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Management of gynecologic cancer during COVID-19 pandemic: South Asian perspective

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Abstract

Management of gynecological cancers has suffered during the pandemic, partly due to the lock down and partly due to directing resources to managing COVID-19 patients. Additionally, oncology centers are urging cancer patients to stay at home as they face an increased risk of morbidity and mortality after contracting the novel coronavirus, often being immune-compromised. Modification of gynecological cancer management during this pandemic is recommended. Radiotherapy and concomitant radio-chemotherapy could replace surgery as first-line treatment for cervical cancer although there are concerns of immunosuppression with chemotherapy. The value of lymph node staging needs to be reconsidered on a case-by-case basis. Neoadjuvant chemotherapy should be given preference over primary cyto-reduction surgery for advanced ovarian cancers. Surgeries, which demand extended surgical time such as Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and pelvic exenterations, should be avoided during this pandemic. For patients scheduled for interval surgery after two or three neoadjuvant cycles, consideration should be given to six cycles of chemotherapy before surgery is performed. For early stage, low-grade endometrial cancer (FIGO Stage IA on MRI or ultrasound) consideration should be given to medical management until surgery is possible. Medical therapy can include high dose medroxy-progesterone, provera, aromatase inhibitors and metformin. At the time of surgery, consideration should be given to sentinel node dissection rather than extensive lymphadenectomies. Oncologists have to think critically and prepare local guidelines to deal with gynecologic cancer patients.

Introduction

India's first case of Coronavirus was reported in Kerala on 30th January, 2020, amid worldwide panic over the viral outbreak. As of 17th April, 2020, 13,835 now, millions of cases of coronavirus have been detected and thousands have died due to this disease. The COVID-19 pandemic has led to unique challenges in managing cancer patients. These challenges are distressing for both cancer patients as well as the health care providers. Management of gynecological cancers has suffered during the pandemic, partly due to the lock down and partly due to directing resources to manage COVID-19 patients. Also, cancer patients are advised to stay home as they face higher risk of morbidity and mortality after contracting the novel coronavirus. At this time, circumstances to treat cancer patients, vary broadly by region and hospital. Managing a cancer patient depends on COVID-19 prevalence, type of hospital, whether these hospitals are managing both COVID and non-COVID patients and available resources. Due to this reason, despite having many practice guidelines, individualizing according to region and area needs is important. The purpose of this document is to highlight considerations in gynecologic oncology surgical practice amid COVID-19 pandemic in Indian scenario.

Gynecological cancer burden in India

According to Globocon, 2018 (Source: International Agency for Research on Cancer), the incidence of new cervical cancer cases was 96,922 (16.5% of all cancers in females), new ovarian cancers 36,170 (6.2% of all cancers in females) and new uterine cancers 13,328 (1.2% of all cancers in females) [1]. The mortality was 60,078 (7.7%) from cervical cancer, 24015 (3.1%) from ovarian cancer and 5010 (0.64%) from uterine cancer.(1) India sees over 150,000 new gynecologic cancer patients every year. This data shows that there is huge gynecological cancer burden in health centers, demanding multiple hospital visits.

Concerns about patients suffering from gynecological malignancy during COVID-19 pandemic

With Covid-19, mortality rates are higher among cancer patients in Italy and China. 20% of patients who expired due to COVID-19 in Italy were cancer patients [2]. In China, COVID-positive Cancer patients recorded a 40% mortality rate, much higher than any other cancer related cause [3]. This study had 2007 COVID-19 patients from 575 hospitals in China. It was reported that 18 patients had a history of cancer, some currently under treatment; others were in follow-up after treatment. About half of these patients had a higher risk of severe events which is defined as ICU admission, need for ventilation or death [3].

Patients with cancer undergoing hospitalization, chemotherapy or radiation therapy may be at an increased risk of COVID-19 infection, according to a recent JAMA Oncology report [4]. Notably, the majority of infected patients in this study had lung cancer and there were no pa-

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tients with gynecologic cancer. Due to this, experts have suggested revising the goals of treatment, expected benefits of treatment and avoiding complications of COVID-19 in an immune-compromised cancer patient. Infectious diseases are the second-leading causes of mortality in patients with cancer, whose immune systems are often compromised and COVID can be one such infection during time of pandemic. The cause of their systemic immunosuppressive state can be malignancy or anti-cancer treatments, such as chemotherapy, targeted therapy and immunotherapy. Most cancer patients are, therefore, asked to avoid non-essential travel to the hospital and urged to take advice online [5].

Challenges faced by gynecologic oncologist

New gynecologic cancer patients usually need surgery. Surgery during the time of this pandemic, especially in high burden areas, may be risky. This needs to be discussed with the patient, before, making any decision. For follow-up of gynecological malignancy cases, oncologists and their patients need to discuss the necessity of avoiding clinic visits, due to higher risk of morbidity and mortality from COVID-19. Another issue of significance is the difficult decision for both patients and oncologists to continue immuno-suppressive treatments during this COVID-19 crisis.

Determining surgical emergency in gynecologic cancer cases

Indication for any surgery is classified as elective/non-urgent, semi-urgent, and urgent/emergent. The Elective Surgery Acuity Scale (ESAS), modified for gynecologic oncology procedures, may assist surgeons with general procedural classification and prioritization; the table of advised tiers is mentioned in the document by Society of Gynecologic Oncology (SGO).(6) Most gynecologic oncology procedural indications will fall into a Tier 3a/b (semi-urgent) category. Tier 3a comprises of high acuity surgery/healthy patient, potentially life threatening or when patient is highly symptomatic and requires in-hospital stay. Tier 3b comprises of high acuity surgery in unhealthy patients. For these two categories, the Society of Gynecologic Oncology (SGO) recommends not to postpone surgery [6]. They also recommend that if there is high COVID-19 census for any tier, case prioritization may change.

Resource considerations

Individual provider decisions about proceeding with elective surgeries should not be made in isolation, as availability of local institutional resources has to be considered. Local authorities looking after preparedness of a facility in managing COVID patients should share information about resource constraints on a regular basis. These resources include protective gear for providers and patients [6]. With this mutual sharing of information, apt decision can be taken, with idea of its potential impact on limiting the hospitals capacity to pandemic response. One needs to balance the risk of delay of surgery against the imminent availability of resources for patients with COVID-19, while operating upon cases with a high likelihood of postoperative ICU or ventilator requirement. These problems will be encountered more frequently as the impact of COVID-19 on communities grows exponentially.

Acceptable delay in gynecologic cancer surgery

From a psychologic perspective, no delay is acceptable, however, from an oncologic perspective, up to 3–8 week delays may be reasonable for select cancer cases if the risks of COVID-19 exposure are deemed high enough. Referral to regional centers, if possible, is a feasible alternative. If semi-urgent cases are no longer operated upon or managed at an institution, patients requesting appointments should be carefully triaged to identify patients requiring early management. It is important to note that patients with advanced or high-grade cancer conditions if delayed for long may develop worsening symptoms or disease progression. If a case is delayed, re-evaluation at every 2– 4 week intervals is necessary. Finally, it is prudent to prioritize patients beforehand, who need to be operated once full services are restored. Priority should be given to highly curable, early-stage, and those with advanced gynecologic malignancies who require surgery or with symptoms necessitating surgical palliation [6].

Modification in management of specific cancers

The International Gynecological Cancer Society (IGCS) recommends that in early-stage cervical cancer, when access to surgery is limited, one must assure that disease is localized by imaging studies, and if so, consideration of postponing procedures that may be considered high-risk of prolonged operative time or complications, should be taken. The procedures need to be postponed for 6–8 weeks or until crisis resolves. In the setting of visible cervical cancer, neoadjuvant chemotherapy should be considered. In cases of locally-advanced disease, hypofractionation (increase dose per day and reduce the number of fractions) should be considered. According to the American Brachytherapy Society, brachytherapy procedures for cervical cancer patients should not be delayed in patients without COVID-19 symptoms [7]. Risk of laparoscopic surgery concerning pneumoperitoneum in the setting of COVID-19 must be weighed against risk of laparotomy. The FRANCOGYN group of the National College of French Gynecologists and Obstetricians also recommended that radiotherapy and concomitant radio-chemotherapy could replace surgery as first-line treatment for cervical cancer [8]. Also, the value of lymph node staging needs to be reconsidered on a case-by-case basis.

The IGCS and FRANCOGYN group also recommended that neoadjuvant chemotherapy should be preferred over primary cytoreduction surgery for ovarian cancers. HIPEC should be avoided during the COVID-19 pandemic [7-8]. For patients scheduled for interval surgery after three neoadjuvant cycles, consideration should be given for six cycles of chemotherapy before surgery [7-8]. For patients with early stage endometrial cancer of low and intermediate preoperative European Society of Medical Oncology (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) [7-8]. For patients of high ESMO risk, the MSKCC (Memorial Sloan Kettering Cancer Center) algorithm combining PET-CT and sentinel lymph node biopsy, should be applied to avoid pelvic and lumbar-aortic lymphadenectomy [9].

Covid-19 positive gynecologic cancer patients

There is no clarity in the management of positive COVID-19 cancer patients and decision-making regarding anti-cancer treatment. There is no clear answer to whether anti-cancer treatment can be provided during quarantine or should patients wait until they've recovered to resume chemotherapy. SGO recommends that whenever possible, one must avoid operating on known COVID-19 positive patients or those with flu-like symptoms and unknown COVID-19 status, unless the case is emergent/urgent [6]. The National College of French Gynecologists and Obstetricians Guidelines say if a patient with a gynecologic cancer presents with COVID-19, surgical management should be postponed for at least 15 days [8].

The guidelines for giving chemotherapy in the context of an infection say that in case of any infection, be it COVID-19 or otherwise, one should wait until the infection is resolved to resume chemotherapy. Ideally, if there were not a test-kit shortage, doctors would be able to

test every patient prior to beginning chemotherapy, symptoms or no symptoms, to determine if they have the virus before compromising their immune systems with chemotherapy. This could be worth considering because the virus has been shown to have roughly a five-day incubation period.

What does international guideline say regarding managing gynecologic cancer patient

The Society of Gynecologic Oncology states that accurate triage is critical to preserving resources and protecting staff and patients. Just as the risks and benefits of any therapeutic intervention are considered, the potential exposure of patients and staff to COVID-19 as a genuine risk needs consideration. Decisions regarding proceeding with semi-urgent and non-urgent surgeries need involvement of state health department and hospital system levels at local level. Informed consent and shared decision making with patients, with attention to counseling patients about the risks of surgical delay versus in hospital COVID-19 exposure, is important while planning a surgery. Documentation of this counseling in the surgical consent or consultation note is recommended. Decisions regarding cancer surgery are based on local/projected resources, prevalence of COVID-19 in community, patient and tumor characteristics and expected outcomes from delays. This guideline also clearly delineates urgent (immediate), semi-urgent (1-4 weeks) and non-urgent (>4-12 weeks) gynecologic oncology surgeries as mentioned earlier in the article [6].

The International Gynecological Cancer Society (IGCS) recommends limiting number of physicians and healthcare providers involved in providing ambulatory care to minimize exposure to all involved [7]. They also recommend postponing all routine follow-up/surveillance visits, or transition to telemedicine/web-based consultation, if resources allow, until crisis has stabilized and it is considered safe to return to normal operating procedures. Patients should notify healthcare team of any new or concerning issues by telephone or electronic correspondence. They advice to consider postponing any type of intervention that is not absolutely necessary, such as routine imaging studies or serum markers, in patients who are asymptomatic and have no evidence of disease based on most recent evaluation [9].

The American College of Surgeons (ACS) has also issued guidance for triage of patients for cancer surgery in general [10]. However, many cancer surgeries cannot be considered as elective. If decision for surgery is taken, it requires multiple hospital visits and treatment related low immunity; these risks need thoughtful consideration. At the same time, the risks of postponing any surgery or chemotherapy also need evaluation. The American College of Surgeons (ACS) have categorized most gynecologic cancer cases as semi-urgent (i.e., non-elective) surgeries, second only to trauma cases and surgical emergencies in order of their importance. The ACS further opines that if cancer cases are significantly delayed, this could result in significant patient harm [11].

There is some guidance from the Centre for Disease Control (CDC), USA, that 'elective surgeries' may be rescheduled, if possible [12].

Mental health of gynecologic cancer patients

Cancer-related anxiety and distress can get aggravated by a situation where no one knows what choices to make for cancer patients and what is the right suggestion to be advocated in view of the fear of cancer recurrence, progression to a higher stage and loss of life due to inability to access the system amid COVID-19 pandemic. It is a dreadful situation for oncologists and more so for cancer patients. Cancer patients should refrain themselves from the myths and misinformation that is being widely circulated on WhatsApp, Facebook and other social media platforms. The misinformation, related to COVID-19 and cancer, can do more harm than good to a patient mentally. The spread of incorrect information is causing trauma and distress in vulnerable populations and adding to the heavy psychological burden of this disease for those who can least afford it. Patients are encouraged to avail of appropriate cancer organizations, including the World Health Organization (WHO) for definitive information.

Role of tele consultation

Tele-health has never played a more important role in saving lives than amid this pandemic. An example is Navya Care, a tele-consultation service provided by the Tata Memorial hospital. These online portals are providing advice from experts online, without stepping out of their homes. On the hospital website, there is a link given to Navya Care. All People have to register on the website. Cancer patients have to upload their case paper, past medical test data and prescription of medicines. Patients, who do not have website access or unaware about how to operate on the website, can contact experts on their mobiles and send the case papers via WhatsApp. After the implementation of the plan, the online team of Navya Care will consult the doctors and forward their suggestions to subscribers within a couple of days. If the patient is not required to come to hospital, they are asked to wait until the lockdown is over.

The Ministry of Health & Family Welfare has launched the COVID-19 National Tele-consultation Centre (CoNTeC) and also interacted with Nodal Officers of Medical Colleges of States and other AIIMS of the country. This teleconsultation service can be used for gynecological cancer patients too. The All India Institute of Medical Sciences, Delhi has started its teleconsultation services on basis of this, for catering to the needs of its outpatients including those with gynecological cancer. CoNTeC has been made operational at AIIMS with a view to connect the Doctors across the country to AIIMS in real time for treatment of the COVID-19 patients.

The major drawbacks of teleconsultation are the need for tests to assess the patient's condition and progress of the disease while on chemotherapy and radiotherapy especially for aggressive types of cancer. There are many concerns among patients of what happens if one stops, delays or switches the cancer treatment. The other problem is feasibility of teleconsultation, which is not possible at all centers. Hence, catering to the needs of all gynecological cancer patients in the Indian scenario is not feasible through teleconsultation.

Advice to gynecologic cancer patients and survivors amid pandemic: 'Stay connected with yourself and others

This is the advice; the care provider should give to all cancer patients including gynecologic cancer. Building up coping mechanisms during this crisis, is quintessential. At this time, family support is most important for cancer patients, but if someone in the family gets sick, cancer patients must start social distancing, wearing gloves and masks, sleeping in a different room if possible, and wiping down the areas with regular hands washing with soap or with alcohol wipes if available.

Recommendations from authors:

- Referral to facilities closer to patients' homes to avoid long-distance travels.
- Universally screen patients prior to clinical visits and surgery for known symptoms of COVID-19.

- Oncologists and patients may discuss the option of postponement of surgery and explore the possibility of neoadjuvant chemotherapy if the option exists.
- The risks postponing any surgery or chemotherapy should be evaluated.
- Cancer patients must continue their treatment unless they are in close contact with someone with COVID-19 or presenting symptoms of cough, shortness of breath, breathing difficulties or high temperature.
- Cancer patients with fever must not be evaluated in oncology day centers. Initial evaluation outside of the area with high concentration of cancer patients or oncology staff. Possibility of coronavirus must be considered and evaluated. Stable patients should be treated with outpatient oral antibiotic therapy.
- Optimize virtual patient encounters through tele-consultation, including select new patient surgical consults.
- When resources are available, consider preoperative COVID-19 testing of all patients undergoing surgery.
- Use personal protective equipment (PPE) per institutional/ professional society recommendations.
- To maintain the smallest possible inpatient footprint and reduce over-utilization of PPE and COVID-19 exposure risks, pursue same day surgical discharges whenever possible.
- Practicing work-place hygiene along with social distancing is essential, as infection to one healthcare professional will force all contacts to go into quarantine affecting the whole system very badly.
- It is essential for cancer care providers to keep abreast of the latest developments in the management of COVID- 2019.

Conclusion

The COVID-19 pandemic will be likely, tackled over a period of time, but it will leave an unforgettable impact on cancer patients and their caregivers along with oncologists who are helpless on deciding whether "to treat or not to treat." Oncologists have to think critically and prepare a guideline to deal with gynecologic cancer patients during the time of health emergencies and how to manage gynecological cancers, as these patients are more prone for adverse outcomes. Very real ethical dilemmas abound for cancer clinicians bearing the hopes and dreams of their patients, who deserve empathy but also a realistic insight into their situation.

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