

2nd Biennial Meeting of Asian Society of Gynecologic Oncology

November 3-5, 2011
The Ritz-Carlton, Seoul, Korea



New Insight into Gynecologic Cancer in Asia



View Details!!
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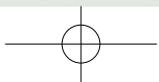


Asian Society of Gynecologic Oncology



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W. E. L. C. O. M. E. M. E. S. S. A. G. E.



On behalf of the Organizing Committee of the 2nd Biennial Meeting of the Asian Society of Gynecologic Oncology, we would like to warmly welcome you to the 2nd ASGO Biennial Meeting on November 3-5, 2011 in Seoul, Korea.

Since its inauguration in 2008, the ASGO has been rapidly growing through the 1st biennial meeting in Japan in 2009 and the 1st International Workshop in Seoul in last July. Both turned out to be great successes thanks to active participation of hundreds of members from over 15 Asian countries. On the basis of precious experience from the history of the ASGO, the ASGO 2011 is sure to be the most highly acclaimed Asian meeting in the field of gynecologic oncology.

Under the theme "New insight into gynecologic cancer in Asia", a wide range of scientific programs will cover the cutting-edge of gynecologic oncology as well as the basic knowledge in this regard. Pertinent hot issues in uterine cervical, endometrial and ovarian cancer will be addressed throughout sessions where every participant will have great opportunities for extensive discussions and informative exchange. In particular, we are preparing an educational session for all the advances in surgical techniques in gynecologic oncology.

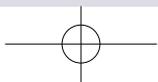
The Organizing Committee has made sincere efforts to provide the participants with memorable experience of the fascinating culture of Korea and the warm spirit of friendship through a variety of socializing programs. We hope that you enjoy our programs in wonderful venues at the heart of Seoul.

We would like to thank the Organizing Committee and the sponsors for playing integral roles in the success of the meeting. We firmly believe that the 2nd Biennial Meeting of the ASGO will contribute to the marvelous advances of the ASGO.

Please enjoy our humble hospitality at the ASGO 2011 in Seoul, Korea.

Soon-Beom Kang, M.D., Ph.D.
President
Asian Society of Gynecology Oncology

Joo-Hyun Nam, M.D., Ph.D.
Chairman
Local Organizing Committee of ASGO 2011



[Meeting Information]

Title

2nd Biennial Meeting of Asian Society of Gynecologic Oncology

Date

November 3(Thu) - 5(Sat), 2011

Venue

The Ritz-Carlton, Seoul, Korea

Theme

New Insight into Gynecologic Cancer in Asia

Language

The official language of the meeting is English

Hosted by

Asian Society of Gynecologic Oncology

Sponsored by

International Gynecologic Cancer Society (IGCS)
Korean Society of Gynecologic Oncology Colposcopy (KSGOC)
Korean Society of Obstetrics and Gynecology (KGOG)
Seoul National University Hospital (SNUH)

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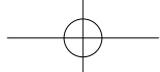


Official Meeting Website

www.asgo2011.org

ASGO 2011 Secretariat

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President-Elect of ASGO

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Noriyuki Inaba (Japan)	Kung Liahng Wang (Taiwan)
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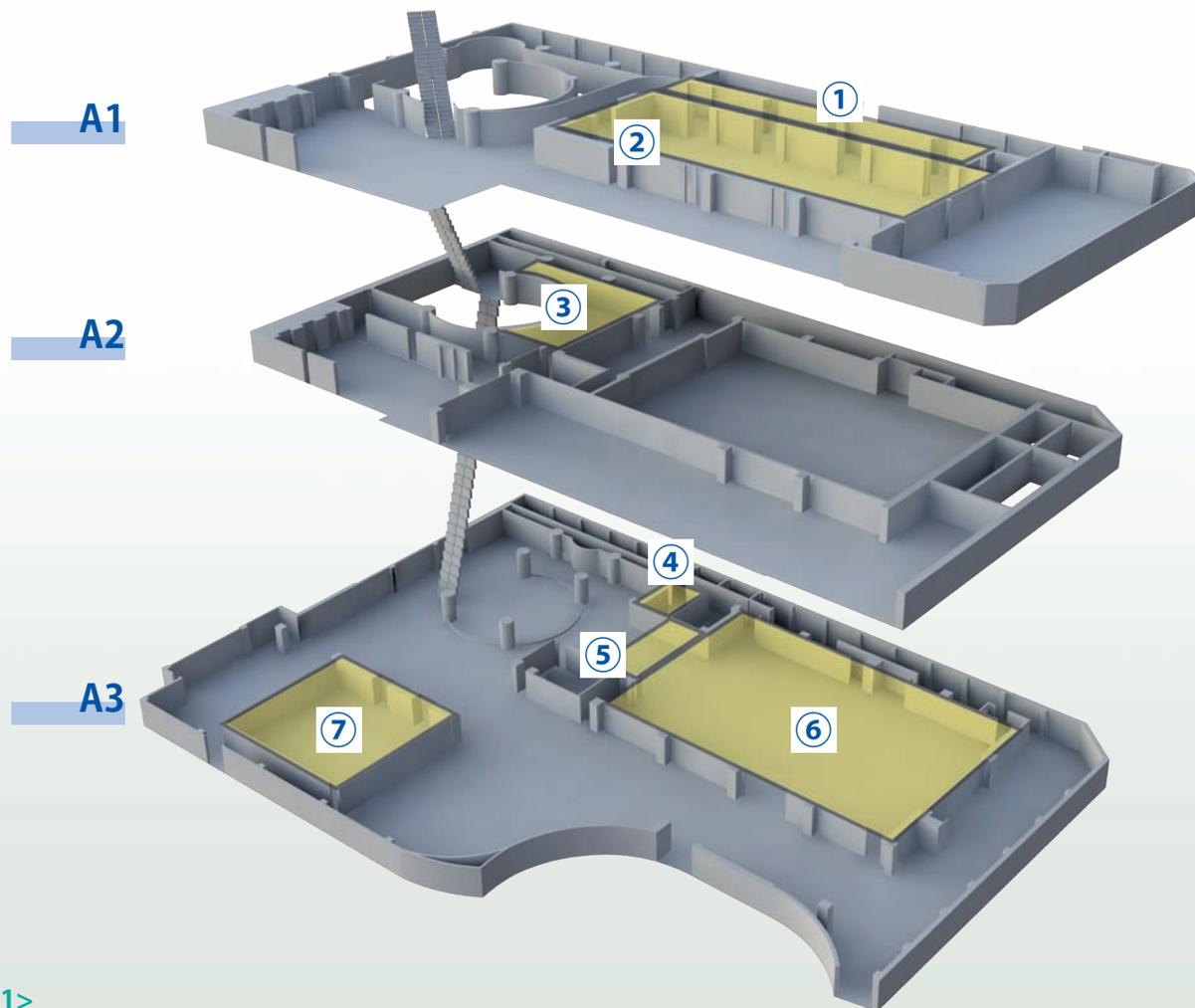
Members

Kyung-Tai Kim, Ki Tae Kim, Sun Haeng Kim, Sung Han Kim, Seung Jo Kim, Jae-Wook Kim, Hak Soon Kim, Sung-Eun Namkoong, Sang Lyun Nam, Heung Tae Noh, Jung-Eun Mok, Hyung Moon, Sang Yoon Park, Yong Won Park, In Sou Park, Il-Soo Park, Jong Sup Park, Tchan Kyu Park, Chan Yong Park, Choong Hak Park, Do Hwan Bae, Dong Han Bae, Jae Uk Shim, Byung Chan Oh, Bock Hi Woo, Man Soo Yoon, Kyung-Hee Lee, Kyu Wan Lee, Sung Ho Lee, Eung Soo Lee, Hun Young Lee, Hyo Pyo Lee, Yoon Seok Chang, Chong Soo Chun, Young Lae Cho, Soon-Do Cha, Ho-Sun Choi, Sei-Jun Han, Chu Yeop Huh, Yoon-Young Hwang

[Program at a Glance]

Date	Thursday, Nov. 3	Friday, Nov. 4	Saturday, Nov. 5	
Time	DAY 1	DAY 2	DAY 3	
	Grand Ballroom (A3)	Grand Ballroom (A3)	Grand Ballroom (A3)	
	Registration			
08:00	Domestic Meeting	Plenary Session I	Plenary Session IV	
08:30				
09:00				
09:30		Coffee Break	Coffee Break	
10:00				
10:30				
11:00		Plenary Session II	Plenary Session V	
11:30				
12:00			Symposium I	Symposium III
12:30			Luncheon	Luncheon
13:00				
13:30		Presidential Address & Invited Lecture		
14:00		Plenary Session III	Free Communication III	
14:30			Educational Session	
15:00		Symposium II		
15:30		Coffee Break	Closing Ceremony	
16:00				
16:30	Special Session: International Collaboration of Clinical Research	Free Communication I	Free Communication II	
17:00				
17:30				
18:00				
18:30	Opening Ceremony & Welcome Dinner	Banquet		
19:00				

[Venue Floor Plan]



<A1>

- ① Poster Exhibition (Hallway)
- ② Booth & Poster Exhibition (Kumkang Room)

<A2>

- ③ Poster Exhibition (Hallway)

<A3>

- ④ Preview Room
- ⑤ Registration Desk
- ⑥ Scientific Sessions, Opening Ceremony & Welcome Dinner, Banquet, Closing Ceremony (Grand Ballroom)
- ⑦ Booth Exhibition (Sorak Room)

[Official Sponsors]

Diamond



Platinum



Gold



Silver



Exhibitors



[Scientific Program]

Thursday, November 3

Special Session. International Collaboration of Clinical Research

SS-01 (16:30-16:45)	Introduction to the Gynecologic Cancer InterGroup (GCIg)
SS-02 (16:45-17:00)	Active Gynecologic Oncology Group (GOG) trials
SS-03 (17:00-17:15)	Status of Japanese Gynecologic Oncology Group (JGOG)
SS-04 (17:15-17:30)	International collaboration of clinical research: status of Korean Gynecologic Oncology Group (KGOG)

Chairperson: Soon-Beom Kang (Korea),
Shingo Fujii (Japan)
Jonathan Ledermann (UK)
Ronald Alvarez (USA)
Kazunori Ochiai (Japan)
Joo-Hyun Nam (Korea)

Welcome Reception & Opening Ceremony

Time & Place: 18:30-20:30, Grand Ballroom (A3)

Friday, November 4

Plenary Session I. Uterine Corpus

PS1-01 (08:00-08:20)	Optimizing surgery for endometrial cancer
PS1-02 (08:20-08:40)	Management of lymph node in endometrial cancer
PS1-03 (08:40-09:00)	Fertility sparing treatment for endometrial cancer in young women
PS1-04 (09:00-09:20)	Postoperative radiotherapy for endometrial cancer
PS1-05 (09:20-09:40)	Recent advances in the treatment of gestational trophoblastic neoplasia

Chairperson: Jung-Eun Mok (Korea),
Toshiharu Kamura (Japan)
Yin Nin Chia (Singapore)
Yukiharu Todo (Japan)
Ronald Alvarez (USA)
Chomporn Sitathanee (Thailand)
Uma Devi (India)

Coffee Break (09:40-10:10)

Plenary Session II. Uterine Cervix

PS2-01 (10:10-10:30)	Abdominal radical trachelectomy from our experience in the past ten years
PS2-02 (10:30-10:50)	Consolidation chemotherapy after concurrent chemoradiotherapy in cervical cancer
PS2-03 (10:50-11:10)	The management of locally advanced cervical cancer in young women
PS2-04 (11:10-11:30)	Advanced robotic surgery in cervical cancer
PS2-05 (11:30-11:50)	Fertility sparing management for cervical cancer
PS2-06 (11:50-12:10)	Quality of life study in cervical cancer patients after radical hysterectomy

Chairperson: Hyo Pyo Lee (Korea),
Zeyi Cao (China)
Takuma Fujii (Japan)
Byoung-Gie Kim (Korea)
Chunling Chen (China)
Young Tae Kim (Korea)
Jericho Thaddeus P. Luna (Philippines)
Xin Lu (China)

Symposium I

S1-01 (12:10-12:30)	Basics of immunology, relevant to HPV
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Chairperson: Seon Kyung Lee (Korea)
Tino Schwarz (Germany)

Presidential Address & Invited Lecture

PA-01 (13:30-13:50)	New Asian leadership for fighting against gynecologic cancer	Chairperson: Joo-Hyun Nam (Korea) Soon-Beom Kang (Korea)
IL-01 (13:50-14:10)	Cervical cancer surgery with metastatic lymph node of the cardinal ligament	Shingo Fujii (Japan)

Plenary Session III. Controversies and Special Issues in Gynecologic Cancers

		Chairperson: Jae-Wook Kim (Korea), Kazunori Ochiai (Japan)
PS3-01 (14:10-14:30)	Management of cervical cancer in low-resource settings	Linus Chuang (USA)
PS3-02 (14:30-14:50)	The intraperitoneal chemotherapy in patients with ovarian cancer	Keiichi Fujiwara (Japan)
PS3-03 (14:50-15:10)	A risk model for secondary cytoreductive surgery in recurrent ovarian cancer: an evidence-based proposal for patient selection	Rongyu Zang (China)
PS3-04 (15:10-15:30)	Hydatidiform mole prevention	Andri Andrijono (Indonesia)

Symposium II

S2-01 (15:30-15:50)	Let's vaccinate Asia: clinical and real world experience for HPV vaccination	Chairperson: Ki Tae Kim (Korea) Sang Young Ryu (Korea)
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Coffee Break (15:50-16:20)

Free Communication I-1. Cervical Cancer

		Chairperson: Young Lae Cho (Korea), Noriyuki Inaba (Japan)
FC1-01 (16:20-16:30)	The establishment of the Korean human papillomavirus cohort study	Tae Jin kim (Korea)
FC1-02 (16:30-16:40)	Multicenter clinical validation of DNA hypermethylation in the detection of cervical neoplasia: a Taiwanese Gynecologic Oncology Group (TGOG) Study	Hung-Cheng Lai (Taiwan)
FC1-03 (16:40-16:50)	Scoring system for predicting a lymph node metastasis in cervical cancer	Yu-Jin Koo (Korea)
FC1-04 (16:50-17:00)	Single node positive revealed good survival as negative node in patients with cervical cancer treated with radical hysterectomy	Prapaporn Suprasert (Thailand)
FC1-05 (17:00-17:10)	Para-aortic lymph node assessment and its surgical indication in patients with stage IB-IIA cervical cancer	Jin Li (China)

Free Communication I-2. Cervical Cancer

		Chairperson: Soon-Do Cha (Korea), Hiroyuki Yoshikawa (Japan)
FC1-06 (17:10-17:20)	Evaluating the learning curve and perioperative outcomes of robot-assisted laparoscopy for cervical cancer: initial experience at the single institution	Ga Won Yim (Korea)
FC1-07 (17:20-17:30)	Prognosis and postsurgical complications of 78 cervical cancer patients who received abdominal radical or simple trachelectomy in our hospital during these 6 years	Hiroaki Kobayashi (Japan)
FC1-08 (17:30-17:40)	Intermediate risk factor grouping in FIGO stage IB-IIA postoperative cervical cancer patients: a multi-center retrospective study of Korean Gynecologic Oncologic Group (KGOG 1021)	Moon Hong Kim (Korea)
FC1-09 (17:40-17:50)	Endoglin (CD105) can be used as a prognostic marker for patients of cervical cancer receiving concurrent chemoradiation	Hao Lin (Taiwan)

Free Communication II-1. Uterine Cancer

Chairperson: Ho-Sun Choi (Korea),
Ikuo Konishi (Japan)

- FC2-01 (16:20-16:30)** Phase II evaluation of irinotecan in leiomyosarcoma of the uterus: a Japan Gynecologic Oncology Group study (JGOG) **Satoshi Takeuchi** (Japan)
- FC2-02 (16:30-16:40)** Expressions of angiotensin II type-1 receptor and miR-155 in endometrial cancers: synergistic inhibitory effect of anti-mir-155 and angiotensin type-1 receptor blocker, losartan, on endometrial cancer cells **Chel-Hun Choi** (Korea)
- FC2-03 (16:40-16:50)** Laser captured microdissection-microarray analysis of the genes involved in endometrial carcinogenesis: stepwise up-regulation of lipocalin2 expression in normal and neoplastic endometria, and its functional relevance **Tsutomu Miyamoto** (Japan)
- FC2-04 (16:50-17:00)** Metronomic doxifluridine chemotherapy combined with the anti-angiogenic agent TNP-470 inhibits the growth of human uterine carcinosarcoma xenografts **Makoto Emoto** (Japan)
- FC2-05 (17:00-17:10)** Overexpression of miR-142-3p in cervical cancer **Yen-Ying Ma** (China)

Free Communication II-2. Interesting Issues in Gynecologic Cancer

Chairperson: Hee-Sug Ryu (Korea),
Ana Dy-Echo (Philippines)

- FC2-06 (17:10-17:20)** Regulation of paclitaxel-induced programmed cell death by autophagic inducer in cervical cancer **Keun Ho Lee** (Korea)
- FC2-07 (17:20-17:30)** Uterine leiomyosarcoma in Asian patients: validation of the new FIGO staging system and identification of prognostic classifiers **Pei Shan Tan** (Singapore)
- FC2-08 (17:30-17:40)** An analysis of thirty-one cases of primary vaginal malignant melanoma **Qidan Huang** (China)
- FC2-09 (17:40-17:50)** Gestational trophoblastic neoplasia and human immunodeficiency virus infection: a 10-year review **Shahila Tayib** (Malaysia)

Saturday, November 5

Plenary Session IV. Translational Research

Chairperson: Sung-Eun Namkoong (Korea),
Yasuhiro Udagawa (Japan)

- PS4-01 (08:00-08:20)** Risk reducing bilateral salpingo-oophorectomy in women at high risk for ovarian cancer **Jonathan Berek** (USA)
- PS4-02 (08:20-08:40)** HPV and cervical cancer from reality to future challenges **Jong Sup Park** (Korea)
- PS4-03 (08:40-09:00)** Immunotherapy in cervical cancer: from bench to bedside **Wen-Fang Cheng** (Taiwan)
- PS4-04 (09:00-09:20)** Effect of estrogen on endometrial carcinogenesis **Tanri Shiozawa** (Japan)
- PS4-05 (09:20-09:40)** Overcoming chemoresistance in ovarian cancer **Chi-Heum Cho** (Korea)

Coffee Break (09:40-10:10)

Plenary Session V. Ovary

Chairperson: Kyung-Tai Kim (Korea),
Mohamad Farid Aziz (Indonesia)
Ginger J. Gardner (USA)

- | | | |
|-----------------------------|---|---------------------------------|
| <p>PS5-01 (10:10-10:30)</p> | <p>An analysis of patients with bulky advanced stage ovarian, tubal, and peritoneal carcinoma treated with primary debulking surgery (PDS) during an identical time period as the randomized EORTC-NCIC trial of PDS vs neoadjuvant chemotherapy (NACT)</p> | |
| <p>PS5-02 (10:30-10:50)</p> | <p>The association between endometriotic lesion and histological aspects of ovarian clear cell carcinoma</p> | <p>Hironori Tashiro (Japan)</p> |
| <p>PS5-03 (10:50-11:10)</p> | <p>PARP inhibitors in ovarian cancer</p> | <p>Jonathan Ledermann (UK)</p> |
| <p>PS5-04 (11:10-11:30)</p> | <p>Novel biomarkers for ovarian cancer screening</p> | <p>Young Tak Kim (Korea)</p> |
| <p>PS5-05 (11:30-11:50)</p> | <p>Dose-dense chemotherapy for ovarian cancer</p> | <p>Chih-Long Chang (Taiwan)</p> |
| <p>PS5-06 (11:50-12:10)</p> | <p>Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient selection</p> | <p>Toyomi Satoh (Japan)</p> |

Symposium III

Chairperson: Seung Cheol Kim (Korea)
Warner Huh (USA)

- | | | |
|----------------------------|---|--|
| <p>S3-01 (12:10-12:30)</p> | <p>Latest findings and results: risk-based cervical cancer screening approach</p> | |
|----------------------------|---|--|

Educational Session. Surgery and surgical pathology of gynecologic malignancies

Chairperson: Kyu Wan Lee (Korea),
Sarikapan Wilailak (Thailand)

- | | | |
|----------------------------|--|----------------------------------|
| <p>ES-01 (13:30-13:50)</p> | <p>Radical hysterectomy</p> | <p>Yoon Soon Lee (Korea)</p> |
| <p>ES-02 (13:50-14:10)</p> | <p>Pelvic and para-aortic lymph node dissection</p> | <p>Kung-Liahng Wang (Taiwan)</p> |
| <p>ES-03 (14:10-14:30)</p> | <p>Principles of bowel resection and anastomosis</p> | <p>Hee Cheol Kim (Korea)</p> |
| <p>ES-04 (14:30-14:50)</p> | <p>Pelvic exenteration for gynecological cancer</p> | <p>Sang-Yoon Park (Korea)</p> |
| <p>ES-05 (14:50-15:10)</p> | <p>Robotics and surgical training: a new paradigm in medical education</p> | <p>Warner Huh (USA)</p> |
| <p>ES-06 (15:10-15:30)</p> | <p>Updates on pathology of uterine sarcoma</p> | <p>Annie Cheung (Hong Kong)</p> |

Free Communication III-1. Ovarian Cancer

Chairperson: Won-Gyu Kim (Korea),
Chyong-Huey Lai (Taiwan)
Ki Hyung Kim (Korea)

- | | | |
|-----------------------------|--|------------------------------|
| <p>FC3-01 (13:30-13:40)</p> | <p>Inhibitory role of ROS on calcineurin and NF-kB activities in LPS-stimulated ovarian cancer cells</p> | |
| <p>FC3-02 (13:40-13:50)</p> | <p>Isolation and characterization of stromal progenitor cells from ascites of patients with epithelial ovarian adenocarcinoma</p> | <p>Chih-Ming Ho (Taiwan)</p> |
| <p>FC3-03 (13:50-14:00)</p> | <p>Comprehensive methylation analyses reveal synchronous hypomethylation of Hnf1 network genes in ovarian clear cell carcinoma</p> | <p>Ken Yamaguchi (Japan)</p> |
| <p>FC3-04 (14:00-14:10)</p> | <p>The effect of HE4 gene silencing on the malignant biological behavior in ovarian cancer</p> | <p>Zou Shuli (China)</p> |
| <p>FC3-05 (14:10-14:20)</p> | <p>Tiam1, negatively regulated by miR-22, miR-183 and miR-31, is involved in migration, invasion and viability of ovarian cancer cells</p> | <p>Jun Li (China)</p> |
| <p>FC3-06 (14:20-14:30)</p> | <p>Ciglitzone sensitize in cisplatin-resistance ovarian cancer cells by targeting glucose metabolism</p> | <p>So Jin Shin (Korea)</p> |

Free Communication III-2. Ovarian Cancer

Chairperson: Duk-Soo Bae (Korea),
Noriaki Sakuragi (Japan)
Hariyono Winarto (Indonesia)

FC3-07 (14:30-14:40) Modification the cut off points of CA 125, HE4, RMI and ROMA scores for Indonesian women who underwent surgery in Dr. Ciptomangunkusumo Hospital from November 2010 until May 2011, in predicting ovarian malignancy: preliminary study

FC3-08 (14:40-14:50) Genome-wide DNA methylation analysis identifies prognostic biomarkers of ovarian cancer

Hung-Cheng Lai (Taiwan)

FC3-09 (14:50-15:00) Feasibility of oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX-4) chemotherapy in heavily pretreated patients with refractory epithelial ovarian cancer: a single institutional experience and comparison with the published reports

Hee Jun Lee (Korea)

FC3-10 (15:00-15:10) A phase I clinical trial of Ad5.SSTR/TK.RGD, a novel infectivity-enhanced bicistronic adenovirus, in patients with recurrent gynecologic cancer

Ronald Alvarez (USA)

FC3-11 (15:10-15:20) Clinical trial of personalized peptide vaccine for recurrent ovarian cancer

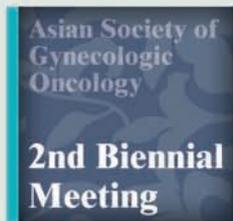
Kouichiro Kawano (Japan)

FC3-12 (15:20-15:30) Health-related quality of life of women with ovarian cancer at initial diagnosis compared with the general population: KORAGC prospective cohort study

Myong Cheol Lim (Korea)

Closing Ceremony & Award Conferment

Time & Place: 15:30-16:00, Grand Ballroom (A3)



Invited Speakers' Session

- **Special Session**
- **Symposium**
- **Invited Lecture**
- **Plenary Session I-V**
- **Educational Session**



Special Session

SS-01

Introduction to the Gynecologic Cancer InterGroup (GCIG)

Jonathan A Ledermann

National Cancer Research Institute (NCRI) Gynaecological Cancer Studies Group, UK

Gynaecological cancers are relatively uncommon and rapid assessment of new therapies requires international collaboration. Commercially sponsored trials are easier to conduct through industry's international connections than academic trials, particularly in an environment of increasing clinical trial regulations. The GCIG was established in 1997 to promote international collaboration in clinical trials, perform studies in rare tumours, stimulate evidence-based medicine through consensus conferences and statements, and to support education in gynaecological oncology. The results of the first GCIG-led trial of cisplatin and paclitaxel were published in 2000, and since then the GCIG has conducted and published many other important studies. Membership through national trials groups, adhering to common clinical trial practices has grown to 20 organisations. There have been 4 consensus conferences in ovarian cancer, guidelines on the use of CA125 to determine progression and evaluate response, and consensus meetings in cervical and endometrial cancer that have led to new trials and discussion of key clinical controversies.

The GCIG faces many challenges, not least of which is the rising cost of clinical trials and complexity of studies that examine treatments in ever smaller biological subsets of disease and rare tumours. For these the academic community must take the lead, and only through international collaboration will progress occur.

SS-02

Active Gynecologic Oncology Group (GOG) trials

Ronald D. Alvarez

Division of Gynecologic Oncology, The University of Alabama at Birmingham, Birmingham AL, USA

The GOG, created over 40 years ago, has 98 full member institutions and 262 affiliates with representation from 12 international countries. Since its establishment, the GOG has conducted over 500 hundred studies and enrolled over 40,000 patients to these trials. These studies have helped set many of the current standards of care for gynecologic cancer and have significantly contributed to the only two NCI Clinical Alerts distributed over the past 12 years. This presentation will review over select recently completed and active phase III and II trials in ovarian, uterine and cervical cancer. Trials in development will also be presented. How the GOG will be affected by efforts to restructure the clinical trials enterprise in the US will also be discussed.

SS-03

Status of Japanese Gynecologic Oncology Group (JGOG)

Kazunori Ochiai, President, JGOG

Department of Obstetrics and Gynecology, The Jikei University, School of Medicine, Tokyo, Japan

The Japanese Gynecologic Oncology Group (JGOG) was founded in 2001. As of July 2011, it is composed of 845 regular members and 203 approved institutions across the country. JGOG works with these members and institutions and has established a system where higher quality clinical research can be performed. JGOG has adopted clinical trial protocols (e.g. JGOG3014) based on protocols proposed by its members and has similarly assumed research that was already being conducted by groups of a small number of institutions, under its umbrella of JGOG studies (e.g. JGOG3016).

JGOG is officially recognized as an international cooperation group of GOG, and it already accepts clinical case entries and audits. JGOG cooperates with the Gynecologic Cancer Intergroup (GCIg), participates in GCIg's consensus conferences, and ensures Japan's views are reflected. It also studies whether protocols proposed by GCIg can be implemented in Japan. JGOG3017 (clear cell cancer study) has been taken up at GCIg as international research, and clinical cases have been registered. JGOG will proudly host the Ovarian Cancer Consensus Conference in 2015 in Japan.

Clinical research in Asia is important as well. There is a nation-wide call to promote clinical research in Asia, and JGOG has helped establish the Asian Gynecologic Oncology Group (AGOG) which is conducting clinical trials together with Korea, Taiwan, India, Thailand and Hong Kong. JGOG also holds close relationship with the Korean Gynecologic Oncology Group (KGOG) and the Korean Society of Gynecologic Oncology (KSGO), two groups in Asia that have the capabilities to conduct clinical research at an international level, and a symposium is held each year alternately in Japan and in Korea. Through these meetings, not only those in leadership positions but also young researchers engaging in actual clinical research are given the opportunity to interact with their peers.

SS-04

International collaboration of clinical research: status of KGOG

Joo-Hyun Nam¹, Sang-Young Ryu²

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In fall 2002, the president Dr. Soon-Beom Kang and some executive members of Korean Society of Gynecologic Oncology & Colposcopy (KSGOC) acknowledged the importance of clinical trial to find evidence-based guideline of clinical practice, but there was no system to do multicenter clinical trials at that time. For this purpose, KGOG was established accepting the advanced multicenter trial models represented by GOG, EORTC, and JGOG. However, there were still negative skepticisms and few resources, so the period of first few years was a really hard time for KGOG.

Beginning with having the first research committee meeting on Apr 17, 2003, the role and goals of KGOG were established as 'to take charge of a well-organized and systemic multicenter trial and to lead standardization and development planning of Korean gynecological cancer specialist education in studying gynecological cancer treatment'. From that time KGOG designed several retrospective multicenter studies and successfully published the data on important SCI journals. Encouraged by the product, KGOG made effort to do not only domestic multicenter trials but also participate in GOG protocols. Until now, KGOG successfully performs almost 60 domestic clinical trials including prospective and retrospective studies and 20 international protocols and published tens of SCI articles.

After several reform processes, KGOG is now composed of research committee and steering subcommittee as the major organizations, and three major tumor-specific subcommittee of cervical cancer, ovarian cancer and endometrial cancer, as well as pathology, radiotherapy, medical oncology and translation research subcommittee as the advisory organizations.

Recently, the new president of KGOG, Dr. Joo-Hyun Nam, focus on that the role of KGOG should be expanded internationally, especially with Asian study group where the cervix cancer burden is very high. The success story of KGOG can be a good model for the Asian study groups which have few government support and low resources. The TACO trial (Tri-weekly Administration of Cisplatin in LOcally advanced Cervical Cancer), a GCIG protocol proposed by KGOG, will be one of major stepping-stone for this international collaboration.

Symposium

S-01

Basics of immunology, relevant to HPV

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Human papillomavirus (HPV) infection differs from other viral diseases in that it is localized to the mucosal epithelia; HPV infection does not lead to viremia or systemic infection. As a result, there is insufficient presentation of the virus to the systemic immune system. Hence, antibody levels following natural HPV infection can be inadequate and may not be protective.

Two prophylactic human papillomavirus (HPV) vaccines are currently licensed: a bivalent HPV-16/18 AS04 adjuvanted vaccine and a quadrivalent HPV-6/11/16/18 vaccine. Clinical trials have demonstrated that the two vaccines may prevent the occurrence of cervical cancer, which takes many years to develop following persistent infection with HPV-16 and 18. A central question that will substantially influence the success of HPV vaccination programs is the duration of vaccine-induced protection.

To predict the duration of protection, the mechanism of HPV infection and the systemic and local immune responses induced by vaccination must be considered. A follow-up study showed that the bivalent HPV vaccine induces high and sustained seropositivity levels against HPV 16 and 18 for at least 9.4 years.

Transudation of vaccine-induced neutralizing antibodies from the blood vessels across the cervical and vaginal epithelium to the site of HPV infection is believed to prevent virus particles from infecting the cervical basal cell layer at the transformation zone. There is a strong correlation between the concentration of antibodies in serum and the cervicovaginal secretion (CVS); i.e., the higher the antibody concentration in serum, the higher the levels measured in CVS. Antibodies can also reach the CVS through the exudation of blood from microlesions, which can occur during sexual intercourse.

A comparative study directly evaluated the immunogenicity of the bivalent and the quadrivalent HPV vaccine in females aged 18 to 45 years. Data from this trial have demonstrated a higher immune response with the bivalent vs. the quadrivalent HPV vaccine in terms of HPV-16 and -18 neutralizing antibodies at all time-points up to month 36 after the start of the vaccination series. The geometric mean ratios of neutralizing antibodies at month 36 for the bivalent HPV vaccine were 2.2–5.9-fold higher for HPV-16 and 8.8–12.5-fold higher for HPV-18 across the age-groups in the total vaccinated cohort.

A recall of vaccine-induced immune memory by natural HPV exposure is unproven. Although an immunological correlate of protection is currently not defined, differences in the magnitude of the immune response between the two vaccines may represent determinants of duration of protection.

S-02

Let's vaccinate Asia: clinical and real world experience for HPV vaccination

Sang Young Ryu

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There are over the 100 strains of HPV, the low-risk HPV type 6 and 11 being associated with about 90% of genital warts, low-grade cervical abnormalities, and recurrent respiratory papillomatosis and the high-risk HPV type 16 and 18 being responsible for around 70% of cervical cancer. Both the bivalent (BHPV) vaccine against HPV 16/18 and quadrivalent (QHPV) vaccines against HPV 6/11/16/18 are approved by US FDA and have shown efficacy in preventing HPV 16/18 persistent infections and the associated CIN 2+. In the FUTURE III trial, the QHPV has shown 97.4% efficacy (95% CI: 84.5, 99.9) in the PPE population in reducing the incidence of any abnormal Pap smear related to vaccine HPV types during follow-up. Additionally, US FDA has approved the indications of QHPV for protecting genital warts, adenocarcinoma in situ (AIS), vulval intraepithelial cancer (VIN), vaginal intraepithelial cancer (VAIN) and related cancers.

However, despite of the great achievement of first anti-cancer vaccine in human history, the longer-term, worldwide, population-based data on HPV vaccine uptake are currently limited. Generally the uptake rate in the most of the developed countries showed at 70% or above. In United Kingdom, overall uptake of all three doses was 80% for 12-13-year olds and 32% for 17-18-year olds. In Australia, where QHPV vaccine was introduced as a national-wide vaccination program in 2007, the overall uptake was 80% for the first dose and 70% completing 3 doses for girls and women aged 12 to 26. In United States, 2010 NIS-Teen data showed slightly lower uptake rate of 48.7% with QHPV vaccine (1st dose of HPV) and 32.0% (3rd dose of HPV).

The WHO in its position paper had advocated for the use of HPV vaccines in developing countries as a part of a comprehensive program to tackle the burden of cervical cancer. However, despite of the high cervical cancer burden with 310,000 new cases per year, there are few reliable population-based data in Asia. Only available data from pharmaceutical company showed around 5% uptake in some of Asian countries and below 1% in most of Asian countries.

Recently, the effect of the socioeconomic factors such as vaccine cost, vaccine knowledge, attitudes and acceptability of the vaccine, and ethnicity were actively investigated. Based on this results, several customized interventions at multiple levels, such as policy-level programs, health systems, school-based clinics, cost-reduction initiatives, education of providers and parents, and dissemination of academic detailing are suggested and introduced in both developed and developing countries.

In this presentation, current status of HPV vaccine uptake, policy-level program, attitude of health provider and the parents are reviewed and discussed.

S-03

Latest findings and results: risk-based cervical cancer screening approach

Warner Huh

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In the US and worldwide, high risk HPV testing plays a growing role in the area of cervical cancer screening. Testing encompasses a broad range of indications including triage for equivocal Pap smears and co-testing in women greater than 30 years of age. Some screening programs have started to incorporate HPV testing for primary screening, as well. The ATHENA trial (Addressing The Need for Advanced HPV Diagnostics) is the largest FDA registration conducted for cervical cancer screening. Over 47,000 women were enrolled in this trial, which sought to evaluate the cobas® 4800 HPV test to identify women with high grade cervical disease (\geq CIN2). In addition to high risk HPV testing, the utility of HPV 16 and 18 genotyping was evaluated in trial.

Initial findings from this trial demonstrated the following:

- 1) The cobas® 4800 HPV test has high sensitivity and is comparable to current HPV testing methods.
- 2) ASC-US cytology with HPV 16/18+ has a high absolute risk of \geq CIN2.
- 3) NILM cytology with HPV 16/18+ has a high absolute risk of \geq CIN2.
- 4) NILM cytology with HPV16/18+ and ASC-US with HR HPV + share a similar absolute risk of \geq CIN3

Presidential Address

PA-01

New Asian leadership for fighting against gynecologic cancer

Soon-Beom Kang, President of ASGO

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More than 80% of world burden of cervical cancer is developing countries in sub-Saharan regions in Africa, central and southern America, and south and middle Asia. For example, out of 500,000 new cases of cervical cancer detected world-wide each year, India contributes 20 percent (100,000) of them. The incidence of cervical cancer in developed countries has been rapidly decreasing due to well organized screening program. Many Asian countries now have national screening program for cervical cancer, though some countries use VIA (visual inspection with acetic acid) as a main screening modality. However, the problem is low coverage caused by several barriers such as lack of infrastructure, poorly trained and limited workforce, patient care costs, and education deficits.

In order to surmount these difficulties and encourage the development of international clinical trials for treatment of gynecologic cancers in Asia, Asian Society of Gynecologic Oncology (ASGO) was inaugurated in Seoul in 2008. ASGO has just three years of history now. It is the beginning for a fight against gynecologic cancer in Asia. Since the great successes of 1st Biennial Meeting in Tokyo in 2009 and 1st International Workshop in Seoul last year, we have made rapid progress and promoted friendly relationships between ASGO member countries. ASGO has its own official journal, Journal of Gynecologic Oncology (JGO, www.gyneoncology.or.kr), and well-organized homepage (www.asiansgo.org) where you can find out lots of precious information regarding the recent advance in gynecologic oncology as well as the history of ASGO.

“Well begun is half done.” However, we have a long way to go ahead of us. ASGO has three goals. First, educational regional meetings and various outreach educational programs should be prepared for education of regional health personnel. Second, establishment of cancer registry in developing countries, propagation of affordable effective screening tools for the detection of cervical cancer, encouragement of vaccination against cervical cancer, and suggesting guidelines for the management of Asian women with gynecologic cancers for the purpose of public health. Third, participation in international multicenter clinical trials with strong partnership with GOG and GCIg should be encouraged for research development.

I believe nothing is impossible. I hope ASGO will become the World Leader, rather than Asian leader, for fighting against gynecologic cancer in near future.

Invited Lecture

IL-01

Cervical cancer surgery with metastatic lymph node of the cardinal ligament

Shingo Fujii

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At least there are three major treatment modalities for cervical cancer such as surgery, radiation, and chemotherapy. Among the prognostic factors of cervical cancer, lymph node metastasis well correlates with poor prognosis of patient. If lymph node metastasis is identified during surgery in the patient of FIGO Stage IB, majority center in the Western country stop the surgery and the patient is usually sent to the chemo–radiotherapy. However, in some other institutions, still lymphadenectomy and radical hysterectomy are done even if there are positive nodes. In such cases, lymphadenectomy is often done up–to the level of the inferior mesenteric artery or higher than this level. According to the post–operative report of pathology, the patients are usually divided into two groups: no adjuvant therapy group and adjuvant therapy group (radiotherapy, chemo–radiotherapy or chemotherapy).

The institutions, where they select no adjuvant therapy group or adjuvant therapy group with chemotherapy, look like to have a tendency to do extensive lymphadenectomy than that of the institutions giving adjuvant radiotherapy. A group in Hungary is doing much more radical surgery if there may be a positive node in IB patients. The group of Dr. Ungar is doing lateral extended parametrectomy (LEP) to these patients who have positive node in either one or both sides. Recently they reported the results of LEP that five year survival of patients with FIGO Stage IB, lymph node positive and free surgical margins without any adjuvant therapy is 91.4%. This study is implying that even if we may have positive lymph node, aggressive surgery such as LEP with appropriate (extensive) lymphadenectomy can get a favorable prognosis to these patients. Although Ungar group started LEP in 1993 and reported as a new surgical method, this surgery was already reported in Japan in 1941 by Ryukichi Mibayashi at Kyoto University during the World War II. The surgery was named as Super–radical Hysterectomy. Although the Ungar group knows the film of Mibayashi surgery, the group ignored the originality of Mibayashi in their published paper. Therefore, I would like to show Mibayashi's original film in 1941 and also show the Mibayashi's surgery, a total removal of internal iliac blood vessel system, to the patient with metastatic lymph node adhering in the cardinal ligament. This surgery is a very good treatment modality and we can preserve the pelvic nerve in the other side.

I would like to recommend this surgery to IB patients with severe adhesive lymph node metastasis in the cardinal ligament, particularly to younger age patients with pathological chemoradio–resistant features.

Plenary Session I

PS1-01

Optimizing surgery for endometrial cancer

Chia Yin Nin

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Majority of endometrial cancer presents early. Surgery therefore is often the main mode of treatment. Proper and adequate surgery is thus important. Optimizing surgery ensures the best outcome and also minimises morbidities. Surgical morbidities e.g. lymphoedema is of important consideration as majority of patients will outlive their cancer and hence quality of life issues becomes important. The role of routine pelvic lymphadenectomy is still controversial although ASTEC trial does not support a survival advantage. The new FIGO staging involves taking into consideration para-aortic lymph node status and hence leads one to question the role of extended surgical staging. Conventional laparotomy appears to be superseded by laparoscopy for the latter is associated with lesser morbidity. Increasingly, robotics is being employed in the surgical management of endometrial cancer. Whether it is superior to laparoscopy await to be answered. Financial cost for robotics needs to be taken into consideration, as majority of surgery for endometrial cancer can be easily undertaken with conventional laparotomy or laparoscopy.

PS1-02

Management of lymph node in endometrial cancer

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Recently, results of two randomized trials concerning therapeutic effect of lymphadenectomy in endometrial cancer were published. However, many physicians have overgeneralized the results of the trials. The RCTs showed that pelvic lymphadenectomy does not have a therapeutic effect in low-risk endometrial cancer. On the other hand, SEPAL study suggested that pelvic and para-aortic lymphadenectomy have a therapeutic effect in intermediate-/high-risk endometrial cancer. In the SEPAL study, the combined pelvic and para-aortic lymphadenectomy included removal of lymph nodes above the inferior mesenteric artery (IMA). Removal of the para-aortic nodes above the IMA might be critical in order to improve survival for patients with intermediate-/high-risk of recurrence. In this study, the rate of para-aortic node (PAN) recurrence was significantly different between the two procedures (pelvic and para-aortic lymphadenectomy << pelvic lymphadenectomy). This difference still exists even in addition of chemotherapy. This suggests that adjuvant chemotherapy cannot replace surgical removal of affected lymph nodes. We also found that an addition of para-aortic lymphadenectomy to pelvic lymphadenectomy did not increase severe complications. Since SEPAL study is a retrospective cohort study, another study is in need for validating a therapeutic effect of pelvic and para-aortic lymphadenectomy. But a high-risk group is not suitable for a randomized surgical trial. A prospective cohort study appears to be the most appropriate method for high-risk patients.

PS1-03

Fertility sparing treatment for endometrial cancer in young women

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The incidence of endometrial cancer has increased over the past decade. Up to 14% of women affected by endometrial cancer will be premenopausal, some of which will desire future fertility. This presentation will review clinical characteristics of premenopausal women affected by endometrial cancer, various fertility sparing treatment options, and long term cancer and reproductive outcomes in these conservatively managed patients.

PS1-04

Postoperative radiotherapy for endometrial cancer

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Endometrial cancer (EC) is common gynecological cancer and primarily affects postmenopausal women. Majority of patients are presented with uterine-confined early stage disease. Surgery is the primary management in most patients, and also to provide disease extension (pathological staging) and other prognostic factors which will be used to decide further adjuvant treatment.

Major prognostic factors for EC include stage, grade, age, histological type, lymph-vascular space invasion. Adjuvant radiotherapy (RT) for EC has increasingly been tailored to these risk factors. For low-risk disease (stage IA, grade 1-2 endometrioid type), standard treatment is surgery alone. For intermediate-risk disease, four randomized trials have studied the benefit of adjuvant RT, either external beam radiotherapy (EBRT) to the pelvis or vaginal brachytherapy (VBT), which are summarized in table 1.

Table 1. Randomized trials of adjuvant RT in stage I EC (Creutzber et al. 2011)

Trial	Patient eligibility	Surgery	Randomization	LRR	Survival
Norwegian (1968-1974)	540 stage I	TAH-BSO	VBT vs. VBT+ EBRT	7% vs. 2% 5 y	89% vs. 91% 5 y (NS)
PORTEC1 (1990-1997)	714 IB, G2-3, IC G1-2	TAH-BSO	No RT vs. EBRT	14% vs. 4% 5 y	85% vs. 81% 5 y (NS)
GOG99 (1987-1995)	392 IB, IC, II (occult)	TAH-BSO + LND	No RT vs. EBRT	12% vs. 3% 2 y	86% vs. 92% 4 y (NS)
ASTEC/EN5 (1996-2005)	905 IA-B G3, IC, II, UPSC/CC	TAH-BSO ± LND	No RT vs. EBRT	7% vs. 4% 5 y	84% vs. 84% 5 y (NS)
PORTEC2 (2002-2006)	427 age >60 IB G3, IC G1-2	TAH-BSO	VBT vs. EBRT	2% vs. 2% 5 y	85% vs. 80% 5 y (NS)

Conclusions from these randomized trials are that EBRT provides a highly significant improvement of local control in the pelvis but without survival advantage. Furthermore, patients who received EBRT had higher risk of GI toxicity, although the severity is mild. So EC patients with very favorable prognosis should be observed after surgery. Postoperative RT should be limited to those with high risk factors. The 10-year locoregional recurrence rates in the PORTEC-high-intermediate risk

group were 4.6% in the RT arm compared with 23.1% in the no-RT arm. In the GOG99, 4-year local recurrent rates in the high-intermediate risk group were 5%, and 13% in RT, and no-RT arm, respectively. In the absence of survival benefit with EBRT and majority (70%) of locoregional recurrences were in the vagina, VBT alone might also be effective in obtaining local control with fewer side effects and more convenient for the patients than EBRT. Result of PORTEC2 trial has shown that VBT is effective in preventing vaginal relapse with no difference in disease-free and overall survival. GI toxicities were significantly lower along with better QOL in the VBT arm. As the result, VBT alone has become standard of care for patients with high-intermediate risk EC, and is increasingly used in many countries.

Patients with high-risk and advanced-stage EC (extrauterine disease) have substantial risks of distant failures and death from EC. Results from trials (table 2) have shown that adjuvant EBRT alone reduced local failures, while chemotherapy alone delayed distant metastasis, and survival rates were similar. At present, the reasonable approach is to combine both treatment modalities, so called “tumor-directed RT with chemotherapy”. A number of trials are currently ongoing to explore this approach regarding how to combine these two modalities and finally the outcomes (table 2). These trials will resolve many questions regarding which patients may benefit from RT, chemotherapy, or both.

Table 2. Randomized trials of adjuvant chemotherapy and/or RT in EC (Creutzber et al. 2011)

Trial	Patient eligibility	Randomization	LRR	Survival
Susumu et al. (2008)	385 stage I-III >50% MI	Pelvic RT vs. chemo (3CAP)	7% vs. 7% (NS)	85% vs. 87% (NS)
Maggi et al. (2006)	345 stage IB-II G3, stage III	Pelvic RT vs. chemo (5CAP)	12% vs. 16% (NS)	69% vs. 66% (NS)
Randall et al. GOG122 (2006)	396 stage III, IV (<2 cm residual)	WAI vs. chemo (8AP)	13% vs. 18%	42% vs. 53%
Kuoppala et al. (2008)	156 stage I-IIIA	Pelvic RT vs. pelvic RT + chemo (3CEP)	3% vs. 2% (NS)	85% vs. 82% (NS)
Hogberg et al. (2010)	382 stage I-III	Pelvic RT vs. pelvic RT + chemo	NA	76% vs. 83% (NS)
Ongoing trials				
PORTEC3	Stage I-III HR, serous/cc	Pelvic RT vs. RT + chemo (2C+RT 4TC)		
GOG249	Stage I-II HR, serous/cc	Pelvic RT vs. VBT + chemo (3TC)		
GOG258	Stage III-IV	RT+ chemo (2C+RT 4TC) vs. chemo (6TC)		

PS1-05

Recent advances in the treatment of gestational trophoblastic neoplasia

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Gestational Trophoblastic Neoplasia (GTN) is a spectrum of heterogeneous conditions which arises from the products of conception, presents mysteriously, may threaten the health of young reproductive women if not properly managed. It arises more frequently in Asia than in North America or Europe.

Most patients who develop GTN after hydatidiform mole are detected early by serum beta hCG monitoring so detailed investigations are rarely required. Pulmonary metastasis are most common, if the lesions are found on chest radiograph, then brain MRI & body CT are recommended to exclude more widespread disease affecting brain or liver which would substantially change the management. Disease vascularity suggests patients who are at risk of treatment resistance. However, the majority of women with this disease will be cured by single agent mono chemotherapy either with methotrexate or dactinomycin by using FIGO report data for GTN of prognostic scoring and anatomical staging systems.

The combined prognostic score predicts potential for development of resistance to monotherapy with methotrexate or dactinomycin. A score of 0–6 suggests low risk & 7 or more indicate high risk. Only 30% of patients scoring 5–6 can be cured with low risk therapy. The amount of vascularisation as detected on Doppler ultrasonography could help to provide the necessary additional information. Such disease has almost no chance of being cured with monotherapy and needs multidrug treatment. Therefore the revision of the FIGO scoring system would be helpful for early identification of 70% of women in this group who subsequently develop resistance to methotrexate with folinic acid rescue & who may need more intensive therapy.

Most patients with high risk GTN present with many metastases months or years after the causative pregnancy of any type. Symptoms & signs vary with disease location. The optimal management of these high risk women depends on prompt diagnosis, proper treatment and reference to centre with expertise in the management of such disease.

EMA–CO as a multidrug chemotherapy remain the preferred treatment of high risk GTN (Etoposide 100 mg/m² on day 1 & 2, dactinomycin on day 1 & 2, Methotrexate 100 mg/m² IV bolus, 200 mg/m² IV infusion on day 1 dactinomycin 10–12 μg/kg on day 1 & 2 & cyclophosphamide 600 mg/m² & vincristine 1–1.5 mg/m² on day 8) and has a successful outcome with minimal toxicity and a cure rate 80–85% reported worldwide.

Those women who progress during or after primary chemotherapy still can be salvaged with EP–alternating every week with EMA chemotherapy. Survival is more than 80% but toxic effects are substantial. PET scanning with 18 F–fluorodeoxyglucose may help to identify the site of active disease to aid surgical resection and cure. Patients with relapsed or refractory neoplasia, Paclitaxel–Cisplatin & Paclitaxel–Etoposide (TP–TE) every 2 weeks seems to be much better tolerated than EP–EMA regimen. High dose chemotherapy with peripheral stem cell transplantation does not cure many patients with refractory disease.

Plenary Session II

PS2-01

Abdominal radical trachelectomy from our experience in the past ten years

Takuma Fujii, Hiroshi Nishio, Juri Sugiyama, Takashi Iwata, Kazuhiro Minegishi, Mamoru Tanaka, Naoaki Kuji, Toshio Hamatani, Yasuhiro Yoshimura, Daisuke Aoki

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Fertility sparing surgery for cervical cancer is in demand due to the increase of cervical cancer in young women. Abdominal radical trachelectomy (RT) is one of the alternative promising surgical option. We reviewed planned 140 abdominal radical trachelectomy of our institution in the past ten years.

Surgical complication, oncological prognosis, and obstetrical outcome were estimated.

The median age of the patients was 33 (23–44) years. The majority of the lesions were stage IA (21.4%) or IB1 (78.6%). In histology, 87% (110/126) were squamous and 13% (16/126) were adenocarcinomas. The median follow-up was 26 (2–104) months. Ten % of patients planned RT were abandoned and converted to hysterectomy due to positive lymph nodes or positive margins of the removed cervix by frozen section in the original operation. Furthermore, additional 10% of patients who underwent RT received adjuvant chemotherapy and/or radiation for those reasons. There were some post operative complications; cervical stenosis, amenorrhea and lymphocele. In the obstetrical outcome, 11 babies were delivered by Caesarean section. Eight of 11 patients conceived with artificial reproductive technology. Nine babies were delivered after 32 weeks.

RT seems to be an oncologically safe procedure in well-selected patients with early-stage diseases. Obstetrical outcomes post RT was tolerable. However, the patients need to be fully informed about perioperative and late complications especially for the risk of premature delivery. Collaboration with gynecologic oncologists, perinatologists, ART specialists and professional nurses were also critical issues for establishing this procedure.

PS2-02

Consolidation chemotherapy after concurrent chemoradiotherapy in cervical cancer

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We compared the efficacy and toxicity of consolidation chemotherapy after concurrent chemoradiation (CCRT) and CCRT alone in patients with locally advanced cervical carcinoma.

Using medical records from January 2001 to December 2007, 39 patients treated with consolidation chemotherapy after CCRT (Group 1) were matched to 39 patients treated with CCRT alone (Group 2). Consolidation chemotherapy consisted of three additional cycles of chemotherapy with cisplatin 60 mg/m² (Day 1) and 5-fluorouracil 1,000 mg/m² per day (Days 1–5) given every 3 weeks. The primary endpoint was overall survival.

During a median follow-up period of 35 months (range, 8–96 months), 10 (25.6%) and 16 (41.0%) patients showed disease progression in Groups 1 and 2, respectively. Distant recurrence with or without locoregional/lymphogenous recurrence occurred more frequently in Group 2 than in Group 1 (23.1% vs. 7.7%, $p=0.06$). By contrast, there was no difference in locoregional or lymphogenous recurrence between the two groups. The rate of overall survival was higher in Group 1 than in Group 2 (92.7% vs. 69.9%, $p=0.042$), whereas the difference in progression-free survival between the groups was not statistically significant (70.1% vs. 55.1%, $p=0.079$). Although the difference was not statistically significant, neutropenia was more common in Group 1 than in Group 2 (10.9% vs. 4.7%, $p=0.07$).

Consolidation chemotherapy after CCRT may improve survival and reduce distant recurrence without additional toxicity compared to CCRT alone in patients with locally advanced cervical carcinoma. Further discussion on other investigator's reported results and ongoing clinical trials for consolidation chemotherapy after CCRT in patients with cervical cancer will be presented.

PS2-03

The management of locally advanced cervical cancer in young women

Chunling Chen

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Cervical cancer is the most common gynecological malignancy. Locally advanced cervical cancer is a group of patients with poor prognostic factors staging from IB2 to IVA. The young cervical cancer patients usually refer to the women younger than 35 years old. The requirements of both improving 5-years survival rate and improving the QOL by maintaining of endocrine function and vaginal function are considered in those women. So the special treatment for this group of patients is investigated.

Current studies support the effectiveness of neoadjuvant chemotherapy in the treatment of locally advanced cervical cancer. Platinum-based combination plan is commonly used, such as TP regimen. The benefit of neoadjuvant intraarterial chemotherapy is controversial compared by intravenous drip. By shrinking the size of the tumor, neoadjuvant chemotherapy can provide operation chance for the locally advanced cervical cancer women whose tumor is too large to be removed. Surgery is the primary treatment for young locally advanced cervical cancer women with early stages. The ovarian transposition surgery can reduce radiation damage to ovary and the vaginal replacement by peritoneum will help restore sexual function of patients underwent radical hysterectomy. Pelvic exenteration could be used in some of the young patients with stage IVA. Concurrent chemoradiotherapy (CCR) offers an absolute survival benefit in many RCT studies in locally advanced women. But it is easy to damage ovaries and vagina for young women.

In conclusion, the main treatment for young women with locally advanced cervical cancer should be surgical excision as chief component of combined therapy or CCR. In order to improve patient's quality of life we should pay special attention to the maintaining of physiological functions.

PS2-04

Advanced robotic surgery in cervical cancer

Young Tae Kim

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Robotic surgery has emerged as an innovative minimally invasive method that is being used in gynecology with increasing frequency. The da Vinci Surgical System (Intuitive Surgical, Inc, Sunnyvale, California) is the only FDA approved and commercially available robot in gynecology. It is now being used in various surgical procedures throughout the world. In Korea, the Korean FDA approved the da Vinci system in July 13th, 2005 and the first robot assisted laparoscopic hysterectomy was conducted by Kim et al. on January 31st, 2006. For the past 4 years, more than 4,000 cases of robotic surgeries in various fields including gynecology, general surgery, urology and thoracic surgery have been performed at our institution.

The robotic system has three components: the patient side surgical cart, the vision system, and the surgical console. The patient side cart has three to four robotic arms for controlling a three-dimensional camera and robotic surgical instruments. The vision system processes high-resolution image signals from the camera to the surgeon console. The surgeon's hand movements from the console are translated into real-time movement of the robotic instruments with less tremor and enhanced precision. The uniquely wristed robotic instruments move with seven degrees of freedom as opposed to conventional laparoscopic instruments that only have four, allowing greater dexterity in the surgical field. There are three types of da Vinci systems currently available. The standard system has three robotic arms with an optional fourth arm. It was soon upgraded to the S system with four arms and high definition vision in 2006. The S system has a wider panoramic view and a digital zoom that is developed to reduce instrument interference. The Si system was the next upgrade launched in 2009, enabling dual-console capability for training and collaboration, enhanced high-definition three-dimensional vision and footswitch controls that allow surgeons to freely swap different types of energy instruments.

In gynecologic oncology, the robot has been used increasingly in a variety of applications, notably for radical hysterectomy in patients with cervical cancer but also for pelvic and paraaortic lymphadenectomy, trachelectomy, simple hysterectomy, and oophorectomy. The technology is in its infancy, with most articles being case series and investigational studies.

There is a growing number of literatures on cervical cancer probably because radical surgery for cervical cancer is one of the most complex surgical procedures in gynecologic oncology due to the amount of dissection required for the bladder, ureter, parametrium, and rectum. The integration of robotic technology into laparoscopic surgery is used with increasing frequency in the treatment and evaluation of patients with early, advanced, and even recurrent cervical cancer. Overall, 126 robot-assisted surgeries were performed in the cohort studies of cervical cancer, each with different perioperative outcomes. Published procedures with robotic assistance include radical hysterectomy, trachelectomy, parametrectomy, lymphadenectomy, pelvic exenteration, and ovarian transposition prior to radiotherapy. Results of the previous studies establish that robot-assisted surgery for cervical cancer is a feasible procedure with reasonable operative time, low blood

loss, comparable lymph node yields, and shorter hospital stay. To date, there are no published randomized trials on robot-assisted radical hysterectomy. The ongoing, phase III randomized clinical trial comparing laparoscopic or robot-assisted radical hysterectomy with abdominal radical hysterectomy in patients with early stage cervical cancer is being performed under the auspices of the American Association of Gynecologic Laparoscopists (AAGL). The aim is to show the equivalence of laparoscopic or robotic approaches versus the abdominal approach by a 2-phase protocol. Phase 1 will evaluate the feasibility of the proposed trial and phase 2 will evaluate the equivalence between open and laparoscopic/robotic radical hysterectomy with regard to disease-free and overall survival. This study is expected to accrue a total of 740 patients internationally.

Over one thousand robotic systems have been installed worldwide and the use of the robot in surgical procedures continues to increase. Due to enhanced precision, autonomy, ergonomics and surgical efficiency, the robotic system appears to have a significant impact on the management of gynecologic malignancies. Surgical management of gynecologic oncology surgeries may take full advantage of robotic assistance in a minimally invasive manner. However, the safety of robot-assisted surgery in gynecologic malignancies regarding recurrence, long term survival, and oncologic outcomes remains to be determined in future randomized trials. Multi-institutional data and randomized clinical trials will be needed to evaluate both the drawbacks and benefits of robot-assisted surgery to ensure the best clinical outcome.

PS2-05

Fertility sparing management for cervical cancer

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With advances in treatment modalities for cancer, the cure rate of women affected with some malignancies is much higher. However, loss of fertility as a consequence of therapy is still a major drawback of some treatments of cancers affecting younger patients still in their reproductive years and desirous of pregnancy.

Efforts have been made in oncology to find ways to prevent fertility loss without lowering the cure rate of selected cancers. Advances in therapeutic modalities have been made in the last decades in order to safely offer young patients affected by some cancers to keep their fertility. There are now ways to procreate even if the reproductive organs have to be removed or irreversibly affected by the cancer treatment.

For cervical cancer, radical trachelectomy has been developed by Dr. Daniel Dargent for the past 15 years. Over 326 cases have been reported so far and accumulating data confirms excellent oncologic outcome with a recurrence rate of < 5% and death rate of < 3%. Over 123 babies have been born after the procedure and the obstetrical results are also encouraging. The majority of pregnant women (67%) have delivered a live baby and 75% have delivered at term. However, second trimester losses as well of prelabor rupture of membranes and preterm delivery are the main obstetrical problems following the trachelectomy procedure. Most patients do not require artificial reproductive techniques to become pregnant and fertility does not seem to be adversely affected by the procedure. The radical trachelectomy is thus becoming a widely accepted fertility-sparing procedure for young women with early-stage cervical cancer.

PS2-06

Quality of life study in cervical cancer patients after radical hysterectomy

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Cervical cancer is the second most common female cancer and ranked third in female cancer-caused death worldwide. Radical hysterectomy (RH) with pelvic lymph node dissection has been the standard treatment choice for patients with early-stage invasive cervical carcinoma. Due to the radicality of RH surgery, many cervical cancer patients who underwent RH may suffer from post-operative symptoms and function losses, including dysuria, urinary incontinence, dysparia and vaginal dryness, constipation and sexual dysfunction.

Evaluating the outcome of RH should incorporate remove the mass, free of disease, relief of symptoms, as well as QoL assessment. Many generic QoL instrument designed in the form of questionnaire have been recently developed according to different cancer types, including Functional Assessment of Cervical Cancer Therapy (FACT-Cx).

During past decades laparoscopic surgical methods are widely adapted to treat gynecological malignancies. Assessment of a new surgical procedure should be found on the comparison with the results generated from standard open surgery.

In order to evaluate the quality of life (QoL) in patients who underwent abdominal radical hysterectomy (ARH) and total laparoscopic radical hysterectomy (TLRH) for early stage cervical carcinoma, total 121 patients with early-stage cervical carcinoma who underwent ARH and TLRH, have been randomly enrolled in a questionnaire-based study at Obstetrics and Gynecology Hospital of Fudan University between January 2008 to June 2010. Among them, 107 patients completed the QoL analysis. The data have shown that no significant differences were found in age, operation time, clinical-pathologic characteristics, adjuvant therapies, and complications between the two groups. The post-surgery QoL analysis showed no significant difference between TLRH group and ARH group in physical wellbeing, social wellbeing, emotional wellbeing, functional wellbeing and symptoms associated with operation.

In conclusion, post-surgical QoL analysis failed to uncover significant difference between TLRH and ARH groups. TLRH could be an alternative micro-invasive management to modify the classical surgery for early stage cervical carcinoma.

Plenary Session III

PS3-01

Management of cervical cancer in low-resource settings

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To help physicians understand the current status and options for the management of cervical cancer in low-resource settings.

There is a paucity of research on cervical cancer in low-resource settings. An expert panel was invited to present and discuss the management of cervical cancer in low-resource settings during the 2011 SGO Annual Meeting. The panel was tasked to make recommendations regarding best options and alternatives for management of patients with cervical cancer in low-resource settings.

Although more than 85% of cervical cancers develop in low-resource settings, few studies addressed the problems facing the management of cervical cancer in this setting. Three areas of deficiency were identified: 1. There is a lack of megavoltage LINAC equipment. Currently 60Co is the standard therapy. 50 Gy whole pelvic radiation is given. Occasionally additional reduced fields are given. There does not seem to be a standard protocol. Additionally, there is no brachytherapy treatment available. 2. Chemoradiation is used infrequently. Probably the main reason is the patient's inability to buy the drug. 3. Surgical management of early stage disease is not done. Possible solutions to these problems may be: 1. Establish a protocol that can be easily followed. 50 Gy whole pelvic radiation seems reasonable but additional therapy, particularly for advanced disease should be considered. This could be 20 Gy in reduced fields. Although considerable data is not available, an extrafascial hysterectomy appears to be a reasonable alternative to brachytherapy after 70 Gy with good regression. 2. How chemotherapy can be obtained as part of chemoradiation is a major problem. Discussion with health authorities may be helpful. The logistics of giving chemotherapy appears to be available as chemotherapy is given for other malignancies. 3. Early stage disease could be managed surgically. Currently a lack of surgical training is the main reason surgery is not considered. This could be improved by regular on-site surgical training of gynecologic surgeons or focused high-intensity teaching module.

Using the three modalities of surgery, radiation, and chemotherapy alone or in combination with modifications may be necessary to overcome the challenges in low-resource settings. In order to improve the clinical outcomes, clinical trials and research are needed to investigate for the optimal treatment for patients with cervical cancer in low-resource settings.

PS3-02

The intraperitoneal chemotherapy in patients with ovarian cancer

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The most significant entity of the ovarian cancer is wide spread of disease in the abdominal cavity, called intraperitoneal (IP) dissemination. Therefore, administration of anticancer drugs into the IP cavity appeared to be an idealistic route of chemotherapy for this disease. It is theoretically reasonable, because disseminated cancer cells can be attacked by extremely high concentration of anticancer drugs. Number of research has shown the advantage of IP chemotherapy pharmacologically and clinically.

In the US, three large-scale randomized clinical trial demonstrated PFS/OS benefit of IP chemotherapy comparing with intravenous (IV) chemotherapy, and meta-analysis confirmed the advantage of IP chemotherapy. Based on these findings, US NCI made a clinical announcement recommending IP chemotherapy for ovarian cancer patients with small residual disease after initial surgery. However, IP chemotherapy has not been accepted as a standard treatment, mainly due to the toxicity issue, therefore, development of IP chemotherapy regimen is required.

Although it has been suggested that IP chemotherapy is applicable for the patient with small residual disease, recent pharmacological research indicated that IP chemotherapy using platinum agents should also be more effective than IV therapy for the patients with bulky residual disease. Retrospective and phase II study confirmed the result.

Neoadjuvant chemotherapy has been becoming a widely accepted new standard. Dose-dense weekly paclitaxel administration has shown dramatic improvement on survival. Bevacizumab showed an improvement of PFS in advanced ovarian cancer patients. Taking in account these information, there are three randomized phase III trials are on-going. One of the IP studies, the iPOcc Trial conducted by JGOG and GOTIC, is now open for international collaborations with KGOG, and collaborators in Austria, Australia, Singapore, and Spain.

It is hoped that these trials will give us an answer how we use IP chemotherapy more effectively and more safely.

PS3-03

A risk model for secondary cytoreductive surgery in recurrent ovarian cancer: an evidence-based proposal for patient selection

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Patient selection and the role of secondary cytoreductive surgery (SCR) are still undetermined since there is no randomized report till now. We started a pooled analysis of international collaborative cohort in December 2008. The aims are to evaluate the efforts of SCR in platinum-sensitive recurrent epithelial ovarian cancer (PSR EOC) and to develop a risk model for predicting SCR in PSR EOC.

Individual data of 1075 patients with PSR EOC undergoing SCR from seven world-wide centers were pooled and analyzed. The risk model was developed based on the factors impacting on SCR surgical outcome. Additional data on 117 patients who were not included in the development of the model were used for external validation and to assess the discrimination of the model.

Of the 1075 patients, 434 (40.4%) underwent complete resection. Complete secondary cytoreduction was associated with six variables: FIGO stage (OR=1.32, 95% CI: 0.97-1.80), residual disease after primary cytoreduction (OR=1.69, 95% CI: 1.26-2.27), progression-free interval (OR=2.27, 95% CI: 1.71-3.01), ECOG performance status (OR=2.23, 95% CI: 1.45-3.44), CA125 (OR=1.85, 95% CI: 1.41-2.44) and ascites at recurrence (OR=2.79, 95% CI: 1.88-4.13). These variables were entered into the risk model and assigned scores ranging from 0 to 11.9. Patients with total scores of 0-4.7 were categorized as the low-risk group, in which the proportion of complete cytoreduction was 53.4% compared to 20.1% in the high-risk group (OR=4.55, 95% CI: 3.43-6.04). In external validation, the sensitivity and specificity was 83.3% and 57.6%, respectively. Area under the curve of the receiver-operating characteristics for predicting complete SCR was 0.68 (95% CI: 0.60-0.79).

This model and scoring system may well predict the outcome of SCR and could potentially be useful in future clinical trials to determine which patients with recurrent ovarian cancer should have SCR as part of their management.

PS3-04

Hydatidiform mole prevention

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As many as 80% of hydatidiform moles experienced spontaneous regression due to apoptosis. On the other hand, 20% of hydatidiform moles would keep proliferating to the point that persistent post-mole occurs. Vitamin A is a vitamin that works to stimulate cell differentiations, control cell proliferation and increase apoptosis. It is interesting to study whether there is a relationship between hydatidiform mole and vitamin A.

The average level of blood retinol of the patients with hydatidiform mole was 10.52 $\mu\text{g}/\text{dl}$, and the average blood retinol of control patients was 12.89 $\mu\text{g}/\text{dl}$ ($p < 0.005$). The risk for the incidence of hydatidiform mole in the pregnant women of ≤ 24 years of age with severe deficiency of vitamin A was 6.29 times higher and the risk for hydatidiform mole in the women of ≤ 24 years with nil parity and severe deficiency of vitamin A was as many as 7 times higher than in control group. The incidence of low retinol deposit in liver on hydatidiform mole cases were 73.22%. The administration of vitamin A (200,000 IU) in post-mole evacuation decreased incidences of persistent mole. In randomized double blind clinical study, it was found that the incidences of persistent mole in the control group was 28.57%, and in the group receiving vitamin A 6.25%.

Retinol level in hydatidiform mole was lower in the group receiving vitamin A than in the control group. The administration of vitamin A following mole evacuation decreased the incidences of persistent mole from 28,57% to 6,25%.

Plenary Session IV

PS4-01

Risk reducing bilateral salpingo-oophorectomy in women at high risk for ovarian cancer

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Although ovarian cancer is relatively uncommon, epidemiologic studies have identified various high risk factors. Women who are carriers of a germline mutation in BRCA1 or BRCA2 have the highest risk of developing ovarian cancer. Mutations in these two genes account for approximately 95% of hereditary ovarian cancers. Mutation carriers have a 15–60% lifetime risk for developing ovarian cancer. For these women, the value of prophylactic salpingo-oophorectomy has been well documented.

BRCA1/2 carriers who undergo risk-reducing prophylactic salpingo-oophorectomy (RRBSO) are sometimes found to already have occult neoplasia: in one series of 98 such operations, 3 (3.1%) patients had a low-stage ovarian malignancy. The protection against the subsequent development of cancer is very high: the performance of a prophylactic salpingo-oophorectomy reduces the risk of BRCA-related gynecologic cancer by 96%. Because some serous epithelial tumors might arise in the fallopian tube and because there is a higher rate of tubal carcinoma in women with BRCA1 and BRCA2 mutations, it is essential that risk-reducing surgery include the removal of both ovaries and both fallopian tubes.

Although the risk of ovarian and fallopian cancers is substantially diminished by RRBSO, there remains a small risk of subsequently developing a peritoneal carcinoma, a tumor that may also have a higher predisposition in women who have mutations in the BRCA1 and BRCA2 genes. In these series, the risk of peritoneal carcinoma following RRBSO was 0.8% and 1%, respectively. Prophylactic salpingo-oophorectomy in premenopausal women reduced the risk of developing subsequent breast cancer by 50% to 80%.

HPV and cervical cancer from reality to future challenges

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Cervical cancer is the 2nd most common female cancer; 493,243 patients worldwide in 2002, and the 3rd most common cause of female cancer mortality with 273,505 deaths reported worldwide. Cervical cancer is preventable and generally curable if detected early. Important strategies to reduce the risk of cervical cancer include screening through the use of the Papanicolaou test, HPV (human papillomavirus) test and prophylactic vaccination.

Studies by zur Hausen and other colleagues have identified HPV, which is transmitted through sexual contact, as the main cause of cervical cancer by defining some potential oncogenic mechanisms. The recognition that oncogenic type-specific HPV infection can induce the initiation and promotion of cervical cancer development allows development of strategies reducing the global burden of cervical cancer through prophylactic vaccination, and possibly through immunotherapy.

Two vaccine strategies have been developed. First, prevention of HPV infection through induction of capsid-specific neutralizing antibodies has been developed. Using non-infectious virus-like particles (VLPs) with HPV type 16 and 18, HPV vaccination has been shown to be virtually 100% effective in preventing persistent type-specific HPV infections as well as their neoplastic sequelae. However these vaccines, at the present, protect against only two of the 15 oncogenic genital HPV types, they are expensive, delivered by intramuscular injection and require cold chain. The challenges are to develop non-expensive, thermo-stable vaccines that can be delivered by non-injectable methods that provide long term protection to most oncogenic HPV types. HPV L1 VLP-based vaccines have no therapeutic properties, but induce high concentrations of neutralizing antibody to L1 resulting in rapid access to local lymph nodes thus circumventing the immune avoidance strategies of viral intra-epithelial infectious cycle.

Second approach of developing therapeutic vaccines by targeting nonstructural early viral antigens has also been developed. HPV E6 and E7 proteins are very promising target proteins for therapeutic vaccines, as they are the only viral proteins constitutively expressed in cervical cancer cells and are required to maintain the disease phenotype. Many groups have focused on recombinant protein strategies for developing therapeutic immunization to induce E6- and/or E7-specific cell-mediated immune responses by the recognition of specific antigens present in the HPV-associated neoplastic lesions. Therapeutic vaccines targeting HPV nonstructural proteins are still at an early stage of development.

Success in developing prophylactic HPV vaccines has demonstrated the potential of prevention of cervical cancer and numerous experimental trials and encouraging preclinical results suggest that effective prophylactic and therapeutic vaccines can be developed through inducing neutralizing antibody as well as therapeutic immune response to achieve clinical useful outcomes.

PS4-03

Immunotherapy in cervical cancer: from bench to bedside

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Over a long period of time, cancer has become the most important health issue in the world. Conventional treatment modalities for cancer such as surgery, radiotherapy, and cytotoxic chemotherapy, though effective to some extent, have a shortcoming in common: these methods may injure normal cells. Indeed, there is a need to decrease the incidence of cervical cancer and develop better forms of its treatment.

The ideal cancer treatment should be able to eradicate systemic tumors at multiple sites in the body while having the specificity to discriminate between neoplastic and nonneoplastic cells. So cancer immunotherapy, especially antigen-specific therapy represents an attractive approach for cancer treatment.

Our research team has focused on different strategies on the development of antigen-specific cancer vaccine immunotherapy, including protein-based vaccine, naked DNA vaccine and cell-based therapy. The past, present and future aspects of cancer immunotherapy will be presented and discussed.

PS4-04

Effect of estrogen on endometrial carcinogenesis

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Impaired mismatch repair (MMR) is reportedly crucial in the early stages of endometrial carcinogenesis. Although estrogen exposure is considered an important risk factor for endometrial carcinoma, the relationship between estrogen and MMR activity remains undetermined. The present study was undertaken to elucidate the effect of estrogen on MMR activity in normal and malignant endometrial cells. The expression of MMR proteins, hMLH1 and hMSH2, and its correlation with estrogen was examined using immunohistochemical and immunofluorescent techniques. The effect of estradiol (E2) on the expression of hMLH1/hMSH2 protein/mRNA and *in vitro* MMR activity using two types of heteroduplex (G/T mismatches, 2-base insertion-deletion loops) was examined in cultured normal endometrial glandular (NEG) cells and in an estrogen receptor-positive endometrial carcinoma Ishikawa cells. Immunohistochemical expression of hMLH1 and hMSH2 in normal endometrial glands was positively correlated with the serum E2 levels. The expression of hMLH1/hMSH2 protein and mRNA were increased in NEG and Ishikawa cells by E2 treatment. *In vitro* MMR activity was up-regulated by E2 in both types of cell and heteroduplex. Immunofluorescent analysis demonstrated that E2 enhanced proliferation and hMLH1/hMSH2 expression in both cells, however, proliferating cells without hMLH1/hMSH2 expressions implying “high risk” cells were more frequently observed under low E2 concentrations. Collectively, the E2-induced up-regulation of MMR activity in endometrial cells suggests that high estrogen levels act as an intrinsic defense against endometrial carcinogenesis, whereas the imbalance between cell growth and MMR under low E2 environment as seen at post-menopause is vulnerable to carcinogenesis.

PS4-05

Overcoming chemoresistance in ovarian cancer

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Ovarian cancer is a leading cause of cancer mortality being the most frequent cause of death from gynecological cancer. Seventy-five percent of ovarian cancer patients present with evidence of metastatic spread beyond the ovaries and require combined surgery and chemotherapy. Although response rates with first-line chemotherapy may exceed 80%, patients with advanced disease invariably relapse with a median progression-free survival of only 18 months. Primary cytoreductive surgery in combination with adjuvant chemotherapy (carboplatin and paclitaxel) has produced higher initial response rates in the range of 65–80%, but long-term overall survival for patients with advanced high-grade ovarian cancer is 10–30%, mainly due to the development of drug resistance. Thus, overcoming chemotherapy resistance remains a key problem in the treatment of advanced ovarian cancer and consequently, new substances to enhance and support the activity of cytotoxic drugs are urgently needed.

A greater understanding of tumor biology and molecular pathways that mediate cancer progression and drug resistance has led to the development of various molecular targeted therapies such as monoclonal antibodies, small molecule receptor tyrosine kinase inhibitors and agents blocking downstream signaling pathways. The last five years has seen a major expansion in the number of clinical trials with molecular targeted agents in ovarian cancer. This review discusses the rationale for molecular targeted therapy in ovarian cancer and the current randomized trials. Results of many other trials with molecular targeted therapy will follow over the next 2–3 years.

This review focuses on the recent developments with new biological agents in the treatment of advanced and recurrent ovarian carcinoma.

Plenary Session V

PS5-01

An analysis of patients with bulky advanced stage ovarian, tubal, and peritoneal carcinoma treated with primary debulking surgery (PDS) during an identical time period as the randomized EORTC-NCIC trial of PDS vs neoadjuvant chemotherapy (NACT)

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The recent EORTC-NCIC randomized trial comparing primary debulking surgery (PDS) to neoadjuvant chemotherapy (NACT) in advanced epithelial ovarian carcinoma (EOC) reported a median progression-free survival (PFS) of 12 months and overall survival (OS) of 30 months for both arms. Due to the equivalent survival and decreased morbidity with NACT, many now consider it the preferred approach. We analyzed the outcomes of patients treated with PDS at our institution during the same time period in which the EORTC-NCIC trial was conducted, using identical inclusion criteria.

We identified all patients undergoing primary treatment for advanced EOC at our institution from 9/98-12/06. Study inclusion and exclusion criteria were identical to those of the EORTC-NCIC trial. Standard statistical tests were used.

Of 316 eligible patients, 285 (90%) underwent PDS and 31 (10%) received NACT due to extra-abdominal disease, medical comorbidities, and/or advanced age (>85 yrs). Of the 285 patients who underwent PDS, most had carcinoma of ovarian origin (248, 87%); stage IIIc disease (249, 87%); grade 3 tumors (237, 83%); and serous histology (249, 87%). Optimal cytoreduction (≤ 1 cm residual) was achieved in 203 patients (71%). Postoperative platinum-based chemotherapy was given to 281 of 285 patients (99%). The median PFS and OS were 17 and 50 months, respectively.

PDS should continue to be the preferred initial management for patients with bulky stage IIIc-IV ovarian carcinoma. NACT should be reserved for those who cannot tolerate PDS and/or for whom optimal cytoreduction is not feasible.

PS5-02

The association between endometriotic lesion and histological aspects of ovarian clear cell carcinoma

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The relationship between endometriotic cyst and ovarian clear cell adenocarcinoma (CCA) is an active area of gynecological research. Although endometriotic lesion is often considered to precede CCA, the relationship is still unresolved due to the diversity of histopathological features observed. Therefore, we conducted a retrospective study to determine the association between endometriosis and the histological aspects of CCA.

We reviewed the pathology of 46 CCAs obtained from a total of 410 ovarian cancer cases that were treated at Kumamoto University Hospital between 1990–2008. We observed two tumor subgroups consisting of either the clear cell components alone (pure-type) or containing clear cell along with endometrioid and/or serous components (mixed-type). The presence of endometriotic lesions within the tumors was analyzed in two types. To assess characteristics of mixed-type tumors, we investigated immunohistochemistry for expressions of ARID1A, PTEN and p53, known as responsible genes for carcinogenesis of clear cell, endometrioid and serous carcinomas, respectively.

The data identified 35 pure-type CCAs, and 11 mixed-type CCAs with endometrioid (3/11) and/or serous (9/11) components. Endometriotic lesions were observed in 28 pure-type CCAs (80.0%), but only in 5 mixed-type tumors (45.0%). Immunohistochemical analysis demonstrated that mixed-type CCAs had altered expressions of PTEN (2/3 of endometrioid components), p53 (5/9 of serous components), and ARID1A (5/11 of clear cell components). Endometriotic lesions were not observed in any CCAs with abnormal expressions of p53 in the serous components.

Immunohistochemical analysis demonstrated that mixed-type CCAs have altered expressions of ARID1A, PTEN, and p53. Furthermore, we noted that CCAs containing serous components with abnormal p53 expressions exhibited carcinogenesis independent of endometriosis. Together, our results show that CCAs appear to represent a heterogeneous group of tumors, requiring specifically tailored clinical therapies.

PS5-03

PARP inhibitors in ovarian cancer

Jonathan A Ledermann on behalf of the 'Study 19' investigators

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Poly ADP Ribose Polymerase (PARP) is a key regulator of the DNA repair pathway. Ovarian tumours with BRCA1/2 mutations are sensitive to inhibition of PARP due to impaired DNA repair by homologous recombination (HR). Phase II studies have demonstrated a tumour response in 28–33 % patients. More recently, HR deficiency has been found in larger proportion patients, particularly in those without BRCA1/2 mutations who have platinum-sensitive high-grade serous cancer, extending the population of patients who could potentially benefit from PARP inhibitors. This has now been tested using olaparib (AZD2281) as maintenance therapy following platinum-based chemotherapy for recurrent high grade serous ovarian cancer in a randomized, double-blind, multicentre, placebo-controlled Phase 2 study (ClinicalTrials.gov NCT00753545).

In this trial 265 patients were randomly allocated olaparib 400mg bd or placebo and the primary endpoint was PFS determined by RECIST. At the time of data analysis with 58% progression events there was a highly statistically significant reduction in the risk of progression in favour of olaparib (HR, 0.35; 95% CI 0.25–0.49; $p < 0.00001$; median progression post chemotherapy 8.4 versus 4.8 months). The treatment was well tolerated with nausea, fatigue and vomiting seen more commonly with olaparib compared to placebo. This was manageable largely through dose reduction and interruption of therapy. Very few patients discontinued treatment due to toxicity and there was no significant reduction in quality of life.

This trial has confirmed clinically meaningful activity of olaparib as maintenance therapy in a population of patients with high-grade serous ovarian cancer with or without BRCA1/2 mutations. It has opened the way forward for future studies to explore how olaparib, alone or in combination with chemotherapy might be incorporated into the treatment of ovarian cancer.

PS5-04

Novel biomarkers for ovarian cancer screening

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Research advances and the introduction of new targeted therapies for the treatment of cancer in the past decade have led to improved outcomes. As a result of these rapid changes, it has become paramount to identify diagnostic biomarkers. The biomarker field is one of the most challenging issues for oncologists today. Therefore, this has prompted us to commission a focus issue on biomarkers.

CA-125 is the most frequently used serum biomarker for ovarian cancer. However, there has long been controversy surrounding the use of CA-125 testing for ovarian cancer. While this biomarker is useful for clinical monitoring of response to chemotherapy, it is far less robust as a tool for treatment initiation for recurrent disease. Furthermore, for initial diagnosis of ovarian cancer, sensitivity is only 50% to 60% for early-stage disease in postmenopausal women when specificity is set at 99%.

The identification of more sensitive and specific biomarkers or biomarker panels for the early detection of ovarian cancer would be immediately beneficial. A lot of researchers reported the validation of serum multi-biomarkers for detection of early-stage ovarian cancer. There are many candidates for novel biomarkers for ovarian cancer, for examples, Eotaxin-1, IL-2R, MMP-2, MMP-3, Cyfra 21-1, ErbB2, EGFR, CEA, CA72-4, IGFBP-1, VCAM-1, FSH, GH, HE4, MMP-7. Despite all of the potentially useful biomarkers, almost none have been incorporated into formal cancer management. However, we are going to find a significant diagnostic biomarker comparable to CA-125, and it will come true soon because the technology has developed with rapid speed.

The pipeline of process for biomarker development begins with the discovery – an unbiased analysis of normal and cancer tissue specimens to identify differences in collections of tissue proteins. Discovery analyses are performed on a small number of very well-characterized cancers, precancers or normal tissue specimens. The objective of the next stage is to reduce this large list of biomarker candidates to identify a much smaller number of the highest quality candidates. Candidates are subjected to an iterative process of verification and assay development, in which highly sensitive, targeted analyses confirms their presence in tissues or plasma. The final stage of the pipeline is evaluation of biomarker candidates in clinical trials in a context most relevant to their eventual clinical application. This process is very time-consuming and requires many efforts. Therefore, the collaborative registry should be created for biomarker studies. The benefits of a comprehensive biomarker study registry are that more balanced evaluation of proposed markers is possible and false positive leads in research can be prevented through the collaboration.

Hopefully, more rapid identification of promising candidate biomarkers will be possible with the collaborative registry.

PS5-05

Dose-dense chemotherapy for ovarian cancer

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Among gynecological malignancies, epithelial ovarian cancer stands out as one that is difficult to be treated, has a high recurrence rate, and unfortunately, presents a high mortality rate for afflicted patients. Evidences have emerged that “dose-dense” (DD) schedule of chemotherapy for ovarian cancer, no matter in the first-line or recurrent setting, has shown a promising therapeutic results. Notably, DD chemotherapy also exhibits therapeutic effect in drug-resistant disease. In the interest of elucidating the reason for the improved responsiveness of platinum-resistant tumor to be re-challenged by platinum-based drugs administered in the dose-dense manner, we investigated and compared the immune profile of mice that received dose-dense administration of platinum-based and taxane-based drugs with that of mice that received the maximum tolerated dose (MTD). We discovered that in the case of drug-resistant ovarian cancer, the responsiveness to DD chemotherapy was greater than the responsiveness to MTD so long as the host-immunity was intact. In athymic mice and when there was selective depletion of macrophage or CD8 effectors cells, the usefulness of DD was abolished. In contrast to MTD, which caused severe bone marrow toxicity in mice, DD chemotherapy was able to preserve major immune effectors cells such as CD8⁺, CD4⁺, NK, CD11b⁺, CD11c⁺, and F4/80⁺. DD chemotherapy also promoted macrophage (CD14⁺ F4/80⁺) numbers and even the recruitment of said macrophage to the site of tumor in the peritoneal cavity. Equally important, DD regimen elicited tumor-specific cytotoxic T cell activity that greatly contributed to the shrinkage of the tumor in the intraperitoneal ovarian tumor model. Finally, we also documented a correlation between the induction of macrophage and activity of chemotherapy with weekly low-dose carboplatin and paclitaxel in the patients having platinum-resistant ovarian cancer.

From our data, we conclude that the immune-dependence of DD chemotherapy contributes to its effectiveness in treating platinum-resistant epithelial ovarian cancer.

PS5-06

Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient selection

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Fertility-sparing surgery (FSS) for stage I epithelial ovarian cancer (EOC) including unilateral salpingo-oophorectomy and optimal surgical staging is an option available to young women. However, the recommended indications for such treatment remain controversial. EOC with clear cell or grade 3 (G3) histology and with bilateral ovarian involvement has been excluded from indications for FSS in almost all guidelines. The recommendations regarding FSS for unilateral and stage IC EOC differ widely among these guidelines, although those for unilateral and stage IA EOC with favorable histology are common to all guidelines. The present study attempted to determine selection criteria for FSS in stage I EOC patients based on clinical outcomes for over 200 stage I EOC patients who underwent FSS. The objective of this study was to assess clinical outcomes and fertility in patients treated conservatively for unilateral, stage I invasive EOC.

A multi-institutional retrospective investigation was undertaken to identify patients with unilateral and stage I EOC treated using FSS. Favorable histology was defined as grade 1 or grade 2 adenocarcinoma, excluding clear cell histology.

A total of 211 patients (stage IA, n=126; stage IC, n=85) were identified from 30 institutions. Median duration of follow-up was 78 months. Five-year overall survival and recurrence-free survival in each group were: 100% and 97.8% for stage IA and favorable histology (n=108); 100% and 100% for stage IA and clear cell histology (n=15); 100% and 33.3% for stage IA and grade 3 (n=3); 96.9% and 92.1% for stage IC and favorable histology (n=67); 93.3% and 66.0% in stage IC and clear cell histology (n=15); and 66.7% and 66.7% for stage IC and grade 3 (n=3). Forty-five of 84 patients (53.6%) who were nulliparous at FSS and married at the time of investigation gave birth to 56 healthy children.

Our data confirm that fertility-sparing surgery is a safe treatment for stage IA patients with favorable histology and suggest that stage IA patients with clear cell histology and stage IC patients with favorable histology can be candidates for FSS followed by adjuvant chemotherapy.

Educational Session

ES-01

Radical hysterectomy

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In 1974, Piver et al. described the following five types of hysterectomy: extrafascial, modified radical, Radical, extended radical, and partial exenteration. Extrafascial hysterectomy (type I) is a simple hysterectomy and is suitable for stage IA1 cervical carcinoma. Modified Radical hysterectomy (type II) is basically the hysterectomy described by Ernst Wertheim. The modified radical hysterectomy is appropriate for stage IA2 cervical cancer. Radical hysterectomy (Type III), the most commonly performed operation, for stage IB cervical cancer is that originally described by Meigs in 1944(107). Extended Radical Hysterectomy (Type IV) differs from the type III operation in three aspects: (i) The ureter is completely dissected from the vesicouterine ligament, (ii) the superior vesicle artery is sacrificed, and (iii) three-fourths of the vagina is excised. The indication for partial Exenteration (Type V) was removal of a central recurrence involving a portion of the distal ureter or bladder.

A new classification for radical hysterectomy was described following a consensus meeting in Kyoto, Japan, The classification is based only on the lateral extent of the resection. Four basic types are described, A–D. Type A corresponds to the extrafascial hysterectomy. Type B corresponds to the modified radical hysterectomy. Type C has C1 type and C2 type. The Q–M classification system distinguishes between a type C1 procedure, which corresponds to the nerve-sparing modification, and the type C2, which aims for a complete parametrial resection. Type D differs from type C2 only in the lateral extent of the lateral parametria resection.

In the 1980s, Japanese gynecologists published the first English article for the pelvic autonomic nerve-sparing concept named the Tokyo method, which was considered as the solution of bladder, rectum, and sexual dysfunction after radical hysterectomy.

Nerve-sparing concepts via a laparotomy approach have focused on the hypogastric nerve, the pelvic splanchnic nerve, and the distal part (vesical and uterovaginal branches) of the inferior hypogastric plexus (IHP, pelvic plexus) during the dissection of the posterior leaf of the vesicouterine ligament (VUL).

I described the laparoscopic pelvic anatomy of nerve-sparing radical hysterectomy. The operative steps were described on the focus of nerve sparing procedures, and in particular, of vessels and nerves in the deep part of the cardinal ligament, uterosacral ligament, and posterior leaf of the VUL under the enhanced view of laparoscopy.

ES-02

Pelvic and para-aortic lymph node dissection

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The presence of lymph node metastasis is the most significant prognostic factor in the management of gynecologic malignancies. Indirect techniques such as lymphography, computerized tomography, magnet-resonance imaging, or guided fine-needle aspiration are of limited sensitivity and specificity in looking for metastasis. Diagnostic lymphadenectomy by laparotomy is costly and uncomfortable, and causes major peri-operative complications and pelvic adhesions.

Laparoscopy results in minimal surgical trauma, less intra-abdominal adhesion formation, lower costs, less pain, and a shorter recovery time than traditional laparotomy. The first case of laparoscopic pelvic lymphadenectomy was reported by Dargent, et al in 1989, followed by Nezhat's description of laparoscopic para-aortic lymphadenectomy three years later. Several reports showed the numbers of nodes harvested by laparoscopy and laparotomy were no significant difference. Debulking of large lymph node metastases can also be achieved at laparoscopy. Recently laparoscopic extraperitoneal techniques were also developed for lymph nodes dissection. Improvements in laparoscopic surgical techniques and instrumentation have made laparoscopic lymphadenectomy in gynecologic malignancies feasible and effective.

Principles of bowel resection and anastomosis

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Anastomotic failure remains the main cause of morbidity and mortality after intestinal surgery. The incidence of overt dehiscence has been reported variably from 0.1% to 30% according to the disease entities, suture techniques, and organs sutured. Many struggles were done to achieve better results and outcomes after anastomosis regarding suture techniques, suture materials, wound healing, and influences of local and systemic factors. Recently, surgical staplers are widely used and gain the importance dealing the bowels. It is necessary to understand the mechanism involving intestinal healing after resection, as well as the technical aspect to obtain the safe anastomosis.

Principles of intestinal anastomosis

- 1) Avoiding ischemia and consequently necrosis
- 2) Hemostasis, preventing hematoma and postoperative bleeding
- 3) Adequate approximation of tissue
- 4) Lack of excessive traction and tension
- 5) Enough intestinal lumen
- 6) Avoiding increment of intraluminal pressure

Factors influencing the wound healing after anastomosis

Many systemic factors have been suggested to influence of intestinal wound healing such as age, malnutrition, shock, diabetes, anemia, hypovitaminemia, chemotherapeutic agents, and so on. To achieve the complete anastomosis, the corrections of these systemic derangements are important as much as possible.

Local factors around anastomosis are much important for safe anastomosis, thus, great effort to maintain the adequate tissue oxygenation and blood flow must be performed during operation. Tension across the anastomosis, trauma, and ischemia must be avoided and fresh lesion of bowel must be used for anastomosis.

Suture materials

Suture materials can act as foreign bodies producing local inflammation. Throughout several decades, there was great amount of investigation to find out the best suture material for bowel anastomosis. Nowadays, many suture materials are widely used: monofilamentary lines vs multifilamentary lines and absorbable materials vs non-absorbable materials.

The ideal material for anastomosis has the following properties as no potentiation of infection, slow absorption, not irritable, and easy to manipulate.

Suture technique

Several manual suture techniques have been proposed but still, there remain a big controversy regarding feasibility and safety among different techniques and no concrete guidelines or evidence are not obvious for selection of optimal technique.

Both single plane and double planes anastomosis were applied. separate stitches and continuous running technique were also used widely. The success of each techniques varies and is closely related to the surgeon's experiences and preference.

Stapled anastomosis

In the last two decade, advances in stapling devices have led to an increased frequency of stapled bowel anastomoses. There are a variety of potential benefits from a stapled technique: better blood supply; reduced tissue manipulation; less edema; uniformity of sutures, adequate, or perhaps wider, lumen at the site of anastomosis; ease and rapidity. A consistently safe method of anastomosis is still an ideal; the achievement of which would not only lower the incidence of dangerous complications but possibly avoid the need for a defunctioning colostomy or ileostomy. Staplers have been used in many kinds of anastomosis, but most frequently in colorectal surgery, particularly for low anastomoses.

Establishing safe anastomosis is crucial step in bowel surgery. For it, understanding healing mechanism as well as choosing the adequate technique and material is mandatory.

ES-04

Pelvic exenteration for gynecological cancer

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Pelvic exenteration (PE) is an ultraradical surgery pioneered first in gynecologic oncology in 1948 by Brunschwig for advanced cancer. This surgery removes basically all pelvic organs, including not only the uterus, ovaries, and vagina but also the adjacent organs, bladder, and rectosigmoid colon. PE have been successfully performed with a team approach, whereby the gynecologist, urologist, and general surgeons, and possibly the plastic surgeon work together in this very extensive procedure.

The prime indication for PE is recurrent cervical cancer after full radiation therapy. PE is largely confined to the treatment of central recurrences. The main shift in the goal of PE has been from a palliative procedure to a potentially curative procedure in patients with advanced pelvic malignancy. Especially in ovarian cancer, PE with curative intent led to much improvement in perioperative mortality and overall survival rates.

The complications related to the exenteration are mostly the results of the denuded pelvic floor and the reconstruction of vital organs using partially radiated structures. Recent advances in patient selection, surgical technique, and perioperative care have led to decreased morbidity.

Total PE and its modifications need to be considered among the treatment options for patients with advanced pelvic malignancies. Recent advances in patient selection, surgical technique, and perioperative care have led to decreased morbidity. Despite this, PE remains a formidable procedure with the potential for both short- and long-term complications.

Experiences at National Cancer Center (NCC) Korea

From January 2001 and April 2011, the PEs were performed for cancer of the cervix (62 patients), vagina (11 patients), vulva (6 patients), uterine sarcoma (3 patients) and 1 endometrium. Median follow-up was 34 (0.7–110) months. Total morbidity rate was 48%; 23 of patients (27%) had early complications (<30 days after PE) whereas 27 patients (32%) had late complications. Wound problem was common among early complications and bowel fistula and obstruction were common among late complications. Five year overall survival and disease free survival were 44% and 39%, respectively. The modified PE was performed for ovarian cancer (239 patients) at NCC. Stage of ovarian cancer was as follows Stage I, 13; Stage II, 18; Stage III, 174; Stage IV, 34. Median follow-up was 31 (1–119) months. Five year overall survival and disease free survival were 62% and 33%, respectively.

ES-05

Robotics and surgical training: a new paradigm in medical education

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In the United States and worldwide, robotic surgery has played an increasingly important role in minimally invasive surgery. For many surgeons, robotics has become the standard approach for women diagnosed with endometrial and cervical cancer. Recently, surgeons have successfully utilized robotics in the obese and morbidly obese while maintaining excellent surgical and oncologic outcomes while minimizing morbidity. However, this unique surgical tool has presented some issues and complexities related to training and education. Presently in the US, every American Board of Obstetrics and Gynecology (ABOG) approved gynecologic oncology fellowship training program has access to a robotic surgical system. However, training is not consistent among institutions, and standard, time-tested educational approaches may not apply or be relevant to robotic surgical training.

This presentation on robotic surgical training will review the following:

- 1) Lessons learned with fellow/resident training at the University of Alabama at Birmingham (UAB)
- 2) The role of simulation based training on the robotic surgical platform.
- 3) Are complication rates higher in cases performed with fellows/residents?
- 4) Suggestions on how to optimize robotic training.

Updates on pathology of uterine sarcoma

Annie NY Cheung

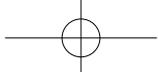
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Uterine leiomyosarcomas and endometrial stromal sarcomas (ESSs) are the two most common uterine sarcomas.

Currently, ESSs are classified into low-grade ESS and undifferentiated endometrial sarcoma (UES). Low-grade ESSs are biologically low-grade uterine sarcomas and typically composed of uniform cells intimately associated with prominent arterioles, resembling the endometrial stroma in proliferative phase. There is usually little cytological atypia or pleomorphism, and mitoses are scanty. In contrast, UESs are frankly malignant, lack specific differentiation and any features of normal endometrial stroma. It is a highly aggressive neoplasm, often exhibiting myometrial invasion, hemorrhage and necrosis, as well as marked nuclear pleomorphism and high mitotic activity. The diagnosis of UES is reached after excluding other uterine tumours with a sarcomatous component, such as adenosarcoma and malignant mixed mullerian tumour.

Preoperative detection of uterine leiomyosarcomas is difficult because of the similarity in clinical presentation with ordinary fibroids. They are highly aggressive tumors and surgery remains the mainstay of treatment. For pathologists, diagnosis of the great majority of leiomyosarcomas using current diagnostic criteria is usually straightforward as most tumors often possess two or more of the diagnostic microscopic features including diffuse atypia, high mitotic count and tumor cell necrosis. The diagnostic difficulties are usually related to tumors having only one of these worrisome features, with or without other unusual morphologic findings. These latter tumors have been labeled as uterine smooth muscle tumors of uncertain malignant potential (STUMP). STUMPs that are followed by a recurrence are biologically low-grade leiomyosarcomas. Epithelioid and myxoid leiomyosarcomas are rare and their diagnostic criteria are different to tumors of usual spindle cell differentiation.

The problems with histologic diagnosis, immunohistochemical studies and molecular pathology are highlighted.



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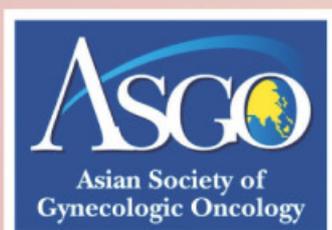
2011: Volume 22

4 issues per volume

Language: English

pISSN 2005-0380

eISSN 2005-0399



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FC-01

The establishment of the Korean human papillomavirus cohort study

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Objective: We established a large prospective multicenter Korean human papillomavirus (HPV) cohort study in September, 2009. The goals of the Korean HPV cohort study were to: study the epidemiology of persistent HPV infection, investigate whether persistent HPV infection increases the risks of low-grade and high-grade cervical lesions, and identify genetic and immunological determinants of persistent HPV infection.

Methods: The Korean HPV cohort study teams included gynecologists, epidemiologists, pathologists, biologists, virologists, religionists, and sociologists. Five hospitals enrolled HPV patients who provided informed consent and completed questionnaires, and collected cervical samples for the Korean HPV cohort study. Cervical samples were analyzed to determine the results of HPV, Pap, and P16 plus Ki67 tests. The Korea Centers for Disease Control received and managed all data and samples.

Results: A pilot project to evaluate the design and establishment of the Korean HPV cohort study was performed for 6 months. The pilot project was successfully completed, and the Korean HPV cohort study has been continued thereafter.

Conclusion: Through analyses of risk factors related to persistent HPV infection and CINs, the epidemiologic, virologic, and clinical results of this cohort study are intended to be used for constructing guidelines and developing educational materials for the primary prevention of cervical cancer. Ultimately, our data may be useful for developing new treatments for HPV infections.

Keywords: Human papillomavirus, Cohort study, Cervical cancer

FC-02

Multicenter clinical validation of DNA hypermethylation in the detection of cervical neoplasia: a Taiwanese Gynecologic Oncology Group (TGOG) study

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Objective: Our previous work discovered some novel genes highly methylated in cervical cancer and demonstrated the high detection rate of cervical intraepithelial neoplasias 3 (CIN3) and worse lesions. To validate further these results, the present study conducted a multicenter study using a standardized testing assay.

Methods: We conducted a multi-center prospective case-control study in 11 medical centers in Taiwan from Dec. 2009 to Nov. 2010. A standardized multiplex QMSP was performed using the LightCycler 480 Real-Time PCR System (Roche). HPV testing was done by Hybrid Capture II. Subjects were separated into training set to generate cut-off value and testing set for validation.

Results: Six hundred and seventy-six patients were recruited including 330 patients in the training set and 346 patients in the testing set. In the training set analysis, the AUCs for the detection of CIN3+ are 0.74 and 0.76, for SOX1 and PAX1, respectively. The sensitivities for CIN3+ detection are 67% and 60%, and the specificities are 81% and 92%, respectively for SOX1 and PAX1. In the testing set, the sensitivities are 64%, 69% and 89%, and the specificities are 90%, 80% and 68% for SOX1, PAX1 and HPV, respectively. When using combination with Pap smear, the sensitivities for CIN3+ detection are 96%, 93% and 97%, and the specificities are 73%, 83% and 66%, respectively for SOX1, PAX1 and HPV testing in combination with Pap smear.

Conclusion: Combined testing of Pap and PAX1 or SOX1 methylation could provide better performance than the combination with HPV testing in cervical cancer screening.

Keywords: Cervical cancer, Epigenetics, Methylation, SOX1, PAX1

FC-03

Scoring system for predicting a lymph node metastasis in cervical cancer

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Objective: Lymph node involvement is the most important prognostic parameter in cervical cancer, however, the therapeutic role of lymphadenectomy is still unclear even in an advanced cervical cancer. To predict nodal metastasis, we investigated the preoperative factors and determined a scoring system in cervical cancer.

Methods: A retrospective review of 321 patients who underwent pelvic lymphadenectomy in cervical cancer between 2009 and 2011 was performed.

Results: Mean number of pelvic lymph node resected was 31.0, and 66 patients (20.6%) had nodal metastasis. Lymphocyst was detected in 15.5% and lymphedema requiring treatment occurred 5.6%. In logistic regression, the preoperative factors associated with metastatic lymph node were as follows; nodal metastasis on PET (OR 5.40) or MRI (OR 3.71), tumor size >2 cm on imaging (OR 6.01), and SCC level ≥ 0.7 ng/ml (OR 2.36). Using these four factors, total score of risk for nodal metastasis was calculated, namely, 5 points in a case of positive on PET, 4 in positive on MRI, 6 in tumor size >2 cm, and 2 in SCC ≥ 0.7 ng/ml. In total score, the cut-off value of 5 points showed only 3.7% of false negative value (FNV), 96.3% of negative predictive value (NPV), 93.2% of sensitivity, and 41.8% of specificity.

Conclusion: In cervical cancer, scoring system consisting of four factors such as nodal metastasis on PET and MRI, tumor size, and SCC level shows high NPV and low FNV for predicting nodal metastasis. This preoperative evaluation can get physicians to avoid inadvertent lymphadenectomy, so decrease surgical risks and complications.

Keywords: Cervical cancer, Lymph node metastasis, Lymphadenectomy

FC-04

Single node positive revealed good survival as negative node in patients with cervical cancer treated with radical hysterectomy

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Objective: Lymph node metastasis is the major independent prognostic factor in cervical cancer patients treated with radical hysterectomy and pelvic node lymphadenectomy (RHPL). However, in patients with single node involvement, the survival of these patients might not be poor. To study the outcome of them, we conducted this retrospective study to identify the disease free survival (DFS) of cervical cancer patients treated with RHPL who had single node positive compared to the patients with negative node

Methods: Medical record of 843 cervical cancer patients undergoing RHPL at Chiang Mai university hospital between January 2002 and December 2008 were reviewed. The patients were divided into 5 groups according to the status of pelvic node as follow; group A=negative nodes (n=706;83.7%), group B=1 positive node (n=65;7.7%), group C=2 positive nodes (n=38;4.5%), group D = 3 positive nodes (13;1.5%) and group E>4 positive nodes (n =21;2.5%). The DFS of patients in each group were compared.

Results: The 5 year DFS in group A (negative node) was 98.5% that was closed to group B (single positive node) that showed 5 year DFS=91.3%. Whereas the remaining groups (group C,D,E) showed 1 year DFS as 77.6%, 74.1%, and 55.6%, respectively. These survival outcome in group A and B were significant difference from the 3 rest groups ($p<0.0001$).

Conclusion: Single node positive showed the similar survival as negative node while the survival outcome in patients with more than one node involvement was very poor.

Keywords: Single node metastasis, Cervical cancer, Radical hysterectomy

FC-05

Para-aortic lymph node (PAN) assessment and its surgical indication in patients with stage IB–IIA cervical cancer

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Objective: To investigate the frequency of PAN involvement in stage IB–IIA cervical carcinoma and to determine the feasibility and indication of para-aortic lymphadenectomy.

Methods: Medical records of 528 patients with Stages IB–IIA cervical carcinoma who underwent radical hysterectomy and systematic pelvic and PAN dissection from 2005 to 2010 were investigated retrospectively. Multiple logistic regression analysis was employed to determine the high-risk factors for PAN metastasis.

Results: The frequency of PAN involvement was 9.7% (51 patients) for all of the 528 patients and was 5.4%, 8.2%, 13.0% and 14.9% in FIGO stage IB1, IB2, IIA1 and IIA2, respectively. 158 (29.9%) patients had pelvic lymph node (PLN) metastases and 61 (11.6%) had common iliac lymph node (CILN) metastases. In a multivariate analysis, FIGO Stage, tumor size, and pelvic nodal involvement were independent risk factors for PAN metastasis. By using a receiver operating characteristic (ROC) curve, we found the optimal cut off point of tumor size to predict PAN metastasis was 3cm (sensitivity, 94.1%; specificity, 35.6%). Median follow-up was 28 months (3–48 m). The mean operating time for para-aortic lymphadenectomy was 30 min (range 20–45 min) and the median blood loss during the overall surgical procedure was 400 ml (range 100–1,450 ml). The rate of surgical complications was 7.7%, but no surgery-related death occurred.

Conclusion: PAN dissection is safe and feasible for cervical cancer patients. It is recommended that paraaortic lymphadenectomy should be routinely done for stage IB–IIA cervical cancer patients whose tumor size is no less than 3cm.

Keywords: Para-aortic lymph node, Surgical indication, Cervical cancer

FC-06

Evaluating the learning curve and perioperative outcomes of robot-assisted laparoscopy for cervical cancer: initial experience at the single institution

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Objective: To evaluate the learning curve and perioperative outcomes of robot-assisted laparoscopic procedure for patients with cervical cancer.

Methods: A series of 65 consecutive robot-assisted laparoscopic radical hysterectomies with bilateral pelvic lymph node dissection for cervical cancer were performed between May 2006 and May 2011. Demographic data and perioperative parameters including docking time (DT), console time (CT), total operative time, blood loss, lymph node retrieval, length of hospital stay, and complications were analyzed. The learning curve was evaluated using the cumulative sum (CUSUM) method.

Results: The mean age of patients was 46.2 years, and the mean BMI was 22.8 kg/m². The learning curve for console time was analyzed. The learning curve consisted of two unique phases: phase 1 (the initial 28 cases), and phase 2 (the subsequent cases). Phase 1 represented the initial learning curve, which spanned 28 cases. Phase 2 represented the mastery phase in which more challenging cases were managed. Docking and console times were significantly decreased after the first 28 cases compared to the rest (5 min vs. 4 min for DT, 160 min vs. 134 min for CT; $p < 0.0006$ and $p = 0.0004$, respectively). No conversion to laparotomy occurred. There was no difference in median blood loss, lymph node retrieval, length of hospital stay, and perioperative complications among the two phases.

Conclusion: The two phases identified with CUSUM analysis of surgeon console time represented characteristic stages of the learning curve for robot-assisted surgery for cervical cancer. The learning phase was achieved after 28 cases.

Keywords: Learning curve, Robot-assisted laparoscopy, Cervical cancer

FC-07

Prognosis and postsurgical complications of 78 cervical cancer patients who received abdominal radical or simple trachelectomy in our hospital during these 6 years

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Objective: To preserve fertility of cervical cancer patients, we started abdominal radical or simple trachelectomy (ART or AST) from 2005. The prognosis, postsurgical complications are reviewed.

Methods: Our eligibility criteria about tumor size for ART are: (1) squamous cell carcinoma (FIGO IA2 to early IIA) and adenocarcinoma (IB1) not over 3cm and 2cm in width, respectively; (2) MRI indicating at least 1cm free space between tumor edge and the amputation site of cervix. In the cases of smaller lesions including FIGO IA1 adenocarcinoma, we performed AST.

Results: Within 86 patients fulfilling the preoperative criteria, 78 cases underwent trachelectomy (ART: 67, AST:11). Seven cases with positive lymph nodes and a case showing positive amputated cervical margin were intraoperatively converted to radical hysterectomy. Within 78 cases, one patient lost her fertility by postoperative pelvic irradiation due to finding micro-metastasis in a lymph node by the postoperative histological re-examination. Main postsurgical complications were infection occurred in 18% cases at the anastomosis site between neo-cervix and vagina, but all cases were easily cured by antibiotics. Another complication was cervical stenosis requiring the cervical dilatation in some cases. Rare but serious complication of uterine amenorrhea occurred in 7% cases. During 32months of a mean follow-up period (1-73 months), none of the cases recurred and two patients had live births at 28 and 37 weeks of gestation.

Conclusion: ART seems to be safely performed without recurrence by our present eligibility criteria. Most of postsurgical complications were mild, except uterine amenorrhea. As for obstetric outcome, the low pregnancy rate must be improved in future.

Keywords: Abdominal trachelectomy, Cervical cancer, Fertility sparing surgery

FC-08

Intermediate risk factor grouping in FIGO stage IB-IIA postoperative cervical cancer patients: a multi-center retrospective study of Korean Gynecologic Oncologic Group (KGOG 1021)

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Objective: To determine which criteria are more feasible in predicting recurrence in cervical cancer patient with intermediate risk factors, KGOG versus GOG criteria

Methods: The medical records of 1,523 patients who had undergone radical surgery for stage Ib-IIa1 cervical cancer were reviewed with collaboration of 13 centers affiliated with KGOG. We set two criteria of intermediate risk group; one was KGOG criteria, which consists of any two or more intermediate risk factors (i.e., lymphovascular involvement, deep stromal invasion, and tumor size 2cm or more), and the other was GOG criteria which are three factor model (i.e., 1. Positive capillary-lymphovascular space involvement and one of the deep third penetration, middle third penetration, and clinical tumor ≥ 2 cm, or superficial third penetration and clinical tumor ≥ 5 cm, 2. Negative capillary-lymphatic space involvement with middle or deep third penetration, and clinical tumor ≥ 4 cm).

Results: Among the 1,523 patients with one or more intermediate risk factor, those who met the KGOG criteria were 1,082 patients (71.0%) and those who met the GOG criteria were 618 patients (40.6%). There were 236 recurrences, 140 in KGOG criteria group and 96 in GOG criteria group. The positive predictive value was not significantly increased using GOG criteria compared to KGOG criteria. Furthermore, the sensitivity was higher in KGOG criteria compared to GOG criteria (78.7% vs. 53.9% respectively. Z-test, $p < .05$) in detecting recurrences.

Conclusion: KGOG criteria are more sensitive than the GOG criteria in predicting recurrences for the patients with intermediate-risk group of cervical cancer after radical hysterectomy.

Keywords: Cervical cancer, Intermediate risk factor, Recurrence

FC-09

Endoglin (CD105) can be used as a prognostic marker for patients of cervical cancer receiving concurrent chemoradiation

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Objective: Endoglin (CD105), a co-receptor for transforming growth factor β 1 (TGF- β 1) in vascular endothelial cells, is highly up-regulated in tumor vessels and therefore is essential for angiogenesis. We attempted to investigate whether endoglin and TGF- β 1 can be used as markers to predict survival for cervical cancer patients.

Methods: We retrospectively analyzed endoglin and TGF- β 1 immunohistochemical expression of tissue samples obtained from 80 patients with different FIGO stages cervical cancer before they received concurrent chemoradiation (CCRT). Plasma levels of endoglin were also quantified prospectively from 15 healthy individuals and 21 cervical cancer patients prior to CCRT. The clinicopathological variables of the 80 patients including microvessel density (MVD) of endoglin and TGF- β 1 staining status were analyzed for treatment outcomes. The association between plasma levels of endoglin and disease extension/spreading was also evaluated.

Results: The median follow-up period was 86 months (range, 2–144) for the 80 patients. With Cox regression analysis, we found that FIGO stage (HR 4.66; 95% CI 2.10–10.32, $p < 0.001$) and endoglin MVD (HR 12.21; 95% CI 3.62–41.16, $p = < 0.001$) were independent factors to predict survival. Interestingly, strong TGF- β 1 expression was significantly associated with poor survival only when endoglin MVD was high. When compared with normal controls, plasma endoglin levels were significantly elevated in the 21 cervical cancer patients and correlated with disease extend.

Conclusion: Endoglin can be used as an independent prognostic marker for cervical cancer patients. TGF- β 1 also had an impact on survival only when endoglin was enriched, suggesting its involvement to tumor progression in the later stage of angiogenesis.

Keywords: Endoglin, TGF- β 1, Cervical cancer

Phase II evaluation of irinotecan in leiomyosarcoma of the uterus: a Japanese Gynecologic Oncology Group (JGOG) study

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Objective: To estimate the antitumor activity of irinotecan in patients with persistent or recurrent leiomyosarcoma of the uterus and to determine the profiles of toxicity of irinotecan in this cohort of patients.

Methods: Eligible patients had measurable advanced or recurrent leiomyosarcoma of the uterus. Irinotecan at a target dose of 100 mg/m² was administered IV on day 1, 8, and 15, every 4 weeks, until progression of disease or adverse events prohibited further therapy.

Results: Sixteen patients were enrolled from 12 institute members that the protocols were approved by each institutional review board. Of the patients entered, 15 patients were eligible, and the one case was not eligible because of wrong histology. Patients characteristics included a median age of 56 years old, with 33.3% (5/15) having prior chemotherapy. The most frequently observed grade 4 toxicities were neutropenia seen in 4 (25%) patients, leucopenia in 1 (6.3%), and thrombocytopenia in 0 (0%). One treatment related death, which was the case with neutropenia resulted in septic shock. There were no complete response, and two (13.6%) partial response, 2 (13.6%) stable disease.

Conclusion: Irinotecan at this dose and schedule appeared to have modest activity in patients with persistent and recurrent leiomyosarcoma, but further pre-chemotherapeutic screening of UGT1A1 polymorphism would be necessary.

Keywords: Leiomyosarcoma, Irinotecan, Chemotherapy

FC-11

Expression of angiotensin II type-1 receptor and miR-155 in endometrial cancers: synergistic inhibitory effect of anti-mir-155 and angiotensin type-1 receptor blocker, losartan, on endometrial cancer cells

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Objective: MicroRNA-155 (miR-155) is one of the micro RNAs (miRNA) most consistently involved in neoplastic diseases, and it is known to repress the angiotensin II type 1 receptor (AGTR1). The aim of the present study was to evaluate the expressions of miR-155 and AGTR1, and to clarify the potential efficacy of anti-miR-155, alone and in combination with AGTR1 blocker in endometrial cancers.

Methods: Expressions of miR-155 and AGTR1 were evaluated using real-time PCR and immunohistochemistry. And the MTT assay was performed in endometrial cancer cells following anti-miR-155 and AGTR1 blocker (losartan) treatment, alone and in combination.

Results: miR-155 was over-expressed and AGTR1 was underexpressed in endometrial carcinoma tissues. AGTR1 immunoreactivity were found in six of ten (60.0%) normal endometrium, 11 of 14 (78.6%) endometrial hyperplasia, and 27 of 62 (43.5%) endometrial carcinoma tissues ($p=0.051$), and patients with AGTR1 expression showed longer disease-free survival ($p=0.019$). We checked that abolishing the function of miR-155 and AGTR1 by anti-miR-155 or losartan inhibited cell survival of endometrial carcinoma cells, respectively, and furthermore, combined treatment showed synergistic effects.

Conclusion: In this study, we characterized the expressions of miR-155 and AGTR1 in endometrial tissues. The combined treatment with anti-miR-155 and losartan have a synergistic antiproliferative effect and an improved understanding is required to clarify whether miR-155 and AGTR1 can be used as a novel therapeutic targets in endometrial cancer.

Keywords: MiR-155, AGTR1, Endometrial carcinoma

FC-12

Laser captured microdissection–microarray analysis of the genes involved in endometrial carcinogenesis: stepwise up–regulation of lipocalin2 expression in normal and neoplastic endometria, and its functional relevance

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Objective: Endometrial carcinoma often arises from normal endometrial glandular cells via a precursor, atypical endometrial hyperplasia. However, the genetic changes involved in this carcinogenetic process are not fully understood.

Methods: Differentially expressed genes were selected from glandular cells of normal proliferative phase endometria, atypical endometrial hyperplasia and endometrial carcinoma using laser–captured microdissection (LCM) and microarray.

Results: The microarray analysis revealed a total of 51 genes to be up–regulated, and 23 genes to be down–regulated in neoplastic endometrial epithelia. We focused on lipocalin2 (LCN2), which showed the largest magnitude of up–regulation. Immunostaining for lipocalin2 confirmed a stepwise increase in its expression in endometrial hyperplasia and carcinoma. The subcellular distribution of lipocalin2 was both cytoplasmic and nuclear, despite reports that lipocalin2 is a secretory protein. Treatment of endometrial carcinoma cells with 5–azacytidine increased the expression of lipocalin2, suggesting the expression to be controlled by methylation of the promoter. The forced expression of lipocalin2 resulted in the enhanced cell proliferation and invasion *in vitro*.

Conclusion: The expression of lipocalin2 increased with the endometrial carcinogenesis, and accumulation of the protein conferred biological aggressiveness to endometrial carcinoma cells. These results suggest lipocalin2 to be a novel target in the treatment of endometrial carcinoma.

Keywords: Endometrial carcinoma, Microarray, Lipocalin2

FC-13

Metronomic doxifluridine chemotherapy combined with the anti-angiogenic agent Tnp-470 inhibits the growth of human uterine carcinosarcoma xenografts

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Objective: Uterine carcinosarcoma is a highly aggressive gynecological neoplasm that responds poorly to conventional chemotherapy and radiotherapy. Metronomic chemotherapy is accepted as a new approach for cancer treatment, and its underlying mechanism seems to involve the suppression of angiogenesis. However, the efficacy of metronomic and anti-angiogenic therapies against uterine carcinosarcoma is unknown.

Methods: The anti-angiogenic effect of doxifluridine was assessed *in vitro* using human umbilical vein endothelial cells (HUVEC) co-cultured with FU-MMT-1 human uterine carcinosarcoma cells (Emoto M. Cancer 1992). The antitumor and anti-angiogenic effects of metronomic doxifluridine (delivered via oral gavage) in combination with TNP-470 were evaluated *in vivo*. Tumor vascularity was assessed by contrast-enhanced color Doppler ultrasound, laser Doppler and microvessel density staining.

Results: Doxifluridine suppressed tube formation of HUVEC and vascular endothelial growth factor production by FU-MMT-1 cells. Metronomic doxifluridine alone significantly suppressed tumor growth compared with the untreated (control) group, while metronomic doxifluridine in combination with TNP-470 significantly inhibited tumor growth compared with each treatment alone. A significant reduction of intratumoral vascularity was observed in FU-MMT-1 xenografts following treatment with metronomic doxifluridine in combination with TNP-470, as compared with each treatment alone. Intestinal bleeding was only observed when the maximum tolerated dose of doxifluridine was administered in combination with TNP-470.

Conclusion: Metronomic doxifluridine chemotherapy in combination with TNP-470 might be effective for uterine carcinosarcoma without marked toxicity, possibly acting via its potent anti-angiogenic effects. Clinical studies are needed to evaluate the safety and efficacy of this treatment in humans.

Keywords: Uterine carcinosarcoma, Metronomicdoxifluridine, Anti-angiogenic effects

Overexpression of miR-142-3p in cervical cancer

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Objective: Cervical cancer is an important gynecologic cancer in Taiwan. MicroRNAs (miRNAs) have been found to be dys-regulated in many cancers, serving as oncogenes or tumor suppressors. In this study, our goal was to explore candidate miRNAs associated with carcinogenesis and prognosis in cervical cancers.

Methods: We quantified the expression levels of 270 human miRNAs in 5 cervical cancers and 3 normal cervical tissues by a stem-loop real-time-PCR method, then validated the results by 17 cancers and 7 normal tissues through Taqman miRNA q PCR. We also performed locked nucleic acid (LNA)-based in situ hybridization (ISH) of miRNA on tissue sections of HSIL, early and advanced invasive cervical cancers.

Results: MiR-142-3p was the most significantly elevated miRNA in cervical cancers. LNA-ISH study showed the ratios of positive staining of miR-142-3p increased stepwise from normal cervical epithelium, then HSIL, to invasive carcinoma. Among 80 cases with advanced cervical cancer, increased expression of miR-142-3p was inversely correlated with their survival. Pathway enrichment analysis by online DAVID tool revealed p53 and TGF-beta pathways involved in growth inhibition/tumor suppression were significantly enriched by miR-142-3p targets.

Conclusion: MiR-142-3p expression may be involved in cervical carcinogenesis and has a prognostic impact in patients with advanced cervical cancer. The clinical significance of miR-142-3p was inferred to be associated with p53 and TGF-beta pathways.

Keywords: MicroRNA, Cervical cancer, Prognosis

FC-15

Regulation of paclitaxel-induced programmed cell death by autophagic inducer in cervical cancer

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Objective: Autophagy has a vital role in homeostasis by combining organelle and proteins with lysosome while starving. Though autophagy provides tumor cells energy sources, continuing state of autophagy induces the cells to the death. Here we aim to see whether autophagic inducer has an effect on conventional chemotherapeutic agents.

Methods: mTOR inhibitor, or Rapamycin, and paclitaxel were used as an autophagic inducer and apoptosis-inducing agents in HeLa cervical cancer cells, respectively.

Results: Growth inhibition of cells were not observed after 0, 10, 20 nM of paclitaxel with or without rapamycin. In 5 nM concentration of paclitaxel, rapamycin administration inhibited the cells growth significantly compared to no treatment, which implying the synergic antitumoral effect of paclitaxel and rapamycin in some condition. Paclitaxel itself didn't show the effect on autophagic cells but that of apoptotic cells by flow cytometry. LC3 spots which reflect autophagy were increased in 5 nM of paclitaxel after pretreatment of 10 nM of rapamycin.

Conclusion: This suggest that autophagic inducer, rapamycin can potentiate the autophagic cell death when adding apoptosis-inducing chemotherapeutic agent. In conclusion, controlling of autophagy may help to find a new adjunctive target for chemotherapy.

Keywords: Autophagy, Apoptosis, Cervical cancer

Uterine leiomyosarcoma in Asian patients: validation of the new FIGO staging system and identification of prognostic classifiers

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Objective: Uterine Leiomyosarcoma (uLMS) is a rare and aggressive malignancy associated with poor survival regardless of stage. Here we compare the performance of the new 2009 FIGO staging system with the older system based on Endometrial cancers and identify important prognostic markers.

Methods: Medical records of 110 uLMS patients from 1974 to 2010 were reviewed and data from 85 analysed using Kaplan–Meier (KM) log rank and Cox proportional hazards models.

Results: Under the new FIGO classification, 73% of women presented with stage I disease, and 4.7%, 4.7% and 17.6% with Stages II, III, and IV respectively. 8 patients were downstaged, and none were upstaged. KM overall survival (OS) analysis did not show any significant improvement in risk discrimination between stages I–IV, although there was improved statistical performance for PFS. The 5–year OS rate for Stage I patients under old FIGO was 0.597 (95% C.I.: 0.443 to 0.751), versus 0.580 (95% C.I.: 0.432 to 0.728) under new FIGO. Advanced patient age, tumor size, tumor grade and lymphovascular invasion were adverse prognostic factors, however only age and grade remained significant on multi–variate analysis. Patients with high grade (HG) stage I tumours had a 10–year OS rate of <20% versus approximately 80% for low grade tumors. For stage I, tumors between 5cm and 10 cm represented an intermediate prognostic group.

Conclusion: The new FIGO classification does not significantly improve risk discrimination between stages and majority of uLMS patients continue to be diagnosed with stage I disease, where prognosis becomes highly dependent on patient age and tumour grade.

Keywords: Uterine Leiomyosarcoma, FIGO staging, Prognostic factors

An analysis of thirty-one cases of primary vaginal malignant melanoma

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Objective: To investigate the diagnosis, treatment and prognostic factors of primary vaginal malignant melanoma.

Methods: Clinical data of 31 patients with primary vaginal malignant melanoma treated in Sun Yat-sen University Cancer from March 1970 to June 2005 were retrospectively analyzed.

Results: The average age was 53 years. The main symptoms were vaginal discharge and bleeding tumor. Tumors were usually located in the anterior wall of the lower 1/3 vagina. The interval from onset of symptoms to treatment averaged 18.6 months. The average overall survival time of the 31 cases was 36.5 months. Twenty-two cases with surgical-based treatment while 8 patients underwent non-surgical treatment. The average overall survival (OS) was 44.0 months in the surgical group versus 18.2 months in the non-surgical group. Eighteen cases secondary received immunotherapy while the other 13 did not. The average overall survival (OS) was 47.2 months in immunotherapy group and 19.7 months in non-immunotherapy group. Multivariate analysis Cox regression showed that age less than 63 years, longer interval from onset of symptoms to treatment, surgery, immunotherapy were significant factors ($p < 0.05$) affected overall survival time of patients.

Conclusion: Patients with primary vaginal melanoma were with poor prognosis. But if diagnosed earlier and applied surgery-based treatment combined with immunotherapy, the prognosis may be better.

Keywords: Vaginal malignancies, Malignant melanoma, Surgical treatment and immunotherapy

Gestational trophoblastic neoplasia and HIV infection: a 10-year review

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Objective: To describe the management of Gestational Trophoblastic Neoplasia (GTN), with particular reference to concurrent HIV infection.

Methods: Retrospective descriptive study of all cases of GTN managed at Groote Schuur Hospital over a 10-year period (1999–2008).

Results: Seventy-six patients (median age 30 years) were included, of whom only 36 (47.4%) patients had known HIV status. Fourteen (18.4%) were HIV-positive and 4 (28.6%) were on anti-retroviral treatment. Histologically, 44 (58%) had hydatidiform mole and 21 (28%) had choriocarcinoma. In the remaining 11 cases, a clinical diagnosis was made. Based on the revised FIGO/modified WHO scoring, 43 (56.6%) patients were low risk and 33 (43.4%) were high risk. Thirty-eight (50%) were staged as FIGO Stage 1. Of 73 patients who received chemotherapy, 56 (76.7%) achieved complete remission, 9 (12.3%) did not achieve any remission, 7 (9.6%) has a relapse and 1 (1.4%) was lost to follow-up. Patients who never went into remission had frequent treatment delays due to poor compliance or inadequate blood counts. The overall survival at 60 months was 81.9%. The overall 5-year survival for FIGO Stage I, II, III and IV were 97.4%, 66.7%, 77.8% and 46.2%, respectively. Survival for HIV-Positive patients was 64.3% versus more than 85% for both the HIV-Negative and HIV-Unknown groups.

Conclusion: Apart from more advanced stage, HIV seropositivity and poor compliance with treatment also portend poorer outcome in GTN patients. In HIV-positive patients with poor CD4, little clarity is available whether ARV should be commenced speedily and the administration of chemotherapy delayed until immune reconstitution occurred.

Keywords: GTN, HIV, Chemotherapy, Mortality

Inhibitory role of ROS on calcineurin and NF- κ B activities in LPS-stimulated ovarian cancer cells

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Objective: Although reactive oxygen species (ROS) are required for the physiologic function of the cells, excessive ROS cause apoptosis through several mechanisms such as activation of protein kinases, disruption of mitochondrial membrane potential, and/or direct activation of caspase cascades. To elucidate the role of ROS as an important regulator in pathogenesis on the secretion of NO that is produced during inflammatory reactions

Methods: β BHP and H₂O₂ were employed in LPS-stimulated ovarian cancer cells. NO secretion and iNOS expression were inhibited by pretreatment with β BHP and H₂O₂ in a dose-dependent manner.

Results: EMSA revealed that LPS-induced activation of NF- κ B was inhibited by pretreatment with β BHP or H₂O₂. LPS-induced inhibition of NF- κ B was induced by blocking the degradation of I κ B α and I κ B β through IKK inactivation by pretreatment with β BHP and H₂O₂. LPS-stimulated ovarian cancer cells treated with β BHP and H₂O₂ exhibited inhibition of calcineurin activity. Furthermore, β BHP also inhibited the protein association of NF- κ B and CBP coactivator, subsequently repressing the NF- κ B-mediated transactivation by calmodulin-dependent protein kinase (CaMK).

Conclusion: Taken together, these results suggest that inhibition of NF- κ B by β BHP and H₂O₂ is due to the inhibition of calcineurin and of IKK activity in LPS-stimulated ovarian cancer cells and the inhibition of CaMK-induced coactivator association of NF- κ B.

Keywords: ROS, NF- κ B, Calcineurin

Isolation and characterization of stromal progenitor cells from ascites of patients with epithelial ovarian adenocarcinoma

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Objective: The components of ascites and their effects on tumor cell microenvironment remained poorly understood. We aim to isolate and characterize stromal progenitor cells in the ascites of patients with epithelial ovarian adenocarcinoma (EOA).

Methods: A total of 17 ascitic fluid samples and 7 fresh tissues were obtained from 16 patients with EOA. Ascites were collected and cultured *in vitro* with different conditions. Using flow cytometry and immunocytochemistry, we isolated and characterized two cell populations with different morphology (epithelial type and mesenchymal type) from ascites in patients with epithelial ovarian adenocarcinomas. The *in vitro* cell culture model was established with conditional culture medium.

Results: The doubling times of epithelial-type and mesenchymal-type cells are 36 hrs and 48 hrs, respectively, indicating the faster growth of epithelial-type cells compared to that of mesenchymal-type cells. At *in vitro* culture condition, these ascitic cells exhibit self-renewing and long-term proliferation potential. They were characterized to be CD44⁺, CD24^{-/low}, and AC133^{+/dim+} that are known as typical cancer stem/progenitor cell makers. These cells not only show higher expressions of BMP-2, BMP4, TGF- β , Rex-1 and AC133 early genes, but express EGFR, integrin $\alpha_2\beta_1$, CD146 and Flt-4 which are highly tumorigenic and metastatic associated. The epithelial type cells express more cytokeratin18 and E-cadherin; in contrast, the mesenchymal type cells express more AC133, CD73, CD105, CD117, EGFR, integrin $\alpha_2\beta_1$, and CD146 surface markers.

Conclusion: The established culture system provides an ideal *in vitro* model for cancer-associated stromal progenitor cells target drug selection and effective ovarian cancer therapy development.

Keywords: Human cancer initiating/stem cell, Stromal progenitor cells, Epithelial ovarian adenocarcinoma

FC-21

Comprehensive methylation analyses reveal synchronous hypomethylation of HNF1 network genes in ovarian clear cell carcinoma

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Objective: Ovarian clear cell carcinomas (CCCs) exhibit frequent *ARID1A* mutations and *HNF1B* overexpression, but epigenomic features that characterize CCC are not elucidated. Our objectives were to identify methylation profiles of CCC using genome-wide data.

Methods: Methylation data were generated using the Illumina Infinium platforms for 46 ovarian cancer cell lines (14 CCCs, 32 non-CCC and 4 normal cell lines) and 93 ovarian cancer tissues (13 CCCs, 72 non-CCC and 8 normal specimens). Functionally methylated genes were identified by student t-tests and correlations between methylation and expression. Categorical analyses (Allez) and network analyses (MetaCore) were used to evaluate biological features. Methylation levels were validated by pyrosequencing. P-values <0.05 were considered significant.

Results: Consensus clustering showed a distinct methylation profile of CCCs from those of non-CCC and normal counterparts. 276 genes were hypermethylated and 22 genes were hypomethylated functionally in CCC. Allez showed that the hypomethylated genes in CCC included many with HNF1 binding sites and were related to oxidative stress ($p < 0.01$). MetaCore showed 9 *HNF1* transcript network genes were synchronously hypomethylated. In external datasets, six (GSE6008) and five (PMID16144910) of nine *HNF1* pathway genes were overexpressed in CCC versus non-CCC ($p < 0.05$). Pyrosequencing validated 11 *HNF1* network hypomethylated genes in CCC ($p < 0.01$).

Conclusion: CCCs possess a distinct methylation profile compared with other histologies of ovarian cancer with hypomethylation of *HNF1B* as well as genes with HNF1 binding sites. These results support a prominent role for epigenetic deregulation of the *HNF1* network in CCC via hypomethylation.

Keywords: Ovarian clear cell carcinoma, HNF1B, Methylation

The effect of HE4 gene silencing on the malignant biological behavior in ovarian cancer

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Objective: Human epididymis secretory protein 4 (HE4) has been proved to be a promising novel biomarker for ovarian cancer. However, its biological role has not yet been reported. We aimed to explore the role of HE4 in the carcinogenesis and progression of ovarian cancer.

Methods: We silenced HE4 gene expression by RNA interference in ovarian cancer cell line SKOV3.ip1. First, we constructed recombinant pcDNA6.2 GW/EmGFP-HE4 shRNA plasmid and stably transfected SKOV3.ip1 cells with it. We examined the effect of HE4 silencing on cell cycle, proliferation, transwell migration and invasion by PI staining assay, CCK-8, Transwell migration and invasion assay respectively in SKOV3.ip1 cells *in vitro*.

Results: HE4 shRNA successfully reduced HE4 mRNA expression by 96.53% and decreased secreted HE4 protein expression by 68% in SKOV3.ip1 cells. HE4 silencing increased the percentage of cells in G0/G1 by 23.66% and decreased that in S phases by 12.97% in SKOV3.ip1 cell lines as compared with negative control. That induced statistically significant cell growth inhibition rate in cell proliferation in SKOV3.ip1 (26.46%~49.45%, $p=0.000$) in CCK-8 assay. Moreover, HE4 silencing significantly reduced the percentage of SKOV3.ip1 cells migrated through the Transwell chamber by 27.18% and cells invaded through the matrigel by 13.2%.

Conclusion: This is the first evidence of HE4 gene function. We found that HE4 may promote the cell cycle progression, migration and invasion in ovarian cancer. It may present a promising target for ovarian cancer gene therapy.

Keywords: Human epididymis protein 4, HE4, Ovarian cancer, Carcinogenesis

Tiam1, negatively regulated by miR-22, miR-183 and miR-31, is involved in migration, invasion and viability of ovarian cancer cells

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Objective: This work is aimed to identify Tiam1's role in ovarian cancer progression *in vitro* and to validate the regulatory effect of specific miRNAs on Tiam1 expression.

Methods: We examined the differential expression of Tiam1 in 17 paired primary and corresponding metastatic ovarian cancer tissues by semiquantitative immunohistochemistry, and in paired high-metastatic human serous ovarian cancer cell SKOV-3ip and low-metastatic human serous ovarian cell SKOV-3 by Real-time RT-PCR and Western Blot. Then, loss-of-function study was performed to characterize Tiam1's role in ovarian cancer cell migration, invasion, viability, and apoptosis. Subsequently, we validate the regulatory effect of miR-22, miR-183, and miR-31 on Tiam1 expression with dual-luciferase reporter assay, Western Blot and Real-time RT-PCR.

Results: There is a positive correlation between Tiam1 expression and the metastatic potential in ovarian cancer. Downregulation of Tiam1 in SKOV-3ip cells lead to reduced cell migration and invasion, and growth inhibition without significantly affecting cell apoptosis. Regulatory study revealed that Tiam1 was a direct target of miR-22, miR-183 and miR-31.

Conclusion: miRNAs may converge on Tiam1 to regulate cell migration, invasion and viability in ovarian cancer.

Keywords: Ovarian cancer, Tiam1, miRNA

Ciglitizone sensitizes cisplatin-resistant ovarian cancer cells by targeting glucose metabolism

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Objective: Resistance to chemotherapy severely limits the effectiveness of chemotherapy drugs in treating cancer. Still, the mechanisms and critical pathways that contribute to chemotherapy resistance are relatively unknown. This study elucidates whether ciglitazone (thiazolidinedione derivative) could sensitize ovarian cancer chemoresistant cells to the effects of cisplatin. Peroxisome proliferator-activated receptor (PPAR)- γ ligands constitute important insulin sensitizers that have already been approved for the treatment of human metabolic disorders.

Methods: In order to confirm the unknown cellular and biochemical responses to ciglitazone and cisplatin co-treatment with ovarian cancer cells, MTT assay and Western blot assay were performed. To analyze mechanism of glucose metabolism related gene regulation by PPAR- γ ligands and cisplatin, RT-PCR and cell cycle analysis were performed.

Results: Ciglitazone increased the sensitivity of cancer cells to the apoptotic effects of cisplatin in cisplatin resistant ovarian cancer cells. Expressions of p-AMPK were greatly increased after co-treatment with ciglitazone and cisplatin. Glut-1 was related with glucose metabolism, and Sp1 was decreased by co-treatment with ciglitazone and cisplatin. Ciglitazone induced Sp1 degradation in a manner paralleling that of glucose starvation.

Conclusion: In summary, the results of this study showed that ciglitazone (PPAR- γ agonist), known as an oral antidiabetic agent, was able to mediate the chemosensitivity of ovarian cancer cells to cisplatin through the inhibition of Sp1 and Sp1-regulated gene products. These results suggest that ciglitazone will be a novel agent for sensitizing therapy against ovarian cancer chemoresistance.

Keywords: Ciglitazone, Resistant ovarian cancer cell line, Sensitize

Modification the cut off points of CA125, HE4, RMI and ROMA scores for Indonesian women who underwent surgery in Dr. Ciptomangunkusumo hospital from November 2010 until May 2011, in predicting ovarian malignancy: preliminary study

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Objective: To have the cut off points of CA 125 and HE4 in predicting ovarian malignancy of Indonesian Women who underwent surgery in dr. Ciptomangunkusumo Jakarta, Indonesia. To have the cut off points of RMI and ROMA scores in predicting ovarian malignancy of Indonesian Women who underwent surgery in dr. Ciptomangunkusumo Jakarta, Indonesia

Methods: Consecutively sera of 134 patients who underwent surgery in dr. Ciptomangunkusumo Hospital for suspected of Ovarian Malignancy of epithelial type were collected. The sera were examined for CA 125 and HE4, the examination were done in private laboratory using Architect Method. The laboratory results were compared to the histopathology results. The data was processed using STATA, by using ROC graphs, the AUC s were analyzed to have our CA 125 and HE 4 cut off points.

Results: The ideal cut off point of CA 125 for our patients was determined 102.2 U/ml compare to previously published is 200 U/ml for premenopausal women. The Ideal cut off point of HE4 that would be used for ROMA is 85.3 pM, while the standard published cut off point is 70 pM. The ideal cut off points of RMI and ROMA are 368.7 and 28.1 (pre-menopause); 51.4 (post-menopause). Both sensitivity and specificity of RMI and ROMA are increase after modifications.

Conclusion: In this preliminary study we see a need to modify the CA 125, HE4, RMI and ROMA scores. These cut off points could be different for every race. More study should be conducted in determining the most reliable cut of points.

Keywords: CA 125 AND RMI, HE4 AND ROMA, Ovarian malignancy

Genome-wide DNA methylation analysis identifies prognostic biomarkers of ovarian cancer

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Objective: Abnormal DNA methylation contributes to tumorigenesis. The clinical significance of epigenetic effects in ovarian cancer is rarely explored. We aim to discover novel DNA methylation as a prognostic biomarker of ovarian cancer.

Methods: We did the methylomic analysis using bead arrays to in 46 malignant ovarian tumors. Bioinformatic analysis including the integration of gene-expression databases on the public domain revealed candidate gene lists. Verifications *in vitro* using RT-PCR and bisulfite pyrosequencing narrowed down the list to 3 genes. We did a comprehensive bisulfite pyrosequencing analysis of 3 genes in 116 ovarian cancer tissues and correlate the methylation patterns to clinicopathological features. Kaplan-Meier survival and Cox regression analysis estimates the competence of prognostic markers.

Results: Patients with high methylator phenotypes had a shorter progression-free survival (PFS) and overall survival (OS). Gene P methylation confers the most significant effects on OS with an adjusted hazard ratio of 7.24 (3.25–15.61) ($p < 0.001$). Patients with methylation of either gene N or H confers shorter PFS (9.1 vs 60.0 months for PFS; $p < .001$), whilst methylation of any two of these 3 genes had a shorter OS (22.2 vs 56.8 months; $p < .001$).

Conclusion: DNA methylation of gene P, N and H are associated with ovarian cancer survival. These DNA methylation may be biomarkers for individualized epigenetic therapy in the future.

Keywords: Ovarian cancer, Methylation, Prognosis, Survival

FC-27

Feasibility of oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX-4) chemotherapy in heavily pretreated patients with refractory epithelial ovarian cancer: a single institutional experience and comparison with the published reports

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Objective: We sought to evaluate the efficacy and toxicity of oxaliplatin, leucovorin (LV) and 5-fluorouracil (5-FU) (FOLFOX-4) in patients with refractory epithelial ovarian cancer (EOC).

Methods: Clinical data were reviewed in 28 patients with refractory EOC who received FOLFOX-4. It was administered as a more than second-line chemotherapy, which consisted of 85 mg/m² of oxaliplatin as a 2-hour infusion on day 1, 200 mg/m² of LV as a 2-hour infusion on day 1 and bolus 400 mg/m² of 5-FU on day 1 followed by a 22-hour infusion of 600 mg/m² of 5-FU on day 1 for 2 consecutive days every 3 weeks. Furthermore, our results were compared with those of 3 previous studies.

Results: The median number of prior lines of chemotherapy was 5 (range, 3-9), and a total of 95 cycles were administered to all patients with the median number of 4 cycles (range, 1-9 cycles). The overall response rate was 19% (complete or 75% response, 0; partial or 50% response, 4) according to the RECIST and Rustin criteria. In regards to hematological toxicity, 1 (4.8%), 2 (9.5%) and 1 (4.8%) patients showed grade 3 anemia, neutropenia and thrombocytopenia, and grade 3 fatigue and peripheral neuropathy were observed as non-hematological toxicity in 1 (4.8%) and 2 (9.5%) patients, respectively. Moreover, there were no differences in tumor response (19-30%) and toxicity (0-29%) of FOLFOX-4 among all 4 studies.

Conclusion: FOLFOX-4 may be a feasible option as salvage chemotherapy with acceptable toxicity for treating EOC.

Keywords: FOLFOX-4, Refractory, Ovarian cancer

A phase I clinical trial of Ad5.SSTR/TK.RGD, a novel infectivity-enhanced bicistronic adenovirus, in patients with recurrent gynecologic cancer

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Objective: Ad5.SSTR/TK.RGD is an infectivity-enhanced bicistronic adenovirus that expresses a therapeutic thymidine kinase suicide gene and a somatostatin type 2 receptor, allowing for noninvasive assessment of gene transfer with nuclear imaging. The purpose of this study was to identify the safety, efficacy and biologic effects of Ad5.SSTR/TK.RGD in patients with recurrent gynecologic cancer.

Methods: Eligible patients were treated intraperitoneally (IP) for 3 consecutive days with 1×10^9 to 1×10^{12} vp/dose of Ad5.SSTR/TK.RGD and subsequently treated with ganciclovir (GCV) for 14 days. Toxicity (utilizing CTC grading) and clinical efficacy (utilizing RECIST criteria) was evaluated. Octreoscans were obtained on patients before and after Ad5.SSTR/TK.RGD treatment. Various tissue samples were obtained to evaluate gene transfer, generation of wild type virus, viral shedding and antibody response.

Results: Twelve patients were treated in three cohorts. There were no vector-attributable dose limiting toxicities noted. The most common toxicities attributable to Ad5/SSTR/TK.RGD were grade 1–2 in nature, generally constitutional or pain symptoms. One patient had a stable disease in the first month by RECIST criteria, and then experienced complete resolution of measurable disease and normalization of her CA125 on further follow-up. Four other patients demonstrated stable disease and seven patients experienced progressive disease. Ancillary studies demonstrated the presence of Ad5.SSTR/TK.RGD virus in ascites collected at various time points.

Conclusion: This study demonstrates the feasibility and tolerance of Ad5.SSTR/TK.RGD as a potential therapeutic option for gynecologic cancer patients.

Keywords: Infectivity-enhanced adenoviral therapy, Suicide gene therapy, Ovarian cancer

Clinical trial of personalized peptide vaccine for recurrent ovarian cancer

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Objective: To investigate the efficacy and the safety of personalized peptide vaccine (PPV) and the usefulness of peptide specific IgG after vaccination as a prognosis predictive marker in recurrent ovarian cancer patients.

Methods: The candidate peptides for PPV were screened from HLA (HLA-2, A11, A24, A26, A31 or A33) matched peptide by measurement of peptide specific IgG antibody in pre-vaccination sera of the patients. Up to 4 peptides showing higher titer of IgG antibody among 31 peptides were given subcutaneously 6 times with 1 week interval followed by 6 times with 2 week interval. Peptide specific humoral immune response was evaluated by Luminex method.

Results: Twenty two patients with recurrent ovarian cancer were enrolled in this study. Increased IgG titer was observed in 2 of 20 patients at the 6th vaccination and in 13 of 14 at 12th vaccination. No serious adverse effects related with PPV were observed.

Conclusion: Safety and enhancement of immune response after 12th vaccination was verified in PPV in recurrent ovarian cancer patients. Further analysis is required to investigate the overall survival and if the increase of peptide specific IgG after vaccination would be the prognosis predictive marker.

Keywords: Ovarian cancer, Cancer vaccine, Peptide

Health-related quality of life of women with ovarian cancer at initial diagnosis compared with the general population: KORAGC prospective cohort study

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Objective: To compare the health-related quality of life (HRQOL) of women with ovarian cancer at the time of diagnosis with that of the general population (GP) from Korean Outcome Research and Analysis in Gynecologic Cancers (KORAGC) prospective cohort to provide new insight for HRQOL among ovarian cancer patients.

Methods: In this prospective cohort study at 9 university hospitals and the National Cancer Center in Korea, we administered European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) and Hospital Anxiety and Depression Scale (HADS) to 177 women with ovarian cancer. HRQOL and HADS scores of subjects were compared with reference data from the 500 GP. After adjusting for propensity scoring using age, level of education, and income, we considered P less than .05 as 'statistically significant' and absolute difference of EORTC-QLQ C30 score 10 or more as 'clinically meaningful difference'.

Results: Women with ovarian cancer reported poorer HRQOL scores in global health status, role, emotional, and social functioning in functional scale and fatigue, pain, insomnia, appetite loss, constipation, diarrhea, and financial problem in symptom scale with clinically meaningful difference ($p < 0.01$ for all). We found no significant difference in HRQOL with regard to physical and cognitive function and nausea/vomiting and dyspnea in symptom scale score and total score of HADS.

Conclusion: HRQOL was lower in women immediately after diagnosis of ovarian cancer than that of GP. This result might be incorporated into to future strategy of ovarian cancer screening or early detection program.

Keywords: Ovarian cancer, Quality of life, Symptom



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PP-001

Correlation between homeodomain-interacting protein kinase 2 and apoptosis in cervical cancer

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Objective: Homeodomain-interacting protein kinase 2 (HIPK2) is a serine/threonine nuclear kinase that involved in the apoptosis through wild type p53 gene, cell growth and is also thought to participate in the process of tumorigenesis. The purpose of this study is to identify the role of HIPK2 in cervical cancer.

Methods: We have examined HIPK2 expression in normal and cervical cancer tissues by quantitative real-time PCR and western blot in mRNA and protein level. To investigate the mechanism of action of HIPK2 in cervical cancer, RNA interference was used to analyze the effect of HIPK2 on apoptosis and cell growth in cervical cell lines.

Results: We found that HIPK2 expression were significantly higher in cervical cancer than in normal cervical tissues both in mRNA and protein level. Moreover, inhibition of HIPK2 promoted the cell growth and decreased the rate of cell apoptosis in cervical cell lines.

Conclusion: HIPK2 expression was higher in cervical cancer tissues and has positive correlation in cervical cancer. HIPK2 may play important role in development of cervical cancer.

Keywords: HIPK2, Cervical cancer, Apoptosis

PP-002

Robot assisted autonomic nerve sparing extended lymphadenectomy including presacral, common iliac and lower paraaortic nodes in the part of radical hysterectomy

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Objective: To date, relatively little data exist to describe the possible benefit of a more extensive lymphadenectomy for early-stage cervical cancer. Robot assisted extended lymphadenectomy is considered a challenging procedure for save the branches of superior hypogastric plexus and hypogastric nerve.

Methods: Robot assisted extended lymphadenectomy was performed after radical hysterectomy and pelvic lymphadenectomy. To obtain the autonomic nerve sparing techniques, it needed supraumbilical telescopy insertion and mobilization of simoid colon, meticulous node dissection to presacral on the promontory, hypogastric vein, common iliac, lower paraaortic area without injury to superior hypogastric plexus and hypogastric nerve.

Results: Since Mar 2011, robot assisted autonomic nerve sparing extended lymphadenectomy was performed for 10 patients with cervical cancer (1 Ia1, 8 Ib1, 1 Ib). In all cases, preservation of superior hypo-

gastric plexus and hypogastric nerve was completed. The mean number of extended harvested nodes was 13.5±7.9. The mean number of harvested pelvic nodes was 25.5±11.4. Total obtained node was 39±15. The mean console time was 230.8±56.7 min, and the blood loss was 38±14 ml. The mean self voiding time was 7.3±2.3 days. One had delayed bleeding after operation. No major morbidity was recorded.

Conclusion: Small number of preliminary experience of robot assisted autonomic nerve sparing extended lymphadenectomy seems to be feasible and safe for the treatment of early-stage. Robot is more efficient than laparoscopy for extended lymphadenectomy. And it needs to evaluate long term survival benefit about early staged or pelvic node metastatic cervical cancer. Also further evaluation of functional benefit of superior hypogastric plexus sparing is needed.

Keywords: Cervical cancer, Radical hysterectomy, Extended lymphadenectomy

PP-003

The incidence and risk factors of lower-extremity lymphedema following radical surgery with or without adjuvant radiotherapy in patients with FIGO stage I-IIa cervical cancer

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Objective: This study aimed to determine the incidence and risk factors of lower-extremity lymphedema (LEL) in women who had radical surgery with or without adjuvant radiotherapy for FIGO stage I-IIa cervical cancer.

Methods: The medical records were reviewed retrospectively on patients with histologically confirmed FIGO stage I-IIa cervical cancer. LEL related to medical problems such as peripheral vascular disease, congestive heart failure or chronic renal disease were excluded. A logistic regression analysis was used to examine the relationship between variable clinical characteristics and development of LEL.

Results: A total 707 patients were evaluated. Among them, we excluded 92 patients who received radiotherapy as the initial therapy and 19 patients with LEL related to medical problems. Seventy-five patients (12.6%) developed LEL. The incidence were significantly high in patients with adjuvant radiotherapy (odds ratio: 3.47; 95% CI: 2.086-5.788; p=0.000). 78.7% of the LEL were developed within 3 years after initial treatment.

Conclusion: Adjuvant radiotherapy was significantly associated with development of LEL in women who had radical surgery with lymphadenectomy for FIGO stage I-IIa cervical cancer. The possibility for the occurrence of LEL must be fully explained prior to the treatment and the appropriate education to prevent LEL must be made. Further prospective studies are needed to confirm the incidence and risk factors of LEL.

Keywords: Cervical cancer, Lymphedema, Risk factor

PP-004

Brain metastasis in patients with uterine cervical cancer

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Objective: The purpose of this study is to describe the features of patients with brain metastasis from cervical cancer.

Methods: We reviewed the medical records of patients with cervical cancer between February 2001 and June 2011 retrospectively. Clinical characteristics, symptom, treatment, and survival in patients with brain metastasis from cervical cancer were analyzed.

Results: Eleven patients with brain metastasis from cervical cancer were identified. The incidence of brain metastasis in our population is 0.48%. Median patient age at initial diagnosis of cervical cancer was 50 years (range 33–75). Three patients had FIGO stage IVB disease; two had stage IIIB disease; two had stage IIB disease; and one each had stage IB, IIIA disease. The median interval from diagnosis of cervical cancer to identification of brain metastasis was 15.4 months (range 1.9–83.3). Nine patients presented with neurologic symptoms such as headache, nausea, vomiting, seizure, and extremity weakness. Initially, six patients received whole brain radiotherapy; three patients received chemotherapy; one underwent surgery; and one patient refused treatment. The median survival time after diagnosis of the brain metastases was 5.9 months (95% CI 1.57–10.23).

Conclusion: The prognosis after diagnosis of the brain metastasis in patients with uterine cervical cancer is poor. Efficient multimodal treatments seems to be needed to control other metastatic tumors including brain tumor and expect the best chance for survival.

Keywords: Brain metastasis, Cervical cancer, Survival

PP-005

Urologic complication of laparoscopic radical hysterectomy and lymphadenectomy

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Objective: The purpose of this study is to evaluate intraoperative and postoperative urologic complication and management of laparoscopic radical hysterectomy and lymphadenectomy for cervical cancer.

Methods: We reviewed the medical records of the 146 patients with cervical cancer and endometrial cancer who underwent total laparoscopic radical hysterectomy with lymphadenectomy between August 2002 and April 2011 retrospectively. The intraoperative and postoperative urologic complications were analyzed.

Results: Prophylactic insertion of double J catheter ureteral stent was done in thirteen patients (8.9%), two of whom experienced post-

operative urologic complications. Nine patients (6.2%) had postoperative urologic complications. Four patients with ureterovaginal fistula; two were treated with cystoscopic placement of double J catheter ureteral stents and two with ureteroneocystostomy. Vesicovaginal fistula occurred in two patients, which were treated with vesicovaginal fistula repair. There was one patient with bladder injury that was repaired under laparoscopy, and one patient with ureter injury that was treated with cystoscopic placement of double J catheter ureteral stents.

Conclusion: Iatrogenic lower urinary tract injury during laparoscopic radical hysterectomy is relatively common complication. Careful postoperative care may be mandatory for patients after laparoscopic radical hysterectomy.

Keywords: Laparoscopic radical hysterectomy, Cervical cancer, Urologic complication

PP-006

A prospective randomized trial for evaluation of therapeutic efficacy and safety of nerve-sparing radical hysterectomy in cervical cancer

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Objective: The radical hysterectomy is often associated with bladder dysfunction. This may arise as a result of pelvic nerve damage during operation. The objectives of this study were to evaluate the efficacy of nerve-sparing radical hysterectomy (NSRH) for reducing postoperative bladder dysfunction, and therapeutic safety.

Methods: From December 2001 to November 2004, 91 patients with cervical cancer stage IA2–IIA enrolled in this prospective randomized trial. We compared pre- and postoperative bladder function by urodynamic study (UDS) and the time to recover the ability to void spontaneously with residual urine less than 50 ml, and counted the number of nerve in paracervical tissue by IHS. Clinicopathologic results were also evaluated.

Results: There were no differences in clinicopathologic parameters between two groups. Operating time was longer in NSRH than conventional RH (CRH) (270±45 min and 298±72 min, respectively, p=0.018). Number of nerve was significantly lower in NSRH than CRH (15.8±6.3 and 30±11.7, respectively, p=0.01). The time taken to obtain a post-void residual urine volume of less than 50 ml was 12.0±5 d in NSRH group and was 17.5±15 d in CRH group (p<0.001). Postoperative UDS showed that preservation of maximal flow rate, first voiding sense and voided volume in NSRH group, but not in CRH (p<0.05). There were 3 cases of clean intermittent catheterization needed only in CRH group. No significant differences in recurrence

and survival could be found.

Conclusion: NSRH appears to be effective in reducing postoperative bladder dysfunction and safe in oncologic aspects. This procedure might be standard procedure in the future.

Keywords: Cervical cancer, Nerve-sparing radical hysterectomy, Bladder dysfunction

PP-007

Downregulation of SOCS genes is due to DNA hypermethylation and histone deacetylation in cervical cancer cells

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Objective: The objectives of this study were twofold: to investigate whether the expression of SOCS genes is downregulated in cervical cancer cell lines and to verify whether the radiosensitivity of cervical cancer cells is modified by alteration of SOCS expression.

Methods: CaSki, HeLa, ME-180, SiHa, SNU-1299, and SNU-1160 were obtained. Realtime RT-PCR, methylation-specific PCR, and bisulfite genomic sequencing were employed to investigate SOCS-1,3,5 status. 5-Aza-2'-deoxycytidine and trichostatin A were used for inhibition experiments. Clonogenic assay was performed to study a possible change in radiosensitivity according to SOCS expression differences.

Results: All cell-lines showed repressed expression of SOCS-1, 3, and 5. MSP and sequencing demonstrated that considerable portion of promoter region of SOCS-1, 3, 5 genes were methylated. Through inhibition test using 5-aza-dC and trichostatin A, both DNA hypermethylation and histone deacetylation were found to play roles in SOCS downregulation. Clonogenic assay showed recovery of SOCS-1 and 3 decreased the radiosensitivity of HeLa cell.

Conclusion: Cervical cancer cell-lines showed repressed expression of SOCS-1, 3, and 5. Both DNA methylation and histone deacetylation may contribute to the downregulation of SOCS-1, 3, 5 genes in cervical cancer cells

Keywords: SOCS, Cervical cancer, DNA methylation

PP-008

Risk factors for abnormal cytology after large loop excision of the transformation zone

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Objective: This study was designed to determine the risk factors for abnormal Papanicolaou (Pap) smear after large loop excision of the

transformation zone (LLETZ).

Methods: We retrospectively reviewed medical records of 343 women who underwent LLETZ between 2006 and 2008. The associations between clinicopathologic characteristics including margin status and risk of abnormal follow-up cytology were analyzed.

Results: Forty two (12.2%) women were found to have abnormal Pap after LLETZ. Old age women at the time of procedure were related with higher rate of postoperative Pap abnormality (21.2% vs. 10.1%, p=0.020). Women with endocervical resection margin involvement had more frequent abnormal Pap after LLETZ (33.3% vs. 10.7%, P=0.004). Interestingly, the histologic grade of LLETZ pathology was inversely correlated with abnormal Pap after procedure. (p=0.018).

Conclusion: Our findings show that a positive endocervical margins is an important risk factor for abnormal Pap after LLETZ suggesting that women with positive exo- or deep cervical margins could be followed up with reassurance.

Keywords: Large loop excision of the transformation zone, Recur, Resection margin

PP-009

Trends in cervical cancer incidence in young women in Korea

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Objective: This study was performed to examine trends in cervical cancer incidence in young women.

Methods: Cases of cervical cancer diagnosed between the year 2004 and 2008 in Korea were extracted from a database registered by National Cancer Information Center. Changes in incidence of cervical cancer were analysed by 10-year age group.

Results: Peak incidence of cervical cancer was in women aged 40-49 years (27-29% of every year cases). New cases of cervical cancer with women aged 20-29 years were 107 of 4,052 cases (2.6%) in the year 2004, 91 of 3,737 cases (2.4%) in the year 2005, 126 of 3,997 cases (3.1%) in the year 2006, 114 of 3,616 cases (3.1%) in the year 2007, and 141 of 3,888 cases (3.6%) in the year 2008. Although the annual incidence of cervical cancer in women decreased between the year 2004 and 2008, cases of cervical cancer in young women aged 20-29 years increased by 27.8%.

Conclusion: The screening for cervical cancer reduces the incidence of cervical cancer. But the incidence of cervical cancer in young women is increasing. It is necessary for young women to receive cervical cancer screening, HPV vaccination and other public health policies, for example sexual health education.

Keywords: Cervical cancer, Incidence, Young women

PP-010

Analysis of prognosis in cervical cancer patients by revised staging system

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Objective: In cervical cancer, stage 0 has been deleted and stage IIA has been separated substages, IIA1 and IIA2 by tumor size according to revised staging system. This study was to compare survival outcome between stage IIA1 and IIA2.

Methods: We retrospectively reviewed a total 212 patients with prior FIGO stage IIA cervical cancer who had radical hysterectomy with bilateral pelvic lymphadenectomy from 1988 to 2006 in our institute. They were divided into stage IIA1 and IIA2 by revised FIGO staging system. And stage IIA1 and IIA2 were compared with clinicopathologic parameters and 5 year-survival.

Results: Of the 159 cases who didn't receive neoadjuvant chemotherapy, 79 (49.7%) had stage IIA1 and 80 (50.3%) had stage IIA2. Stage IIA2 patients were younger than stage IIA1 (mean age, 51.7±12.2 years vs 56.1±11.3 years; p=0.0178). There were no difference between stage IIA1 and IIA2 for clinicopathologic parameters such as histologic type, invasion depth, lymphovascular space involvement, parametrial invasion, resection margin involvement, and lymph node metastasis (p>0.05). The 5-year survival was significantly different between IIA1 and IIA2 (63.2% vs 41.3%, p=0.0226).

Conclusion: Patients with stage IIA1 had better survival than stage IIA2. Therefore this subdivision would affect management for patient's prognosis. We consider that cervical cancer patients with stage IIA2 need more aggressive treatment and strict follow-up than stage IIA1.

Keywords: Cervical cancer, Revised staging system, Prognosis

PP-011

Analysis of the risk factors for the recurrence of cervical cancer following ovarian transposition in China

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Objective: To investigate the potential risk factors related to the recurrence of cervical cancer following ovarian transposition.

Methods: A total of 105 patients with cervical carcinoma were retrospectively analyzed. Each patient underwent surgical therapy in combination with ovarian transposition at the Department of Gynaecology and Obstetrics of Peking University People's Hospital between September 2000 and November 2009. The potential risk factors were analyzed using a univariate method. Survival analysis was conducted using the Kaplan-Meier method.

Results: The average age of the 105 patients was 38.7 years. 12 pa-

tients were placed in stage IA, 65 in IB, 12 in IIA, and 16 in IIB. According to the differentiation degree, patients were categorized as having well-differentiated cancer (G1, n=25), moderately differentiated cancer (G2, n=48), and poorly differentiated cancer (G3, n=32). Unilateral (n=39) or bilateral intraperitoneal (n=66) ovarian transposition was also performed during the surgery. In our population, five patients (4.8%) had a recurrence, two of whom (1.9%) had ovarian metastasis. Univariate analysis showed that the pathological type (p=0.005) and degree of differentiation (p=0.001) were potential risk factors for recurrence of cervical carcinoma following ovarian transposition. Cancer embolus in vessels or lymphatic metastasis was observed in four of the five patients who suffered a recurrence; however, these phenomena were not correlated with the recurrence (p=0.054).

Conclusion: Pathological type, differentiated degree and cancer embolus in vessels or lymphatic metastasis were identified as potential risk factors for the recurrence of cervical carcinoma after ovarian transposition.

Keywords: Cervical carcinoma, Ovarian transposition, Recurrence

PP-012

Evaluating the learning curve and perioperative outcomes of robotic-assisted laparoscopy for gynecology cancer: initial experience with one hundred consecutive procedures at the single institution

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Objective: The purpose of this study was to describe the learning curve and perioperative outcomes of robotic-assisted laparoscopic procedure for patients with gynecology cancer.

Methods: 121 consecutive patients underwent robotic assisted laparoscopic surgical staging (n=56) or radical hysterectomy with bilateral pelvic lymph node dissection (n=65) from May 2006 to May 2011 at Severance hospital, Yonsei university college of medicine. Cases were arranged in order based on surgery date and perioperative outcomes were compared between 2 groups (case 1-56, 57-121). The outcomes included docking time (DT; from incision to docking robot), console time (CT; sitting time in console), operating time, blood loss, lymph node retrieval, and surgery related complication.

Results: Demographic difference was not observed between surgical staging group and radical surgery group except age (49.7 vs 46.2, p<0.001), console time (130 vs 141, p<0.029), blood loss (50 vs 100, p<0.017) and postoperative hospital stay (8 vs 12, p<0.001). No conversion to laparotomy occurred. 2 cases of complication including 1 external iliac vein injury, 1 bladder trauma, 3 bleeding cases requiring treatment took place during robotic surgery. DT, CT and total operation

time were significantly decreased after the first 56 cases compared to next 65 cases ($p=0.0027$, $p=0.0025$, $p=0.0008$, respectively). There was no difference in lymph node retrieval and perioperative complications among those groups.

Conclusion: The learning curve of both robotic-assisted laparoscopic surgical staging and radical surgery improves DT and CT in the first 56 cases without increasing the number of complication.

Keywords: Learning curve, Robotic-assisted laparoscopy, Gynecology cancer

PP-013

Weekly cisplatin therapy compared with triweekly combination chemotherapy as concurrent adjuvant chemoradiation therapy after radical hysterectomy for cervical cancer

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Objective: To evaluate whether the use of triweekly combination chemotherapy together with radiation exerts a more beneficial systemic effect than weekly cisplatin chemoradiation in patients with cervical cancer after radical surgery.

Methods: We retrospectively analyzed patients with stage IB1 to stage IIB cervical cancer who had undergone radical hysterectomy with pelvic lymph node dissection, followed by concurrent adjuvant chemoradiation therapy. The patients were divided into 2 groups: the triweekly combination chemotherapy group and the weekly cisplatin chemotherapy group. We evaluated the survival and adverse effects of the 2 groups.

Results: In total, 201 patients were included. The mean duration of follow-up was 52.2 months. Of the 201 patients, 130 received triweekly combination chemotherapy, and 71 patients received weekly cisplatin chemotherapy as an adjuvant treatment. The 5-year disease-free survival was 82.2% for patients treated with weekly cisplatin chemotherapy and 74.3% for those treated with triweekly combination chemotherapy ($p=0.3929$). The 5-year overall survival was 81.4% and 79.3% for the same treatment groups, respectively ($p=0.9833$). The overall survival of the patients with stage IIB cervical cancer was marginally higher in the triweekly combination chemotherapy group than in the weekly cisplatin group ($p=0.0582$). Leukopenia, neutropenia, thrombocytopenia, anemia, and hepatopathy were significantly more common in the triweekly combination chemotherapy group.

Conclusion: The weekly cisplatin chemotherapy group experienced the same therapeutic effect as the triweekly combination chemotherapy group but with less toxicity. Therefore, weekly cisplatin chemotherapy is considered the more useful concurrent adjuvant chemoradiation

regimen after radical surgery.

Keywords: Cervical cancer, Adjuvant therapy, Chemoradiation

PP-014

Sentinel node detection with (^{99m}Tc) phytate alone is satisfactory for cervical cancer patients undergoing radical hysterectomy and pelvic lymphadenectomy

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Objective: If the sentinel-lymph-node (SLN) concept is valid in cervical cancer, most patients could avoid pelvic lymphadenectomy when absence of metastasis is intraoperatively confirmed in the SLN. We assessed feasibility and accuracy of SLN detection using (^{99m}Tc) phytate in patients with cervical cancer.

Methods: Eighty-two women with stage Ia–IIb cervical cancer enrolled in this study. All underwent hysterectomy or tarachelectomy with accompanying total pelvic lymphadenectomy. On the day before surgery, we injected fluid containing (^{99m}Tc)-labeled phytate subepithelially into four cervical quadrants outside the tumor. Intraoperatively, SLNs were identified as radioactive "hot nodes" by gamma probe. Systematic bilateral pelvic lymphadenectomy was performed after the hot node sampling to evaluate the predictive ability of hot nodes.

Results: A total of 157 lymph nodes were detected as SLNs in 72 of 82 patients. SLN detection rate was 88%. Detection rate was 95% for the subgroups of patients with stage Ia–Ib1 disease and smaller tumor size (≤ 3 cm in maximal diameter). Lymph node metastasis was found in 15 patients. In 3 of them, no SLNs were detected. In the remaining 12 patients, each ipsilateral SLN contained metastasis when the pelvic lymph nodes contained metastases. Sensitivity was 100%, the false negative rate was 0%, and the negative predictive value of SLN was 100%.

Conclusion: We conclude SLN detection using (^{99m}Tc)-labeled phytate is satisfactory to assess pelvic nodes in patients with early cervical cancer; if validated with other research, it should be incorporated into clinical practice.

Keywords: Sentinel lymph node, Cervical cancer, Pelvic lymphadenectomy

PP-015

Distribution of HPV genotypes in glandular and squamous cervical precancer and cancer in Korean women

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Objective: The objective of the study was to compare the distribution of

HPV genotypes in glandular and squamous cervical precancer and cancer.

Methods: 2213 women diagnosed with cervical intraepithelial neoplasia 2–3 (CIN 2–3), 614 women with squamous cell carcinoma (SCC), 65 women with adenocarcinoma in situ (AIS) and 218 women with adenocarcinoma (ADC) were enrolled in this study. Samples obtained from liquid-based cytology were analyzed for HPV genotyping using HPV DNA chip test and other samples were underwent Hybrid capture II system. The HPV DNA chip test harbor 24 HPV probes (15 high-risk types and 9 low-risk types) and has the advantage of being able to detect 24 HPV types simultaneously.

Results: The most common HPV types in CIN 2–3 were HPV 16, 58, 33, 31 and 18 (37.1%, 15.8%, 8.2%, 7.7%, 6.6%, respectively). In SCC the most common types were HPV 16, 18, 58, 33 and 31 (54.1%, 10.6%, 9.6%, 5.4%, 5.0%, respectively). In AIS, HPV 16, 18, 45, 53 were 40%, 40%, 3.3%, 3.3% respectively. In ADC, most common genotypes were HPV 18 (54.6%), 16 (27.8%) and 45 (7.2%). The proportion of samples that resulted in negative of high-risk HPV by Hybrid capture II system in ADC was 18.8% compared to 11.8% in SCC ($p < 0.01$).

Conclusion: There was a difference between common HPV genotypes in squamous cell carcinoma and adenocarcinoma. In adenocarcinoma, negativity of high-risk HPV was common than squamous cell carcinoma which suggest that adenocarcinoma may have a different carcinogenesis from squamous cell cancer other than HPV infection.

Keywords: HPV genotypes, Cervical cancer, Cervical precancer

PP-016

Prognostic significance of the number of dissected lymph nodes in cervical cancer patients treated with radical hysterectomy and lymphadenectomy

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Objective: Lymph node (LN) metastasis is known as one of the important prognostic factors in cervical cancer. However, regardless of LN metastasis, the clinical importance of the total number of dissected LN and prognosis is controversial. The purpose of this study is to determine impact of the number of dissected LN and other prognostic factors for survival in cervical cancer.

Methods: Patients who underwent radical hysterectomy and lymphadenectomy for cervical cancer between January 2003 and May 2011 were included. Pathological data including age, body mass index, stage, histologic subtype, tumor size were collected. The prognostic effects of total number of dissected lymph node were analyzed.

Results: Of 134 patients with cervical cancer (FIGO stage IB1–IIA2), we selected 101 patients with negative LN metastasis. The number of dissected LN was related to tumor size ($p = 0.013$) and depth of cervical

stromal invasion ($p = 0.002$). However the number of dissected LN had no significant correlation with the overall survival (OS) ($p = 0.240$) and disease free survival (DFS) ($p = 0.679$). In a separate analysis, the removal of more than 30 LN was associated with increased overall survival, but the statistical analysis failed to show a significant correlation.

Conclusion: Our findings suggest that a complete pelvic lymphadenectomy is important for a good prognosis of patients with early stage cervical cancer.

Keywords: Cervical cancer, Lymph node, Prognosis

PP-017

Radical hysterectomy followed by tailored adjuvant therapy versus primary chemoradiation therapy in patients with bulky early-stage cervical cancer: a Korean multicenter retrospective study

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Objective: To compare survival outcomes and treatment-related morbidities between radical hysterectomy (RH) followed by tailored adjuvant therapy and concurrent chemoradiation therapy (CCRT) in patients with bulky early-stage cervical cancer.

Methods: We retrospectively evaluated 413 patients with stage IB, IIA cervical cancer (tumor diameter >4 cm on MRI) who underwent RH followed by tailored adjuvant therapy or CCRT at three tertiary centers.

Results: About 35.9% of patients were successfully salvaged by RH alone and that these experienced the best survival outcomes with the lowest morbidity rates. Mean patient age was significantly higher in the CCRT than in the RH group (51.5 vs. 46.9 years, $p = 0.001$), but there was no between-group difference in other clinical and prognostic factors including tumor size, parametrial invasion, or lymph node metastasis as shown by MRI. Multivariate analysis showed that the CCRT group was at higher risk for tumor recurrence (odds ratio [OR], 1.70; 95% confidence interval [CI], 1.03–2.80; $P = 0.038$) and death (OR, 1.65; 95% CI, 0.95–2.87; $p = 0.076$) than was the RH group. Grade 2–4 acute (7.3% vs. 41.0% vs. 69.1%, $p < 0.001$) and chronic (6.5% vs. 6.5% vs. 27.9%; $p < 0.001$) complications were significantly less frequent in the RH-alone and RH+(CC)RT groups than in the primary CCRT group.

Conclusion: A significant proportion of patients with bulky early-stage cervical cancer were successfully salvaged by RH alone. Disease-free survival rate was significantly greater and treatment-related morbidity was significantly lower in patients who received RH followed by tailored adjuvant therapy.

Keywords: Bulky early-stage cervical cancer, Radical hysterectomy, Current chemoradiation therapy

PP-018

Factors associated with parametrial involvement in stage Ib1 cervical cancer and identification of patients suitable for less radical surgery

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Objective: The purpose of the present study was to determine possible factors associated with parametrial spread in patients with stage IB1 cervical cancer and define parameters associated with a low risk for parametrial spread, in order to identify candidates for less radical surgery.

Methods: We retrospectively reviewed 200 patients with stage IB1 cervical cancer who had undergone radical hysterectomy (class III) and pelvic lymphadenectomy.

Results: Overall, 20 (10.0%) of the 200 patients revealed parametrial spread, of which 11 had only direct microscopic extension of the disease, 3 had only disease spread to parametrial lymph nodes, 1 had both direct microscopic extension and disease spread to parametrial lymph nodes, and 5 had only tumor emboli within the lymph vascular channels in the parametrial tissue. Elderly age, depth of invasion, tumor size, lymph vascular space invasion (LVSI), positive pelvic nodes, and ovarian metastasis were significantly associated with parametrial involvement. The multivariate analysis model included factors that could be determined by a cone biopsy and showed LVSI, deep stromal invasion, and elderly age to be the independent predictors of parametrial involvement. Ninety-one patients had a depth of invasion of ≤ 10 mm and no LVSI, of which only 1 (1.1%) had parametrial involvement. When patients aged ≤ 50 years were further stratified into those with a depth of invasion of ≤ 10 mm and no LVSI, parametrial involvement was found to be 0.0% (0/68).

Conclusion: Patients with a tumor depth of invasion of ≤ 10 mm, no LVSI, and aged ≤ 50 years, could be considered for less radical surgery.

Keywords: Cervical cancer stage 1B1, Parametrial involvement, Less radical surgery

PP-019

The prevalence of human papillomavirus infection among Korean pregnant women and transmission rate of human papillomavirus to their infants

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Objective: To assess the prevalence of human papillomavirus (HPV) infection among pregnant women and to evaluate the rate of vertical transmission of HPVs to their infants.

Methods: 391 pregnant women and their infants were prospectively recruited for this study between February 2010 and November 2010. Cervical swabs and blood samples were collected from the women at 32–36 weeks of gestation. Neonatal buccal swabs and cord blood were taken immediately after birth. HPV positive neonates were rechecked HPV DNA at 6 months postpartum. HPV genotyping with HPV DNA chip (MyGene Co., Seoul, Korea) was used to detect the HPV of mothers and neonates. Type specific PCR was performed to see HPV DNA in the maternal and cord blood in cases of mother and infant infected same types of HPV DNA.

Results: HPV DNA was positive in 18.4% (72/391) of mothers and 4.3% (17/391) of neonates. The rate of vertical transmission of HPV to their infant was 23.6% (17/72). HPV DNA type-specific maternal/neonate concordance was 100%. 16 HPV positive infants were delivered vaginally and 1 HPV positive infant was delivered by cesarean section. All HPV positive neonates were converted HPV negative at 6 months after birth. There was no viremia in maternal and cord blood in cases of mother and infant infected same type of HPV DNA.

Conclusion: Prevalence of HPV DNA in neonates born from HPV positive mothers was significantly high. However, these data suggest that neonatal HPV DNA positive is not true vertical infection but contamination during vaginal delivery.

Keywords: Human papillomavirus, Vertical transmission, Korean

PP-020

Obesity, physical activity, calorie intake and the risk of cervical intraepithelial neoplasia and cervical cancer

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Objective: The objective of this study was to determine whether or not obesity, height, weight, physical activity, and calorie intake are associated with the risk of cervical intraepithelial neoplasia (CIN) and cervical cancer.

Methods: We enrolled 1,125 women, 18–65 years of age, to participate in a human papillomavirus (HPV) cohort study from March 2006 to the present; 582 cases and 543 controls were recruited and interviewed.

Results: Multinomial logistic analysis showed that obesity (≥ 25 kg/m²) was positively associated with the risk of cervical cancer (OR [95% CI]=1.68 [1.09–2.57]). On the other hand, physical activity was inversely associated with the risk of CIN 2/3 and cervical cancer. Compared to women in the lowest tertile of physical activity, risks were reduced among the highest tertile for CIN2/3 (OR=0.58 [0.36–0.93], p

for trend=0.02), and cervical cancer (OR=0.61 [0.38–0.98], *p* for trend=0.03), respectively.

Conclusion: The findings of this study suggested that obesity was positively associated with cervical cancer risk, while physical activity was inversely associated with the risk of high-grade cervical lesions and cancer.

Keywords: Obesity, Physical activity, Cervical cancer

PP-021

Nomogram for predicting overall survival in cervical cancer patients treated with definitive concurrent chemoradiotherapy—adjusting the effect of pretreatment [¹⁸F]—fluorodeoxyglucose PET

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Objective: The aim of this study was to develop a nomogram for predicting the probability of 3-year survival after definitive concurrent chemoradiotherapy (CCRT) in cervical cancer.

Methods: Between 1998 and 2008, 209 patients of cervical cancer were treated with definitive CCRT in our institution. Before CCRT, [¹⁸F]—fluorodeoxyglucose PET (¹⁸F—FDG—PET) was performed in 91 patients. Multivariate analysis using Cox proportional hazards regression model was performed. The authors developed a nomogram based on this Cox model. Internal validation of the nomogram was performed with bootstrapping and performance was assessed by concordance index and a calibration curve.

Results: By multivariate regression analysis, histology, International Federation of Gynecology and Obstetrics (FIGO) stage, and para-aortic lymph node metastasis were identified as independent predictors for overall survival. Whether ¹⁸F—FDG—PET was performed before CCRT did not make a difference to identify the factors for survival except pelvic lymph node metastasis. Pelvic lymph node metastasis detected by ¹⁸F—FDG—PET also predicted overall survival. The nomogram for predicting the 3-year survival was constructed incorporating these 4 variables. The concordance index was 0.69. The predictive ability of the nomogram proved to be superior to FIGO stage (*p*<0.05).

Conclusion: The constructed nomogram appears to be a better predictive model for overall survival than the FIGO staging system. If the nomogram is externally validated, it can be used to counsel patients choosing additional treatment modalities after definitive CCRT.

Keywords: Nomogram, Cervical cancer, Concurrent chemoradiotherapy

PP-022

Role of adjuvant radiotherapy after radical hysterectomy in node-negative stage Ib–IIa cervical cancer with intermediate risk factors

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Objective: Radical hysterectomy and pelvic lymphadenectomy is the optional effective treatment of early stage cervical cancer. Some authors proposed to use adjuvant radiotherapy (RT) in patients who had intermediate risk factors for recurrence. We attempted to assess the benefit of radiotherapy after radical hysterectomy in node-negative stage IB–IIA cervical cancer patients with intermediate risk factors.

Methods: The medical records and pathologic slides of patients FIGO stage IB–IIA cervical cancer underwent radical hysterectomy with negative pelvic node between January 2000 and December 2007 were reviewed. The histologic variables were confirmed. Recurrence-free survival and treatment related complications were investigated.

Results: Of the 573 node-negative stage IB–IIA cervical cancer patients, 56 (48.7%) had single intermediate risk factor and 59 (51.3%) had two or more intermediate risk factors. Only 18 patients received adjuvant radiotherapy (RT group) while 97 patients did not receive (non RT group). Sixteen patients (13.9%) developed recurrence, 11 patients had two or more intermediate risk factors. Three patients (20.0%) in the RT group developed recurrences whereas 8 patients (18.2%) in the non RT group developed recurrences. No locoregional recurrence occurred in patients received adjuvant radiotherapy. The 5-year recurrence free survival rates in patients with two or more risk factor received adjuvant radiotherapy and those without adjuvant radiotherapy were 77.8% and 83.0%, respectively (*p*=0.904). Three patients had treatment related complications, 2 with leg lymphedema and 1 with radiation proctitis.

Conclusion: Adjuvant radiotherapy after radical hysterectomy in node-negative stage IB–IIA cervical cancer patients with intermediate risk factors reduced only the incidence of locoregional recurrence.

Keywords: Node-negative cervical cancer, Intermediate risk, Adjuvant radiotherapy

PP-023

A phase II study of tri-weekly cisplatin and irinotecan as neoadjuvant chemotherapy for locally advanced cervical cancer

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Objective: An approach employing preoperative neoadjuvant chemotherapy (NAC) for bulky cervical carcinoma of stages IB2 to IIB has been introduced in clinical practice. We retrospectively investigated the usefulness and safety of NAC for cervical cancer treatment.

Methods: Twenty-three patients with locally advanced squamous cell

carcinoma of the uterine cervix of clinical stages IB2 to IIB were studied between January 2002 and September 2010. Their median age was 40 years (range, 25–63). Two 21–day regimens consisting of intravenous administration of cisplatin at 70 mg/m² (day 1) and irinotecan at 70 mg/m² (days 1 and 8) were administered followed by 2 courses of NAC. Antitumor response, adverse events, and surgery completion rate were investigated.

Results: Clinical staging revealed stage IB2 in 5 cases; stage IIA, 2 cases; and stage IIB, 16 cases. Two courses of NAC were administered in all cases. Regarding anti–tumor effects, CR was observed in 5 cases (21.7%), PR in 15 (65.2%), SD in 2 (8.7%), and PD in one (4.3%). The response rate was 87.0%. Grade 3 or higher hematological toxicities included 6 cases (26.1%) with leukopenia, 14 (60.9%) with neutropenia, and 2 (8.7%) with anemia, while none had thrombocytopenia. Grade 3 or higher non–hematological toxicities included 2 cases (8.7%) with nausea and one (4.3%) with vomiting. The completion rate of radical hysterectomy was 100%.

Conclusion: NAC with irinotecan plus cisplatin for cervical cancer showed potent antitumor effects. The adverse events that occurred because of these regimens were manageable, allowing us to safely treat cervical cancer.

Keywords: Neoadjuvant chemotherapy, Cervical cancer, Squamous cell carcinoma

PP-024

Neoadjuvant weekly carboplatin and paclitaxel followed by radical hysterectomy for locally advanced cervical cancer: long-term results

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Objective: To determine the long–term effect of neoadjuvant chemotherapy (NAC) with paclitaxel and carboplatin on a weekly schedule followed by radical surgery for patients with locally advanced cervical cancer.

Methods: Thirty patients with stage Ib2 to IIIb uterine cervical cancer were treated with paclitaxel (60 mg/m²) and carboplatin (AUC 2) every week for six cycles. A radical hysterectomy was performed six days after the final administration of NAC. The patients were followed up and five–year progression free survival (PFS) and overall survival (OS) were evaluated.

Results: Of 30 patients, 28 were followed up. The median follow–up period was 55.6 months. An objective response (CR+PR) was observed in 26 patients (87%). Two had CR, four had SD, and the remaining patients had PR, while PD was not seen in this study. A radical hysterectomy was performed in 28 patients without delay. The five–year PFS and OS rates were 78.6% and 81.8%, respectively. The five–

year PFS and OS for patients with stage Ib2–IIb cervical cancer were 79.2% and 83.1%, respectively, which is comparable to the concurrent chemoradiation therapy (CCRT) study previously reported. Larger initial tumor size and lymph node metastasis tended to be negatively correlated with survival.

Conclusion: NAC with paclitaxel and carboplatin on a weekly schedule followed by radical surgery for patients with locally advanced cervical cancer is a promising mode of therapy that may improve the prognosis. It would be worthwhile to conduct larger–scale trials for comparison with the results of the CCRT study.

Keywords: Neoadjuvant chemotherapy, Paclitaxel, Weekly schedule

PP-025

Combination of Irinotecan (CPT-11) and Nedaplatin (NDP) for recurrent uterine cervical cancer patients.

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Objective: The clinical activity of combination of CPT–11 and NDP for recurrent uterine cervical cancer patients was evaluated retrospectively.

Methods: Intravenous CPT–11 was given 60 mg/m² (day1, 8, 15) followed by NDP 80 mg/m² (day 1) every 4 weeks. According to the medical records, totally 29 cases from 2000 were received this regimen.

Results: Median age was 57 years (range: 29–80), and performance status (PS) of the patients was 18 cases for PS 0, 10 cases for 1, one case for 2, respectively. Clinical stage was as follows: 3 cases of stage IB1, one case of IB2, 2 cases of IIA, 10 cases of IIB, 8 cases of IIIb, and 4 cases of IVB. Histologically, there were 27 cases of squamous cell carcinoma and 2 cases of adenocarcinoma. About hematological toxicity of grade 3 or more, neutropenia, leukopenia, and febrile neutropenia were observed in 79.3%, 96.5%, and 13.7% cases, respectively. About non–hematological toxicity, vomiting, appetite loss, arthralgia, and distraction were observed in only one case, respectively, and as a result, in seven cases chemotherapy was not completed. Among 26 cases with clinically evaluable lesions, there were 7 complete responses (CR), partial responses (PR), 7 stable diseases (SD), and 9 progressive diseases (PD), and clinical response rate was 38.4%. Median progression–free survival was 7 months (0–38 months).

Conclusion: Combination of CPT–11 and NDP seems to be active for recurrent uterine cervical cancer patients.

Keywords: Recurrent uterine cervical cancer, Chemotherapy, Irinotecan and nedaplatin

PP-026

Passive smoking facilitate the risk of CIN 1 in high risk HPV-positive women: Korean HPV cohort study

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Objective: To investigate associations between passive smoking and risk of cervical intraepithelial neoplasia (CIN), and cervical cancer in high risk HPV-positive women in the Korean HPV cohort study (KHPV).

Methods: The KHPV recruited 1,306 women, aged 18–65, including HPV-positive women with normal cytology (n=577), CIN1 (n=419), CIN2/3 (n=165), and cervical cancer (n=145) from March 2006 to December 2009. Detailed information on passive smoking and other lifestyle factors were collected by questionnaires. Multinomial logistic analysis was performed to estimate multivariate-adjusted odds ratios.

Results: Ex- and current smoker had an increased risk of CIN1 (OR=1.81; 95% CI: 1.26–2.60) as compared to nonsmokers. The risk of CIN1 increased with increasing exposure time of passive smoking regardless of smoking after adjusting for potential confounder (OR=2.09; 95% CI: 1.33–3.28, p for trend=0.0023). In non-smoker, the subject with passive smoking had an increased of CIN1 (OR=1.48; 95% CI: 1.04–2.10, p for trend=0.0276) after adjusting for potential confounder. In smoker, the effects of passive smoking were not statistically significant. Both of exposure time separated by two hours per day (p for trend=0.0003), and 1 hour and 2 hours per day (p for trend=0.0006) of passive smoking demonstrated significant associations with development of CIN1.

Conclusion: This is the first study to demonstrate that passive smoking is an independent and combined risk factor of CIN1. HPV viral load and alcohol synergize to increase the risk of CIN1 among high-risk HPV-positive women.

Keywords: Passive smoking, CIN1, High-risk HPV

PP-027

Prospective randomized controlled trial for development of new cervical cancer screening and prevention model in Korea: HPV DNA test with cervical cytology—preliminary study

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Objective: To develop the new cervical cancer screening and prevention model in Korea

Methods: We conducted a prospective, randomized controlled trial in females admitted to the 10 sub-centers for cervical cancer screening. The enrolled people were separated into two groups, cervical cytology alone vs. HPV DNA test (Hybrid Capture 2, HC2) with cervical cytology, through randomization. In addition, all subjects were underwent a questionnaire about demographic variables and lifestyle. Our primary endpoint was the detection of cervical precancerous lesion or cancer

by colposcopy-guided biopsy.

Results: The study enrolled 1,596 women, with 1,285 evaluable for cytology and HC2, and 970 for questionnaire. Total 862 women were enrolled for final analysis, 468 in cervical cytology alone and 394 in combination group, with results of tests and questionnaire. Abnormal cytology in each group is 1.3% (4 of ASC-US and 2 of HSIL) and 0.5% (1 of LSIL and 1 of HSIL). HPV prevalence by age quinquennial and HPV viral load appeared the peak in 35–39 and tended to decreased with increasing age. In the questionnaire about lifestyle, it showed similar results in a comparison between the two groups (Parity, BMI, coitache, disease history, familial history, smoking, and drinking history).

Conclusion: As a result of preliminary analysis, no differences were found in both screening methods. To obtain accurate results, the large-scale is needed including the final pathologic results and screening costs.

Keywords: Cervical cancer screening, Cytology, HPV DNA test

PP-028

Primary treatment and prognostic factors of small cell neuroendocrine carcinoma of the uterine cervix: a Taiwanese Gynecologic Oncology Group (TGOG) Study

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Objective: To investigate the treatment and clinicopathological variables in correlation to prognosis in small cell neuroendocrine cervical carcinoma (SCNECC).

Methods: Clinical data of SCNECC patients with International Federation of Gynecology and Obstetrics (FIGO) stages I–IV treated between 1987 and 2009 at the member hospitals of TGOG were retrospectively reviewed.

Results: Of 179 eligible patients, 3 were of FIGO stage IA, 69 IB1, 32 IB2, 19 IIA, 23 IIB, 1 IIIA, 8 IIIB, 3 IVA, and 21 IVB. The median follow-up of survivors was 51.2 months. Median failure-free survival (FFS) was 16.0 months, and median cancer-specific survival (CSS) was 24.8 months. In multivariate analysis, FIGO stage and lymph node (LN) metastasis were selected as independent variables (FFS and CSS) in stages I–IV, while FIGO stage was selected for CSS and surgical margins for FFS in patients receiving surgery at primary treatment. In stages IIB–IVB, primary treatment containing etoposide and platinum (EP) for ≥5 cycles was associated with significantly better FFS (p=0.041) and CSS (p=0.035) than other treatments. Further—

more, concurrent chemoradiation with at least 4 cycles of EP (CCRT-EP4+) was associated with even better 5-year FFS ($p=0.025$) and CSS (75.0% vs 16.9%, $p=0.016$). In contrast, 5-year CSS for node-negative stages IB1-IIA patients undergoing primary surgery with/without adjuvant therapy was 57.5%.

Conclusion: FIGO stage and LN metastasis are significant prognostic factors in SCNECC. In stages IIB-IVB, cycle number of EP has significant impact on survival, and CCRT-EP4+ might be the treatment of choice.

Keywords: Neuroendocrine carcinoma, Small cell, Uterine cervix

PP-029

Failure pattern and salvage therapy of small cell neuroendocrine carcinoma of the uterine cervix: A Taiwanese Gynecologic Oncology Group (TGOG) Study

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Objective: To investigate failure pattern and salvage therapy following treatment failure of small cell neuroendocrine carcinoma of the uterine cervix (SCNECC).

Methods: Clinical data of 179 SCNECC patients treated between 1987 and 2009 at the member hospitals of TGOG were retrospectively reviewed. Clinicopathological variables, primary treatment, sites of failure, failure pattern, salvage treatment, and outcomes were analyzed.

Results: Up to the date of analysis (June 28, 2011), treatment failure was documented in 105 at a median time to failure (TTF) of 10.1 months (0-91.3), death was documented in 91. Assessable failure patterns ($n=81$) included loco-regional (LR) in 38.3%, distant (D) in 51.9%, and combined (L+D) in 9.9%. There was significant difference in median TTF among initial stage (stages I-II vs III-IV; 12.3 vs 5.7 months, $p<0.001$). Curative salvage therapy consisted of 1 with surgery (S) alone, 5 with radiotherapy (RT) alone, 8 with concurrent chemoradiation (CCRT), and 1 with S+RT. Median survival after failure (SAF) was 3.8 months (range 0-207.5). Median SAF for LR, D, and L+D were 4.5, 6.1, and 5.8 months, respectively ($p=0.830$). Of all the failures, only 3 with LR were successfully salvaged with long-term SAF (54, 124 and 208 months). Those receiving pelvic RT/CCRT (definitive or adjuvant) at primary treatment rarely failed local-regionally (2/54, 3.7%) as compared to those without (29/125, 23.2%) ($p=0.001$).

Conclusion: The success or failure of primary treatment determines overall survival. Future research should be directed in improving primary treatment (systemic and local-regional control).

Keywords: Neuroendocrine carcinoma, Small cell, Uterine cervix

PP-030

The role of human papillomavirus (HPV) types 16 E6/E7 oncoproteins in fibroblast growth factor (FGF) 2 and 4 induced cervical epithelial-mesenchymal transition (EMT) and carcinogenesis

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Objective: Cervical cancer is one of the most globally common cancers in women and leading cause of death from gynaecological malignancy, it is also a common gynecologic cancer in Taiwan. Although HPV infection is the major cause of cervical cancer formation, however, only a small fraction of those HPV infected female will develop cervical cancer, indicating that there will be some other factors contribute to the progression of cervical cancer lesion to invasive cervical cancer. Studies have been initiated to investigate whether HPV16 E6/7 transfection could contribute to the tumorigenesis by FGF 2 and 4 in human malignant cervical cancer cells.

Methods: Cell culture, immunoblotting, invasive assay cell proliferation assay

Results: The HPV16 E6/E7 transfection will induce the EMT in cervical epithelial cells, increased cell proliferation ability and induced cell invasive activity

Conclusion: In this study have indicated that the HPV 16 E6/7 transfection in CxWJ cells, which make it have different response to FGFs ligand stimulation and gain more invasive ability. Further study about the change of epithelium and mesenchymal characteristics will be done to elucidate the role of HPV16 E6/7 and FGF alteration in cervical carcinogenesis.

Keywords: Cervical cancer carcinogenesis, HPV E6, E7, FGF2, 4, EMT

PP-031

Safety and feasibility of robotic radical trachelectomy in patients with early-stage cervical cancer

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Objective: To evaluate the safety and feasibility of robotic radical trachelectomy in patients with early stage cervical cancer.

Methods: We retrospectively reviewed the medical records of patients who underwent robotic radical trachelectomy and bilateral pelvic lymphadenectomy between May 2004 and March 2011. All surgical procedures were performed with the Da Vinci S robot or SI robot.

Results: Six patients with cervical cancer IA1 (n=1), cervical cancer IB1 (n=4) and cervical cancer IIA1 (n=1) were included in this analysis. Procedures included radical trachelectomy and bilateral pelvic lymphadenectomy with or without cerclage. The median operative time was 303.5 min (range, 257–453 min), the median blood loss was 125 ml (range, 30–300 ml), and the median hospital day was 10 days (range, 7–17 days). No perioperative complications occurred. There was no recurrence during the median follow-up time of 9 months.

Conclusion: Robotic radical trachelectomy is technically feasible and safe in patients with early stage cervical cancer who want to preserve fertility.

Keywords: Robotic surgery, Trachelectomy, Gynecology

PP-032

Prognostic implication of human papillomavirus DNA load in adenocarcinoma of the uterine cervix

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Objective: To determine the relationship between HPV DNA load gained by the Hybrid Capture 2 HPV DNA test and clinicopathologic features of cervical adenocarcinomas.

Methods: We retrospectively reviewed the medical records of patients who were diagnosed adenocarcinomas of cervix between January 2001 and March 2008. HPV DNA titers were measured by the Hybrid Capture 2 HPV DNA Test (HC2).

Results: The results of HC II titer between 2 groups were separated by stage, lymphovascular space invasion, LN metastasis (preop/postop), invasion depth, tumor size. In 34 patients without lymphovascular space invasion, the mean HC II titer was higher than those 6 patient who had lymphovascular space invasion (282.98 RLU vs 34.75 RLU) ($p=0.017$). In 26 patients who had no lymph node metastasis in pathologic finding after hysterectomy, the HC II titer was 352.49 RLU. Comparing that 5 patient who had lymph node metastasis had mean HC II titer 2.12 RLU ($p=0.006$). In 3 patient who has lower than 3mm cervical cancer invasion, the mean HC II titer was higher than that in 40 patients who had deeper invasion than 3mm (1136.31 RLU vs 237.75 RLU) ($p=0.016$).

Conclusion: We demonstrated low HC II titer in advanced cervical adenocarcinoma and higher titer in early stage. The HC II titer was associated with cervical carcinogenesis, but not with the metastasis or tumor cell growing.

Keywords: HPV DNA hybrid capture II titer, Cervical adenocarcinomas, HC II titer

PP-033

What are pros and cons of robotic hysterectomy in early advanced cervical cancer comparing with conventional radical hysterectomy and laparoscopic hysterectomy?

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Objective: The purpose of this study was to evaluate the operation outcomes in cervical cancer patients who received robotic (RRH, n=9), laparoscopic (LRH, n=12), or radical abdominal hysterectomy (RAH, n=6) at the time of initiation of the robotic and laparoscopic radical hysterectomy program.

Methods: The characteristics and operation outcomes of patients were collected from January 2009 to July 2011. All patients were diagnosed with early-stage cervical cancer and were treated by a single gynecologic oncologist. Based on the operation method, patients were divided into three groups.

Results: Difference in age, BMI, estimated blood loss, number of lymph node yield, hospitalization days, previous operation history, cancer stage, cancer type, operation complication, transfusion provided, resection margin outcomes, and number of injected additional pain killers were negligible. However compared with other procedures, RAH had significantly shorter operation time. (274.8 ± 58.8 vs 282.8 ± 107.1 vs 175.8 ± 43.4 , LRH vs RRH vs RAH, respectively, $p=0.04$)

Conclusion: Compared to RAH, operation time of LRH and RRH may be longer especially during the learning curve period (LCP). Surgical outcomes can be affected by surgeon's skill during the LCP, though we could not find any significant difference between the outcome of LRH and RRH. Further randomized controlled studies should be carried out to achieve more accurate results on the comparability of these two minimal invasive techniques. However in an aspect of cosmetic outcomes, LRH and RRH might be superior to RAH due to minimally invasive surgical practices.

Keywords: Robotic hysterectomy, Conventional radical hysterectomy, Laparoscopic hysterectomy, cervical cancer

PP-034

The histologic profile of LSIL with the follow-up data

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Objective: To know the histologic profile of LSIL

Methods: From 1999 to 2011 medical records were reviewed retrospectively to find the patients whose Pap smear results were LSIL. Their age and plan to care and histologic results including punch biopsy, conization or hysterectomy procedure were reviewed.

Results: There were 191 patients whose Pap smear results were LSIL.

There were 151 patients who underwent biopsies and 40 who did not. There were 72 patients (47.7%) who had no intraepithelial lesions. Their ages were 42.0 ± 11.5 years old. 68 patients were followed without treatment and 2 underwent cone and 2 did hysterectomy. There were 64 patients (42.4%) who had CIN 1. Their ages were 42.4 ± 10.3 years old. 61 patients were followed without treatment and 3 underwent cone. There were 9 patients (6.0%) who had CIN 2. Their ages were 36.9 ± 9.0 years old. 1 patient was followed without treatment and 7 underwent cone. There were 4 patients (4.0%) who had CIN 3. Their ages were 48.1 ± 8.3 years old. Every patient underwent cone. There were 40 patients who did not undergo biopsies.

Conclusion: Among patients with LSIL, there are 10% of high grade cervical intraepithelial lesions. Colposcopy guided punch biopsy is strongly suggested.

Keywords: LSIL, Histology, Follow-up

PP-035

Quantification and genotyping of human papillomavirus

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Objective: We introduce improved useful method based on Real-time PCR (RT-PCR) and microarray HPV genotyping.

Methods: We tested novel primer sets (GPM7 Forward/Reverse) that target in the conserved L1 region of HPV genome to detect the broad range HPV types, at least 36 types, and evaluation of viral loads per cell. Generated RT-PCR products that are Cy-5 labeled in reverse primers are directly used to screen genotype on microarray.

Results: This assay applied on 150 genital samples that were presented cytological abnormality, and were HC II positive in 64% (n=96) and negative in 36% (n=54). In our results, when RT-PCR negative range was adjusted at below 100 copy, RT-PCR Positive was 80% (n=120) and negative was 20% (n=30). Genotyping was sequentially performed with RT-PCR Positive samples by microarray. 85.5% of 55 ASC-US (Atypical Squamous Cells of Undetermined Significance) classified samples were identified genotype, mainly type 16 (16.4%), and 14.5% of them were negative. Each HPV positive ratio was 85.5%, 86.7%, 96.9% and 100% in ASC-US, LSIL, HSIL and Cancer.

Conclusion: Although the relation of statistical significance between viral load and cytology was not cleared, we verified its increased pattern in high grade lesion. We will study with more clinical samples for precise statistical significance test. Quantification and identification of HPV by connected methods with RT-PCR and DNA chip will be helpful to predict the progression of cervical cancer.

Keywords: HPV, Quantification, Genotyping

PP-036

Validation of viral load of HPV4A ACE according to HPV genotype by comparison with of hybrid capture 2, PCR, and cervical pathology

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Objective: To validate the viral load of HPV4A ACE according to HPV genotype compared with Hybrid Capture 2 viral load, PCR, and cervical pathology

Methods: We enrolled 106 women with Hybrid Capture 2 positive, admitted for cervical cancer screening from December 2008 to May 2011. Cervical cytology was diagnosed according to 2001 Bethesda System.

Results: HPV genotype distribution showed similar results with previous studies in Korea. Viral load of HPV4A ACE were similar to that of Hybrid Capture 2 (HC2) in ascending order. Viral load of HC2 increased according to severity of the cytologic and histologic results, but was not statistically significant. Depending on the results of PCR and HPV4A ACE, Total cases were classified as HPV16, HPV18, and other high risk (HRC). In each group, viral load of HPV4A ACE had similar distribution with that of HC2.

Conclusion: This study will be useful to understand the association between the viral load by HPV genotype and cervical pathology. The large-scale studies are needed to investigate the association of viral load by genotype and cervical pathology.

Keywords: High-risk HPV, Genotype, HPV4A ACE

PP-037

Current suitable screening method for cervical cancer in China

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Objective: To evaluate the current suitable screening method for cervical cancer in China.

Methods: To evaluate the current opportunistic screening (OS) in diagnosis of cervical cancer and pre-cancer in Chinese hospitals. To analyze the value of cytology and colposcopy in cervical lesion screening, 795 women in Beijing and 642 women living in Neimenggu province were screened for cervical lesion by the visual inspection with VIA/VILI as cervical cancer screening tools.

Results: A total of 1,242,952 women came to the outpatient department of the 12 hospitals in 2005 and 202,231 (16.27%) of them received OS. Cervical lesions pre-cancer were diagnosed in 5146 cases (2.54%) and cervical cancer in 1134 (0.56%). In the 795 women, 1 early invasive cervical cancer, 4 CIN3, 3 CIN2 and 7 CIN1 were found out. In the 323 women,

2 invasive cervical cancer, 1 CIN3, 1 CIN2 and 3 CIN1 were found out. In six areas, 12,208 women were recruited. The positive rate of VIA/VILI was 11.50%, 17.95%, 21.88%, 6.19%, 2.95%, 6.11%, respectively. The diagnosis rate of high grade cervical intraepithelial neoplasia is 6.49%, 15.67%, 18.42%, 1.67%, 18.33%, 21.51%, respectively. For high grade lesion, the diagnosis rate of VIA/VILI is 5.22%, 13.06%, 1.52%, 0.80%, 18.33%, 16.00%, respectively.

Conclusion: We should pay more attention to cervical lesion screening of people living in poor health condition area and use variable method for screening.

Keywords: Cervical cancer screening, Human papillomavirus, Cytology

PP-038

Pre-operative diagnosis and the management of minimal deviation adenocarcinoma (MDA) and lobular endocervical glandular hyperplasia (LEGH) of the uterine cervix: a multi-center, retrospective study

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Objective: To clarify the preoperative differential diagnosis and management of minimal deviation adenocarcinoma (MDA) and lobular endocervical glandular hyperplasia (LEGH), a multicenter study was performed.

Methods: A total of 112 patients who underwent conization or a hysterectomy for suspected MDA were collected from 24 hospitals. The pathological diagnosis in each case was determined by a central pathological review (CPR) board. The diagnostic significance of clinicopathological findings including results of magnetic resonance imaging (MRI), Pap smears, and testing for gastric mucin was analyzed.

Results: The CPR identified 37 cases of Nabothian cyst or tunnel cluster, 54 cases of LEGH, 6 cases of MDA, 11 cases of adenocarcinoma. LEGH was often associated with AIS, MDA, and mucinous adenocarcinoma. Three MDA patients recurred, whereas none of LEGH patients recurred irrespective of the type of surgery. On MRI, LEGH appeared as a characteristic multicystic lesion with an inner solid component, whereas MDA showed a predominantly solid pattern. A Pap smear or gastric mucin alone had limited diagnostic power. However, a combination of these findings is useful, i.e., a cystic structure with inner solid components on MRI associated with mild glandular atypia and gastric mucin strongly suggested LEGH (24/26, 92%). A solid structure with atypical glandular cells was indicative of MDA or adenocarcinoma (5/5, 100%).

Conclusion: The combination of MRI, Pap smears, and gastric mucin will improve the accuracy of the preoperative diagnosis of MDA and LEGH. Patients suspected of having LEGH may need to be treated with less aggressive methods.

Keywords: MDA, LEGH, Diagnosis

PP-039

HPV L1 capsid protein immunocytochemistry and E2/E6 ratio in abnormal cervical cytology with HPV Type 16 single infection

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Objective: The purpose was to evaluate immunocytochemistry of L1 capsid protein and E2/E6 ratio in abnormal cytology with human papillomavirus (HPV) type 16.

Methods: A total of 137 specimens were collected at Seoul St. Mary's Hospital. Cytology was evaluated by immunostaining of HPV L1 capsid protein and E2/E6 ratio of HPV 16 was performed with RT-PCR.

The immunocytochemistry were performed using Cytoactiv[®] HPV L1. The staining was considered positive when at least one nuclei of the cell showed red staining. The status of HPV 16 was grouped in episomal, mixed and integrated forms using E2/E6 ratio.

Results: A total of 137 cases were eligible for the study, consisting of 21 cases of ASCUS, 59 cases of LSIL, 38 cases of HSIL, and 19 cases of cervical cancer. The HPV L1 positivity were found in 52.4%, 49.2%, 42.1%, 10.5% of ASCUS, LSIL, HSIL, cancer groups, respectively. Interestingly, 89.5% of cancer cytology showed HPV L1 capsid protein negative for immunocytochemistry. The mean ratio of abnormal cytology showed significant difference according to cytology grades (ANOVA, $p < 0.05$). The mean of E2/E6 ratio in cancer cytology was 0.22 and significantly lower than those of the other groups ($p < 0.05$). Cervical cancer cytology had a prevalence of mixed form (57.9%), integrated form (36.8%) and 5.3% of episomal form.

Conclusion: The pattern of HPV L1 capsid immunocytochemistry and E2/E6 ratio showed statistical significance according to the grades of abnormal cytology. Cancer cytology expressed extremely low ratio of E2/E6.

Keywords: Human papillomavirus, HPV L1 capsid protein, E2/E6 ratio

PP-040

Study on the clinical strategy of cervical lesion in gestation period

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Objective: To study the clinical strategy of cervical lesion in Gestation period

Methods: 28 cases of pregnant women with abnormal cytological results attended the colposcopy clinic in our hospital. The patients' average age is 29.4 years old. They all have colposcopy detection.

Results: In these 28 cases, no complication was occurred induced by colposcopy. Biopsy was given in 18 cases. For 16 cases with ASC-US, only seven cases were taken biopsy. 3 cases with CIN1, 1 case with

CIN3, the other 3 is metaplasia. The 4 cases with CIN are all positive for HR-HPV. The other 3 case is negative. For 4 cases with LSIL, 3 of them is HR-HPV positive, the pathological results is 1 with CIN2, 1 with CIN1, 1 negative. After delivery, the patient with CIN2 was checked and the pathology is CIN3. 8 cases with HSIL, their HR-HPV are all positive. Pathology is 7 cases with CIN3, 1 with CIN2. One of CIN3 is ended in early pregnancy. The other 6 cases with CIN3 was check during pregnancy. After delivery, they were checked again, 3 cases with CIN1, 2 with CIN2, 1 with CIN3. The CIN2 during pregnancy is missed.

Conclusion: HR-HPV testing is a useful strategy for pregnant women with abnormal cytological result. The colposcopy evaluation is very important for the women with cervical lesion during pregnancy.

Keywords: Cervical lesion, Gestation period, Management

PP-041

Human lysyl-tRNA synthetase is increased in uterine cervical cancer

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Objective: Human lysyl-tRNA synthetase (KRS) has diverse functions in the regulation of cellular processes via its versatile molecular interactions and catalytic ability. Although overexpression of KRS has been observed in a few cancer cell lines, there is no report of its expression in uterine cervical cancer.

Methods: We assessed the expression of KRS in normal cervical and cervical cancer tissue by western blot analysis. The band intensity was analyzed to compare the expression level between normal and cancer tissue in relation to the tumor stage and whether there was lymph node metastasis.

Results: The expression of KRS in cervical cancer was significantly increased compared with that in normal cervix tissue. However, the expression of KRS was not associated with tumor stage or lymph node metastasis.

Conclusion: KRS expression is increased in cervical cancer, and this could be a clue for further research to understand the pathophysiology of the tumor and to develop a possible target for therapy.

Keywords: Cervical cancer, Lysyl-tRNA synthetase, KRS

PP-042

Clusterin expression is associated with decreased disease-free survival of patients with adenocarcinoma of the uterine cervix

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Objective: The aim of this study was to evaluate the prognostic significance of clusterin expression in tissues of cervical cancer.

Methods: Cervical cancer specimens were obtained from 88 patients who underwent radical hysterectomy and systematic lymphadenectomy at the Busan Paik Hospital, Inje University from the year 2001 to the year 2008. The expression of clusterin protein was analyzed by immunohistochemical staining. The relationship between clusterin expression and clinicopathologic factors for cervical cancer was analyzed by chi-square test. Survival analyses were performed by the Kaplan-Meier curves and the log-rank test.

Results: Clusterin was present in the cytoplasm of cervical cancer cells. Clusterin expression was significantly higher in adenocarcinoma (50.0%, 24/48) than in squamous cell carcinoma (10.0%, 4/40) ($p=0.0002$). Clusterin expression in cervical cancer tissues was not related to any clinicopathologic factors analyzed. However, clusterin expression in adenocarcinoma was significantly associated with a decrease in disease-free survival ($p=0.0104$).

Conclusion: Clusterin might be a new molecular marker to predict the survival of patients with adenocarcinoma of the uterine cervix and may help identify patients with more aggressive tumors who may benefit from targeted therapy.

Keywords: Cervical cancer, Adenocarcinoma, Clusterin

PP-043

Reproductive concerns and QOL of cervical cancer patients treated with abdominal radical trachelectomy

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Objective: To investigate reproductive concerns and QOL in women treated with abdominal radical trachelectomy.

Methods: We assessed psychosocial and reproductive concerns and QOL in 59 cervical cancer patients enrolled in an ongoing study. Prospective data of them were evaluated in combination with a medical chart review.

Results: Between February 2004 and October 2010, 61 cervical cancer patients were enrolled in the study. Two patients were excluded because they did not undergo the planned surgery. 53 (89.8%) responded and 43 (72.89%) offered complete data. Greater reproductive concerns were significantly associated with lower QOL on numerous dimensions ($p<.001$). In a multiple regression model, social support, physical and sexual problems, and reproductive concerns accounted for 70% of the variance in QOL scores. Women who reported wanting to conceive after surgery, but were in instable partnership with their boyfriends or husbands, reported significantly more reproductive concerns than those who were in stable partnership ($p<.001$). Future childbearing was the main reason most women chose to

undergo this fertility-preserving procedure. However, 20.9% of the patients had high expectations for future conception at their enrollment, admitted that their expectations declined over time, accompanied by an increasing distress.

Conclusion: These preliminary data suggested that the issue of reproductive concerns and QOL is worthy of additional investigation to assist post-trachelectomy cervical cancer patients with a better life.

Keywords: Reproductive concerns, Quality of life, Post-trachelectomy patient

PP-044

Pregnancy outcomes in women who had cervical intraepithelial neoplasia requiring treatment and future childbearing after cervical photodynamic therapy

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Objective: To evaluate pregnancy outcomes after cervical photodynamic therapy (PDT)

Methods: From December 2001 to August 2009 in our institution, cervical PDT was performed for 94 patients to treat the CIN. Among them, 38 patients had wanted subsequent pregnancy. After IV photosensitizer administration, optimal doses of light were irradiated at cervical lesion in 48 and 96 hours.

Results: 38 women underwent cervical PDT, and 10 women achieved pregnancies. 8 women delivered vaginally between 37 and 40 weeks, 1 twin pregnancy had cesarean section at 35 weeks, and only 1 woman had preterm delivery at 36 weeks of gestation.

Conclusion: Conization of cervix for the treatment of CIN is known to be related with adverse pregnancy outcomes in subsequent pregnancies, including preterm delivery. So we suggest that topical PDT of cervix is a helpful method for women who want future childbearing.

Keywords: Photodynamic therapy, Cervical intraepithelial neoplasia, Pregnancy

PP-045

DNA load is prognostic factor for VAIN development after hysterectomy especially that without cervical lesion

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Objective: This study will consider contributing factors of the VAIN development after hysterectomy with or without cervical lesion and it can help to evaluation for VAIN after hysterectomy.

Methods: Between January 2000 and March 2011, we retrospectively reviewed the medical records of patients with VAIN after hysterectomy at the Department of Obstetrics & Gynecology, Korea University College

of Medicine, Guro Hospital, Seoul, Korea.

Results: Forty three women were histologically confirmed VAIN by colposcopy guided biopsy. The mean age at diagnosis of VAIN was 52.2 years (range, 37–73). The mean period for the diagnosis of VAIN following hysterectomy was 61.9 months (range, 3–182). Twenty seven patients underwent hysterectomy with cervical lesion; 8 cases of cervical dysplasia, 19 cases of early stage cervical cancer (13; CIS, 4; stage Ia1, 2; stage Ia2). Sixteen patients underwent hysterectomy without cervical lesion. In previously hysterectomized women without cervical lesion has significantly high HPV DNA load ($p=0.026$) and high grade of VAIN ($p=0.04$). The age, parity, vaginal cytology, and period until the diagnosis of VAIN were not significantly different between two groups. Twenty-five patients were tested for HPV DNA load in two years after hysterectomy. There was a negative correlation of HPV DNA load and period until the diagnosis of VAIN ($r=-0.736$, $p=0.000$).

Conclusion: Development of VAIN after hysterectomy without cervical lesion is associated with higher HPV loads and more severe lesions than that with cervical lesion. Further studies are needed to clarify the pathogenesis of VAIN on the point of HPV replication.

Keywords: Vaginal intraepithelial neoplasia (VAIN), HPV DNA test, Hysterectomy

PP-046

Outcome and reproductive function after treatment of ovarian germ cell malignancy

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Objective: This study is undertaken to evaluate the outcome of patients diagnosed with Ovarian Germ Cell Malignancy (OGCM) who underwent fertility sparing surgery and adjuvant chemotherapy treated in our center, focusing on reproductive function, survival, recurrence rate and their prognostic factors.

Methods: We retrospectively reviewed 33 patients who had fertility sparing surgery and adjuvant chemotherapy in our center from 2000–2010. Gynaecology oncology record and histopathology database were reviewed. Patients were contacted, assessed and interviewed via telephone questionnaire to assess their menstrual, reproductive function and disease status after treatment, post therapeutic status of pregnancy or delivery and overall survival

Results: Thirty three patients diagnosed with OGCM underwent unilateral salpingo oophorectomy and adjuvant chemotherapy (BEP regimen). The mean age at presentation was 19.8 years (range, 9–34 years). Histological subtypes were 21.2% dysgerminoma, 21.2% immature teratoma, 42.4% yolk sac tumour and 15.2% mixed germ cell tumour. After treatment, 71.4% recovered their menstrual cycles within 6 months. During follow up, 5 patients conceived with 5 live birth deliveries and 3 miscarriages. The overall survival rate was 87.9% with

median follow up of 45.2 months. Recurrence or disease progression occurred in 36.3% of patients and those with histology of yolk sac tumour element (non DSG/IMT) was significant prognostic factor for early relapsed/ recurrence.

Conclusion: Fertility sparing surgery and adjuvant chemotherapy appear to have little effect on fertility and menstrual cycle with a good overall survival. Patients diagnosed with histopathological yolk sac tumour element are poor prognosis for early recurrence, thus aggressive treatment should be initialized earlier.

Keywords: Germ cell ovarian malignancy, Reproductive function, Fertility preserving surgery

PP-047

Squamous cell carcinoma arising from mature cystic teratoma of the ovary

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Objective: Squamous cell carcinoma (SCC) is the most common type of malignant transformation in mature cystic teratoma (MCT) of the ovary. It is difficult to preoperatively diagnose. This retrospective study aims to seek the possible risk/ prognostic factors and treatments for SCC arising from MCT of the ovary.

Methods: Using an institutional database, 3 women treated for SCC arising from a MCT of the ovary at the Kaohsiung Veteran General Hospital. A retrospective chart review was conducted.

Results: A total of 1551 cases of MCT were diagnosed at Kaohsiung Veteran General Hospital from 1990 to 2009, of which, malignant teratoma SCC type was noted in 3 cases (0.19%). The median age of the subjects was 39 years. Abdominal fullness was the most common symptom (3/3 cases). The mean diameter of the ovarian tumor was 17.3 cm, ranging from 16 to 18 cm. All 3 patients received simple right salpingo-oophorectomy or debulking surgery. Two of the patients reached stage IIIC and died.

Conclusion: We recommend being cautious of the following risk factors: patient age, tumor size, ultrasound characteristics, sonar tumor vessel wave form, computed tomography, and levels of SCC and CA125 tumor markers. Based on our literature review, stage IA patients who undergo standardized operational procedures do well without adjuvant treatment, but such patients must be confirmed accurately with complete surgical staging to be in stage IA before undergoing conservative management. The optimal approach to the management of patients with advanced stage and recurrent disease is unclear.

Keywords: Squamous cell carcinoma, Dermoid cyst, Malignant transformation

PP-048

Sertoli-leydig cell tumors of the ovary: a Taiwanese Gynecologic Oncology Group (TGOG) study

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Objective: We report the natural history and prognosis of this uncommon ovarian tumor from a TGOG study.

Methods: A 20 year-period retrospective review was conducted by TGOG including 9 tertiary medical centers from different regions in Taiwan. Medical records of 40 cases of ovarian SLCT were collected. Pathology review was carried out by a panel of expert pathologists.

Results: After pathological review, seventeen patients were subsequently excluded because pathology slides were not available in 5 cases and discrepant results from initial diagnosis were found in 12 cases (34%). For the remaining 23 patients, the median age was 41 years. The most common symptom was irregular vaginal bleeding followed by an abdominal palpable mass or amenorrhea. Most of the tumors were unilateral and confined to right ovary with the average size of 8.2cm. Preoperative serum markers were available for 12 patients and were elevated for 3 patients. All patients accepted primary surgery and 11 patients (48%) had staging operation. Six patients accepted adjuvant chemotherapy and bleomycin, etoposide and cisplatin were used in 4 of them. Clinical follow-up information was available in 21 patients with the average of 35.6 months. Eighty-two percent of patients were alive and free of disease. Two patients died of disease.

Conclusion: This study demonstrates the extreme rarity of ovarian SLCT in Taiwan. Histological discordance between diagnosis and central review proves the need for expertise review before treatment. To further improve our understanding of biologic behavior and treatment strategy of this unique tumor, international collaboration is imperative.

Keywords: Sertoli-Leydig cell tumors of the ovary, TGOG, Sex cord-stromal tumor of ovary

PP-049

Residual tumor after the salvage surgery is the risk factors for primary treatment failure in malignant ovarian germ cell tumors: a retrospective study of single institution

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Objective: This study was conducted to evaluate the clinicopathologic characteristics of malignant ovarian germ cell tumors (MOGCTs) and to determine the association of their prognostic factors to primary treatment failure.

Methods: The medical records of 57 patients with stages I to IV MOGCT were retrospectively reviewed, and their clinicopathologic and treatment-related data were collected and analyzed.

Results: The median age at the diagnosis was 23.3 years (range: 8–65 years). The histology of the tumors were immature teratoma (n=24), dysgerminoma (n=20), endodermal sinus tumor (n=8), mixed germ cell tumor (n=4), and choriocarcinoma (n=1). 66.7% of the patients had stage I disease; 5.2%, stage II; 26.3%, stage III; and 1.8%, stage IV. After the initial surgery, 49 patients (86%) received cisplatin-based chemotherapy. The five-year survival rate was 96.5%. There were six primary treatment failures, with two of the patients dying of the disease. In the multivariate analysis, the residual tumor after the salvage surgery was the only significant variable associated with primary treatment failure ($p=0.0011$, HR = 29.046, 95% CI 3.832–220.181).

Conclusion: Most MOGCTs have excellent prognoses with primary treatment, and good reproductive outcomes can be expected. Because primary treatment failure is associated with the residual disease after the salvage surgery, knowledge of the presence or absence of this risk factor may be helpful in risk stratification and individualization of adjuvant therapy in MOGCTs.

Keywords: Malignant ovarian germ cell tumor, Primary treatment failure, Prognostic factors

PP-050

Evaluation of local radiotherapy for isolated lymph node recurrence of epithelial ovarian cancer: therapeutic effect and safety

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Objective: Isolated lymph node recurrence (ILNR) of epithelial ovarian cancer (EOC) has been reported to have less aggressive progression and favorable outcome, especially when treated with surgery. However, the role of radiotherapy in ILNR is seldom discussed. We sought to determine the therapeutic effect and safety of local radiotherapy in ILNR of EOC, and compare them with those of surgery.

Methods: We reviewed the medical records of EOC patients undergoing surgery or radiotherapy for ILNR between January 1995 and December 2008. Patient characteristics, feature of recurrence, survival, and treatment-associated morbidity were evaluated and compared according to treatment modality.

Results: Of a total of 33 identified patients, 14 and 19 underwent local radiotherapy and secondary cytoreductive surgery for ILNR, respectively. There was no significant difference in patient age, FIGO stage, time to ILNR and size of node disease between the two groups ($p>0.05$). Optimal cytoreductive surgery was achieved in all patients undergoing surgery, while complete response was achieved in 12 of 14 patients undergoing radiotherapy. Follow-up time ranged from 26 to

140 months (median 78). Six patients in the surgery group and 5 in the radiotherapy group died from the disease. The 5-year post-recurrence survival rate is 68.8% and 66.7% in surgery and radiotherapy group, respectively ($p>0.05$). There was no significant difference in overall and progress-free survival between the two groups ($p>0.05$). The treatment-associated toxicity in radiotherapy group was acceptable and comparable to morbidity of surgery group.

Conclusion: Local radiotherapy is a safe and effective procedure as secondary cytoreductive surgery for ILNR of EOC.

Keywords: Epithelial ovarian cancer, Lymph node recurrence, Radiotherapy

PP-051

Micropapillary pattern in serous borderline ovarian tumors: does it matter?

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Objective: To evaluate the clinical and prognostic impact of micropapillary pattern in patients with serous borderline ovarian tumors (SBOT).

Methods: We retrospectively assessed 130 consecutive patients with typical (n=97) or micropapillary (n=33) SBOT. Clinicopathologic factors and outcomes were compared.

Results: There were no significant between-group differences in age, menopausal status, parity, body mass index, cancer antigen 125 concentration, tumor size, tumor rupture, positive cytology, ovarian surface involvement, retrieved lymph nodes, use of laparoscopy, fertility-sparing and ovary-sparing procedures, complete staging and restaging, and adjuvant chemotherapy. However, the incidences of advanced stage (II–III) tumors (10.3% vs 36.4%, $p=0.001$), microinvasion (2.1% vs 15.2%, $p=0.012$), peritoneal implants (8.3% vs 33.4%, $p<0.001$), and lymph node involvement (0% vs 21.2%, $p<0.001$) were significantly higher in patients with micropapillary than with typical SBOT. Five patients with typical (5.2%) and three with micropapillary (9.1%) SBOT had recurrent disease ($p=0.418$), and one patient (3%) in micropapillary SBOT group died due to the disease ($p=0.254$). The 5-year disease-free survival (DFS) rates for patients with typical and micropapillary SBOT were 96% and 86%, respectively ($p=0.148$). All three patients with micropapillary SBOT who had recurrence had peritoneal implants (one noninvasive and two invasive). Multivariate analysis showed that peritoneal implant was the only significant factor related to DFS ($p=0.002$).

Conclusion: Because micropapillary SBOT was significantly associated with peritoneal implants, especially invasive implants, and lymph node involvement, complete staging procedures, including

lymph node dissection, are recommended. However, micropapillary SBOT itself was not significantly associated with DFS. Peritoneal implant was the only factor independently associated with tumor recurrence.

Keywords: Serous borderline ovarian tumor, Micropapillary, Prognosis

PP-052

Prognostic significance of nutritional risk index in advanced epithelial ovarian cancer

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Objective: The purpose of this study was to evaluate the feasibility of principal recommended nutritional risk index (NRI) as a prognostic factor in patients with advanced epithelial ovarian cancer.

Methods: A total of 150 advanced epithelial ovarian cancer patients were treated with debulking surgery, followed by taxane and platinum-based chemotherapy in the single institution. The NRI was derived from the serum albumin concentration and the ratio of actual to usual weight and was analyzed before surgery, and on the start and the end of chemotherapy (NRI1, NRI2, and NRI3, respectively).

Results: The NRI was not related to the number of chemotherapy cycles. The median duration of the follow-up was 37 months. The median progression-free survival of patients with low and very-low NRI3 were 17 and 7 months, respectively, whereas that of patients with normal NRI3 were 23 months (95% CI, 18–28 months) ($p=0.008$). The median overall survival (OS) of patients with very-low NRI3 was shortest among groups (13 months, 95% CI, 8–18 months, $p<0.001$). Independent predictor for OS included NRI2 and NRI3 (hazard ratio 1.19 and 1.65; $p=0.018$ and $p<0.001$, respectively).

Conclusion: The NRI before and after chemotherapy was a significant prognostic factor in patients with epithelial ovarian cancer who were treated with debulking surgery and adjuvant taxane and platinum-based chemotherapy.

Keywords: Ovarian cancer, Nutrition, Survival

PP-053

Therapeutic efficacy of oral paclitaxel (DHP 107) in an orthotopic mouse model of ovarian cancer

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Objective: Paclitaxel has been used as a chemotherapeutic agent against a various type of cancers. Recently, clinical mucoadhesive lipid-based oral paclitaxel formulation (DHP107) was newly developed.

We designed to compare the in vivo anti-tumor efficacy of DHP107 with traditional IV Paclitaxel using an orthotopic mouse model.

Methods: DHP107 was administered p.o. at dose of 0, 25, and 50 mg/kg twice a week. Paclitaxel IP injections at traditional dose of 5 mg/kg were used as controls. The significant tumor weight reductions were observed in mice with DHP107 p.o. administration at dose of 25 mg/kg ($p<0.01$) and 50 mg/kg ($p<0.01$). DHP 25mg/kg twice a week was selected as a therapeutic dose.

Results: Mice were administrated with DHP 107 p.o at dose of 0,25mg/kg twice a week or 50 mg/kg once a week. DHP 107 administration at low dose (25 mg/kg, tumor weight reduction by 88%, $p<0.01$) twice a week was effective as a therapeutic schedule in inhibiting tumor growth compared with administration at high dose DHP107 (50mg/kg, by 36%, $p<0.2$) and IP Paclitaxel (5mg/kg, by 82%, $p<0.01$) once a week

Conclusion: Our results define the in vivo anti-tumor efficacy by metronomic oral chemotherapy of DHP107 for alternative systemic administration of paclitaxel.

Keywords: Oral paclitaxel, Ovarian cancer, DHP107

PP-054

Ovarian cancer screening by the information of low-mass metabolic ions in blood

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Objective: Most women with ovarian cancer are diagnosed at advanced stage. Earlier diagnosis could improve survival outcome. The present study focused on the question whether low-mass metabolic ions in blood may provide important information for ovarian cancer screening.

Methods: Low-mass metabolic ions in sera from 25 patients with ovarian cancer and 22 controls have been extracted by methanol/chloroform, and analyzed by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry. From 6 times independent mass analyses, information of low-mass metabolic ions less than 2,000 m/z were obtained and used for principle component analysis-discriminant analysis (PCA-DA) to calculate discriminant score for ovarian cancer.

Results: Discriminant scores completely separated ovarian cancer from controls. The range of Fisher's discriminant ratio was 0.8969 to 1.6130, and the difference between lowest discriminant score of ovarian cancer and highest discriminant score of controls was 173.7. At least more than 125 low-mass metabolic ions were required for satisfying 100% of sensitivity and specificity.

Conclusion: Despite the small sample size, our present study suggests

information on unexploited low-mass metabolic ions in blood can be useful for ovarian cancer screening.

Keywords: Ovarian cancer, Screening, Low-mass metabolic ion

PP-055

Prognostic factors of advanced ovarian cancer patients treated with neoadjuvant chemotherapy

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Objective: The purpose of this study was to describe the prognostic factors of the advanced ovarian cancer patients who received interval debulking surgery (IDS) following neoadjuvant chemotherapy (NAC).

Methods: We investigated the prognostic significance of FIGO stage (III vs IV), histological response evaluation, cytology of ascites, the size of the residual tumor, and treatment free interval (TFI) by comparing Kaplan-Meier curves of the subgroups with the long-rank test. Cox's proportional hazard regression model was applied in risk indicator evaluation.

Results: From 2005 to 2009 a total of 66 patients were included. The median PFS was 12.5 months, and the median OS was 25 months. Univariate analysis revealed that the size of residual tumor >1cm, lower histological response rate, the positive of cytology of ascites, TFI <6month were significant prognostic factors in terms of overall survival. Multivariate analysis revealed that the size of residual tumor and TFI were significant prognostic factors.

Conclusion: The size of residual tumor and TFI are significant prognostic factor among the patients with treatment starting NAC followed by IDS.

Keywords: Ovarian cancer, Neoadjuvant chemotherapy, Prognostic factor

PP-056

Effects of neoadjuvant chemotherapy on patterns of initial recurrence in advanced-stage epithelial ovarian cancer

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Objective: The aim of this study is to compare the patterns of initial recurrence in patients with advanced-stage epithelial ovarian cancer who received neoadjuvant chemotherapy followed by interval debulking surgery (NAC) or primary debulking surgery (PDS).

Methods: Between 2000 and 2009, 255 patients with stage IIIC-IV ovarian cancer were treated in Seoul National University Hospital. Of these, 117 patients who received optimal debulking surgery followed by taxane/platinum-based adjuvant chemotherapy +/- preoperative

chemotherapy were included in the study population to analyze the patterns of initial recurrence. The clinicopathologic variables, including sites of initial recurrence, were compared between NAC and PDS groups using chi-square or Fisher's exact test, as appropriate.

Results: Thirty-seven patients received neoadjuvant chemotherapy, whereas 80 patients received primary debulking surgery. Clinicopathologic variables were similar between the two groups except the stage IV disease was more prevalent in NAC group (48.6% vs. 10.0%; $p < .001$). With a median follow-up period of 34.5 months (range 3.9 to 127.4 months), recurrence rates in PDS and NAC groups were similar with 71.3% (57/80) and 83.8% (31/37), respectively ($p = .144$). In overall, NAC group showed higher rates of distant metastases ($p = .044$). However, when the comparison was stratified by the stage, there were no statistically significant differences in sites of initial recurrence ($p > .05$).

Conclusion: Neoadjuvant chemotherapy did not affect the patterns of initial recurrence as well as the recurrence rates.

Keywords: Epithelial ovarian cancer, Neoadjuvant chemotherapy, Recurrence

PP-057

Expressions of emmprin and MCT1 in ovarian epithelial tumors

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Objective: Monocarboxylate transporter 1 (MCT1) and MCT1 associated molecule, emmprin, have been recognized as promising targets for cancer therapy. The aim of this study is to investigate the clinical significance of MCT1 and emmprin in human ovarian cancer.

Methods: Expressions of emmprin and MCT1 were analyzed by real time RT-PCR, immunoblot, and immunohistochemistry (IH).

Results: H was done in 205 patients with adenoma (A: 48 cases), borderline tumor (B: 48 cases) and carcinoma (C: 109 cases). The statistical analysis was performed using Whitney U test or χ^2 test. $p < 0.05$ was regarded as significant. Expression of MCT1 and emmprin were significantly high in C, compared to that in A ($p < 0.05$), whereas no significant difference in expression levels of MCT1 and emmprin was found between B and C ($p > 0.1$). The localization of emmprin at apical cell membrane was found in 4 of 48 cases (8%) in B and 108 of 109 cases (99%) in C, indicating that there was significant difference in the expression of apically localized emmprin between B and C ($p < 0.05$). In recurrent ovarian cancer, the signal of emmprin was also detected at cell membrane, indicating that emmprin at cell membrane was highly expressed in primary as well as recurrent ovarian cancer. The expression or localization of emmprin and MCT1 in carcinomas was not significantly associated with prognosis.

Conclusion: Emmprin may play a role in tumorigenesis in ovarian cancer, suggesting that emmprin is a validating target for ovarian cancer therapy.

Keywords: Ovarian cancer, Emmprin, MCT1

PP-058

A long-term follow-up of 176 Taiwanese with adult-type ovarian granulosa cell tumors - TAGO study group

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Objective: Because of rarity, indulgent clinical course, and of most importance, small sample size studies of adult-type ovarian granulosa cell tumors (A-OGCTs: GCTs) before, this study was conducted to report 176 pathology-confirmed GCTs.

Methods: Between 1984 and 2010, 176 Taiwanese patients from the multiple medical centers in Taiwan (TAGO Study Group) were evaluated.

Results: Mean age at the diagnosis was 46 years (range, 15-83), and near half of patients (45.7%) were fourth and fifth decades of life. The most common symptoms included abdominal pain (28.5%, n=58), following by irregular menstruation (16.7%, n=34). The mean size was 10.4 cm (range, 0.2-40). The stage distribution was 77.8%, 5.1%, 6.1%, and 11% in the stage I, II, III-V, and unknown, respectively. The median follow-up period was 60.7 months (range, 1-316 months). Recurrence rate was 21%. The overall 5- and 10-year survival rates were 96.5% and 94.1%, respectively. In univariate Cox-regression analysis, initial stage, presence of residual tumor after initial surgery, need for adjuvant chemotherapy and tumor size were associated with disease recurrence. Statistically presence of residual tumor after initial surgery and tumor size were significant.

Conclusion: The outcome of GCTs was good with near to 95% 5- and 10-year survival rates. The prognosis might be related to initial tumor status, such as initial stage, present of residual tumor after initial surgery, and tumor size (>13.5cm), suggesting complete removal of tumor at the initial operation was encouraged.

Keywords: Ovarian granulosa cell tumors, Long term follow up, Outcomes

PP-059

Expression profile and mutation of EGFR gene in epithelial ovarian cancer

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Objective: To investigate the correlation between EGFR expression profile, EGFR gene mutation and clinicopathological characteristics, in order to provide evidence for the treatment of ovarian carcinoma with EGFR-TKIs.

Methods: The 96 patients with FIGO stage III and IV epithelial ovarian cancer were included, who were treated in Sun Yat-Sen University Cancer Center during Jan 2003 to April 2009. The EGFR expression was detected in paraffin-embedded cancer tissues with immunohistochemistry assay. For the cases with positive EGFR staining, real-time PCR was employed to detect EGFR gene mutation. The correlation between EGFR expression profile with gene mutation status and clinicopathological characteristics was analyzed by chi-square test.

Results: EGFR expression rate was 78.2% in all cases with different levels. Patients who were with stage III disease, with poor differentiated tumor, ascites cytology positive and underwent suboptimal cytoreduction presented high expression level of EGFR in their tumor tissues. Four specimens harbored tyrosine kinase domain mutation and were in-frame deletion of 15 nucleotides (2235del15; E746_A750del) in exon 19 of EGFR gene. These four patients with the mutation presented similar clinicopathological characteristics, they were older than 50 years at diagnosis and had FIGO stage IIIC, poor differentiated diseases with high expression level of EGFR.

Conclusion: In most cases with epithelial ovarian cancer, EGFR expression were positive. The old patients with high level of EGFR expression in advanced and poorly differentiated ovarian carcinomas are likely to harbor EGFR mutation E746_A750del, and they might have better response to EGFR-TKIs.

Keywords: Epidermal growth factor receptor, Gene mutation, Epithelial ovarian cancer

PP-060

Body mass index during the chemotherapy may not affect the survival in patient with ovarian cancer: a multicenter analysis

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Objective: The purpose of this study was to evaluate the effect of change in body mass index (BMI) during the chemotherapy after cancer surgery on the progression free survival (PFS) and overall survival (OS) in patients with ovarian cancer.

Methods: Data was collected from three different hospitals from May 1997 to December 2010 retrospectively. Patients diagnosed with ovarian cancer, stage III or IV were included. We evaluated the basic patients' characteristics and clinical outcomes including BMI before operation, and before/after chemotherapy.

Results: Of those, a total of 101 patients met the inclusion criteria. The mean age and BMI were 56.7±11.1 (range: 29-78) and 23.9±2.9 (range: 15.9-30.5), respectively. Two patients (2.0%) were included in underweight, 36 (35.6%) in ideal, 52 (51.5%) in overweight, 11 patients (10.9%) in obese group based on the Asian criteria of BMI. There

was no difference in age, BMI, optimality of cytoreductive surgery (OCS), cancer stage, and histology among the hospitals. PFS and OS were affected by OSC, and OS was also affected by cancer stage. However, BMI before operation, Asian criteria of BMI, or the change in BMI before and after chemotherapy including the second line of chemotherapy had no impact on both PFS and OS. There was no significant difference in PFS and OS between patients with decreased BMI more than 3 and those with increased more than 3 during the chemotherapy.

Conclusion: BMI had no association with PFS and OS in ovarian cancer. Further large study will be needed to support our results.

Keywords: BMI, Ovarian cancer, Survival

PP-061

Prognostic factors responsible for recurrence in granulosa cell tumor of the ovary

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Objective: Granulosa cell tumor (GCT) of the ovary is an uncommon type of ovarian neoplasm and limited data are available in the literature to guide optimal treatment and follow-up protocol. The goal of this study was to evaluate clinicopathologic findings, surgical procedures, and prognostic factors for recurrence in GCT.

Methods: Between 1989 and 2011, 89 cases of GCT were treated in our institution. Patient characteristics, surgical treatment, adjuvant therapy, pathologic and follow-up information were collected from hospital charts and clinic records retrospectively. Kaplan-Meier and Cox proportional hazards analyses were used to identify the predictors for recurrence.

Results: GCT constituted 3% of all ovarian cancers in our institution during the study period. The median age was 45 (4-85) years. The median follow-up period was 42 (1-228) months. Eighty were stage I, 3 stage II, and 6 stage III. There were 14 cases of recurrence and 5 cases of disease-related death. The median time to relapse was 33 (3-100) months. Factors affecting the recurrence were FIGO stage ($p < 0.05$), tumor size ($p < 0.05$) and absence of postoperative residual tumor ($p < 0.05$), while intraoperative rupture of tumor, adjuvant chemotherapy and surgical staging including pelvic lymphadenectomy were not. Twenty-eight of 80 stage I patients underwent fertility sparing surgery with three recurrences. In multivariate analysis, tumor size and absence of postoperative residual tumor remained as independent risk factors for recurrence.

Conclusion: Recurrence in GCT might be associated with tumor size and absence of postoperative residual tumor. If there are no residuals, fertility sparing surgery for early staged patients with GCT wishing to

preserve fertility appears to be a safe alternative.

Keywords: Granulosa cell tumor, Recurrence, Prognostic factors

PP-062

The relationship between podoplanin expression and cell proliferation in ovarian clear cell adenocarcinoma

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Objective: Podoplanin is used as a marker for malignant mesothelioma or lymphatic vessels, and its expression has been investigated in various types of cancer cells. However, its cellular functions haven't yet been resolved in detail. We previously reported that podoplanin immunoreactivity was observed in epithelial ovarian carcinomas, and that it is expressed in 54.5% of clear cell adenocarcinomas (CCC), which is significantly more frequently than its expression in other histological types. We have also confirmed a significant inverse correlation between podoplanin expression and Ki-67 staining in CCC. In this study, we investigated the relationship between podoplanin expression and cell proliferation using CCC cell lines.

Methods: We established a podoplanin gene-transfected CCC cell line, designated RMG-1-PDPN, derived from RMG-1 cells (which do not express podoplanin). We also established a podoplanin down-regulated CCC cell line, designated OVMANA-PDPN-ND from OVMANA cells (which express podoplanin) by siRNA transfection. We investigated the expression of Ki-67, p27 and cyclin D1 mRNA by RT-PCR in each cell lines.

Results: Ki-67 expression decreased and p27 expression increased in RMG-1-PDPN cells compared with wild type cells. Ki-67 expression increased and p27 expression decreased in OVMANA-PDPN-ND cells compared with wild type cells. Cyclin D1 expression was not affected by podoplanin gene transfection or RNA interference.

Conclusion: These findings suggest that podoplanin inhibits cell proliferation. Recently, it was also reported that low proliferative activity may be associated with biological behavior and chemoresistance in CCC. Therefore, podoplanin may play a role of this biological characteristic of CCC.

Keywords: Ovarian clear cell adenocarcinoma, Podoplanin, Cell proliferation

PP-063

A possible clinical adaptation of CRM197 in combination with conventional chemotherapeutic agents for ovarian cancer

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Objective: Heparin-binding epidermal growth factorlike growth factor (HB-EGF) is a promising target for cancer therapy. We have already started a phase I study of CRM197, a specific HB-EGF inhibitor, for advanced ovarian cancer. In this study, we evaluated possible clinical adaptations of CRM197 in combination with conventional chemotherapeutic agents.

Methods: CRM197, bevacizumab, and paclitaxel were intraperitoneally administered either alone or in combination to ES2 human ovarian cancer cell-xenografted mice. The tumor volumes and microvessel densities (MVD) were determined.

Results: Enhanced antitumor effects were observed when paclitaxel was used in combination with bevacizumab or CRM197. The antitumor effect of paclitaxel/CRM197 was significantly higher than that of paclitaxel/bevacizumab. The MVD of mice treated with paclitaxel/CRM197 was significantly lower than that of mice treated with paclitaxel/bevacizumab.

Conclusion: CRM197 in combination with paclitaxel significantly blocked tumor formation and angiogenesis. These results suggest that paclitaxel is a suitable candidate for CRM197 combination therapy.

Keywords: HB-EGF, Targeted therapy, CRM197

PP-064

The complete cytoreductive surgery of the metastatic tumors on the diaphragm in patients with primary fallopian tube and ovarian cancer at advanced stage using ligasure system

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Objective: To explore the possibility, safety and effectiveness of the management of the metastatic tumors on the diaphragm in patients with primary fallopian tube and ovarian cancer at advanced stage.

Methods: The metastatic tumors on the diaphragm of the primary fallopian tube and ovarian cancer at stage IIIc were managed using the vessel sealing instrument (LigaSystem, ValleyLab, Tyko, USA).

Results: The metastatic tumors on the diaphragm of six cases of patients with primary fallopian tube and ovarian carcinoma at the stage IIIc were managed using LigaSure. The visible tumor-free states were reached in all cases. The serum CA125 value were decreased dramatically to normal after the operation and 1 regimen or 2 regimens of chemotherapies with platinum and paclitaxel in five cases, and the serum CA125 was decreased by more than 73% after the operation and one regimen of the chemotherapy in one case. No complication was occurred in this study. The blood loss during the operation was minimal. No blood transfusion was needed.

Conclusion: The management of the diaphragm involvement of the primary fallopian tube and ovarian carcinoma at advanced stage using vessel sealing instrument is simple, safe and effective.

Keywords: Ovarian cancer, Cytoreductive surgery, Diaphragm involvement

PP-065

Multiple modalities treatments had a survival benefit for the patients with brain metastasis from epithelial ovarian carcinoma - a Taiwan Gynecological Oncology Group (TGOG) study

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Objective: To evaluate the clinical characteristics and outcome of patients with brain metastases from epithelial ovarian carcinoma.

Methods: The medical records of patients with brain metastases from epithelial ovarian carcinoma were retrospectively reviewed from multiple medical centers in Taiwan under the TGOG. The clinical characteristics, treatments for primary ovarian cancer and brain metastases, and outcomes were analyzed.

Results: Totally 64 patients were recruited in this study. In univariate analysis, the survival from brain metastasis of patients with mucinous or clear cell carcinoma, resistant response to initial adjuvant chemotherapy, previous history of cancer relapse before brain metastasis, synchronous extra-brain metastasis and more than one brain metastatic lesions was poor. Longer interval between ovarian cancer and brain metastasis and multiple modalities treatments had positive impact on survival. In multivariate analysis, the most important prognostic factors were previous history of cancer relapse before brain metastasis (HR:4.39, 95 % CI:1.61-11.99, p=0.0039), numbers of brain metastatic lesions (HR:4.99, 95 % CI:1.71-14.60, p=0.0033) and multiple modalities treatments [two kinds of therapy (HR:4.31, 95 % CI:1.18-15.72, p=0.0272), one kind of therapy (HR:19.24, 95 % CI:4.57-81.02, p<0.0001), no treatment (HR:240.04, 95 % CI:29.72-1939.98, p<0.0001)].

Conclusion: Patients with brain metastases from epithelial ovarian carcinoma generally had a poor prognosis. Clinicians should keep alert to the neurological complaints of ovarian cancer patients and arrange appropriate image studies for early detection. Aggressive multiple modalities treatments had a benefit of the survival for these patients.

Keywords: Ovarian cancer, Brain metastases, Multiple modalities treatments

PP-066

Cost-utility analysis of combination therapy of pegylated Liposomal Doxorubicin (PLD) and carboplatin for Korean women with platinum-sensitive ovarian cancer

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Objective: Our objective was to perform the cost-utility analysis of comparing the combination therapy of Pegylated Liposomal Doxorubicin (PLD)/ Carboplatin with that of Paclitaxel/Carboplatin as a second-line treatment for women with Platinum-sensitive ovarian cancer among the Koreans.

Methods: Markov model was constructed with 10-year time horizon. Treatment sequence was consisted of 1st – 6th line chemotherapy and best supportive care. Cycle length, time interval for efficacy evaluation of chemotherapy, was 9 weeks. The model consists of four health states: Responsive, Progressive, Clinical Remission and Death. At any given time, a patient may either remain at the current therapy line or make a transition to the next therapy or death. Median time to progression (TTP) and survival were obtained through a systematic literature review and were pooled using meta-analytical approach. These outcomes were then converted into transition probabilities using formula. Direct cost included drug acquisition costs, costs for test, monitoring, best supportive care, and out-of-pocket cost.

Results: PLD/Carboplatin combination as the 2nd line therapy turned out to be more effective but with higher costs, showing incremental cost-effective ratio of Korean Won (KRW) 19,712,349 (equivalent to US\$ 18,093). This result was robust in all the deterministic sensitivity analyses, only except when the median TTPs were varied. The probability of cost-effectiveness for PLD/Carboplatin combination therapy was 50.6% at the willingness to pay of KRW 22,000,000 (US\$ 20,202), which is 2010 Korean GDP per capita.

Conclusion: It could be safe to assert that the PLD/Carboplatin combination therapy is an economically valuable option.

Keywords: Cost-utility analysis, Pegylated liposomal doxorubicin, Platinum-sensitive ovarian cancer

PP-067

Can preoperative serum human epididymis protein 4 (HE4) predict the primary cytoreductive outcome for advanced ovarian, tubal or peritoneal carcinomas?

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Objective: To evaluate the ability of preoperative serum human epididymis protein 4 (HE4) to predict the primary cytoreductive outcome in advanced epithelial ovarian carcinoma (EOC), tubal or peritoneal carcinomas.

Methods: The study reviewed the records of 90 patients with advanced ovarian, tubal or peritoneal carcinoma who underwent primary cytoreduction at our institution (from Nov. 2005 to Oct. 2010). Preoperative serum HE4 levels were detected using ELISA.

Results: Optimal debulking (OD) was achieved in 48% (43) of patients. The median HE4 level for patients with OD versus suboptimal debulking was 423 and 820 pmol/l, respectively ($p < 0.001$). The areas under the ROC curve for HE4 and CA125 were 0.716 and 0.594, respectively. The most useful HE4 cutoff value was 473 pmol/l. Suboptimal cytoreduction was obtained in 66.7% (38/57) of cases with HE4 \geq 473 pmol/l compared with only 27.3% (9/33) of cases with HE4 $<$ 473 pmol/l. At this threshold, the sensitivity, specificity, positive predictive value and negative predictive values to diagnose suboptimal debulking were 81%, 56%, 67%, and 73%, respectively. Logistic regression analysis showed that patients with HE4 levels \geq 473 pmol/l were less likely to achieve OD (odds ratio=5.044, $p=0.002$).

Conclusion: Serum HE4 is an important factor on preoperative assessment of ovarian cancer. Patients with HE4 levels \geq 473 pmol/l were less likely to achieve OC and the value of 473 pmol/L may be the threshold of predicting primary optimal cytoreduction. Larger prospective studies are needed to confirm the value of these findings.

Keywords: Human epididymis protein 4, Advanced ovarian cancer, Optimal debulking

PP-068

Apoptotic effect of NV-196, an isoflavone derivative

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Objective: The objectives of this study were to determine the efficacy of NV-196, a synthetic isoflavone derivative, as a chemosensitizer in chemoresistant CP70 and R182 epithelial ovarian cancer (EOC) cells and to characterize the mechanism behind its sensitizing effect.

Methods: EOC cells were treated with tenfold dilutions of NV-196 (0.1 to 10 μ g/ml) for 24 and 48 hours. Cell viability was determined by the CellTiter 96 Aqueous One Solution Cell Proliferation Assay. Apoptosis was assessed by Caspase-Glo assays and apoptotic cascade XIAP, caspase-2 and Bid were characterized by Western blot analyses.

Results: As a monotherapy, NV-196 showed decreased cell viability in a time- and dose-dependent manner in both CP70 and R182 cells. A significant increase in caspase-3 activity was observed in both cells. Caspase-8 and -9 activations were also observed. Western blots demonstrated Bid and caspase-2 activation and cleavage of XIAP. NV-196 enhances the cytotoxic effects of carboplatin and paclitaxel.

Conclusion: NV-196 induces cell death through the induction of apoptosis. Pretreatment with NV-196 may sensitize the ovarian cancer cells to carboplatin or paclitaxel. NV-196 may act as a chemosensitizing agent in epithelial ovarian cancer cells.

Keywords: Epithelial ovarian cancer, Apoptosis, NV-196

PP-069

Clinical significance of Galectin-1 expression in ovarian carcinomas

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Objective: Galectin-1 (gal-1) is a 14-kDa laminin-binding galectin involved in several biologic events including regulation of cancer cell proliferation and adhesion to the matrix. In this study, we investigated the clinical significance of Gal-1 expression including roles of prognostic marker or therapeutic target in epithelial ovarian carcinomas.

Methods: The expression of Gal-1 was evaluated by immunohistochemistry in 71 patients with ovarian carcinomas including 49 serous, 12 endometrioid and 4 mucinous types. We compared the expression of Gal-1 with participants' clinicopathological findings. In vitro experiments were conducted to elucidate the potential biologic role of gal-1 in ovarian cancer progression and invasion.

Results: Gal-1 immunostaining was significantly increased in the cancer-associated stromal cells compared with the normal, noninvaded stroma ($p < 0.001$). For Gal-1 peritumoral expression, strong staining group (score 2-3) has a poorer progression-free survival (PFS) compared with weak staining group (score 0-1) ($p = 0.03$; 34 and 55 months, respectively). With inhibition of galectin-1 gene expression by Gal-1 siRNA transfection and addition of anginex in two ovarian cancer cell lines, there was modest effect on cell growth inhibition assessed by MTT assay. The level of cell migration was significantly reduced by gal-1 siRNA and increased by added recombinant gal-1 protein.

Conclusion: Our results shows that cancer-associated stromal expression of Gal-1 was associated with poor PFS and expression of Gal-1 in cancer cell or fibroblast could mediate tumor progression and migration in ovarian carcinoma

Keywords: Ovarian carcinoma, Galectin-1, Prognosis

PP-070

The activation of Akt and ERK by platinum-based chemotherapy in ovarian cancer is associated with favorable patient outcome

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Objective: Several studies indicate that the phosphatidylinositol 3-kinase (PI3K)-Akt and the ERK (extracellular signal regulated protein kinase) activation is associated with poor prognosis in various cancers. However, these reports are the results in the specimens obtained prior to chemotherapy. Here, we tested if chemotherapy activates the Akt and ERK pathways and changes in their activation affect the prognosis in ovarian cancer patients whose specimens obtained before and after chemotherapy. We also examined the effect of chemotherapy on the cell proliferation and apoptosis to identify their role in the biology of ovarian cancers.

Methods: This study was carried out in a series of 10 ovarian cancer patients. PI3K-Akt and ERK activation was evaluated by immunohistochemical staining for phosphorylated Akt and ERK. Their correlation with patient outcomes was investigated using the Kaplan-Meier method. Cell proliferation and apoptosis were evaluated by Ki67, and by caspase-3 and cleaved PARP, respectively using immunofluorescent staining.

Results: Increase in Akt and ERK phosphorylation after chemotherapy was observed in five and eight patients, respectively out of ten patients examined. Interestingly, patients with Akt and ERK activation by chemotherapy showed a favorable overall survival compared with those with decrease or no change of Akt and ERK expression. In almost all patients, Ki67 expression was initially high and largely decreased after chemotherapy. Apoptotic markers expression was increased in almost all patients exposed to chemotherapy.

Conclusion: Our findings suggest that the Akt and ERK activation by chemotherapy may be associated with favorable prognosis in ovarian cancer.

Keywords: Ovarian cancer, Akt, ERK

PP-071

Feasibility of intraoperative intraperitoneal chemotherapy with paclitaxel in patients with epithelial ovarian cancer

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Objective: The aim of this study was to determine whether intraoperative intraperitoneal (IP) chemotherapy with paclitaxel improve progression-free and overall survival among patients with epithelial ovarian cancer.

Methods: Between January 2000 and December 2006, we reviewed the medical records of patients who underwent surgery for epithelial ovarian cancer except stage I. Univariate and multivariate analyses were executed to evaluate the potential variables for survival analysis.

Results: Of a total of 51 patients, 33 patients (64.7%) were intraoperative IP group and 18 patients (35.3%) were non intraoperative IP

group. Univariate analysis revealed that stage IV (HR, 6.7; 95% CI, 2.0–21.9; $p=0.002$ and HR, 6.2; 95% CI, 2.0–19.1; $p=0.001$, respectively) and level of postoperative CA 125 (HR, 1.5; 95% CI, 1.1–1.9; $p=0.004$ and HR, 1.4; 95% CI, 1.1–1.8; $p=0.017$, respectively) were significantly associated with overall survival (OS) and progression-free survival (PFS). On multivariate analysis, parity ≥ 3 (HR, 4.4; 95% CI, 1.1–18.6; $p=0.041$), stage IV (HR, 12.0; 95% CI, 2.2–65.5; $p=0.004$), intraoperative IP chemotherapy (HR, 0.3; 95% CI, 0.08–0.8; $p=0.021$) and number of chemotherapy (9–12) (HR, 0.2; 95% CI, 0.5–0.9; $p=0.039$) were significantly associated with OS. Stage IV (HR, 16.7; 95% CI, 3.2–86.7; $p=0.001$), intraoperative IP chemotherapy (HR, 0.5; 95% CI, 0.07–0.6; $p=0.05$) and number of chemotherapy (9–12) (HR, 0.1; 95% CI, 0.03–0.6; $p=0.01$) were significantly associated with PFS.

Conclusion: Adding IP chemotherapy with paclitaxel during operation significantly reduced the risk of death and disease recurrence in patient with epithelial ovarian cancer.

Keywords: Epithelial ovarian cancer, Intraoperative intraperitoneal chemotherapy, Paclitaxel

PP-072

The use of weekly topotecan in gynecologic cancer: Kaohsiung Chang Gung experience

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Objective: The prognoses of patients with recurrent epithelial ovarian cancer and cervical cancer are poor after first line platinum-based chemotherapy. This situation becomes more and more difficult to handle in the presence of a platinum-resistant condition. Topotecan 1.5 mg/m² on day 1–5 of a 21-day cycle is often employed as a second-line therapy however with a significant high rate of grade 3,4 hematologic toxicities. We attempted to investigate the safety and efficacy of weekly topotecan in heavily pretreated recurrent ovarian and cervical cancer patients.

Methods: We retrospectively review medical records of patients with recurrent epithelial ovarian cancer and cervical cancer who had received weekly topotecan between Nov 2008 and Nov 2009. Eighteen patients (12 ovarian cancer, 6 cervical cancer) were identified and they all had received at least 1 prior lines of platinum-based chemotherapy. Topotecan was administered at the dose of 2.75–4 mg/m² via a 30-minute IV infusion on day 1, 8, 15 of a 28-day cycle until disease progression or unacceptable toxicity occurred.

Results: Thirteen patients (72.2%) had received 2 prior lines of chemotherapy. Median number of chemotherapy cycles was 2 (range 1–6). A total of 41 cycles were administered. Main toxicities (grade 3,4) included anemia (0%), leukopenia (17%), and thrombocytopenia

(11%). One patient (5.6%) showed clinical partial response, while 7 patients with stable disease (38.9%) were observed. Ten patients (55.6%) progressed on therapy.

Conclusion: Although topotecan administered at weekly dosage (2.75–4 mg/m²) is not active in our study, it seems also to be a more tolerable regimen compared to the classical 5-day schedule.

Keywords: Ovarian cancer, Topotecan, Chemotherapy

PP-073

A study of long term survival after recurrence of epithelial ovarian cancer

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Objective: Recurrent ovarian cancer mostly cause poor prognosis, while there are a few case which show long survival. The aim of this study was to investigate the prognostic factors of long-term survival case, and establish the treatment plan for recurrent ovarian cancer.

Methods: We retrospectively retrieved 61 women with recurrent ovarian cancer who were received primary treatment between 1996 and 2006. A variety of clinicopathological factors were recorded.

Results: Median survival of all recurrent case was 37.3 months. 5-year survival after recurrence was 35%, and 10-year survival was 20%. FIGO stage, histological type, peritoneal dissemination at primary status, metastasis at primary status, or the accomplishment of primary operation were not correlate with prognosis after recurrence. Disease-free interval after primary treatment, the number of the recurrent tumor, and dissemination at recurrent status correlate with prognosis. 23 case of recurrent patient received debulking surgery. 5-year survival after recurrence was 50%, and 10-year survival was 35%. Noticeably, complete debulking surgery associates with longer survival. 17 case of recurrent patient received irradiation therapy. 5-year survival after recurrence was 50%, and 10-year survival was 45%.

Conclusion: Recurrent ovarian cancer often show poor outcome, but some cases that received complete surgery or irradiation therapy for localized recurrent tumor show long survival. We remain in need to evaluate the tumor status and indication of local complete therapy.

Keywords: Recurrent ovarian cancer, Long term survival, Prognostic factor

PP-074

Risk of malignancy index for diagnosis of ovarian cancer

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Objective: To evaluate the ability of the risk of malignancy index (RMI I) for discriminating between benign and borderline or malignant ovarian tumor.

Methods: A prospective study was conducted in 69 women with pelvic masses admitted for gynecologic surgery at Ramathibodi Hospital, from January 2011 to June 2011. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of RMI I were calculated.

Results: In our study, there were 12 cases (17.4%), 1 case (1.5%), 56 cases (81.2%) diagnosed ovarian cancer, borderline ovarian tumors and benign ovarian tumors, respectively. Using a cut-off level of 200 to indicate malignancy and borderline ovarian tumor, the RMI I gave sensitivity of 46.1%, specificity of 85.7%, PPV of 42.9%, and NPV of 87.3%. The optimal cut point of RMI I was generated at the level of more than 150 which gave sensitivity of 69.2%, specificity of 83.9%.

Conclusion: In the present study, the RMI I is able to discriminate between benign and borderline or malignant ovarian tumor.

Keywords: Risk of malignancy index, Ovarian cancer, Diagnosis

PP-075

Epigenetic regulation and promoter methylation of ovarian cancer stem cell marker CD133

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Objective: To confirm epigenetic regulation of the expression of CD133 being considered as a candidate marker of cancer stem cell in epithelial ovarian cancer

Methods: We used the epithelial ovarian cancer cell line (IGROV, OVCAR8, and SKOV3) and the endometrial adenocarcinoma cell line (Ishikawa) for control.

Results: To determine the influence of microenvironment, IGROV, OVCAR8, SKOV3, and Ishikawa were incubated in 37°C with 5% CO₂/94% N₂/1% O₂ in a hypoxic chamber and with treatment of TGF-β1, respectively. CD133 mRNA of all cell line decreased over time than in normoxia and no TGF-β1, confirmed by real-time PCR and flow cytometry (FACS). For check of factors of other epigenetic regulation, we used 5'-aza-2'-deoxycytidine (DAC) and trichostatin A (TSA), respectively. And then, CD133 mRNA and protein level was measured by real-time PCR, FACS, and methylation-specific PCR (MSP). The expression of CD133 was increased after treatment of DAC, but decreased after treatment of TSA.

Conclusion: This study means that cancer stem cell of epithelial ovarian cancer can be regulated epigenetically. With further study, epigenetic regulation of cancer stem cell will be applied in the treatment of epithelial ovarian cancer.

Keywords: Cancer stem cell, CD133, Epigenesis

PP-076

Trends in clinicopathologic characteristics in Japanese women with endometrial cancer, 1990-2010

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Objective: Over the past 20 years, the incidence of endometrial cancer is increased remarkably in Japan. The rate of elderly women is also increased in the population of Japan. We examined the impact of advanced age on surgical outcomes, clinicopathologic factors of the tumor and survival in women with endometrial cancer.

Methods: We reviewed the medical records of 319 women, undergoing surgery for endometrial cancer between 1990 and 2010. Patient demographics, surgical outcomes, clinicopathologic factors and survival were compared based on two groups (A, 1990-2000, 116cases) and (B, 2001-2010, 203cases). The histologic subtypes were reevaluated with immunohistochemical expressions of p53, estrogen receptor and Ki-67.

Results: Women more than 70 years of age in groups A and B were 11 (9%) and 54 (27%), respectively ($p < 0.001$). Women with serous carcinoma, clear cell adenocarcinoma and carcinosarcoma in groups A and B were 6 vs. 24, 1 vs. 7 and 5 vs. 13, respectively ($p < 0.001$). The averages of age in women with serous carcinoma, clear cell adenocarcinoma and carcinosarcoma were 69.5, 69.6 and 68.3 years of age, respectively. The surgical stage, survival of patients, body mass index (BMI) and parity showed no significant difference between groups A and B. Women more than 70 years of age received less aggressive care than younger women.

Conclusion: The increase in number of elderly women in the Japanese population is probably related to the increase in that of high-risk endometrial cancers. A study is needed to investigate prevention strategies and to improve the treatment of elderly patients with high-risk endometrial cancer.

Keywords: Endometrial cancer, Japanese women, Clinicopathologic outcomes

PP-077

Therapeutic effect of EZH2 silencing in orthotopic endometrial cancer model

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Objective: EZH2 is overexpressed in a number of malignancies, and might be an attractive target for treatment. However, the biological significance and effect of its silencing has not been known in endo-

metrial cancer. Here, we examined therapeutic efficacy of EZH2 silencing alone or combined with chemotherapy, and revealed its downstream molecular mechanism.

Methods: EZH2 expression, silencing by siRNA, and resulting molecular downstream mechanism were examined in endometrial cancer cell lines by Western Blot. Viability, apoptosis and invasion ability were investigated in endometrial cancer cells. Therapeutic effect of in vivo EZH2 silencing single or combined with chemotherapy was examined using siRNA incorporated into chitosan nanoparticles (siRNA/CH-NP) via orthotopic endometrial cancer models.

Results: EZH2 was expressed in all endometrial cell lines which we examined, Ishikawa, Hec-1A, Spec-2 and KLE. In vitro cell viability, apoptosis and invasion assays showed that EZH2 silencing decreased cell viability and invasion ability, and increased apoptosis. Also, EZH2 silencing enhanced cytotoxicity of paclitaxel, docetaxel and CDDP. EZH2 silencing using siRNA/CH-NP resulted in significant inhibition of tumor growth compared to control siRNA/CH-NP (76.7% reduction in Ishikawa, $p < 0.0001$; 70.7% reduction in Hec-1A, $p < 0.0001$; 81.8% reduction in Spec-2, $p = 0.02$). In addition, EZH2 siRNA/CH-NP in combination with taxane showed significant chemo-sensitizing anti-tumor effect compared to taxane with control siRNA/CH-NP (92.3% for Ishikawa, $p < 0.001$; 92.5% for Hec-1A, $p < 0.001$; 84.9% for Spec-2, $p < 0.0001$). These effects were mediated by decreased tumor cell proliferation and angiogenesis, and increased apoptosis.

Conclusion: The preclinical data for endometrial cancer treatment by EZH2 silencing is promising and supports further clinical trial for endometrial cancer.

Keywords: EZH2, Endometrial cancer, siRNA

PP-078

Fludarabine therapy in endometrial cancer: a possible alternative treatment

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Objective: Endometrial cancer is one of the most common gynecologic malignancies, and the numbers of patients has been increased almost twice in this decade in Japan. Accompanied with the increasing rate, we sometimes encountered patients resistant to conventional chemotherapy with platinum agents, and it is keen to discover new drug which is effective to chemo-resistant cases. Fludarabine is a nucleoside analog used for chronic lymphocytic leukemia and also effective to some NCI60 cell lines which are resistant to cisplatin, doxorubicin, and paclitaxel.

Methods: To predict the effectiveness of fludarabine in endometrial cancer, we did a binary analysis of microarray data. We did the cell cy-

toxicity assay and apoptosis assay to see the cytotoxic effect of fludarabine. We also measured the Caspase 3/7 activity in vitro. Finally, we measure the effect of fludarabine in endometrial xenograft tumor.

Results: Binary analysis of microarray data predicted fludarabine might be specifically effective to endometrial cancers resistant to conventional therapies. In our study, fludarabine inhibited cells proliferation and increased apoptosis rate more significantly in a cisplatin-resistant endometrial cancer cell line, HEC-1A, than HEC-50B ($p < 0.001$). By fludarabine treatment, Caspase 3/7 activity was induced higher in HEC-1A than HEC-50B ($p < 0.001$), and the growth of HEC-1A inoculated tumor was superior inhibited than cisplatin ($p < 0.05$)

Conclusion: These results indicate that fludarabine may play a potent role in the treatment for chemo-resistant endometrial cancer.

Keywords: Fludarabine, Endometrial cancer, Chemotherapy

PP-079

Patterns of recurrence in endometrial cancer patients at risk of lymph node metastasis or recurrence according to extent of lymphadenectomy

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Objective: The purpose of this study was to compare the patterns of recurrence and survival in patients with risk of lymph node metastasis or recurrence according to the extent of lymphadenectomy (LND).

Methods: We selected 257 patients with risk of lymph node metastasis or recurrence who underwent definitive surgery as the first treatment between 1995 and 2009. These patients underwent hysterectomy, bilateral salpingo-oophorectomy and systematic pelvic lymphadenectomy (PLND) with or without para-aortic lymphadenectomy (PALND). We identified the patterns of recurrence according to the type of LND and compared survival between intrapelvic and extrapelvic recurrence.

Results: Among the 257 patients, 164 patients had PLND, and 93 patients had PLND+PALND. Regarding lymph node metastasis in PLND+PALND group, approximately 40% patients had involvement of para-aortic nodes. Thirty-six patients (14%) out of the 257 patients showed recurrence. The rate of extrapelvic recurrence was significantly higher in the PLND group compared to the PLND+PALND group (96.0% vs. 36.4%, respectively, $p < 0.001$). In the analysis of recurrent patients, survival defined at the time from first evidence of recurrent disease to their last follow-up was significantly poor in the extrapelvic recurrent group than in the intrapelvic recurrent group ($p = 0.027$).

Conclusion: The incidence of extrapelvic recurrence was significantly higher in the PLND group than in the PLND+PALND group.

Keywords: Endometrial cancer, Para-aortic lymphadenectomy, Recurrence

PP-080

Accuracy of intraoperative frozen section of endometrial cancer using the revised FIGO staging system compared with previous one

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Objective: The objective of this study was to assess the value of intraoperative frozen section (IFS) diagnosis for myometrial invasion and histology of endometrial cancer using the revised FIGO staging system.

Methods: The medical records of 303 patients with endometrial cancer who underwent surgery with intraoperative diagnosis at the Osaka University Hospital between January 1999 and December 2008 were reviewed. IFS diagnosis was retrospectively analyzed for the accuracy rates of myometrial invasion and histology compared with the final diagnosis, and with preoperative prediction by MRI and endometrial curettage.

Results: When using the previous FIGO staging system, the accuracy rate of IFS for the diagnosis of myometrial invasion was 77%, while the accuracy rate of preoperative prediction by MRI was 54%. However, using the newly revised FIGO staging system for myometrial invasion, the accuracy rate of IFS was 87% and preoperative prediction by MRI was 82%, respectively. The accuracy rate of IFS for the diagnosis of histology was 71%, whereas the accuracy rate of preoperative prediction by endometrial curettage was 68%.

Conclusion: We still find IFS diagnosis to be a necessary and reliable method for accurate staging and adequate surgical management for endometrial cancer. We also found that preoperative diagnosis by MRI was also an effective method for surgical management of endometrial cancer. Therefore, we cannot conclude that MRI and D&C for preoperative diagnosis can replace IFS diagnosis, even when using the revised FIGO staging system

Keywords: Endometrial cancer, Frozen section, Revised FIGO staging system

PP-081

Feasibility and outcome in obese patients with endometrial cancer: a Korean outcome research & analysis in gynecologic cancers study

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Objective: To compare clinicopathologic characteristics and surgical outcomes in women with endometrial cancer according to body mass index (BMI).

Methods: From June 2009 to October 2010, prospective observational study without randomization of 219 patients treated by surgery from 10 hospitals nationwide.

Results: Patients were divided according to the WHO guidelines for Asia-Pacific populations and the distributions of BMI were as follows: 3 (1.4%) patients in underweight (BMI <18.5 kg/m²), 69 (31.5%) patients in normal weight (BMI, 18.5–22.9 kg/m²), 52 (23.7%) patients in overweight (BMI, 23.0–24.9 kg/m²), 72 (32.9%) patients in obese (BMI, 25.0–29.9 kg/m²), and 17 (7.8%) patients in morbid obese (BMI ≥30.0 kg/m²). Age, co-morbidities, operation method (laparoscopy or laparotomy), surgery type and postoperative adjuvant therapy were not different between non-obese patients (BMI <25.0 kg/m²) and obese patients (BMI ≥25.0 kg/m²) but history of previous surgery was more common in obese patients but marginally significant (21.8% vs. 33.7%, p=0.060). Regarding to surgical outcomes, operation time was significantly longer in obese patients (206min vs. 236 min, p=0.008) but blood loss, lymph node yield, hospital stay, foley removal, transfusion rate and perioperative complication were not statistically significant. Regarding to pathologic results, lymph node metastasis was more common in non-obese patients (4.8% vs. 0%, p=0.042) but there were no difference in terms of lymphovascular space invasion, tumor grade, histologic type and FIGO stage.

Conclusion: Surgical outcomes do not seem to be significantly influenced by BMI except operation time so the laparoscopic approach can be the alternative method for obese patients. Lymph node metastasis is more common in non-obese women but long-term follow-up is needed.

Keywords: Endometrial cancer, Multicenter prospective study, Body mass index

PP-082

The adjuvant management of FIGO stage IIIA–IVB uterine endometrioid adenocarcinoma—short term, single institute experience

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Objective: Endometrioid adenocarcinoma (EA) is the most common uterine malignancy. Comprehensive surgical staging and/or debulking procedure is the standard primary therapy of EA. However, the following adjuvant therapy in stage IIIA–IVB cases is still controversial and debated because of insufficient case number and lacking of effective

evidence. Our aim is to review the recent accepted adjuvant therapy after surgery.

Methods: A retrospective chart review was carried out after IRB approval in a medical center—Mackay memorial hospital, Taipei, Taiwan from 2007 to 2011. Histology was restricted within only endometrioid adenocarcinoma. Survivor analysis was performed with Kaplan–Meier’s method, compared with log–rank test.

Results: Twenty–nine cases were eligible into this retrospective review, 6 (20.7%), 10 (34.5%), 11 (37.9%) and 2 (10%) cases were stage IIIA, IIIC1, IIIC2 and IVB. In adjuvant settings, two (6.9%) cases received follow–up without post–operative therapy. Twenty (69.0%) cases had primary combination chemotherapy—8 received cisplatin plus doxorubicin, 4 received paclitaxel plus carboplatin, 5 received additional radiotherapy after completing the chemotherapy and 3 received sandwich setting (chemotherapy–radiation therapy–chemotherapy). Five (17.2%) cases received primary whole pelvic radiation therapy and vaginal brachytherapy, one of them had additional following courses of chemotherapy. Two (6.9%) cases received primary concurrent chemo–radiation therapy with weekly cisplatin. In the analysis of progression free survival and overall survival, no significant difference is observed so far.

Conclusion: In this short–time–interval, small scale retrospective review, various adjuvant therapy of stage IIIA–IVB EA can not demonstrate the survival difference.

Keywords: Uterine endometrioid adenocarcinoma, Adjuvant therapy, Advanced stage

PP–083

Preoperative systemic inflammatory response markers in predicting lymph node metastasis in endometrioid endometrial adenocarcinoma

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Objective: To evaluate the predictive value of preoperative systemic inflammatory response (SIR) markers for diagnosis of lymph node (LN) metastasis in endometrioid endometrial adenocarcinoma.

Methods: A total of 319 patients who were pathologically proven as endometrioid endometrial adenocarcinoma after staging operations from 2001 to 2009 were retrospectively reviewed. Serum CA–125 levels and preoperative SIR markers were assessed regarding LN metastasis: neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), C–reactive protein (CRP), albumin, platelet and fibrinogen. The receiver operating characteristic (ROC) curves were plotted for each SIR marker and their combinations.

Results: NLR, PLR, CRP, and serum CA–125 levels of LN positive group

were higher than those of LN negative group ($p < 0.001$, 0.001, 0.045, and < 0.001 , respectively). Serum albumin level of LN positive group was significantly lower than that of LN negative group ($p = 0.005$). The ROC curve demonstrated the best cut–off values of NLR (≥ 1.73), PLR (≥ 10.37), CRP (≥ 0.79 mg/dl), albumin (≤ 4.05 g/dl), and CA–125 (≥ 43.00 U/ml) for the preoperative diagnosis of LN metastasis. Four combination tests of NLR, PLR, albumin, and fibrinogen showed 96.8%/31.9% of sensitivity/specificity and 13.3%/98.9% of positive predictive value/negative predictive value. Addition of CA–125 did not improve the test profiles of the four combination tests.

Conclusion: The preoperative SIR evaluation appears to be a useful method of predicting preoperative LN metastasis in endometrioid endometrial adenocarcinoma.

Keywords: Systemic inflammatory response markers, Lymph node metastasis, Endometrioid endometrial adenocarcinoma

PP–084

Endometrial carcinoma: where do we stand? A review of clinicopathological profile over a decade

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Objective: To study the clinicopathological profile and management of patients diagnosed with endometrial carcinoma

Methods: 217 cases of endometrial carcinoma treated at gynaecology department of Safdarjung hospital from 2001–2010 were reviewed retrospectively with regard to presentation, management and outcome.

Results: The median age was 56 years. Irregular cycles were the main presenting complaint in young women. Postmenopausal women presented with bleeding 2–22 years after menopause. Endometrial aspiration biopsy diagnosed 78% cases, while in remaining 22% hysteroscopy directed biopsy clinched diagnosis. Endometrial thickness on ultrasound varied from 3–30mm in menopausal women. 72% cases were diagnosed at early stage (I–II). Adenocarcinoma accounted for 79% cases. Lymph node metastasis was found in 13% of stage I disease, non–endometrioid variety accounted for 80% of these cases. Distant metastasis was seen in 10% cases. Adjuvant therapy was required in 74% cases. Recurrence and relapse was seen in 20% cases.

Conclusion: In all cases of irregular bleeding / PMB endometrial aspiration biopsy should be performed for early diagnosis. Hysteroscopy directed biopsy is must in symptomatic cases even with negative EB. Staging laprotomy with selective pelvic lymphadenectomy should be performed in all diagnosed cases. Adenocarcinoma responds well to radiotherapy and has better prognosis as compared to other variants.

Keywords: Endometrial carcinoma, Endometrioid carcinoma, Pelvic lymphadenectomy

PP-085

Molecular pathological analysis of single tumor gland using crypt isolation method in 25 endometrial carcinoma cases

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Objective: Genetic alterations of endometrial adenocarcinoma are accumulated in individual tumor glands during progression. We aimed to clarify whether endometrial carcinoma consists of various single tumor glands with different molecular abnormalities by analyzing the molecular abnormalities of single tumor glands by using the crypt isolation method. In addition, we investigated the relationship between the forms of molecular abnormalities in single tumor glands and prognosis.

Methods: 25 cases of endometrial endometrioid adenocarcinoma subjected to surgery were examined. To elucidate the differences in molecular abnormalities among single tumor glands, individual tumor glands were analyzed for loss of heterozygosity (LOH), microsatellite instability (MSI), and the target gene of MSI. Furthermore, DNA methylation was examined by the methylation-specific polymerase chain reaction (PCR).

Results: Frequencies of LOH at some loci in representative tumor glands sample that was used crypt isolation method were higher than frequencies of LOH in conventional method that was not used crypt isolation method, containing interstitial tissue. MSI was detected in 40% (10/25) of endometrioid carcinoma. In 16 of 25 cases, diversity of gene abnormalities among single tumor gland samples was confirmed. Poor prognosis 4 cases had Heterogeneity among single tumor glands, and LOH in a plurality of regions.

Conclusion: It became clear that even within the same sample, tumor was composed of various tumor glands with different molecular abnormalities. Further, it suggested that the form of gene abnormalities in single tumor glands is related to prognosis.

Keywords: Crypt isolation method, Loss of heterozygosity, Microsatellite instability

PP-086

Insulin receptor isoform a can affects biological characteristics and signaling pathway of endometrial carcinoma cells

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Objective: To investigate insulin receptor isoform A's effects of the biological characteristics and signaling pathways in endometrial carcinoma cell line RL95-2.

Methods: IR-A-pc DNA3.1 was constructed and transfected RL95-2 cell, Normal and pcDNA3.1-Null cell line were utilized as the control groups. To analyze the influence of IR-A over expression, the cell growth rate was detected with MTS, cell cycle progression and apoptosis rate was analyzed by Flow cytometry. After 0min, 5min, 10min, 20min, 30min and 60min stimulated with insulin, IGF-I and IGF-II (10^{-8} mmol/L) as well as 10min with increasing concentration (10^{-8} mmol/L, 10^{-7} mmol/L, 10^{-6} mmol/L), we examined the activation of extracellular signal-regulated kinase (ERK) 1/2 phosphorylation, a key molecule in the mitogen-activated protein kinase (MAPK) pathway.

Results: The growth rate of RL95-2-IR-A cell was significantly lower than those in the two controls. The DNA content in S phase of RL95-2-IR-A was higher than those in the two controls ($p < 0.05$). The percentage of apoptotic cells has no significant differences in three cell lines. The levels of ERK 1/2 phosphorylation in RL95-2-IR-A is increased than two controls, but not increased after stimulated than before.

Conclusion: IR-A over expression can raise the growth rate of RL95-2 by increase the DNA content in S phase. (MAPK) pathway may be Activated through IR-A, but the level is not dependent on the stimulation time and the concentration of insulin, IGF-I and IGF-II.

Keywords: Endometrial carcinoma, Insulin receptor isoform A, Signaling pathway

PP-087

The expression and clinical significance of clusterin and Ki67 in endometrial cancer

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Objective: To explore the expression pattern and clinical significance of the CLU and proliferation indices ki67 in endometrial cancer.

Methods: 64 cases treated at The Third affiliated hospital of Sun Yat-sen University during 2005-2010 were enrolled in the study group. The relationship was analyzed for the expressions of CLU and Ki67 with clinical factors.

Results: In this study positivity of CLU in endometrial cancer, 40 cases of Adenocarcinoma, 37.5% (15/40) moderate staining, 42.5% (17/40) strong staining, 15% (6/40) weak staining. Positivity of clusterin in secretory phase of endometrium 18% (2/11) moderate stained, 64% (7/11) strong stained. Similarly in proliferative phase 61% (8/13) moderate staining, 8% (1/13) strong staining. The Ki67 positivity in endometrial cancer comprised 41% (16/39) of weak staining, 23% (9/39) of moderate staining, and 13% (5/39) of strong staining. In secretory phase with Ki67, 9% (1/11) weak staining, 18% (2/11) moderate staining. In proliferative phase, total 14 cases stained among them 7% (1/14) weak staining, 7% (1/14) moderate stained. Clusterin was significantly more highly ex-

pressed to age, stage and grade. We found higher expression of clusterin in endometroid carcinoma using immunohistochemistry ($p < 0.05$). The correlation of clusterin and Ki-67, showed no significant relationship. Non parametric correlation p value=0.667, $r_s=0.05$.

Conclusion: Our data suggests that clusterin in immunohistochemistry might be the clinically significant in tumorigenesis and progression of disease. Therefore it showed that Clusterin expression have distinct role in carcinogenesis.

Keywords: Clusterin, Endometrial cancer, Immunohistochemistry

PP-088

The investigation of expression and role of insulin receptor isoforms in endometrial carcinoma

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Objective: Hyperinsulinemia/diabetes in women is high-risk factors associated with endometrial carcinoma (EC), the molecular mechanism of which remains unclear. The aim of the study is to explore the expression and role of insulin receptor isoforms (IR-A and IR-B) in EC. Hyperinsulinemia/diabetes in women is high-risk factors associated with endometrial carcinoma (EC), the molecular mechanism of which remains unclear. The aim of the study is to explore the expression and role of insulin receptor isoforms (IR-A and IR-B) in EC.

Methods: The expression of IR isoforms were detected by RT-PCR and real-time PCR in four EC cells (Ishikawa, KLE, RL95-2, HEC-1-A) and EC tissues from 42 cases. The relationships between the expression of IR isoforms and the clinicopathological parameters of EC tissues were analyzed. A eukaryotic IR-A expression plasmid was constructed for overexpression of IR-A in RL95-2 cells, which originally has a low expression of IR-A. MTS method was used to determine the proliferation curves in RL95-2 cells with or without IR-A transfected.

Results: IR-A and IR-B were co-expressed in four EC cells and EC tissues. The expression of IR-A and IR-B in EC tissues had no significant relevance with FIGO stage ($p=0.838$, $p=0.146$), cell differentiation ($p=0.556$, $p=0.272$), depth of myometrial invasion ($p=0.440$, $p=0.206$), invasion of lympho-vascular space ($p=0.115$, $p=0.104$) and lymphonodes metastasis ($p=0.864$, $p=0.166$). The expression of IR-A in EC patients with type 2 diabetes mellitus (DM) was significantly higher than that in patients without DM ($p=0.043$). The overexpression of IR-A showed a significant proliferation-promoting effect on RL95-2 cells.

Conclusion: The two isoforms of IR are co-expressed in EC, and the overexpression of IR-A may have the potential of promoting EC cell proliferation.

Keywords: Endometrial carcinoma, Insulin receptor isoform, Hyperinsulinemia

PP-089

Evaluation of risk factors in surgically staged endometrial cancer

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Objective: To evaluate the risk factors and lymph node status in surgically staged endometrial cancer patients.

Methods: Medical records of 141 biopsy proven endometrial cancer patients who underwent surgical staging including pelvic and para-aortic lymphadenectomy at Cheil General Hospital & Women's Healthcare Center from January 2008 to September 2010 were retrospectively analyzed. Magnetic resonance imaging (MRI) and intraoperative frozen section (IFS) of uterus were used as pre- and intraoperative risk factor evaluation, respectively. Both methods were correlated with final pathology.

Results: The mean age of the patients was 53.0 years (range, 31-82 years). Of the 141 cases reviewed, 97 patients had an MRI preoperatively and depth of myometrial invasion, cervical stromal invasion and lymph node (LN) enlargement on MRI correlated with final pathology in 87.6%, 89.7% and 85.6%, respectively. 97 patients were evaluated with IFS of uterus and depth of myometrial invasion, cervical stromal invasion, histologic grade and histologic type on uterine IFS correlated with final pathology in 93.8%, 90.7%, 86.6% and 83.5%, respectively. Of the 30 patients who were identified as low-risk in both MRI and uterine frozen section, 14 patients had one or more risk factors in final pathology and 6 underwent adjuvant therapy. All 30 patients had no pelvic or para-aortic LN metastasis in final pathology.

Conclusion: Correlation rate for pre- and intraoperative evaluation of risk factors using MRI and IFS are substantial. But, surgical staging for endometrial cancer patients may be needed to accurately evaluate the risk factors and guide postoperative adjuvant therapy.

Keywords: Endometrial cancer, Risk factors, Surgical staging

PP-090

Effects of a selective COX-2 inhibitor in patients with uterine endometrial cancers

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Objective: COX-2 is highly expressed in endometrial cancers, suggesting that a selective COX-2 inhibitor could be valuable for treating endometrial cancers that overexpress COX-2. In this study we investigated the anti-tumor effects of the selective COX-2 inhibitor etodolac on endometrial cancer patients.

Methods: Etodolac [400 mg, bid, for two weeks] was administered

preoperatively to 21 endometrial cancer patients who had provided informed consent. Using pre-treatment biopsies and post-treatment surgical specimens, the expression levels of COX-2, Ki-67, p53, p21, p27, and cyclin D1 were evaluated by immunohistochemistry and the apoptotic index [AI] was determined by TUNEL staining. Preoperative biopsies and surgical specimens from 32 patients with endometrial cancer not treated with etodolac served as controls.

Results: Surgical specimens from COX-2 positive endometrial cancer patients treated with etodolac had significantly reduced expression levels of COX-2, Ki-67, p53, p21, p27, and cyclin D1 as determined by immunohistochemistry, while AI was not affected. These markers were unchanged for COX-2 negative endometrial cancer patients treated with etodolac and the control group.

Conclusion: The selective COX-2 inhibitor etodolac showed anti-proliferative effects by suppressing COX-2 and cell-cycle regulator protein expression in patients with endometrial cancer positive for COX-2 expression. This study demonstrates that a selective COX-2 inhibitor is a potentially beneficial treatment for COX-2 positive endometrial cancers.

Keywords: Endometrial cancer, COX-2, COX-2 inhibitor

PP-091

Prediction of hidden malignancy in endometrial hyperplasia patients

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Objective: To examine clinical parameters of hidden endometrial carcinoma if endometrial biopsy results in endometrial hyperplasia

Methods: Of 210 patients with endometrial hyperplasia on endometrial biopsy, 121 women underwent hysterectomy from 2000 to 2010 in SNUH. Clinical parameters were reviewed retrospectively and analyzed with Student t-test and Pearson's chi-square test.

Results: 121 women who underwent hysterectomy preceding endometrial biopsy were grouped by endometrial biopsy results into complex atypical hyperplasia, complex hyperplasia without atypia, simple atypical hyperplasia, simple hyperplasia without atypia: 34 (28.1%), 38 (31.4%), 13 (10.7%), 36 (29.8%), respectively. Final pathological results after hysterectomy were endometrial hyperplasia (40, 33.1%), endometrial carcinoma (24, 19.8%), mixture of endometrial hyperplasia and carcinoma (33, 27.3%), and no abnormal lesion (24, 19.8%). Statistically significant clinical risk factors were infertility, hormone replacement therapy ($p=.098, .046$, respectively). Age at diagnosis and age at menopause were the other risk factors of hidden endometrial carcinoma ($p=.000, .013$, respectively). However preoperative serum CA 19-9 and CA 125 levels were not statistically sig-

nificant clinical parameters, we estimate cut-off values with receiver operator characteristic curve: 10.55U/mL (sensitivity 0.750, specificity 0.679), 12.6U/mL (sensitivity 0.647, specificity 0.659), respectively.

Conclusion: It is important issue to treat endometrial biopsy results of endometrial hyperplasia because of the possibility of hidden malignancy. We evaluated several risk factors associated with hidden endometrial carcinoma. These clinical parameters and cut-off values may be useful to discriminate endometrial carcinoma from endometrial hyperplasia only after endometrial biopsy.

Keywords: Endometrial hyperplasia, Endometrial carcinoma, Endometrial biopsy

PP-092

Introduction of laparoscopic pelvic lymphadenectomy for endometrial cancer in a facility in Japan

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Objective: Laparoscopic surgery for gynecologic cancer is widely employed in Western countries as well as in Asian countries including Korea. It is because laparoscopic surgery is now recognized as a procedure that is equal to open surgery in terms of radicality, safety and outcome of the patient. However, in Japan, only a few facilities actively perform laparoscopic surgery for gynecologic malignancy. Recently, in our facility, we tried to introduce laparoscopic total hysterectomy along with pelvic lymphadenectomy for the patient with Grade 1-2, clinical stage IA-IB endometrial cancer.

Methods: The operator of the laparoscopy had an experience of over 50 cases of laparoscopic simple hysterectomy and also more than 100 cases of abdominal hysterectomy with lymphadenectomy. As a part of the training, the surgeon to be involved in the laparoscopic surgery visited several facilities in Japan, Korea, France, etc. to introduce appropriate surgical techniques as well as suitable management.

Several surgical parameters were compared between four cases of initial laparoscopic surgery with 10 cases of total abdominal hysterectomy with pelvic lymphadenectomy performed in the same period.

Results: The average operation time is 259 min. for laparoscopy vs. 265 min. in laparotomy. The average amount of bleeding is 159g in laparoscopy compared with 286g in laparotomy. The average number of resected lymph node was 18.2 compared with 33.8 in laparotomy.

Conclusion: These data suggest that even in the very initial cases, laparoscopic surgery could be safely performed with less operation time. However, radicality, namely resected lymph nodes, tended to be less in laparoscopic surgery.

Keywords: Laparoscopic pelvic lymphadenectomy, Endometrial cancer, Introduction

PP-093

HER-2 overexpression and amplification in type 2 endometrial carcinoma

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Objective: Recently, it was reported that HER-2 overexpression or amplification was more common in type 2 endometrial carcinomas than in type 1 tumors. Herein, we attempted to verify the difference of HER-2 overexpression or amplification between in original tumors and in metastatic or recurrent tumors of type 2 endometrial carcinomas.

Methods: Immunohistochemical staining (Ventana) and FISH (PathVysion HER-2 DNA Probe kit) were performed on the tumor tissues obtained from 46 patients with type 2 endometrial carcinoma. Histological subtypes were as follows: grade 3 adenocarcinoma, 19 patients; serous type, 6; clear cell type, 16; poorly differentiated carcinoma, 5. The relationship between HER-2 expression and clinicopathological factors or prognosis was investigated.

Results: HER-2 overexpression (>2+ immunostaining) and HER-2 amplification (a ratio of HER-2 copies to chromosome 17 (CEP17) copies >2.0) were detected in 30.4% (14 of 46) and 4.3% (2 of 46) in original tumors, respectively. HER-2 overexpression was not associated with clinicopathological factors or prognosis. On the other hand, in 20 tumor tissues obtained from metastatic or recurrent tumors, HER-2 overexpression and HER-2 amplification were detected in 55% (11 of 20) and 15% (3 of 20), respectively. The patients with HER-2 overexpression had somewhat worse prognosis.

Conclusion: HER-2 overexpression or amplification in metastatic or recurrent tumors were more frequent than in original tumors of type 2 endometrial carcinomas. Therefore, there might be possibility of treatment for these patients with trastuzumab as option.

Keywords: HER-2, Type 2 endometrial carcinoma, FISH

PP-094

Immunohistochemical expression of core2 β -1,6-N-acetylglucosaminyl transferase 1 (C2GnT1) in the endometrial carcinoma; a novel potential prognostic factor

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Objective: The expression of core 2 β -1,6-N-acetylglucosaminyl-transferase 1 (C2GnT1), synthesizing core 2 branching structure on O-glycans, was reported to be associated with biological aggressiveness of tumor cells. We examined the relationship between the expression of C2GnT1 and clinicopathological parameters of the pa-

tients with endometrial carcinoma.

Methods: The immunohistochemical expression of C2GnT1 was examined using 73 cases of endometrial carcinoma and 20 cases of adjacent normal endometrium. The result of staining was described as a positivity index (PI, full score 100) calculated according to the percentage of positive cells.

Results: The expression of C2GnT1 of endometrial carcinoma (PI: 7.26–10.08) was significantly higher than that of normal endometrium (0.4–0.99, $p < 0.0005$). The expression of C2GnT1 was frequently observed at the site of deep myometrial invasion and/or lymphovascular space invasion. The patients with C2GnT1 overexpression (PI ≥ 10) showed significantly shorter survival ($p < 0.0005$). Moreover, the overexpression of C2GnT1 was indicated to be an independent prognostic factor by multivariable analysis ($p = 0.031$).

Conclusion: These results suggested that C2GnT1 may be a novel prognostic factor and a novel potential target for the treatment of endometrial carcinoma.

Keywords: Endometrial carcinoma, C2GnT1, Immunohistochemistry

PP-095

Detection of sugar chains of glycoproteins expressed by normal endometrium and uterine endometrial cancer with the lectin arrays

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Objective: Sugar chains of glycoproteins or glycolipids on the cell membrane are known to be involved in recognition between cells and in cell and differentiation, and thus are attracting attention in the fields of reproductive medicine and oncology. We analyzed the expression of glycoprotein sugar chains in the normal endometrium and the endometrial cancer, and searched for sugar chains that were specifically expressed in each case.

Methods: We analyzed the profile of sugar chains with lectin arrays containing 40 immobilized lectins and detected sugar chains by fluorescent labeling of membrane proteins extracted from the cultured cells and tissues. Then we compared the profile obtained from cultured cells derived from the normal endometrium, and the endometrial cancer.

Results: 1. There were differences in the expression of glycoproteins recognized by UEA-1 (α -fucose), SSA and SNA (sialic acid), and BPL and ACA (β -galactose) between the cells derived from well-differentiated and poorly-differentiated uterine cancer. 2. The lectin profile was useful to differentiate normal endometrium from endometrial cancer.

Conclusion: Sugar chains on the cell membrane showed changes of expression due to carcinogenesis of the endometrium and differentiation of cancer cells. It was suggested that analysis of the sugar chain profile expressed on the cell membrane in various gynecological cancers with lectin arrays may help us to assess the characteristics of tumors.

Keywords: Endometrial cancer, Lectin microarrays, Sugar chains

PP-096

Risk factor analysis of concurrent endometrial carcinoma in patients with a tissue-diagnosed endometrial hyperplasia: a Taiwanese Gynecologic Oncology Group (TGOG) Study

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Objective: The aim of this multi-center investigation is to explore the risk factors for coexisting endometrial carcinoma in patients with endometrial hyperplasia.

Methods: Four hundred and four cases were included in this study. These patients were divided into two groups – the non-endometrial carcinoma group and the endometrial carcinoma group. We investigated them by clinical parameters including age, menopausal status, obstetrical history, medical history of diabetes, hypertension and hyperlipidemia, BMI and preoperative pathologic results. The distribution of risk factors among the studied population was further analyzed.

Results: After adjusting the potential confounders by binary logistic regression, the risks of age (OR=1.04; 95% CI: 1.01–1.08), BMI (OR=1.15; 95% CI: 1.08–1.23), menopause (OR=2.37; 95% CI: 1.18–4.76), diabetes (OR=7.25; 95% CI: 2.29–22.93), and cytological atypia (OR=4.95; 95% CI: 2.55–9.62) were independent risk factors for endometrial hyperplasia coexisting with endometrial carcinoma. When patients had two of the four risk factors, more than 50% (51/96) of them had co-existing endometrial carcinoma. Seven of the 137 (5.1%) women with concurrent endometrial carcinoma had disease relapse during the follow-up period.

Conclusion: Physicians should take the possibility of coexistent malignancy into consideration when endometrial hyperplasia patients with the risk factors, including menopause, diabetes, high BMI and cytologic atypia, especially those with two or more risk factors.

Keywords: Concurrent endometrial carcinoma, Endometrial hyperplasia, Risk factor

PP-097

Value of preoperative serum CA125 level for prediction of prognosis in endometrial cancer patients

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Objective: High preoperative CA125 levels in endometrial cancer patients might be related to lymph nodal metastasis and poor prognosis. To evaluate whether the value of preoperative CA125 (cancer antigen 125) is associated with lymph node metastasis and prognosis of endometrial cancer patients.

Methods: 120 women endometrial cancer patients with preoperative CA125 levels were retrospectively reviewed. The results were also correlated to clinicopathological outcome.

Results: Elevated CA125 (>40 U/mL) significantly correlated with higher stage, higher grade, increased depth of myometrial invasion, lymph node metastasis, and presence of LVSI in endometrial cancer. For endometrial cancer patients, the 5-year overall survival (OS) and recurrence-free survival (RFS) was significantly longer in patients with CA125 ≤ 40 U/mL than those with CA125 > 40 U/mL ($p < 0.001$). When patients were further stratified by CA125 levels and lymph node status, OS and RFS was best for those with CA125 ≤ 40 U/mL and without lymph node metastasis and worst for those with lymph node metastasis and CA125 > 40 U/mL ($p < 0.001$).

Conclusion: Therefore, testing of preoperative CA125 levels might be considered as a part of the management for the endometrial cancer patients.

Keywords: Preoperative CA125, Endometrial carcinoma, Survival

PP-098

The significance of prognostic evaluation of FIGO 2009 staging system on stage I endometrioid adenocarcinoma

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Objective: To explore the impact of 2009 FIGO staging system for stage I endometrioid adenocarcinoma on its prognosis assessing.

Methods: A retrospective study was carried out. The patients were divided into FIGO 2009 Ia and Ib group (200 cases and 44 cases), also FIGO 1988 IA, IB and IC group (34 cases, 156 cases and 29 cases).

Results: The grade of FIGO 1988 IA group was lower than FIGO 2009 IA group ($p = 0.003$). The tumor-free survival curves and total survival curves of FIGO 1988 IA group and IB group all did not differ much compared with FIGO 2009 Ia group ($p > 0.05$). The tumor-free survival curves did not differ much between the FIGO 1988 Ic group and FIGO 2009 IB group ($p > 0.05$). FIGO 2009 IA group patients was younger than FIGO 2009 IB group ($p < 0.001$). The grade of FIGO 2009 IA group

was lower than FIGO 2009 IB group ($p=0.029$). The percentages of chemotherapy and radiotherapy of FIGO 2009 Ia group were lower than FIGO 2009 IB group remarkably ($p<0.001$). The tumor-free survival curve and total survival curves also did not differ much between the two groups ($p>0.05$).

Conclusion: The prognosis of FIGO 1988 IA group and FIGO 1988 IB group all did not differ much when compared with FIGO 2009 Ia group. The prognosis of FIGO 2009 IA group and FIGO 2009 IB group were also not differ much. But it may be due to more FIGO 2009 IB patients accepted chemotherapy and radiotherapy than FIGO 2009 Ia patients.

Keywords: Endometrial carcinoma, Staging system, Prognosis

PP-099

Is the revised 2009 FIGO staging system for uterine sarcomas more discriminating?

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Objective: The aim of this study was to compare survival outcomes for patients with uterine sarcoma using the 1988 and 2009 FIGO staging systems.

Methods: A total of 83 patients with leiomyosarcoma and endometrial stromal sarcoma treated at Yonsei University Health System between March of 1989 and November of 2009 were reviewed. Due to incomplete surgery and difficulty in classification, 19 patients were excluded. The prognostic validity of both FIGO staging systems, as well as other factors were analyzed.

Results: Leiomyosarcoma and endometrial stromal sarcoma comprised 48.2% and 51.8% of the study population, respectively. During a median follow-up of 57 months (range, 1–265 mo), 26 patients died. Using the new staging system, 43 (67.2%) of 64 eligible patients were reclassified. Among those 64 patients, 45 (70.3%) patients with limited uterine corpus involvement were divided into stage IA ($n=14$) and IB ($n=31$). Univariate analysis demonstrated a significant difference between stages I and II and the other stages in both staging systems ($p<0.001$) with respect to disease-free survival (DFS) and overall survival (OS). Age, menopausal status, tumor size, and cell type were significantly associated with OS ($p=0.011$, $p=0.031$, $p=0.044$, $p=0.009$, respectively). In multivariate analysis, a revised FIGO stage $>III$ was an independent poor prognostic factor with a hazard ratio of 9.06 (95% confidence interval [CI] 2.49–33.0, $p=0.001$).

Conclusion: The 2009 FIGO staging system is more accurate than the previous FIGO system for LMS and ESS with respect to its ability to distinguish early-stage patients from advanced-stage patients.

Keywords: Uterine sarcoma, FIGO staging, Leiomyosarcoma

PP-100

Early identification of persistent trophoblastic disease with serum hCG ratio

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Objective: The aim of this study was to ascertain whether serum human chorionic gonadotropin (hCG) level within 2 weeks after evacuation is predictive of persistent gestational trophoblastic neoplasia (GTN) in patients with complete molar pregnancy.

Methods: Between January 2000 and June 2010, a total of 467 patients with complete molar pregnancy were diagnosed. Ninety-seven patients with the second curettage, prophylactic chemotherapy, and insufficient data were excluded. A receiver operating characteristic curve was used to determine the most useful predicting factor in persistent GTN and multivariate logistic regression was used for analyses.

Results: Persistent GTN was diagnosed in 104 of the 371 patients (28.0%) on the basis of the 2000 FIGO criteria. The optimal cutoff point of hCG in 1 week after evacuation and 2 weeks after evacuation were 6400 mIU/mL (sensitivity, 54.8%; specificity, 62.9%) and 2400 mIU/mL (sensitivity, 63.5%; specificity, 76.4%). The optimal cutoff point of the ratio of pre-evacuation hCG to hCG after 2 weeks after evacuation was 30 (sensitivity, 61.5%; specificity, 85.4%). On multivariate analysis, this ratio <30 was an independent predicting factor for persistent GTN (odds ratio=8.137; 95% confidence interval, 4.867–13.604; $p<0.001$).

Conclusion: The ratio of hCG level before evacuation to second week after evacuation is an early valid prognostic marker of GTN and is more accurate than ratio of hCG level before evacuation to first week, first week to second week after evacuation, and hCG level of first week and second week.

Keywords: Gestational trophoblastic neoplasia, Complete molar pregnancy, Human chorionic gonadotropin

PP-101

Evaluation of diagnostic needle biopsy in patients with gynecologic malignant tumors

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Objective: To evaluate the usefulness and limitations of diagnostic needle biopsy in patients with gynecologic malignant tumors, we retrospectively analyzed the case of patients with pelvic tumors who had undergone needle biopsy.

Methods: During the past 7 years, 16 patients with pelvic tumors who had undergone abdominal or vaginal diagnostic needle biopsy with informed consent in our hospital. Needle biopsy was indicated in pa-

tients with pelvic tumors as their malignancy was predictable. The procedure was also performed in some patients with severe complications and a high surgical risk. All suspicious areas were sampled for detailed histological study. The diagnostic results, complications and outcomes of this procedure for gynecologic malignant tumors were analyzed.

Results: The needle biopsy was performed in 7 patients via abdominal approach and in 9 patients vaginally. Eight cases were diagnosed as malignancy by biopsy and 11 malignancies were diagnosed finally. Eleven cases containing 3 patients with leiomyomas had undergone additional procedures such as surgical removal or chemotherapy. The patients did not show any complication after needle biopsy.

Conclusion: The needle biopsy might to be safe and effective as diagnostic tool in patients with gynecologic malignant tumors. The limitations of the procedure should be considered because of difficulties in attempting to diagnose from several small specimens histologically.

Keywords: Needle biopsy, Gynecologic malignant tumors, Diagnosis

PP-102

Oncothermia in gynecologic oncology

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Objective: Ewha Womens Hospital intensively uses oncothermia for gynecological malignancies. The time for the application of the new technology is not enough to present statistically evaluable number of patients in cohorts, so our objective is reporting only an interesting case, having multiple primer metastases.

Methods: We apply for the treatment the EHY-2000 oncothermia device with variable electrode sizes. A treatment cycle contains 10 sessions in average, made 2-3 times a week, having at least a day between the treatments. Every session was performed in duration of 60 min. Patients of advanced uterine cervix and ovary tumors are treated. Oncothermia was applied complementary to various chemotherapies.

Results: Diagnosis in June shows curative improvement: Decreased extent of mass in uterine cervix and in right ovary. Improvement of hepatic metastasis in both lobes of the liver with residual lesion. Improvement of peritoneal carcinomatosis with residual lesion. PET shows impressive improvement of cure. The operative results in August showed the pelvic cavity with a vengeance 4×3×3 cm³ a nodular mass with a thick wall of the right ovary was observed in peritoneum, omentum, rectal serosa findings necrotic nodular mass. Abnormalities are not visible on the left ovary. The CA-125 and CA-19-9 tumor-markers had been normalized.

Conclusion: Oncothermia treatment looks feasible to treat advanced gynecologic malignancies. For evidences perspective, randomized studies, and measuring the overall survival as end-point are desired.

Keywords: Oncothermia, Gynecologic oncology, Cervical cancer

PP-103

Chance of hereditary risk in sequential endometrial and colon cancer with regard to Lynch syndrome: a pilot study

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Objective: Two common cancer types related with Lynch syndrome are colon and endometrium. Several mismatch repair genes (MLH1, MSH2, and MSH6) are reported to be associated with hereditary nature of Lynch syndrome. The aim of our study was to estimate the frequency of Lynch syndrome in sequential tumor patients.

Methods: Women who have been treated for 2 primary colorectal/endometrial cancers were identified from Samsung Medical Center. Patients' information about age at cancer diagnosis, order of cancer development and other characteristics were obtained. Immunohistochemistry of MLH1, MSH2, and MSH6 were done for two tumor sites. And other genetic tests (microsatellite instability, gene sequencing) were done.

Results: A total of 15 women with dual primary cancers were identified. In 2 women, colon cancer and endometrial cancer were diagnosed simultaneously. Of the remaining 13 women, 6 (46%) women had an endometrial diagnosed first. Fifty four (54%) women had a colon cancer diagnosed first. Mean age at diagnosis and median time to second cancer for endometrial /colon cancer were 54/51.7 and 5.3/2.9 years. Patients with a family history of cancer were 9 (60%). Suspicious immunohistochemistry of MLH1/MSH2/MSH6 were 3/3/3 (20/20/20%). Microsatellite unstable population were 5 (33%). There were 3 Lynch syndrome/HNPCC patients after gene sequencing tests.

First cancer	No	Age, median (range)	Median time to second cancer
Metachronous			
Colon	7	51.7 (41-63)	5.3
Endometrium	6	54 (44-68)	2.9
Synchronous	2	55.5 (47, 64)	N/A

Conclusion: After reviewing cases of women with dual cancer patients, preceding endometrial cancer patients including synchronous tumor were above half of the cases. Therefore, careful consideration of gynecologic oncologist for selecting Lynch syndrome should be provided to suspicious patients.

Keywords: Lynch syndrome, Endometrial cancer, Colon cancer

PP-104

Synchronous gynecologic malignancy and preliminary results of Lynch syndrome

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Objective: Lynch syndrome is a hereditary cancer syndrome that increases the risks of colorectal and gynecologic malignancies such as endometrial and ovarian cancer. Several mismatch repair genes (MSH2, MSH6, and MLH1) are reported to be associated with hereditary nature of Lynch syndrome. The aim of our study was to estimate the value of MSH2, MSH6, and MLH1 immunohistochemistry (IHC) based on family history in a Korean sample.

Methods: 36 women with synchronous gynecologic tumors of endometrial and ovarian cancer were identified among patients being treated at our institution. Among them, 32 patients had tumor blocks (total 62 slides) available for analysis. According to a diagnostic algorithm, we performed IHC analyses. Staining was scored based on intensity and proportion

Results: Among 32 eligible patients, 9 (28%) had a family history of cancer. Six patients (19%) were negative for MLH1; among them, four (4/6) were negative at both sites. Ten patients (31%) were negative for MSH2 or MSH6 at both sites or negative for both MSH2 and MSH6. Among these four patients (4/10) showed negative staining for both sites. The three patients showing negative staining for MLH1, MSH2 and MSH6 at both sites with family history were considered to be screening positive groups of Lynch syndrome.

Conclusion: In this study, the frequency of Lynch syndrome associated immunohistochemical staining (MLH1, MSH2 and MSH6) group was estimated as 9% (3/36) among Korean women with synchronous gynecologic tumors.

Keywords: Lynch syndrome, Synchronous gynecologic tumor, Hereditary tumor

PP-105

Changes in biologic markers of oxidative stress and plasma endotoxin level in patients treated with pelvic radiotherapy

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Objective: The purpose of this study was to evaluate the effects of pelvic radiotherapy on biologic markers of oxidative stress and plasma endotoxin levels, and to assess the relationship between the changes of such factors and radiotherapy-related complications.

Methods: Twelve gynecologic cancer patients who were treated via pelvic radiotherapy with or without concurrent chemotherapy were enrolled in this study. Biologic markers of oxidative stress, such as glutathione (GSH) and oxidized glutathione (GSSG), as well as endotoxin levels, were measured weekly during treatment. Subjective symptoms were assessed using the Korean version of the EORTC-QLQ-c30 at

the baseline and on the 5th week of radiotherapy.

Results: No changes were noted in the level of GSH in whole blood, but the GSH/GSSG ratio was reduced dramatically after the initiation of radiotherapy. The mean plasma endotoxin for all patients tended to increase and persisted during radiotherapy, and the number of patients who evidenced clinically significant endotoxin levels (defined as > 0.005 EU/ml) also increased. Nausea/vomiting and diarrhea were significantly changed ($p=0.019$ and $p<0.001$, respectively). A significant relationship was noted to exist between the changes in the endotoxin level and nausea/vomiting ($p=0.001$). However, such symptoms did not correlate with the changes of oxidative stress markers.

Conclusion: Pelvic radiotherapy oxidized the glutathione redox system and increased plasma endotoxin. Further investigations containing interventional and longitudinal studies will be required to assess the effects of the changes in oxidative stress markers and endotoxin on radiotherapy-related adverse events.

Keywords: Radiotherapy, Oxidative stress, Endotoxin

PP-106

Safe and simple critical steps in laparoscopic ovarian transposition

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Objective: To review the critical steps in laparoscopic ovarian transposition, from the points of view of successfulness ovarian function preservation and simplicity of the surgical steps itself.

Methods: Steps and technique of laparoscopic ovarian transposition in Gynecologic Oncology Division is reviewed from the point of view of ovarian function safety & simplicity of the surgery. Field of radiation was considered as critical to determine anatomical landmarks to hang the ovary in a certain level that is high enough and lateral enough to avoid high dose irradiation. The technical simplicity of surgery is reviewed also to achieve a simple and easy ovarian transposition by laparoscopy.

Results: Transpose the ovary as high as caudal to lowest costae or at the subhepatic level, in the paracolic gut considered to be optimal in preserving ovarian function. Making a parieto-colic peritoneal tunnel or ring to hold the ovarian pedicle make the surgery simpler, compare to suture it. Some anatomical landmarks are important in the steps to be noticed. Notify the close ureter structure dorsal to the ovarian pedicle is critical. Make a loop of ovarian pedicle along the caudal aspect of cecum, just trough the parieto-colical peritoneal tunnel is not just simpler but also important to preserve the ovarian vascularization.

Conclusion: A safe and simple technical steps are needed, in order to be more reproducible especially to be done by gynecologic oncologist and even also general gynecologist.

Keywords: Laparoscopic, Ovarian, Transposition

PP-107

Effect of lumbar sympathetic ganglion block in patients with lymphedema after the treatment of gynecologic cancer: a preliminary report

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Objective: To evaluate the effect of lumbar sympathetic ganglion block (LSGB) in patients with lymphedema after the treatment of gynecologic cancer.

Methods: We performed LSGB to seven patients who had suffered from severe lower-extremity lymphedema after radical surgery and/or irradiation. The circumference of each thigh was measured at the uppermost portion of thigh in standing position. The level of discomfort from symptoms was estimated by visual analog scale (VAS) from 0 (absent) to 10 (very severe). We compare the initial circumference of thigh and VAS score with those of one day after intervention.

Results: After the block, lymphedema was relieved dramatically in some patients; Overall response rate was 71.4% (5/7), and average reduction of thigh circumference was 1.3cm (1–2) at the next day. Initial VAS score (mostly 3–5) was dropped to 0 or 1 after intervention. As expected, patients who experienced the response were strongly hoped to receive LSGB again in the future. Lastly, there were no complications associated with LSGB.

Conclusion: LSGB may be very effective in some patients with lymphedema after gynecologic cancer treatment. Clinical studies should be performed to validate the effect and safety of LSGB as a therapy for intractable lower-extremity lymphedema.

Keywords: Lymphedema, Lumbar sympathetic ganglion block, Gynecologic cancer

PP-108

Interstitial implantation of ¹²⁵Iodine seeds as salvage therapy for recurrent ovarian cancer and cervical cancer

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Objective: To investigate the feasibility, short-term efficacy and adverse effects of ¹²⁵I seeds implantation in the treatment of recurrent ovarian cancer and cervical cancer.

Methods: A total of 12 patients with recurrent ovarian cancer and 17 patients with cervical cancer treated in Sun Yat-sen University Cancer Center from June 2009 to December 2010 enrolled into the study. There were 49 lesions including 25 ovarian cancer lesions and 24 cervical ones. Forty-five lesions were treated with ¹²⁵I seed implantation. Forty-four were treated under the guidance of CT while only one lesion under the guidance of ultrasonography. The treating plan was calculated using computerized treatment planning system (TPS) and

Memorial Sloan-Ketterin nomograph. The prescribed matched peripheral dose (MPD) was 100–160 Gy. The total number of sources implanted were 6–68 with a median number of 20.5. Additional chemotherapy was given to 13 patients. Tumor status were evaluated with CT and ¹⁸F-FDG PET/CT findings.

Results: Nineteen patients were still alive after a median follow-up of 15 months (range from 5 to 19 months). Thirteen patients showed complete remission, seven patients showed partial remission. The effective rate was 69.0% (20/29). There were three patients suffered from Sciatic nerve injury symptoms. No complication was found in the other patients.

Conclusion: ¹²⁵I seed implantation was feasible, effective and safe as a salvage local treatment for patients with recurrent gynecologic malignancies, it was worth of development and promotion. The efficacy seems better in recurrent ovarian cancer than in cervical cancer patients.

Keywords: Ovarian and cervical cancer, Recurrent, ¹²⁵I seed implantation

PP-109

The feasibility and surgical outcomes of laparoscopic metastasectomy in the treatment of ovarian metastases from gastric cancer

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Objective: To evaluate the feasibility of laparoscopic metastasectomy (LM) in the treatment of ovarian metastases from gastric cancer, and to compare the surgical outcomes with patients who underwent open metastasectomy (OM).

Methods: The cases of 73 patients who underwent LM (n=16) or OM (n=57) were retrospectively reviewed. All patients were diagnosed with gastric cancer and subsequently underwent a metastasectomy at Yonsei University Health System between December 2002 and March 2011.

Results: Sixteen operations were completed laparoscopically with no conversion to laparotomy. Complete cytoreduction surgery was achievable in 13 patients (81.3%). Operating time, complete cytoreduction, and occurrence of perioperative complications were comparable between the two groups. The LM group had less blood loss (25 mL vs. 400 mL, p<0.0001), earlier return to a general diet (3 days vs. 4 days, p=0.005), shorter postoperative hospital stay (4.5 days vs. 7 days, p<0.0001), and lower postoperative pain scores after 6, 24, and 48 hours than those in the OM group. There were no operative complications in the LM group.

Conclusion: As a surgical treatment for ovarian metastases from gastric cancer, LM is feasible and provides benefits to patients without

detrimental effects on the clinical outcomes for selected patients.

Keywords: Laparoscopy, Metastasectomy, Ovarian metastases, Gastric cancer

PP-110

The effect of photodynamic therapy for the breast cancer in a BALB/c mouse model

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Objective: Photodynamic therapy (PDT) has been used for the superficial neoplasm however, its uses has been extended to other lesions. The purpose of this study is to observe whether the PDT can cure breast cancer in the solid tumor model or not and to define the critical point of laser amount for killing the cancer cell.

Methods: Twenty four BALB/c mouse models with subcutaneous EMT6 mammary carcinomas were prepared each. Mice were into eight groups depends on the amount of illumination. And the tumor size was between 6mm and 10mm. We began by peritoneal infiltration of photosensitizer (PHOTOFRIN[®][HpD], Axcan Pharma Inc, Canada) 48 hours before applying the laser light, and then we applied a non-thermal laser light (CERALAS[™] Diode Laser 632 System, Biolitec, Germany). The wave length was from 350 J/Cm² to 30 J/Cm² on four directions of cancer margin.

Results: Regardless of the tumor size, all of mice were shown effectiveness of PDT. The color of breast cancer lesion began to be changed with dark on 2nd day and the tumor regression was beginning simultaneously. And, we could confirm the complete regression of the breast cancer 14 days after PDT. There was no recurrence of cancer. Also, 90 J/Cm² is might be minimum energy to destruct the cancer cells.

Conclusion: Therefore we can expect that PDT could be utilized to treat the breast cancer, but we need more experience and skills for clinical trials.

Keywords: Photodynamic therapy, Breast cancer, BALB/c mouse model

PP-111

Endometrial pathologies associated with tamoxifen treatment in breast cancer patients

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Objective: The purpose of this study is to evaluate various endometrial pathologies associated with Tamoxifen treatment in breast cancer patients.

Methods: A single institution retrospective review was performed for all

breast cancer patients treated with Tamoxifen from 2000 to 2011 at Asan Medical Center. We compared the pathologic results proven by biopsy in cases with endometrial pathology detected on ultrasonography.

Results: There were total of 259 patients who underwent pathologic-proven by dilatation & curettage or aspiration biopsy. Most cases (n=126, 48.6%) were proven to have EM polyps. The second largest number of cases (n=107, 41.3%) had normal endometrial tissue. There were 13 cases of endometrial hyperplasia and nine cases of simple hyperplasia (3.5%). There were four, complex hyperplasia cases (1.5%) and 10 cases (3.9%) which revealed the presence of endometrial cancer. There were eight endometrioid type endometrial cancer cases. Other diagnoses included uterine papillary serous carcinoma (UPSC) and malignant mixed mesodermal tumors (MMMT).

Conclusion: As breast cancer patients are usually treated using tamoxifen, gynecologists should be alerted to these pathologies which indicated the presence of endometrial cancer and endometrial hyperplasia.

Keywords: Tamoxifen, Breast cancer, Endometrial pathology

PP-112

FDG-PET/CT and gynaecological malignancies: hospital sultanah bahiyah experience

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Objective: To evaluate the role of PET/CT in diagnosing and evaluating patients with suspected gynaecological tumour recurrence or persistent disease following treatment.

Methods: A cross-sectional study carried out at Hospital Sultanah Bahiyah, Malaysia between 2006 and 2008 involving 26 patients with confirmed gynaecological malignancies.

Results: The standard imaging modalities disclosed possible tumour recurrence or persistent disease in 24 of 26 patients (92.3 percent). Two patients with negative CT were subjected to PET/CT due to persistently elevated serum tumour markers. PET/CT confirmed tumour recurrence in 9 (34.6 percent) patients and was inconclusive in 2 (7.7 percent) patients. PET/CT did not show any abnormal uptake in 15 (57.7 percent) patients. Of the 9 patients with positive PET/CT, 7 (77.8 percent) had a repeat PET/CT and 2 (22.2 percent) had a CT following subsequent treatment which confirmed no further evidence of disease. Patients with negative or inconclusive PET/CT were either continued with routine follow-up every 6 months or had a close monitoring by either CT or serum tumour markers.

Conclusion: With the availability of PET/CT, almost two-third of patients with inconclusive findings on CT Scan and/or rising tumour markers did not have to undergo unnecessary chemotherapy or

radiotherapy. Integrated PET/CT imaging is accurate in both diagnosing and evaluating patients with suspected tumour recurrence or persistent disease in gynaecological malignancies.

Keywords: PET Scan, CT Scan, Gynaecological Malignancies

PP-113 (Case Report)

Combination of cisplatin and ifosfamide as neoadjuvant chemotherapy in bulky stage Ib cervical cancer: Case series /preliminary report

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Objective: To explore the possibility to use combination of cisplatin and ifosfamide as a regimen of neo adjuvant chemotherapy in bulky stage IB cervical cancer. The management of bulky stage IB cervical cancer remains controversial. Neo adjuvant chemotherapy has proved as one alternative method to improve resectability and control micro metastasis. Our data in Jakarta while used cisplatin, vincristine and bleomycin showed 9% completed respond, 41% partial respond and 50% stable disease. Change the regimen of combination cisplatin and ifosfamide may have a chance to improve respond rate.

Methods: Patient who has bulky stage IB cervical cancer, no medical contra indicated of chemotherapy and consent to follow the new protocol of neo adjuvant chemotherapy use cisplatin 60 mg/m² and Ifosfamide 4 g/m² while uromitexan used 170% of ifosfamide. Ifosfamide give by infusion for 24 hours. Monitoring side effect of standard NCI. After 3 courses we evaluated used clinical examination and proceed for radical hysterectomy and pelvic lymphadenectomy. We compare the histology from biopsy and specimen of surgery

Results: This preliminary report of 3 cases showed pathology completed respond. All of Histology are squamous cell carcinoma. The side effect of chemotherapy who has dominant are myelosuppressive as anemia, leukopenia and thrombocytopenia grade 2-3. The other side effect is emetogenic grade 3. All of side effects are manageable.

Conclusion: The combination of cisplatin and ifosfamide has a chance as a new regimen in neo adjuvant chemotherapy for bulky stage IB cervical cancer. We need further study to calculate the risk and benefit of this regimen.

Keywords: Bulky stage IB, Cervical cancer, Neo adjuvant chemotherapy

PP-114 (Case Report)

Extrauterine smooth muscle tumors with atypical symptoms

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Objective: Extrauterine smooth muscle tumors including intravenous leiomyomatosis (IVL), benign metastasizing leiomyoma (BML), which have recurrent or metastatic potential, are uncommon benign tumor. They are usually asymptomatic, and when symptoms are manifested, they are often secondary to direct intracardiac or pulmonary involvement.

Methods: This was a retrospective review of 5 patients diagnosed with extrauterine smooth muscle tumors with cardiovascular or pulmonary extension which arising from uterine leiomyoma from 2002 to 2010 at single institution.

Results: Two patients presented with dyspnea or chest discomfort. Other three patients presented with abdominal pain, menorrhagia, and syncope respectively. Mean age at presentation was 42.4 years (range, 26-55). Extension site was lung in two patients, cardiopulmonary system in two patients and there was a rare case of leiomyomatosis with lymphatic extension. Three patients underwent total abdominal hysterectomy with mass resection. One patient underwent mass excision only with injection of GnRH agonist and the other patient underwent only mass biopsy at ovaries and pelvic wall due to young age. Only two patients with cardiac extension case experienced recurrence. They underwent mass excision with explore laparotomy and one of them followed up with additional GnRH agonist use.

Conclusion: Awareness of these extrauterine smooth muscle tumors is important for early diagnosis, adequate treatment and exact differential diagnosis. Successful therapy depends on comprehensive excision of the tumor. And if the tumor is unresectable, hormone therapy should be considered. After excision of the tumor, regular long term follow up is necessary due to its recurrent and metastatic potential.

Keywords: Intravenous leiomyomatosis, Benign metastasizing leiomyoma, Cardiovascular or pulmonary extension

PP-115 (Case Report)

Single-port total laparoscopic radical hysterectomy with pelvic lymph node dissection in cervical cancer

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Objective: To evaluate the feasibility of single-port total laparoscopic radical hysterectomy (TLRH) with pelvic lymph node dissection (PLND) on cervical cancer patients.

Methods: We present two single-port TLRH with PLND cases. All procedures including vaginal cuff suturing were done laparoscopically. After making a single 1.5- to 2.0-cm umbilical incision, we inserted one laparoscope and two other instruments into three cannulas of the port created by a wound retractor and a surgical glove. The operation was executed with conventional rigid straight laparoscopic instruments. Transumbilical drainage tubes were inserted into the pelvic cavity. Transumbilical drainage tubes were inserted into the pelvic cavity.

Results: One of cases is the case of 36-year old woman (G 2, P 2) with moderately differentiated cervical squamous cell carcinoma (stage Ia2). We performed single-port TLRH with PLND. Twenty nine lymph nodes were obtained and no lymph node invasion was noted. The depth of tumor invasion was 4 mm and the resected vaginal margin was clear. The operative time was 240 minutes, and the hemoglobin change between preoperative phase and postoperative day 1 was 1.8 g/dl. The drainage tube was removed on discharge day, 7 days after the surgery. There were no post-operative complications or visible scars outside the umbilicus.

Conclusion: Single-port TLRH with PLND on early stage cervical cancer patients is feasible.

Keywords: Single-port, Total laparoscopic radical hysterectomy, Cervical cancer

PP-116 (Case Report)

Successful pregnancy following radical vaginal trachelectomy for early stage cervical carcinoma

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To report a case of a 32 year old, healthy primipara, diagnosed at age 30 with squamous cell carcinoma of the cervix stage 1, who had a successful pregnancy outcome after she underwent the fertility-sparing radical vaginal trachelectomy in our institution. With emphasis on increased frequency of sexual intercourse, our patient achieved spontaneous pregnancy seventeen months following the radical vaginal trachelectomy with extraperitoneal bilateral lymph node dissection and delivered a live, preterm baby girl, weighing 1.9 kilograms, with APGAR score of eight and nine, at one and nine minutes of life, respectively, with Ballard score of 32 weeks. Indeed radical vaginal trachelectomy though a relatively new procedure fulfils the aggressiveness called for in cervical carcinoma and its fertility-preserving nature. At present, there are only 535 cases being reported worldwide since it was pioneered by Daniel Dargent in 1987 in France. (Balaquit RC and Luna JT, 2008) In the Philippines, this is the third in a case series of radical vaginal trachelectomy for fertility preservation in early stage cervical carcinoma since 2007, the very first of its kind in the region and the only one yet ever reported locally to have a successful pregnancy. The case demonstrates how early detection of a potentially invasive and lethal condition using inexpensive tools such as Visual Inspection with Acetic acid (VIA) and Pap smear allowed a more conservative procedure to be carried out.

Keywords: Radical vaginal trachelectomy, Fertility-sparing, Stage 1A cervical cancer, Pregnancy

PP-117 (Case resort)

An effective case of CAV-EP as a neoadjuvant chemotherapy for small cell carcinoma of the uterine cervix

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Small cell carcinoma of the uterine cervix is very rare and has a poor prognosis which is likely to become widespread metastasis. An effective case is reported of combined cyclophosphamide, adriamycin, vincristine, etoposide and cisplatin therapy (CAV-EP) as a neoadjuvant chemotherapy for small cell carcinoma of the uterine cervix. The patient was 35 year-old woman, 2 para, who was referred to our outpatients ward under the diagnosis of uterine cervical tumor. A pap smear showed class V and the pathological diagnosis was made as small cell carcinoma of the uterine cervix. The tumor was found to infiltrate into bilateral parametria by rectal examination. Because MRI showed about 7cm diameter tumor in the uterine cervix and PET showed no metastasis, her disease was diagnosed as stage IIb of cervical cancer. After CAV-EP was given for 3 cycles as neoadjuvant chemotherapy, the tumor disappeared on speculum examination. The chemotherapy effect was diagnosed as partial response by MRI and PET, and so radical hysterectomy and bilateral salpingo-oophorectomy with pelvic lymphadenectomy was performed. The pathological examination of excised specimen revealed neither residual carcinoma nor lymphnode metastasis. She is observed in our outpatients ward with no recurrence and metastasis after 3 cycles of CAV-EP therapy as adjuvant chemotherapy.

Keywords: Small cell carcinoma of the uterine cervix, Neoadjuvant chemotherapy, CAV-EP

PP-118 (Case report)

An effective case of CPT-11 + Nedaplatin for uterine cervical cancer bone metastases

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As therapies for bone metastases caused by uterine cervical cancer, a radiation therapy and/or bisphosphonates or a strontium chloride radioisotope are considered. An effective case is reported of combined CPT-11 and nedaplatin therapy for bone metastases after postoperative concurrent chemoradiation therapy (CCRT) for uterine cervical cancer. A 67 year-old woman was observed in our outpatients ward, who had received a radical hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy followed by CCRT under the diagnosis of uterine cervical cancer stage IIa in another hospital. After 6 years of CCRT,

a tumor marker SCC was increased to 6.0ng/mL and the patient complained a low back pain. The patient was referred to our hospital. After a positron emission computerized-tomography (PET) taken for an investigation, it showed multiple spinal metastases with maximum accumulation in L4 vertebra. Since an irradiation area for L4 vertebra was overlapped by previous irradiation, the patient received a combined CPT-11 and nedaplatin therapy. After 3 cycles of CPT-11 +nedaplatin therapy, a low back pain was cured and the SCC level was decreased to the below of normal limit. Because chemotherapy was considered effective according to the PET showing lower accumulation for metastatic areas, a total 9 cycles of combined CPT-11 and nedaplatin therapy was performed. After 9 cycles of chemotherapies, this disease was diagnosed as CR and no new focus was detected.

Keywords: Bone metastasis, CPT-11, Nedaplatin

PP-119 (Case Report)

Case report on radical abdominal trachelectomy for stage Ib1 cervical cancer performed in singapore and a review of current literature

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We reported the 1st case of radical abdominal trachelectomy for Stage IB1 cervical cancer performed in Singapore in a woman desiring fertility and reviewed the current literature on this novel technique. The patient was a 35 year old woman who has Stage IB1 cervical cancer diagnosed on cone biopsy. Her tumor was less than 2cm and she had no radiological evidence of regional or distant metastases. She has no children and desired to keep her fertility. The radical abdominal trachelectomy performed was based on the technique described by NR Abu-Rustum. The patient underwent radical abdominal trachelectomy and bilateral pelvic lymphadenectomy successfully in August 2010. She did not require any adjuvant treatment after her surgery and she is disease free for 9 months. Her menses resumed 2 months after surgery. Though radical abdominal trachelectomy is a relatively new fertility sparing surgical technique with less than 200 cases described worldwide, it appears to be a good alternative technique to radical vaginal trachelectomy. Recent literature review suggest good oncologic outcome with this technique.

Keywords: Cervix cancer, Abdominal trachelectomy, Fertility sparing

PP-120 (Case report)

Robotic assisted laparoscopic hysterectomy in cervical intraepithelial neoplasia: a case report

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The aim of this paper is to report the first case of hysterectomy using robot

assisted laparoscopic surgery device in Thailand. A 57-year-old woman with CIN II cannot be completely removed with LEEP was referred for robotic-assisted laparoscopic hysterectomy. Operative time 87 minutes; duration time for setting robot 15 minutes; estimated blood loss (EBL) less than 50 ml; post-operative hospital stay 2 days. No robot-related complications. The using robotic assisted laparoscopic hysterectomy in cervical intraepithelial neoplasia (CIN) can be safely performed.

Keywords: Cervical intraepithelial neoplasia (CIN), Robotic surgery, Laparoscopic hysterectomy

PP-121 (Case Report)

Primary transitional cell carcinoma of the ovary: a case report

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Transitional cell carcinoma (TCC) of the ovary is a rare, recently recognized, subtype of ovarian surface epithelial carcinoma. Most patients with ovarian TCC seek medical attention because of abdominal pain, abdominal distension, bowel or urinary symptoms; therefore, the clinical presentation is indistinguishable from other types of epithelial ovarian carcinoma. Primary TCC of the ovary accounts for 1% to 2% of all ovarian tumors. TCC of the ovary is reportedly more sensitive to platinum-based chemotherapy and has a better prognosis than other types of common epithelial ovarian carcinomas. We present a case of primary TCC of the ovary with a brief review of the literature.

Keywords: Transitional cell carcinoma, Ovarian carcinoma, Chemotherapy

PP-122 (Case Report)

Trousseau's syndrome in a patient with clear cell carcinoma of the ovary

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We report a case of trousseau's syndrome who developed both TIA and brain infarction repeatedly and who found ovarian cancer as the result of systemic research. The medical records of this patient who presented for surgery for ovarian cancer were analyzed retrospectively for demographic data, final tumor histology, stage, and clinical course. She was 64 years old, 2 para. She became vertigo and headache from March 2011, and diagnosed transient ischemic attack (TIA) as the result of detailed medical check. After that, she lost consciousness at home in MAY 2011, and diagnosed multiple brain infarction by brain magnetic resonance imaging. Blood test revealed hypercoagulability, and abdominal CT showed pelvic solid cystic mass, 20cm in diameter. However, the cause of thrombosis due to brain infarction was

unexplained. We considered Trousseau's syndrome with left ovarian cancer as the result of these data. We planned surgical treatment, but her general condition was very poor. Thereby, she underwent left salpingo-oophorectomy only. The pathological results for the resected tumor were compatible with a clear cell carcinoma of the left ovary. After the surgery, hypercoagulability was improved. However, her consciousness wasn't yet improved. Trousseau's syndrome is hypercoagulability associated with malignancy. Malignancy caused by Trousseau's syndrome is mostly solid tumors. Gynecological malignancies such as ovarian cancer and breast cancer often set up this situation. We need to take into consider the fact that gynecologic malignancies also influence the development of thrombosis.

Keywords: Trousseau's syndrome, Clear cell carcinoma of the ovary, Hypercoagulability

PP-123 (Case Report)

A useful case of PET-CT in the diagnosis of malignant transformation of mature cystic teratoma

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Objective: Although mature cystic teratoma (MCT) is a benign ovarian tumor, there are few cases which show malignant transformation (MT) at the rates of 1%. The preoperative diagnosis of MT is very difficult, as only one case was true MT among our 4 MT suspected cases. Since PET-CT was very useful in the diagnosis of MT, we report it.

Methods: Subjects were 4 patients who showed an ovarian tumor with solid part. For all patients, we have performed tumor markers' check and MRI and they were suspected as MT.

Results: Case 1: 50 y.o. SCC 32.5 ng/ml, CA19-9 108.5 U/ml. The accumulation of FDG (SUV 11.64) in PET-CT was observed at a solid part. We performed bilateral adnexectomy and identified it as an MCT with MT. Case 2: 74 y.o. SCC 6.4, CA19-9 45,100, CA125 116.2 U/ml. We performed total abdominal hysterectomy and bilateral adnexectomy. The pathological diagnosis was a benign MCT. Case 3: 70 y.o. SCC 29.4, CA19-9 5050, CA125 49.6, CEA 50.1 U/ml. Tumor was very large and uterus could not be identified by the usual examination. Modified radical hysterectomy, bilateral adnexectomy and retroperitoneal lymph node dissection was performed. The pathological diagnosis was a metastasis to ovary of the endometrial cancer. Case 4: 22 y/o, 16 weeks of gestation. We carried out the unilateral oophorectomy only. The result was a MCT and mucinous cystadenocarcinoma.

Conclusion: The diagnosis of MT of MCT is difficult only with MRI and tumor markers. As we showed in Case 1, PET-CT might be useful for the diagnosis.

Keywords: Malignant transformation, Mature cystic teratoma, PET-CT

PP-124 (Case Report)

Recurrence choriocarcinoma treated surgically with laparoscopic resection of intraperitoneal pelvic tumour: case report

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Gestational choriocarcinoma is a relatively rare and aggressive tumour. More than 80% is chemosensitive and majority of cases are cured with combination of surgical evacuation of uterus and chemotherapy. We present a case of 32 years old lady, P2+2 diagnosed as recurrence choriocarcinoma with intraperitoneal pelvic metastases. Despite completed second line chemotherapy (EMA CO regimen) and in remission for seven months, her hCG levels elevated during follow up. MRI (magnetic resonance imaging) and PET CT (positron emission tomography) showed a suspicious F-18 FDG avid lesion at right lower pelvic area. Laparoscopic resection of pelvic lesion was performed and histopathology examination confirmed recurrence choriocarcinoma. She achieved a complete response after laparoscopic surgical resection of tumour without requiring adjuvant chemotherapy and remains disease free for 26 months. Choriocarcinoma is a highly malignant variant of gestational trophoblastic disease. Curative for recurrence choriocarcinoma is usually managed by polychemotherapy, but it can also be achieved by only surgical resection of focal tumour without adjuvant chemotherapy.

Keywords: Choriocarcinoma, Human chorionic gonadotrophin, Laparoscopic

PP-125 (Case Report)

A case of endometrial adenocarcinoma in a patient having 45, X Turner syndrome with spontaneous menarche

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Patients with Turner syndrome receiving estrogen replacement therapy have an increased risk of endometrial carcinoma. There have been nine cases reported who had not been treated with unopposed estrogen to have developed endometrial carcinoma. We report a case of endometrial adenocarcinoma in a patient having 45, X Turner Syndrome with spontaneous menarche. A 26-year-old single nulligravid woman with Turner syndrome, spontaneous puberty, and karyotype 45,X/46,XX from peripheral blood, was administered to our hospital for continuous dysfunctional genital bleeding and severe anemia. On pelvic examination, there was a myoma 3cm large at the cervix. Transcervical resection of the myoma and endometrial curettage were performed. Histological findings confirmed a leiomyoma and endometrial adenocarcinoma of the uterus,

grade 2. Serum levels of CEA, CA125, CA19–9, and SCC were not elevated. Magnetic resonance imaging suspected myometrium invasion. Hysterectomy with bilateral salpingo–oophorectomy and pelvic lymphadenectomy was conducted. She was mobilized on the next day of the surgery and was discharged on the 7th postoperative day. Histological examination identified the endometrial tumor as well–differentiated FIGO stage IA adenocarcinoma that had no invasion in the myometrium. There is no sign of recurrence 3 months after the operation. The incidence of spontaneous menarche in Turner syndrome is reported to be between 5–10%. However, in patients with Turner syndrome who have developed endometrial carcinoma, the incidence of spontaneous menarche was 80%. These data suggest that in patients with Turner syndrome, spontaneous menarche may be a major risk factor of endometrial adenocarcinoma.

Keywords: Endometrial adenocarcinoma, Turner syndrome, Spontaneous menarche

PP–126 (Case report)

A rare case of synchronous tumour of the endometrium and rectovaginal septum without evidence of endometriosis: a case report

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We present a case of 39–year–old nulliparous woman who was referred to our hospital with ovarian cyst noted on a scan done in a private hospital. She gave history of dysmenorrhea and menorrhagia for 6 months. Repeat US pelvis at our hospital did not show any ovarian cyst. An endometrial polyp and a subserosal posterior fibroid were noted. She underwent Hysteroscopy, dilatation & curettage with removal of polyp. Histology showed Grade 1 endometrioid adenocarcinoma. During staging for Ca endometrium, a rectovaginal tumour was discovered. There was no evidence of endometriosis. Total hysterectomy, bilateral salpingo–oophorectomy, was performed en bloc with anterior resection and primary reanastomosis. Full Surgical staging was done with bilateral pelvic lymphadenectomy and omentectomy. The final histology showed synchronous carcinoma endometrium, FIGO Stage 1A well differentiated endometrioid adenocarcinoma, and carcinoma of rectovaginal septum, poorly differentiated adenosquamous carcinoma with invasion into myometrium and rectal muscularis propria, FIGO Stage II. She recovered well postoperatively and is planned for adjuvant chemotherapy for the rectovaginal septum carcinoma. Rectovaginal septum carcinoma is rare with very few cases reported in the literature. Most of the cases arise in a background of endometriosis. This case illustrates a primary rectovaginal septum carcinoma arising simultaneously with endometrial carcinoma without any evidence of endometriosis.

Keywords: Rectovaginal septum, Endometrial, Carcinoma

PP–127 (Case Report)

Serous borderline tumor with microinvasion; a case report

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This is to present one case of ovarian borderline malignancy with microinvasion. Typical serous borderline tumors that contain small foci of stromal invasion were reported sometimes. The malignant transformation of low malignant potential tumor is less than 0.5%. These tumors are common in the premenstrual age group. They have prognosis similar to that of the normal serous borderline tumor that conservation of the contralateral ovary and may be acceptable therapy in young woman who wish to preserve their fertility. Advanced stage disease and microinvasion were associated with significant higher recurrence and mortality later. So, careful follow up is recommended. We present one case of borderline malignancy with microinvasion according to clinical findings and pathologic background.

Keywords: Borderline tumor, Microinvasion, Low malignant potential tumor

PP–128 (Case Report)

Degenerating fibroid mimicking complex ovarian cyst in pregnancy

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A case of a primigravida presenting with a large complex cystic mass with internal echogenic components with septations diagnosed on ultrasound. She was co–managed with the gynae–oncology team and advised to undergo an open salpingo–oophorectomy. She underwent surgery at 19 weeks gestation. Intraoperatively, both ovaries were normal. There was a large 10 cm posterior wall degenerated fibroid. No ascites was present and intraperitoneal survey normal. Decision was made to close up. She recovered well post op and followed up with ultrasound. Degenerated fibroid in pregnancy can mimic complex ovarian cyst in pregnancy. Ultrasound features are somewhat similar. The use of tumor markers to evaluate the mass is not accurate in pregnancy. There have been reports on the use of MRI as an alternative form of imaging in pregnancy.

Keywords: Degenerating fibroid, Complex ovarian cyst, Pregnancy

PP–129 (Case Report)

A 17–year–old female presenting with anti–n–methyl–d–aspartate receptor antibody encephalitis caused by an ovarian teratoma

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Objective: Anti-N-methyl-D-aspartate receptor encephalitis (anti-NMDARE) is rare, but occurs most commonly in young females. It is often associated with ovarian teratomas and induces various neurological symptoms.

Methods: We report the adolescent case of a tiny mature cystic teratoma within a normal-sized ovary, which resulted in anti-NMDARE that improved after surgical treatment.

Results: A 17-year-old Japanese woman presented with fever, headache, and seizures. She was first diagnosed with meningitis. Her consciousness and respiration deteriorated, and she advanced to respiratory failure requiring mechanical ventilation. One month after onset, CT-scan and MRI indicated a small-sized teratoma within the right normal-sized ovary. Then, the patient underwent right oophorectomy. The ovary was grossly normal in appearance, but a cross section revealed the presence of a small tumor. Histologically, the tumor was diagnosed as a mature cystic teratoma. Later, NMDAR antibodies were confirmed, allowing a diagnosis of anti-NMDARE. Six months after the operation, her condition became gradually better and she was released from mechanical ventilation. The following five months have been uneventful.

Conclusion: In young patients, anti-NMDARE occasionally results in severe symptoms regardless of the small size of the ovarian teratoma. Hence, an accurate diagnosis of ovarian teratoma followed by surgical resection of the tumor is required for the treatment of anti-NMDARE.

Keywords: Anti-N-methyl-D-aspartate receptor antibody encephalitis, Ovarian teratoma, Paraneoplastic syndrome

PP-130 (Case Report)

A Case of vulva cancer and CIS in almost virgin

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Objective: It is well known that the occurrence of cervical uterine cancer and vulvar cancer are associated with HPV infection. Recently, however, we encountered a 63-year-old woman of invasive vulvar carcinoma and cervical uterine carcinoma in situ (CIS) with little opportunity for HPV infection.

Methods: A 63-year-old woman visited our out-patient clinic complaining of left vulvar tumor. Examination of exophytic tumor measuring 2 cm in diameter showed class V in scrubbed Pap smear and squamous cell carcinoma in histology. She had experienced only one sexual intercourse about 20 years ago, and then appeared to have vaginal introitus. She was diagnosed as having vulvar SCC, FIGO stage I.

Results: Local wide excision of the vulva and its reconstruction using femoral-skin flap were successfully performed. During postoperative follow-up period, however, repeated (several) cytological examination of uterine cervix demonstrated abnormal. Hysterectomized uterus

showed CIS of the uterine cervix. HPV type 58 was detected in both cervical and vulvar carcinoma.

Conclusion: This case is almost virgin woman with invasive vulvar cancer and CIS of the uterine cervix. Thus, in this patient, the discussion on the association between sexual intercourse and HPV infection is worthwhile.

Keywords: HPV, Virgin, CIS

PP-131 (Case Report)

Primary extraskeletal myxoid chondrosarcoma of the vulva: a case report

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Primary extraskeletal myxoid chondrosarcoma (EMC) of the vulva is extremely rare. We report a rare case of primary EMC of the vulva treated surgically. A 24-year-old Japanese woman with no gravida noticed a small and elastic mass in her vulva. Inspection revealed a globular mass of about 3 cm diameter in the upper part of the right labium majus. The patient underwent enucleation of the mass for surgical diagnosis at another hospital. We histopathologically examined the thin sections provided by the other hospital. On microscopic examination of hematoxylin and eosin-stained sections, only tumor tissue was found to be enucleated. The tumor was mainly composed of abundant myxoid matrices and short spindle cells arranged in trabeculae or cords. Solid areas with high cellular content, high level of mitotic activity, and a scattering of amianthoid fibers were evident in the tumor. Tumor necrosis was not detected. The tumor was positive for vimentin and NSE, and the maximum Ki-67 labeling index was 20%. Consequently, we diagnosed the tumor as a primary EMC of the vulva. The patient subsequently underwent modified vulvectomy and vulvoperineal reconstruction with bilateral lotus petal flaps. Microscopic examination of the resected specimens revealed residual tumor nodules of EMC. Approximately 3 years after the surgery was performed, the patient is doing well and no recurrence of EMC is evident. Here, we report a second case of primary EMC of the vulva that was surgically treated and discuss the relevant literature.

Keywords: Vulvar sarcoma, Extraskeletal myxoid chondrosarcoma, Soft tissue sarcoma

PP-132 (Case Report)

Pleomorphic type of malignant fibrous histiocytoma with myxoid stroma of the vulva in a young woman

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Malignant fibrous histiocytoma (MFH) of the vulva is extremely rare. We encountered a 21-year-old woman who showed a 4.5×2.6 cm exophytic tumor as a superficial localized tumor of the right vulva. The patient underwent wide local excision of the vulva. The extirpated specimen demonstrated the pleomorphic type of MFH with myxoid stroma of the vulva. Chromosomal analysis of the tumor using the conventional G-band method was normal (46, XX). This seems to be a very rare case of MFH of the vulva in a young woman. Physicians must include MFH in the differential diagnosis of vulvar tumor, even though it is a rare disease.

Keywords: Chromosomal analysis, Malignant fibrous histiocytoma, Vulva

PP-133 (Case report)
Glomus tumor of the uterus

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Glomus tumors are composed of epithelioid smooth muscle cells similar to those described in glomus body. This structure is a specialized arteriovenous anastomosis found in the reticular dermis and is involved in thermoregulation. Glomus tumor usually occur in the extremities, especially the nail bed, but have been described in many other sites, including the stomach, intestines, trachea, lung, urinary tract, bone, and vein. To our knowledge, only Anna M recorded in the literature that glomus tumor occur in the uterus. We report the first case of recurrent glomus tumor of the uterus which show uncertain malignant potentials.

Keywords: Glomus tumor, Uterus, Immunohistochemistry

PP_134
Examination of octreotide starting time for malignant bowel obstruction in gynecologic cancer

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Objective: Malignant bowel obstruction (MBO) due to progression or recurrence of cancer remarkably impairs patient quality of life (QOL). Octreotide is a palliative care drug for symptoms of MBO. We examined symptomatic improvement in cases (early intervention) of MBO at the time of salvage chemotherapy after second line treatment with octreotide, as well as the cancer terminal period.

Methods: We prescribed octreotide to 46 patients with MBO between 2008 and 2011. Octreotide was administered over 24 hours, and this dosage method resulted in 300ug per day and a classification as early intervention and palliative care (versus latter term intervention). For the period of examination, symptoms improved, and meal intake became possible with the aim of continuing treatment. We administered a questionnaire on symptoms, focusing on early intervention at the beginning of use.

Results: Patients with nausea, vomiting, abdominal pain, flatulence and lack of appetite before the dosage showed significant improvement based on the questionnaire method by the seventh day of administration (Wilcoxon order official approval). The insertion of an esophageal and ileus tube was avoided in the early intervention cases, and in several cases continuation of chemotherapy was possible. In the latter term intervention cases, the conditions of some patients deteriorated making comparison with the early stage difficult.

Conclusion: As a matter of course, for digestive organ symptoms with MBO in gynecologic cancer patients, as for the use of octreotide in the terminal stage, there is a possibility of improving patient QOL if administered early during salvage chemotherapy.

Keywords: Malignant bowel obstruction, Octreotide, Gynecologic cancer

PP_135
The measurement of SUVmax of the primary tumor is predictive of prognosis for patients with endometrial cancer

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Objective: The purpose of this study was to evaluate if preoperative measurements of the maximum standardized uptake value (SUVmax) on positron emission tomography/computed tomography (PET/CT) and tumor marker CA125 are correlated with clinical characteristics and prognosis in patients with endometrial cancer.

Methods: The distribution of cases that scored positive for each of the biological parameters examined and the correlations with the SUVmax of the primary tumor and the serum tumor marker CA125 were examined for 106 patients with preoperative assessment of primary endometrial cancer.

Results: There were significant correlations between the SUVmax of the primary tumor and the FIGO stage, histology, depth of myometrial invasion and tumor maximum size. The serum CA125 level was significantly associated with the FIGO stage. The disease-free survival (DFS) and overall survival (OS) rates of patients exhibiting a high SUVmax of the primary tumor were significantly lower than those of patients exhibiting a low SUVmax of the primary tumor. Furthermore,

the DFS and OS rates of patients exhibiting a high SUVmax of the primary tumor were significantly lower than those of patients exhibiting a low SUVmax of the primary tumor at advanced stages (stages III-IV). In particular, the SUVmax of the primary tumor was an independent prognostic factor for OS by a multivariate analysis.

Conclusion: The present findings indicate that for patients with endometrial cancer, a high preoperative SUVmax of the primary tumor is an important predictive factor for identifying endometrial cancer patients with a poor prognosis.

Keywords: Positron emission tomography/computed tomography, Maximum standardized uptake value, Predictor for poor prognosis

PP_136

Diabetes and metformin use in patients with endometrial cancer

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Objective: Epidemiologic studies have suggested that metformin lowers the risk of various cancers among diabetics, while a recent clinical study demonstrated that metformin may enhance chemotherapy in patients with early stage breast cancer. The development of type 1 endometrial cancers is driven by obesity, diabetes and insulin-resistance. Preclinical evidence has shown that metformin inhibits the growth of endometrial cancer cells in vitro. The objective of our retrospective study is to investigate the relationship between diabetes and metformin use in patients with early-stage endometrial cancer.

Methods: Medical records of patients diagnosed with early stage endometrial cancer between January 2000 and December 2010 were reviewed. Patient demographics, clinico-pathologic factors, recurrence rates and survival were compared between non-diabetics, diabetics taking metformin and diabetics not taking metformin. Factors predictive of recurrence and mortality were assessed using a multivariate logistic regression model.

Results: Out of a total of 268 patients identified, 36 were diabetic. Twenty-two diabetic patients took metformin while 14 diabetic patients were not on metformin. Patients in the diabetic groups were older than those in the non-diabetic group and were more overweight and obese according to their body mass index (BMI), regardless of metformin use. Diabetic patients, including metformin users, had significantly increased risk of recurrence and mortality from endometrial cancer.

Conclusion: Diabetes significantly increases recurrence and decreases survival in endometrial cancer. Metformin use does not appear to be of any benefit in reducing relapses or improving survival. Further studies to evaluate the biology and molecular pathways in endometrial cancer are warranted.

Keywords: Endometrial cancer, Diabetes mellitus, Metformin

PP_137

High risk type human papillomavirus (HPV) indicates increasing high grade squamous intraepithelial lesion (HSIL) incidence in cytological low grade squamous intraepithelial lesion (LSIL) patients

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Objective: Human papillomavirus (HPV) is known as the causal agent of cervical cancer. The Papanicolaou smear is the most popular screening tool for cervical cancer. Some cytological low grade squamous intraepithelial lesions (LSILs) are in the developmental stage of HSIL and cervical cancer metaphases. Our purpose is to disclose the significance of high risk type (HRT) HPV in LSIL.

Methods: Documentation of 200 cases of cone biopsy at Hallym University Sacred Heart Hospital from February 2006 to February 2008 was reviewed retrospectively. HPV typing with DNA microarray results were found in 20 of the LSIL patients. Chi-square and student-t tests were used in the statistical analysis.

Results: In the cytological LSIL patients, HRT-HPV positive patients were 16/20 (80%) and one low risk type (LRT) HPV positive patient was 1/20 (5%). In the cytological LSIL patients, postoperative pathological diagnoses were cervical intraepithelial neoplasia 1 (CIN 1) 16/26 (61.5%), CIN2 2/26 (7.7%), CIN3 5/26 (19.2%), CIS (carcinoma in situ) 1/26 (3.8%). Among the 16 HRT-HPV positive patients, there were six that were above HSIL 6/16 (37.5%) in pathologic diagnoses. In the HRT-HPV negative 10 cytologic LSIL patients, there were two that were above HSIL 2/10 (20%) in pathologic diagnoses.

Conclusion: In HRT-HPV positive LSIL, the risk of HSIL of the cervix seems to be increasing. The HPV test is helpful in LSIL patient strategies and should be done in LSIL patients in order to discriminate between the nature and prognosis of cytological LSIL.

Keywords: HPV, Low grade squamous intraepithelial lesion, Cervical cancer

PP_138

Uterine leiomyosarcoma in asian patients - validation of the new FIGO staging system and identification of prognostic classifiers

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Objective: Uterine Leiomyosarcoma (uLMS) is a rare and aggressive malignancy associated with poor survival regardless of stage. Here we compare the performance of the new 2009 FIGO staging system with the older system based on endometrial cancers and identify important prognostic markers.

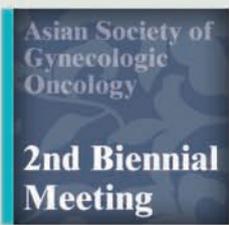
Methods: Medical records of 110 uLMS patients from 1974 to 2010 were reviewed and data from 85 analysed using Kaplan–Meier (KM) log rank and Cox proportional hazards models.

Results: Under the new FIGO classification, 73% of women presented with stage I disease, and 4.7%, 4.7% and 17.6% with Stages II, III, and IV respectively. 8 patients were downstaged, and none were upstaged. KM overall survival (OS) analysis did not show any significant improvement in risk discrimination between stages I–IV, although there was improved statistical performance for PFS. The 5–year OS rate for

Stage 1 patients under old FIGO was 0.597 (95% C.I.: 0.443 to 0.751), versus 0.580 (95% C.I.: 0.432 to 0.728) under new FIGO. Advanced patient age, tumor size, tumor grade and lymphovascular invasion were adverse prognostic factors, however only age and grade remained significant on multi–variate analysis. Patients with high grade (HG) stage I tumours had a 10–year OS rate of <20% versus approximately 80% for low grade tumors. For stage I, tumors between 5 and 10cm represented an intermediate prognostic group.

Conclusion: The new FIGO classification does not significantly improve risk discrimination between stages and majority of uLMS patients continue to be diagnosed with stage I disease, where prognosis becomes highly dependent on patient age and tumour grade.

Keywords: Uterine leiomyosarcoma, FIGO staging, Prognostic factors



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The 3rd Biennial Meeting Asian Society of Gynecologic Oncology

Date December 13 (Fri) ~ 15 (Sun), 2013

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