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Analysis of Gynecologic Cancer Management at Sanglah Hospital during COVID- 19 Pandemic

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ABSTRACT

The COVID-19 pandemic presents its own challenges in treating cancer, especially gynecological cancer. The condition of cancer patients who have been immunocompromised either because of their disease or side effects of the drugs given, has the potential to increase the risk of cancer patients to experience severe COVID-19 infection. The main management of cancer, which is based on three axes, namely surgery, chemotherapy, and radiotherapy, needs to be adapted to increase survival rates. rates in patients.

Keywords: COVID-19, chemotherapy, gynecological cancer, operative, radiotherapy.

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I. Introduction

An outbreak of coronavirus disease-2019 (COVID-19) occurred at the end of 2019 which started in the city of Wuhan, China and spread rapidly throughout the world. Based on the data from Komite Penanganan COVID-19 dan Pemulihan Ekonomi Nasional, confirmed positive cases of COVID-19 in Indonesia has already broken 1 million by the end of January 2021 [1]. The World Health Organization (WHO) has declared COVID-19 as a community health emergency in need of special attention, including the field of gynecology.

In the context of the current COVID-19 pandemic and the limitations of resuscitation services, for the next 2-3 months, the things that must be considered are not only focused on handling but also reducing the risk of infection in cancer patients. To reduce the risk of infection, two priorities are important: limiting high-risk situations such as surgery, chemotherapy, radiotherapy; and to limit the patient's contact with health care workers and, in particular with the care setting [2].

Cancer patients are more at risk towards severe infections. This is exacerbated by the use of chemotherapy regimens and other anticancer drugs that have an impact on the immunocompromised condition of cancer patients, which makes patients more susceptible to infections, both viral infections and other infectious diseases [2].

A study conducted in a tertiary level hospital in Southeast Nigeria from 2000-2010, revealed that the challenges of gynecological cancer treatment vary from late early detection, non-adherence to therapy, lacking use of more up-to-date cytotoxic drugs, unfavorable results of operative procedures, and lack of functional radiotherapy facilities [3]. This can be a concern in an effort to increase survival rates of gynecologic cancer sufferers during the pandemic era in the midst of current therapeutic limitations.

In between all existing problems, this writing will be specifically discussing the handling of COVID-19 related with cancer, especially cancer gynecology. Even without the existence COVID-19 pandemic, cancer alone is a big burden for human health. The thing that creates friction among cancer and COVID-19 is the management of cancer. The main management of cancer pivots on three methods, namely: surgery, chemotherapy, and radiotherapy. The three methods provide a separate burden on the body's immune system. Considerations for managing gynecological cancer require special strategies during this pandemic [4].

II. Discussion

A. Chemotherapy

In selecting a chemotherapy regimen, it is recommended to choose a regimen that requires the least number of visits, such as the 3-week paclitaxel/carboplatin regimen. Consideration should be given to avoid or limit high-dose, intraperitoneal, and hyperthermic intraperitoneal chemotherapy (HIPEC). Things to consider before, during, and after chemotherapy are listed in Table I.

The challenges of chemotherapy treatment during the pandemic, especially in developing countries, include the limited supply of chemotherapy drugs due to disruption of the production process and supply chain of drugs. In addition, there are efforts to avoid immunocompromised conditions in patients so that they do not experience severe infections so that patients do not receive proper therapy [6].

Recommendations for first-line chemotherapy regimens according to The Society of Gynecology Oncology is divided by stage malignancy in patients. A more detailed description is in Table II and Table III.

TABLE I: CONSIDERATION BEFORE, DURING, AND AFTER CHEMOTHERAPY IN CANCER PATIENT THAT NEED TO BE CARRIED OUT IN THE PANDEMIC ERA

Before Chemotherapy	• Consider the goals of therapy: First-line curative therapy should be prioritized. Maintenance therapy (pemeliharaan) should be evaluated to assess the survival benefit in patients and palliative therapy should be done to reduce symptoms of cancer that is not controlled. • Patients should not be treated in hospitals that are referral centers for COVID-19 patients. • It is necessary to consider the administration of a chemotherapy regimen if the patient's residence is far from a health facility or if the patient has plans to visit an area prone to high COVID-19 cases. • Try to reduce the frequency of chemotherapy infusions and weekly infusions. • Need special consideration for single therapy agent or delaying chemotherapy in patients > 65 years of age, patients with comorbid disease (DM, COPD, and cardiovascular disease) or ECOG status 2. • Consider using oral therapy instead of infusion-based therapy if possible. However, it should also be noted that some oral regimens are more toxic than infusion regimens . • Try to outpatient chemotherapy patients if possible. • Screening of all patients for symptoms of COVID-19 and measurement of temperature < 37.5 o C before treatment and testing before undergoing chemotherapy.
During Chemotherapy	• Integrating therapy with telemedicine to reduce the frequency of patient visits for evaluation at the health facility and patients can go directly to the chemotherapy center for treatment. • Consider outpatient treatment for neutropenic fever if the patient is clinically stable with moxifloxacin 400 mg orally once daily or ciprofloxacin 500-750 mg orally twice daily and Augmentin 875 mg orally twice daily. Follow-up can be done using telephone contact for at least 3 days to ensure the clinical condition of the patient.
After Chemotherapy	• Postpone radiology except for emergency or critical care. • Ensure the purpose of health services by discussing it with the patient is prioritized before or shortly after hospitalization, communication using telemedicine or the telephone can be used. • Extend port interval regular flush to 8-12 weeks.

TABLE II: RECOMMENDATIONS FOR FIRST-LINE CHEMOTHERAPY REGIMENS FOR EACH TYPE OF EARLY-STAGE GYNECOLOGIC CANCER DURING THE COVID-19 PANDEMIC

High-grade ovaries stage	Low- grade ovaries stage 1/2	Endometrium	Cervix	Gestational trophoblastic neoplasia (GTN)
Platinum/ taxane chemotherapy every 3 weeks	monotherapy oral aromatase inhibitors vs. Observation	Platinum/ taxane chemotherapy every 3 weeks (high risk histologic subtype)	Chemo radiation	D&C before treatment can be done if there are indications and conditions allow Methotrexate (MTX) IM daily x 5 (0.4 mg / kgBW ~ 14 days) MTX (1 mg / kgBW or 50 mg) IM D 1,3,5,6 w/ folinic acid ~ 14 days
		Consider oral or intrauterine options if available; Levonorgestrel or megestrol acetate IUD for grade 1/2 endometrioid histology		Consider daily MTX po x 5 0.4 mg / kgBW . Dose cap = 25 mg / day Repeat in 14 days Consider for a score of 0-1: Weekly MTX 50 mg /m2 IM, dactinomycin may also be considered for all low-risk GTDs to reduce the number of visits but with due regard for toxicity and the need for central venous access.

TABLE III: RECOMMENDATIONS FOR FIRST-LINE CHEMOTHERAPY REGIMENS FOR EACH TYPE OF ADVANCED-STAGE GYNECOLOGIC CANCER DURING THE COVID-19 PANDEMIC

High-grade ovaries stage	Low- grade ovaries stage 1/2	Endometrium	Cervix	Vulva	Gestational trophoblastic neoplasia (GTN)
Platinum/ taxane chemotherapy every 3 weeks; consider the use of bevacizumab (as in stage 4, severe ascites)	Chemotherapy followed by aromatase inhibitor therapy vs. monotherapy aromatase inhibitor	Platinum/ taxane chemotherapy every 3 weeks	Chemo -radiation for curative cases	Neoadjuvant chemo - radiation	Hospitalization of patients with choriocarcinoma and placental site trophoblastic tumor (PSTT)

TABLE III: RECOMMENDATIONS FOR FIRST-LINE CHEMOTHERAPY REGIMENS FOR EACH TYPE OF ADVANCED-STAGE GYNECOLOGIC CANCER DURING THE COVID-19 PANDEMIC *(CONT)*

Considerations for maintenance therapy using Poly (ADP - ribose) polymerase inhibitor (PARPi) vs. Bevacizumab is based on an assessment of the risk of exposure to COVID-19 with benefit or observation only.	Low threshold for transition to maintenance hormonal oral	Avoid radiotherapy unless there is a curative purpose as indicated	Paclitaxel / carboplatin or taxane /platinum with bevacizumab every 3 weeks (note survival benefit vs fistula risk)
		Consider oral megestrol acetate or megestrol acetate interspersed with tamoxifen , everolimus / oral letrozole , note increased risk of toxicity with hormonal therapy regimens stage 4 (high-grade) and high risk of COVID-19 morbidity, consider postponing therapy and discussing it with the patient.	stage 4 and the high risk of COVID-19 morbidity, consider postponing therapy and discussing it with the patient.

B. Radiotherapy

1) Cervical cancer

In post-operative patients, radiotherapy in cervical cancer patients can be delayed up to 8-12 weeks depending on the clinical condition. In patients who cannot receive systemic therapy and require external radiotherapy, accelerated radiotherapy may be given 6 days per week. All treatment should be completed within 8 weeks with the appropriate dose and delay is not recommended because it will affect the survival rate [6].

2) Endometrial Cancer

In patients who cannot be operated on and are symptomatic, radiotherapy with or without chemotherapy should be given as soon as possible. For patients with endometrioid histology, hormonal therapy may be used to delay the initiation of radiotherapy. Brachytherapy is preferable to stereotactic body radiation therapy (SBRT) to reduce the risk of toxicity [6].

In post - operative patients, adjuvant radiotherapy can be given with a delay of 6-8 weeks after surgery depending on the clinical condition. regimen Brachytherapy is recommended to reduce the number of hospital visits [6].

3) Ovarian Cancer

Patients who have undergone surgery and chemotherapy before, may involve radiotherapy as adjuvant therapy [6].

4) Vaginal Cancer

Vaginal cancer patients with new disease are recommended to receive definitive radiotherapy with or without chemotherapy and should be treated as soon as possible. For radiotherapy with external beam, boost needs to be done using simultaneous integrated boost (SIB). In post - operative patients, adjuvant radiotherapy can be delayed for 6-8 weeks after surgery depending on the clinical condition [6].

5) Vulvar Cancer

Vulvar cancer patients with new disease are recommended to receive definitive radiotherapy with or without chemotherapy and should be treated as soon as possible. In post - operative patients, adjuvant radiotherapy can be delayed for 6-8 weeks after surgery depending on the clinical condition. Post -operative patients who are found to have nodular involvement at the time of surgery require rapid initiation of radiotherapy [6].

C. Operative

1) Cancer Cervix

Lesions pre-invasive cervical: According recommendation American Society for Colposcopy and Cervical Pathology (ASCCP), individual with test screening cancer cervix level low can experience delay evaluation diagnostic for 6-12 months. Patient with high cervical screening test results must schedule evaluation diagnostics within 3 months' time

Early stage cervical cancer: In circumstances where oncological surgery is still allowed, it is recommended to continue with standard care. However, if access to surgery is limited, these steps may be considered. Ensure that the disease is localized with imaging studies, such as a CT scan. If so, consider postponing a procedure that may be considered high risk for a prolonged operative time, or intraoperative potential. and/or postoperative complications, such as radical trachelectomy or radical hysterectomy, for a period of 6-8 weeks, or until the crisis resolves [7].

2) Endometrium Cancer

Low-risk patients: Patients with grade 1 disease may be considered for conservative management with non-surgical options, including systemic hormonal therapy or birth control [7].

High-risk patients: Patients with high-risk disease (grade 2 or 3 or high-risk histology) should be considered for simple hysterectomy and single bilateral salpingo-oophorectomy ± sentinel lymph nodes, if available and possible, and/or based on postoperative management of risk factors uterus. The risk of laparoscopic surgery associated with pneumoperitoneum in a COVID-19 scenario must be weighed against the risk of laparotomy [7].

3) Ovarian Cancer

In suspected early stage disease, consideration of several factors, such as age and family history of breast/ovarian cancer, physical examination, and thorough radiological evaluation with color Doppler pelvic USG, MRI, and/or serum markers, such as CA125 and HE4, to assess risk malignancy in adnexal masses [7].

In patients with advanced disease, consideration of tissue biopsy to confirm the diagnosis of disease and continued neo-adjuvant chemotherapy until the crisis resolves and consideration of surgery at a later time [7].

III. Considerations for the Era of the COVID-19 Pandemic

In March 2020, recommendations issued by the American College of Surgeons (ACS), the US Surgeon General, and some associations of medical and surgical professionals to postpone elective surgical intervention. This recommendation is based on the desire to protect patients and medical personnel from complications related to COVID-19 and conserve hospital resources to increase the capacity of COVID-19 patients. Ultimately, the pandemic has challenged the ability of medical personnel to provide timely care for patients, including patients with gynecologic cancer. Patients with gynecologic malignancies often require surgical intervention throughout the course of their cancer treatment, which has been interrupted during this time [8].

IV. Conclusion

Adaptation in the pandemic era to the management of gynecological cancer needs to be done as an effort to increase survival outcomes in patients both in terms of surgery, chemotherapy, and radiotherapy. The focus of the current management of gynecologic cancer is not only on gynecological disease itself but also on controlling the risk of COVID-19 infection to increase survival benefits and reduce patient mortality and morbidity.

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