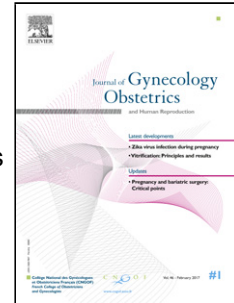


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Recommendations for the surgical management of gynecological cancers during the COVID-19 pandemic - FRANCOGYN group for the CNGOF¹

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Summary :

Introduction: In the context of the COVID-19 pandemic, specific recommendations are required for the management of patients with gynecologic cancer.

Materials and method: The FRANCOGYN group of the National College of French Gynecologists and Obstetricians (CNGOF) convened to develop recommendations based on the consensus conference model.

Results: If a patient with a gynecologic cancer presents with COVID-19, surgical management should be postponed for at least 15 days. For cervical cancer, radiotherapy and concomitant radiochemotherapy could replace surgery as first-line treatment and the value of lymph node staging should be reviewed on a case-by-case basis. For advanced ovarian cancers, neoadjuvant chemotherapy should be preferred over primary cytoreduction surgery. It is legitimate not to perform hyperthermic intraperitoneal chemotherapy during the COVID-19 pandemic. For patients who are scheduled to undergo interval surgery, chemotherapy can be continued and surgery performed after 6 cycles. For patients with early stage endometrial cancer of low and intermediate preoperative ESMO risk, hysterectomy with bilateral adnexectomy combined with a sentinel lymph node procedure is recommended. Surgery can be postponed for 1 to 2 months in low-risk endometrial cancers (FIGO Ia stage on MRI and grade 1-2 endometrioid cancer on endometrial biopsy). For patients of high ESMO risk, the

MSKCC algorithm (combining PET-CT and sentinel lymph node biopsy) should be applied to avoid pelvic and lumbar-aortic lymphadenectomy.

Conclusion: During the COVID-19 pandemic, management of a patient with cancer should be adapted to limit the risks associated with the virus without incurring loss of chance.

Keywords : Gynaecological cancer ; COVID-19 ; Guideline ; Management

These recommendations are based on current knowledge but may evolve as new data emerges.

In the current pandemic context of COVID-19 and the subsequent saturation of resuscitation services, over the next 2 to 3 months we must not only reconsider our therapeutic indications but also limit the risk of infection in our cancer patients. To reduce the risk of infections two priorities are crucial: to limit high risk situations such as surgery and chemotherapy; and to limit the patient's contact with healthcare workers and, in particular, with places of care.

While bearing in mind that the main objective for our patients with pelvic gynecologic cancer remains therapeutic management, all alternatives to surgery must be considered. In particular, the risk-benefit ratio for surgical procedures must be analyzed on a case-by-case basis and in multidisciplinary meeting, taking into account the risk of loss of chance that could result from an alternative strategy that has not been proven. The main objective is to avoid postoperative complications and the need for ensuing postoperative intensive care and in particular the occupation of a resuscitation bed. However, in as far as it is possible according to the saturation of the structure of care related to COVID-19, it is advisable to apply traditional recommendations.

If a patient presents with COVID-19, surgical management and all other oncological treatment should be postponed for at least 15 days.

Cancer patients are 4 to 8 times more likely than the general population to develop severe respiratory complications related to COVID-19 marked by rapid onset and often fatal outcome. The risk is more acute if they have undergone surgery or chemotherapy in the preceding weeks. These patients' vital prognosis is at risk in addition to the risk linked to cancer. They should be provided with a mask and use hand sanitizers on arrival at the hospital.

Preamble.

Management of the oncology patient is conventionally based on two strategies:

1) Curative: for localized diseases, or for certain advanced / metastatic cancers characterized by a particular sensitivity to treatments or a disease course which makes them curable by medical, surgical or radiotherapeutic treatment

2) Palliative (non-curative): for diseases too advanced to be curable.

In the current COVID-19 context, patient prioritization should integrate the nature of the therapeutic strategy (curative versus palliative), their age, estimated life expectancy, and whether the diagnosis is recent or not.

Taking into account the duration of incubation and the high percentage of asymptomatic patients, all pathologic samples should be considered as potentially infected. A recent publication has shown that fixation in formalin can inactivate the COVID-19 virus. The risk of toxicity linked to formalin exposure appears to be less serious than that linked to the handling of fresh, non-fixed tissue potentially carrying COVID-19. If necessary, operating samples from patients included in clinical trials can be sent fresh to the laboratory but all the necessary precautions should be applied.

Imaging tests should be maintained or postponed according to their importance and the impact on the choice of treatment strategy.

1. All multidisciplinary meetings should be organized following the recommendations of the ONCORIF group (<https://www.oncorif.fr/2020/03/coronavirus-recommandations-et-contenus-fiabiles/>). As far as possible, multidisciplinary meetings should be held with a triple objective: not to delay the care of patients who need it; not to unnecessarily mobilize doctors who are not absolutely necessary for the discussion; not to promote the transmission of the virus between cardiopulmonary resuscitation (CPR) doctors. It is strongly advised to hold dematerialized meetings when possible based on video or teleconferencing even if the doctors practice in the same establishment.

2. We propose the following adaptations for the management of patients with gynecologic pelvic cancer during the COVID-19 pandemic period.

2.1. For cervical cancer:

Radiotherapy and concomitant radiochemotherapy should replace surgery as first-line treatment whenever possible. In particular, the value of lymph node staging surgeries must be reviewed on a case-by-case basis depending on the site, the results of imaging tests and the disease stage. Hysterectomy after concomitant radiochemotherapy is only indicated if a post-therapeutic tumor residue is identified.

2.2. For ovarian cancer:

For advanced cancers which may require the use of postoperative resuscitation for cytoreduction surgery, neoadjuvant chemotherapy should be the preferred option even if primary cytoreduction surgery could be envisaged. It is legitimate not to offer hyperthermic intraperitoneal chemotherapy (HIPEC) to patients during the COVID-19 pandemic period when resuscitation resources are saturated. If access to the operating theater is restricted due to the crisis, patients scheduled to undergo interval surgery after 3 or 4 cycles of chemotherapy could continue their chemotherapy and surgery be performed after 6 cycles of chemotherapy. The patient should then undergo at least two new cycles of chemotherapy after their closing surgery (in agreement with INCa recommendations <https://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Summary-Initial-management-of-epithelial-ovarian-cancer-cases>).

For presumed early stage ovarian cancers according to adnexectomy, restaging surgery can be deferred from 1 to 2 months if access to anesthesia-resuscitation is saturated.

Furthermore, in case of saturation of access to anesthesia-resuscitation, a 2-step strategy is recommended for images suggestive of ovarian cancer on an isolated ovarian mass: adnexectomy of the suspect mass, and decision to perform complete staging surgery on final histologic analysis and decision of a CPR doctor.

2.3. For endometrial cancer:

Early stage cancers:

Surgical treatment remains the gold standard for early stage endometrial cancer. The minimally invasive laparoscopic robot-assisted or non-assisted route is the preferred option. Total hysterectomy with bilateral adnexectomy associated with a sentinel node procedure should be performed in patients of low and intermediate preoperative ESMO risk. Surgery can be postponed for 1 to 2 months for low-risk endometrial cancers (FIGO Ia stage on MRI and grade 1-2 endometrioid cancer on endometrial biopsy) if there is no element of discrepancy on the initial assessment, especially if the patient is elderly and / or with comorbidities, without loss of oncological chance for the patient.

For patients at high ESMO risk according to pelvic and lumbar-aortic lymphadenectomy staging, comorbidities and the terrain (obesity, anticoagulant treatment, diabetes, age) should be taken into account. In this context, it would be legitimate to apply the MSKCC algorithm (associating PET CT and GS procedure) to avoid lymphadenectomy which increases the risk of per- and postoperative complications and the subsequent risk of requiring postoperative resuscitation.

For advanced endometrial cancers (stages III and IV), first-line medical treatment should be administered.

For suspected endometrial cancer

For a patient who presents postmenopausal metrorrhagia and endometrial thickening on ultrasound, endometrial pipelle sampling should be performed in consultation. Diagnostic hysteroscopy in consultation should be avoided unless performed at the same time (to limit the number of patient trips). In the event of a non-contributory diagnostic assessment, the date of the diagnostic hysteroscopy and biopsy curettage should be adjusted according to the degree of suspicion of endometrial cancer and the constraints of access to the operating room. If the risk of cancer appears low and the patient is elderly, the procedure under general anesthesia can be postponed until after the confinement period for COVID-19.

2.3. For vulvar cancers:

The management of vulvar cancers, for which surgery remains the standard and often the only treatment option, should not change. However, this cancer often affects the elderly and if a tumor has not progressed much in an elderly patient, treatment may be postponed for a few

weeks. The patient should be discharged as early as possible and cared for at home to reduce the duration of hospitalization.

When surgical management involves heavy surgery (amputation), the use of concomitant radiochemotherapy should be discussed in CPR.

2.4. For vaginal cancer:

Most patients presenting with vaginal cancer are at an advanced stage and will require exclusive radio- / chemo- / brachytherapy treatment. The value of lymph node staging surgery must be reviewed on a case-by-case basis depending on the location, the results of imaging tests, and the disease stage.

2.5. For trophoblastic tumors:

Trophoblastic tumors are considered curable but have a high metastatic potential. This justifies maintaining the care of these young patients without delay.

- Patients with low risk trophoblastic tumors (FIGO score ≤ 6) should be administered methotrexate at home to avoid the four injections of each cure in an outpatient setting.
- Patients with high-risk tumors should be administered multidrug regimens without delay given the generally multi-metastatic nature from the outset.

Finally, hydatidiform moles should be managed by the standard treatment of curettage suction under ultrasound control and not by medicinal evacuation which carries a high risk of retention.

The French Reference Center for Trophoblastic Diseases is available for case-by-case discussion and can provide the treatment protocol with methotrexate at home if necessary (touria.hajri@chu-lyon.fr).

3. Post-therapeutic follow-up

Post-therapeutic oncological follow-up consultations should be postponed for 2 months (i.e., after the COVID-19 confinement period), because there is no obvious loss of chance. Follow-up can be performed by teleconsultation when the technical tools are available. However, follow-up of endometrial and / or cervical cancer is based on clinical examination, which cannot be replaced by teleconsultation, and avoid a follow-up consultation 2 months later.