

Performing gynecologic cancer surgery during the COVID-19 pandemic in Turkey: A multicenter retrospective observational study

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Abstract

Objective: To report the perioperative outcomes of 200 patients with gynecologic cancer who underwent surgery during the Novel Coronavirus Disease (COVID-19) pandemic and the safety of surgical approach.

Methods: Data of patients operated between March 10 and May 20, 2020, were collected retrospectively. Data were statistically analyzed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows v. SP21.0.

Results: Data of 200 patients were included. Their mean age was 56 years. Of the patients, 54% (n=108), 27.5% (n=55), 12.5% (n=25), and 2% (n=4) were diagnosed as having endometrial, ovarian, cervical, and vulvar cancer, respectively. Of them, 98% underwent non-emergent surgery. A minimally invasive surgical approach was used in 18%. Stage 1 cancer was found in 68% of patients. Surgeons reported COVID-related changes in 10% of the cases. The rate of postoperative complications was 12%. Only two patients had cough and suspected pneumonic lesions on thoracic computed tomography postoperatively, but neither was positive for COVID-19 on polymerase chain reaction testing.

Conclusion: Based on the present findings, it is thought that gynecologic cancer surgery should continue during the COVID-19 pandemic while adhering to the measures. Postponement or non-surgical management should only be considered in patients with documented infection.

Gynecologic cancer surgery should continue during the COVID-19 pandemic while adhering to measures. Only 1% of patients developed COVID-19-related symptoms during the postoperative follow-up period.

KEYWORDS

COVID-19; Gynecologic surgical procedures; Lymph node excision; Ovarian neoplasms; Severe acute respiratory syndrome coronavirus 2; Uterine cervical neoplasms; Uterine neoplasms; Vulvar neoplasms

1 | INTRODUCTION

The Novel Coronavirus Disease (COVID-19) pandemic is a rapidly emerging situation with devastating consequences. To date, WHO¹ has reported more than 5 million positive cases and 300 000 deaths in 216 countries. It is clear that these numbers will continue to increase.

Initial assumptions estimated that the pandemic has consumed healthcare resources; therefore, it has a significant impact on the healthcare services. Hospital bed, medical staff, intensive care unit (ICU), and mechanical ventilator capacity are now primarily occupied by COVID-19 patients in the majority of hospitals.² Worldwide, many hospitals are restricting non-emergent surgical procedures. Furthermore, government authorities and some medical societies have published recommendations and guidelines for curtailing or postponing cancer diagnostics, treatment, and/or surgery in order to reallocate resources to the treatment of COVID-19 patients and to save patients with cancer and healthcare staff from the Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2).³

Postponing treatment for cancer can have significantly negative effects. A recent study⁴ showed that there is a significant relationship between delay in surgery and reduced overall survival in patients with solid cancers. The researchers concluded that a surgical delay of more than 40 days is associated with poor outcome in patients with colon cancer. Similar findings have been reported in patients with cervical cancer in a nationwide analysis and concluded that "longer intervals between diagnosis and treatment are associated with poorer prognosis among cervical cancer patients".⁵ Nevertheless, an editorial in the *International Journal of Gynecologic Cancer (IJGC)* suggests the modification of the current standards of care in gynecological cancer from surgery to chemotherapy/hormonotherapy or radiotherapy due to concerns about COVID-19.⁶

All clinical decisions should be made in consideration of the risks and benefits of cancer treatment against the risks of COVID-19 infection. A PubMed search showed that there is a large number of papers on the COVID-19 pandemic; however, most are about guidelines, opinions, reviews, and recommendations. Experience

on surgical management of gynecologic cancers and COVID-related complications have only been rarely and anecdotally reported. During the pandemic, some hospitals in Turkey have postponed cancer surgeries, as in other parts of the world. The aim of the present study was to report on the perioperative outcomes in 200 patients with gynecologic cancer operated during the pandemic, as well as the safety of this approach.

2 | MATERIALS AND METHODS

After approval from the ethical committee the Institutional Review Board of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital and the Ministry of Health Scientific Research Platform, data of patients with gynecologic cancer operated from March 10 to May 20, 2020, were retrospectively collected from 12 gynecologic cancer centers across Turkey. The surgeons responsible were asked to provide data on general patient characteristics, co-morbidities, preoperative and postoperative disease stage, some blood parameters, surgical procedure, the postoperative follow-up process, and both preoperative and postoperative COVID-19-related data (symptoms/screening/testing). All human participants gave written/verbal informed consent before the study began. As the proper use of resources is of great importance during the pandemic, the prevalence of COVID-19 and the caseload in all associated units were carefully evaluated and considered. In addition, careful attention was paid to reach a consensus with anesthesiologists and ICUs during planning.

All patients scheduled for surgery were screened for symptoms of COVID-19 in the preoperative period. Most were hospitalized 24–48 hours preoperatively. Considering the importance of preoperative imaging in the management of gynecologic cancer, most of the patients had a thoracic chest X-ray or computed tomography (CT) scan. Only one companion was allowed and a no-visitors policy was implemented. All wore face masks during the hospital stay. On the day of surgery, patients were transferred directly to the operating room (OR), with a face mask, without stopping in any areas, in order to minimize exposure.

Stretcher personnel wore personal protective equipment (PPE) and were trained to perform disinfection immediately after completion of each transfer. During induction of anesthesia and endotracheal intubation, only the most experienced team were in the room. All OR staff were required to practice enhanced droplet and contact precautions, including the use of an N95 respirator, eye protection, gown, and gloves. When a negative-pressure OR was not available, a high air exchange cycle rate (≥ 25 cycles h^{-1}) was maintained for lower viral load. Equipment was minimized to those pieces most necessary for the procedure and transiting was limited. The most suitable procedure according to disease characteristics was performed.

During the postoperative period, early recovery procedures and early discharge was encouraged. None of the patients or healthcare personnel received prophylactic COVID-19 treatment. During follow-up, general condition, wound status, and symptoms of COVID-19 were recorded. Visitors were not allowed for at least 1 month.

Data were statistically analyzed using International Business Machines (IBM, Armonk, NY, USA) Statistical Package for the Social Sciences (SPSS) Statistics for Windows v.21.0 (IBM Corp.). Descriptive statistics are presented as number and percentage.

3 | RESULTS

Data for 212 patients were collected, but 12 were excluded due to incomplete data. The mean patient age was 56 years (range 24–85 years). The most common type of gynecologic cancer was endometrial carcinoma ($n=108$ [54%]), followed by ovarian ($n=55$ [27.5%]), cervical ($n=25$ [12.5%]), and vulvar ($n=4$ [2%]). Other types of gynecologic cancer (vaginal carcinoma, sarcoma, and gestational trophoblastic disease) comprised another 4%. Of the patients, 98% had non-emergent surgery, whereas four had emergent surgery due to tumor rupture, bleeding, and bowel obstruction.

Of the patients, 80% underwent open-route laparotomy, whereas a minimally invasive approach was performed in 18%. In 2% of the cases, laparoscopic surgery had to be converted to an open approach. Of the patients, 68% were stage 1 and 30% were stages 3–4. Type 1 hysterectomy \pm bilateral salpingo-oophorectomy (BSO) without lymph node dissection (LND) was performed in 10% of the patients, most of which had low-risk early-stage endometrial carcinoma. Lymphadenectomy was added in 25% of the patients. Type 3 hysterectomy was performed in 7% of the patients, most of whom had cervical carcinoma. In the patients with disseminated ovarian tumors (49%), maximal cytoreduction was performed. Vulvectomy was performed in 2% of the patients.

Lymphadenectomy was performed in 80% of the cases. Bowel resection and ileocolostomy was performed in 2.5%. Surgeons reported that they decided to change the surgical approach and/or radicality of surgery in 10% of the cases due to the pandemic. The rate of postoperative complications was 12% ($n=24$). The most common complication was need of a blood transfusion (33%) followed by wound complications (29%). In all, 15% of the patients required observation in an ICU. Only two patients developed symptoms related

to COVID-19 during the postoperative follow-up and neither was polymerase chain reaction (PCR)-positive in multiple samples. Both patients developed respiratory distress after extubation. They had suspected lesions on thoracic CT and were admitted as suspected cases for COVID-19, according to the Novel Coronavirus Pneumonia Prevention and Control Program (14 April 2020) published by the Science Board and Ministry of Health of Turkey. Extubation was performed on postoperative days 7 and 9, respectively, and both patients were monitored in the postoperative pandemic units. No medication specific to COVID-19 was administered. None of the surgical staff was infected and no mortality was reported. Clinicopathologic features of the patients are summarized in Table 1, and postoperative complications and COVID-19-specific effects are summarized in Table 2.

4 | DISCUSSION

Principally, surgery is the cornerstone of the treatment of gynecologic cancers. There is a lack of sufficient data related to the management of patients with gynecological cancers during the COVID-19 pandemic. The significant impact of the pandemic on both medical practitioners and patients cannot be denied, and COVID-19 has dramatically impacted the care of patients with gynecologic cancer. The degree of this impact is related to the burden of COVID-19, especially the availability of local resources.

Several reasons can be considered, including the potential shortage of PPE, hospital beds, ICU beds, and ventilators, as well as the potential shortage of healthcare personnel, and the desire to maximize social distancing.⁷ Non-operative strategies have been suggested as a primary treatment approach, but the short- and long-term effects on survival remain unknown. Recent guidelines and recommendations for non-surgical management of cancers are generally based on personal/expert opinions, and some of the aforementioned fear.⁶

A study from The Netherlands reported that diagnoses of cancer have dramatically decreased during the pandemic, indicating that patients cannot reach the hospitals and will be diagnosed at later stages.⁸ Chen et al.⁵ performed a nationwide analysis of cervical cancer and concluded that the increase in the interval between diagnosis and treatment is associated with poorer prognosis among patients with cervical cancer. A cost-effectiveness analysis from the UK⁹ reported that as a result of the pandemic measures, there might be a significant disruption in the management of cancers, and that a delay of 3–6 months in the surgical management of all stages of cancer might cause 4755/10760 attributable deaths with the loss of 92214/208275 lives per year. Another study¹⁰ estimated that during the peak phase of the pandemic, 2324069 cancer surgery procedures would be postponed globally. These clearly show that the postponement of cancer surgeries can have a devastating effect on the survival of patients and mid- and long-term health economics worldwide.

In a paper published on March 24, 2020,¹¹ the American College of Surgeons classified most gynecologic cancer cases as semi-urgent and added significant delay would cause serious harm to patients.

TABLE 1 Clinicopathologic features of patients.

Mean age (years)	56 (range 24–85)
Preoperative COVID-19-associated symptoms (%)	1
Preoperative COVID-19 diagnosis (%)	0
ASA score (%)	
ASA 1	20
ASA 2	49.5
ASA 3	30
ASA 4	0.5
Mean BMI (kg/m ²)	31 (range 18–49)
Preoperative co-morbidity (%)	
No disease	50
DM	10
HT	21.5
CAH	1
≥2 co-morbidities	13.5
Type of cancer (%)	
Endometrial cancer	54
Ovarian cancer	27.5
Cervical cancer	12.5
Vulvar cancer	2
Others	4
Stages (all tumors) (n)	
Stage 1	68
Stage 2	2
Stage 3	22
Stage 4	8
Type of surgery (%)	
Type 1 HYS ± BSO/No LND	10
Type 1 HYS ± BSO + LND	25
Type 2 HYS + LND	2
Type 3 HYS	7
Debulking Surgery (HYS + BSO + LND + omentectomy ± appendectomy ± bowel resection ± peritonectomy-maximal tumor reduction)	49
Radical vulvectomy ± IFLND	2
Fertility-sparing surgery	2.5
Ileostomy/colostomy	2.5
Lymphadenectomy performed (%)	
Yes	80
No	20
Emergent operations (%)	2
Non-emergent conditions (%)	98
Surgical approach (n)	
Open	80
MIS	18
Converted to open	2

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; BSO, bilateral salpingo-oophorectomy; HYS, hysterectomy; IFLND, inguino-femoral LND; LND, lymph node dissection; MIS, minimal invasive surgery.

TABLE 2 Postoperative complications and analysis of COVID-19 effects.^a

Mean surgical duration (min)	204 (range 60–540)
Mean duration of hospitalization (days)	6 (range 1–21)
Implementation of preoperative COVID-19 screening	
Symptom-based screening	100
Preoperative CT	42
PCR	1.5
PCR + CT	3
Postoperative complications	
Yes	12
No	88
ICU	
Yes	15
No	85
COVID-19-related change in management (less radicality)	10
Postoperative COVID-19	1
Postoperative mortality	0
Healthcare staff infected with COVID-19 (n)	0

Abbreviations: CT, computed tomography; ICU, intensive care unit; PCR, polymerase chain reaction.

^aValues are given as percentage unless otherwise specified.

The Society of Gynecologic Oncology suggested use of the Elective Surgery Acuity Scale (ESAS) for planning,⁷ in which most cases of gynecologic cancer fall into tier 3a/b, and the recommended action is not to delay surgery.¹²

The Turkish Ministry of Health has declared a state of emergency, issuing very strict regulations for postponing all non-urgent surgical procedures and permitting only urgent surgeries for oncological indications. As of May 25, 2020, there were 157 814 cases of COVID-19 and 4369 COVID-19 deaths in Turkey.¹³ During this period, 200 cases of gynecologic cancer that underwent surgery were identified and 1% were considered “suspected” cases of COVID-19 postoperatively (by CT findings). The primary concern for surgery in gynecologic cancers is that most cases are old and have pre-existing co-morbidities and radical procedures are needed for the vast majority, which increases the complication risk and the subsequent risk of requiring care in the ICU.¹⁴ Furthermore, the risk of hospital-acquired COVID-19 infection and concerns about operating asymptomatic positive cases are other issues. Moreover, resources at blood banks have been depleted due to decreased donating and the increase in the need from patients with COVID-19. Reallocation of hospital resources are other concerns policymakers must contend with.¹⁵

Although there are various recommendations from societies, data on the clinical features, prognosis, and COVID-related risks in operated patients with gynecologic cancer are extremely limited. In an analysis from China,¹⁶ in 18 cases positive for COVID-19 with a history of cancer—25% of which received chemotherapy or surgery

in the previous month and 75% were cancer survivors (most dominantly lung cancer)—patients with cancer deteriorated more rapidly than those without. A more specific analysis¹⁷ in 389 hospitalized patients (189 of whom underwent surgery) reported that among the 189 operated patients, 3 (1.59%) patients with gynecologic cancer with no history of COVID-19 contact and normal preoperative thoracic radiographs and CT scans were diagnosed with COVID-19 postoperatively versus a COVID-19 positive rate of 0.77% for the entire cohort. The researchers reported that the risk factors were malignancy, co-morbidities, age over 45 years, and postoperative fever persisting for more than 2 days.

In the present study, 200 patients with gynecologic cancer underwent surgery during the COVID-19 pandemic and the post-surgery rate of COVID-19 positivity (2/200 [1%]) was similar to that reported by Yang et al.¹⁷ Chai et al.¹⁸ reported the results of five COVID-19-infected and 22 non-infected patients that required surgery during the initial phase of the pandemic in Wuhan. They concluded that “surgeons must be more positive when making surgical decisions. Hospital mortality might be higher not because of COVID-19, but because of the panic caused by COVID-19.” A recent study¹⁹ showed that 39 patients with cancer without any symptoms of COVID-19 underwent surgery and none of them or the hospital staff developed any complications related to the pandemic. On the other hand, 6/65 (9%) patients who underwent positron emission tomography (PET)/CT for various malignancies showed unexpected signs of interstitial pneumonia on CT.²⁰

Perrone et al.²¹ reported on surgery for ovarian cancer during the peak phase of the pandemic, emphasizing the importance of preoperative screening/testing via symptom screening and PCR testing 48 hours preoperatively, and only admitting patients with a negative PCR result to hospital for surgery. The interview for screening of symptoms was also repeated upon admission the day before surgery due to false negativity of the tests and no relatives were admitted to the wards. They also recommend that patients avoid contact for 1 month after hospital discharge. Based on the described management scheme, treatment was postponed/canceled only in cases of suspected COVID-19 infection.²¹

The findings of the present study show that gynecologic cancer surgery can be performed safely when appropriate and timely measures for COVID-19 safety are taken preoperatively, intraoperatively, and postoperatively. Only 1% of the cases in the present study developed symptoms of COVID-19 after surgery, although none of the surgical team did. To the best of the authors' knowledge, the present study is the largest to report the frequency of post-surgery COVID-19 infection in patients with gynecologic cancer and the safety profile of the surgical management of gynecologic cancers during the COVID-19 pandemic.

The present study does have some limitations, including the size of the cohort and retrospective design, but the findings clearly indicate that during the COVID-19 pandemic, surgery for gynecologic cancers remains a more viable option than non-surgical management. Non-surgical management of gynecologic and other cancers should be restricted to patients with documented COVID-19 infection. There is

an ongoing study²² by the COVIDSurg Collaborative on the safety of cancer surgery during the COVID-19 pandemic and the findings are eagerly awaited.

The route of surgery is another concern during the COVID-19 pandemic, especially dissemination of the virus during minimally invasive procedures as a result of pneumoperitoneum-associated aerosolization of particles, and the presence of the virus in blood and stool.²³ This is currently only a theoretical risk based on earlier studies on the hepatitis B (HBV) virus and HPV.²⁴ Similar findings related to Severe Acute Respiratory Syndrome Coronavirus-1 (SARS-CoV-1) (the virus responsible for a multinational disease outbreak in 2002–2003), specifically nosocomial transmission and superspreading events, raised doubts about the possibility of aerosol and fomite transmission of SARS-CoV-2. Nonetheless, it is important to emphasize that to date there are no data showing that the risk of surgical exposure to COVID-19 is greater via laparoscopy than via laparotomy. The risk of laparoscopic surgery during the COVID-19 pandemic must be weighed against the risk of laparotomy.²⁵ In the present study, almost 20% of all the surgeries were performed via laparoscopy, which was not associated with an increased risk of COVID-19 infection; therefore, it is believed that laparoscopy should be a contraindication only in patients with gynecologic cancer positive for COVID-19.

Health workers reportedly make up 3%–20% of the population infected with COVID-19, 15% of whom develop severe symptoms leading to death.¹⁸ Although there are no official data on the number of infected healthcare professionals in Turkey who have died, personal experience indicates the number is significant. Unfortunately, this risk of viral infection is an accepted part of surgical practice; in addition to COVID-19, there is a risk of exposure to HBV, HCV, and HIV. The present findings show that only 1% of asymptomatic patients with gynecologic cancer who underwent surgery were positive for COVID-19 after surgery. These preliminary data must be confirmed by other researchers, which it is expected will occur as the pandemic continues to spread worldwide. Fear of COVID-19 infection and lack of knowledge about the transmission might be considered significant factors that affect physician's decisions regarding treatment. Nevertheless, in order to prevent hospital-acquired COVID-19 among healthcare workers and patients, preoperative thoracic CT, PCR, antibody testing, 14-day quarantine, performing surgery in negative pressure ORs, providing the necessary PPE, and early discharge policies should be instituted.

In the light of the findings of the present retrospective multicenter study, it is thought that surgical treatment of patients with gynecologic cancers should not be canceled or postponed during the COVID-19 pandemic. Gynecologic cancer surgery must remain the principal treatment and should be the last treatment modality to be modified or canceled/postponed.

AUTHOR CONTRIBUTIONS

PD, HD, and MD: concept and design of study, manuscript preparation, editing and review; PD and MD: data analysis and interpretation; PD: statistical analysis. All authors performed data acquisition.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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