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Recommendations for gynecologic cancer care during the COVID-19 pandemic

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Dear Editor,

The novel coronavirus disease 2019 (COVID-19), viral respiratory illness, is developed by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its outbreak was firstly observed at Wuhan, China, in 2019 [1]. The World Health Organization (WHO) has developed practical recommendations for every specific situation [2]. In line with WHO's proposal, each country of the globe has announced applicable guidelines for the prevention of COVID-19 transmission. Despite strong quarantine, nationwide lockdown, social distancing, and hygiene education, the COVID-19 spread unfortunately continues with different patterns of occurrence in each country [3].

With these backgrounds, the standard of care in gynecologic cancers has been inevitably hampered by the COVID-19 crisis. As a result, patients and medical staffs are facing unprecedented challenges in treating cancer. In this letter, we have provided specialized recommendations beneficial for clinicians to take care of patients with gynecologic cancers during the pandemic of COVID-19. It is desirable to selectively apply this recommendation in consideration of the hospital's resources and the situation of COVID-19 transmission. For more clear understanding, we divided possible situation of diseases into three priorities, depending on the severity of patient's condition with gynecologic malignancies.

In **Table 1**, we described the priority of disease condition which was modified referring to the clinical guidelines from Ontario Health [4,5]. Management was indicated with A, B, and C in the order of higher priority to adequately cope with specific conditions in cervical, endometrial, and ovarian cancer (**Tables 2-4**) [6-15].

We strongly believe that this recommendation is expected to provide clinicians with practical assistance in dealing with gynecologic cancer by prioritization and minimize potential risk of exposure to COVID-19.

Table 1. The classification of priorities according to the severity of disease condition

Priority	Description of disease severity
A	Life-threatening or needs emergency care
B	Non-life threatening and could be deferred 6–8 weeks during the COVID-19 pandemic
C	Stable even in the discontinuation of treatment during the current COVID-19 crisis

COVID-19, coronavirus disease 2019.

Table 2. Recommendations for cervical cancer care during the COVID-19 pandemic

Priority	Patient's status	Management
A	New diagnosis or screening test	Assessment should be performed as soon as possible based on the level of institution resources or regional circumstances of COVID-19
C	Massive and/or persistent bleeding from cervix	It is preferable to discontinue all routine check-up during COVID-19 pandemic or consider to refer to the accessible local clinic
	Routine screening	
	Abnormal Pap result	
B	Suspected of low-grade cervical disease	Assessment could be deferred up to 6-12 months
B	Suspected of high-grade cervical disease without invasive cancer	It is appropriate to evaluate lesions within 3 months
B	Suspected of invasive cervical cancer	Diagnosis of the lesion could be prioritized within 2 weeks
	Early-stage cervical cancer	
C	Stage IA1 based on LLETZ pathology	It might be possible to observe the lesion without further treatment until COVID-19 outbreak wanes
B	Stage IA2 based on LLETZ pathology	It could be postponed to perform further treatment up to 6-8 weeks
B	Stage IB1, IB2, and IIA1	Radical hysterectomy can be postponed up to 6-8 weeks and can be replaced by alternatives such as trachelectomy, neoadjuvant chemotherapy, or radiation therapy in consideration of fertility preservation, operation morbidity, and patient condition
C	Postoperative status - low risk of recurrence	Adjuvant therapy might be discontinued during the crisis of COVID-19
B	Postoperative status - intermediate risk of recurrence	(CC)RT can be deferred up to 8 weeks after surgery in consideration of risk of Sedlis criteria
B	Postoperative status - high risk of recurrence	It is preferable to perform CCRT on schedule
B	Stage IB3, and IIA2	It is appropriate to perform EBRT using hypofractionation to reduce the number of visit to clinic. Radical hysterectomy can be chosen on the decision of physician.
B	Locally advanced cervical cancer (IIB- IVA)	CCRT is recommended on schedule, and could consider hypofractionation to reduce the number of visit to clinic. Brachytherapy should be done on time unless there is COVID-19 symptom.
B	Stage IVB cervical cancer	It is preferable to perform chemotherapy consisting of cisplatin and paclitaxel, (+/-) bevacizumab on schedule.
	Recurrent cervical cancer	
B	Cervical stump recurrence	Surgical resection or radiation therapy can be considered according to the level of institutional resources on schedule
B	Vaginal recurrence with bleeding	It is recommended to perform brachytherapy or EBRT on schedule
B	Local recurrence within pelvis	(CC)RT is recommended on schedule, and could consider hypofractionation to reduce the number of visit to clinic. Brachytherapy should be done on time unless there is COVID-19 symptom.
B	Distant recurrence - chest only	Chemotherapy is recommended on schedule, but it can be deferred for several week in case of no adverse effect caused by the delay of treatment
B	Distant multiple recurrence	Chemotherapy is recommended on schedule, but it can be deferred for several week in case of no adverse effect caused by the delay of treatment
B	Pelvic side wall recurrence	Ultra-radical surgery or radiation could be recommended according to the level of institution resources
	Follow-up	
C	Follow-up after curative operation	Surveillance can be deferred based on the level of risk for recurrence
C	Follow-up after curative radiation	Surveillance can be deferred based on the level of risk for recurrence
	Special situation	
B	Occult cervical cancer after simple hysterectomy	The treatment can be chosen among observation, surgery, or radiation after pathologic review. It can be deferred for several week in case of no adverse effect caused by delay of treatment
C	Condition requiring palliative treatment	The treatment can be postponed after consultation with multidisciplinary team
A	Serious toxicity (i.e. fever, pain, dyspnea, bowel perforation, and unstable vital sign)	Immediate management of toxicity should be required as soon as possible even in the circumstances of COVID-19 pandemic
B	Neutropenia	Administration of hematologic growth factor is recommended as quickly as possible

COVID-19, coronavirus disease 2019; CCRT, concurrent chemo-radiation treatment; EBRT, external beam radiation therapy; LLETZ, large loop excision of the transformation zone.

Table 3. Recommendations for endometrial cancer care during the COVID-19 pandemic

Priority	Patient's status	Management
A	Diagnostic approach	
	Vaginal bleeding, suspicious uterine pathology	In case of clinically significant AUB, office-based endometrial biopsy should be performed in outpatient setting based on the level of institution resources or regional circumstances of COVID-19
B	Premalignant disease	
	EIN, wants preserving fertility	Start conservative treatment such as oral progestin and LNG-IUD
B	EIN, not wants preserving fertility	Simple hysterectomy might be postponed up to 8 weeks. Conservative treatment such as oral progestin and LNG-IUD can be applied alternatively until the pandemic is over.
A	Surgical staging	MIS approach with SLN mapping is recommended because it confers fast recovery and less complication, and accurate nodal staging
	Surgical staging in patients with active bleeding	Staging operation with hysterectomy should be performed as soon as possible.
	Surgical staging in patients without active bleeding	Staging operation can be delayed up to 8 weeks.
	Clinical stage IA, grade I	Conservative treatment such as oral progestin and LNG-IUD can be applied alternatively until the pandemic is over.
C	Adjuvant treatment	Adjuvant treatment can be deferred up to 9 weeks after surgery.
	Surgical stage I, II with low risk factor	Adjuvant therapy might be discontinued during the crisis of COVID-19
B	Surgical stage I, II with intermediate to high risk factors	Brachytherapy is preferred considering fewer visit and less complication risk
B	Surgical stage III	Depending on the discretion of the physician, adjuvant chemotherapy or radiotherapy is considered. Use chemotherapy regimens that will avoid frequent patient visits (e.g. paclitaxel + carboplatin). In case of pelvic RT, consider hypofractionation to reduce the number of visit to clinic.
	Surgical stage IVA	Depending on the discretion of the physician, adjuvant chemotherapy or radiotherapy is considered. Use chemotherapy regimens that will avoid frequent patient visits (e.g. paclitaxel + carboplatin). In case of pelvic RT, consider hypofractionation to reduce the number of visit to clinic.
B	Inoperable condition	
	Inoperable clinical stage III	Chemotherapy is recommended on schedule. Use chemotherapy regimens that will avoid frequent patient visits (e.g. paclitaxel + carboplatin)
B	Inoperable clinical stage IV	Chemotherapy is recommended on schedule.
B	Stage IVB	Use chemotherapy regimens that will avoid frequent patient visits (e.g. paclitaxel + carboplatin)
	Stage IVB	Chemotherapy is recommended on schedule. Use chemotherapy regimens that will avoid frequent patient visits (e.g. paclitaxel + carboplatin)
C	Follow-up	Routine imaging study is not recommended until the pandemic is over
	Follow-up after primary treatment	Surveillance can be deferred based on the level of risk for recurrence
B	Recurrent disease	Choice of therapy should minimize exposure to other contacts, risk from therapy, and prognosis.
	Isolated vaginal recurrence	Brachytherapy is recommended on schedule, but it can be deferred for several week in case of no adverse effect caused by delay of treatment
B	Pelvic recurrence	RT is recommended on schedule, and consider hypofractionation to reduce the number of visit to clinic.
B	Distant recurrence with symptom	Chemotherapy is recommended on schedule. Use chemotherapy regimens that will avoid frequent patient visits
C	Distant recurrence without symptom	Consider hormonal treatment
	Distant recurrence without symptom	Use chemotherapy regimens that will avoid frequent patient visits
B	Second or more line chemotherapy after recurrence	Consider hormonal treatment
	Second or more line chemotherapy after recurrence	Use chemotherapy regimens that will avoid frequent patient visits

COVID-19, coronavirus disease 2019; AUB, abnormal uterine bleeding; EIN, endometrial intraepithelial neoplasia; LNG-IUD, levonorgestrel intrauterine device; MIS, minimally invasive surgery; RT, radiotherapy; SLN, sentinel lymph node.

Table 4. Recommendations for epithelial ovarian cancer care during the COVID-19 pandemic

Priority	Patient's status	Management
A	Newly diagnosed ovarian cancer	Assessment should be performed as soon as possible.
B	Suspected ovarian cancer with symptoms indicating bowel obstruction/perforation, massive ascites, or peritonitis	For presumed early stage ovarian cancer according to salpingo-oophorectomy, restaging surgery can be deferred from 6–8 weeks.
B	Suspected ovarian cancer with no symptom and looks confined to pelvis	Delaying interval debulking surgery beyond 3–4 cycles of neoadjuvant chemotherapy should be considered.
B	Suspected ovarian cancer with no symptom and looks spread beyond pelvis	Choose regimens scheduled with the fewest infusion visits.
B	After 3 cycles neoadjuvant chemotherapy in suspected advanced stage ovarian cancer	Consider lower dosing intensity and less myelosuppressive regimens to reduce neutropenia.
A	Suspected postoperative complications (e.g. anastomotic leak)	Avoid the prescription of dose-dense, intraperitoneal, and HIPEC regimens.
B	Incidentally found ovarian cancer	Consider extending the chemotherapy plan to 6 cycles before the interval cytoreductive surgery in women who have already started neoadjuvant chemotherapy.
		Assessment should be performed as soon as possible.
		For presumed early stage ovarian cancer according to salpingo-oophorectomy, restaging surgery can be deferred from 6–8 weeks.
		If residual suspected, reoperation should be performed.
A	Early stage (I–IIA) ovarian cancer requiring postoperative adjuvant chemotherapy	Adjuvant chemotherapy should be performed as soon as possible.
B	High-grade serous/endometrioid	Adjuvant chemotherapy can be an option, but should be considered less essential and discussed with the patient about minimizing the infusion visits.
	Non-high-grade serous/endometrioid	
	Adjuvant chemotherapy in advanced stage ovarian cancer	
A	High-grade serous/endometrioid	Adjuvant chemotherapy should be performed as soon as possible.
A	High-grade serous with <i>BRCA</i> mutation	In patients who have a <i>BRCA</i> mutation and are PARP naïve, consider rucaparib monotherapy in situations where platinum therapy cannot be given.
B	Clear cell or mucinous tumor	Adjuvant chemotherapy can be an option, but should be considered less essential and discussed with the patient about minimizing the infusion visits.
C	Low-grade serous tumor	Consider deferring the adjuvant therapy as possible.
C	After upfront adjuvant chemotherapy	Consider deferring the maintenance chemotherapy as possible.
		If utilizing PARPi maintenance therapy, consider the risk of the immunosuppression and exposure to COVID-19 during infusion.
	Follow-up visit	Routine surveillance of asymptomatic patients should be postponed as possible.
C	Patients with PARPi maintenance	Utilize telemedicine and reduce the frequency of in-person evaluation.
C	Patients with bevacizumab maintenance	Most can be managed through telemedicine with scheduled blood tests and imaging done close to home.
		If facilities exist to continue, supervision can be performed by telemedicine, ensuring BP and urinalysis are monitored.
B	Recurrent disease	Choice of therapy should minimize exposure to other contacts, risk from therapy, and prognosis.
C	Symptomatic platinum-sensitive recurrent disease	Adjuvant chemotherapy can be an option, but should be considered less essential and discussed with the patient about minimizing the infusion visits.
C	Symptomatic platinum-resistant recurrent disease	Non platinum-based regimen are low priority and should be used after careful review of the risk/benefit.
C	Symptomatic slowly growing recurrent disease	Decision should be based on clinical judgement.
C	Asymptomatic recurrent disease	Decision should be based on clinical judgement.
	Special situation	
C	Risk-reducing salpingo-oophorectomy for genetic predisposition to gynecological cancer	Consider deferring the surgery as possible.

COVID-19, coronavirus disease 2019; *BRCA*, breast cancer gene; BP, blood pressure; HIPEC, hyperthermic intraperitoneal chemotherapy; PARPi, poly ADP ribose polymerase inhibitor.

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