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Original Article

Impact of COVID-19 on gynecologic cancer treatment in Japan: a nationwide survey by the Japan Society of Gynecologic Oncology (JSGO)

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ABSTRACT

Objective: As coronavirus disease 2019 (COVID-19) rages on, it is a challenging task to balance resources for treatment of COVID-19 and malignancy-based treatment. For the development of optimal strategies, assessing the conditions and constrains in treatment during the COVID-19 pandemic is pertinent. This study reported about a nationwide survey conducted by the Japan Society of Gynecologic Oncology.
Methods: We interviewed 265 designated training facilities about the state of their clinical practice from the time period between March and December 2020. We asked the facility doctors in charge to fill a web-based questionnaire.
Results: A total of 232 facilities (87.5%) responded. A decrease in the number of outpatient visits was reported, and the major reason attributed was reluctance of patients to visit hospitals rather than facility restrictions. The actual number of surgeries decreased by 3.9%, compared to 2019. There was a significant difference when the variable of "Prefectures operating under special safety precautions" or not was introduced. There was no increase in the rate of advanced stages in the three cancer types studied. However, 34.1% participants perceived COVID-19 affected management and prognosis.
Conclusion: Refraining from visiting hospitals based on the patient's judgment may be expected to be an issue in the future. No significant decrease in surgeries was observed, and it would seem that there were few forced changes in treatment plans, but "the State of Emergency" had an impact. There was no increase in the rate of advanced cancers, but this will need to be monitored.

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Synopsis
Japan Society of Gynecologic Oncology conducted a nationwide survey about gynecologic malignancy in Japan under coronavirus disease 2019 pandemic. Patients refrained from visiting hospitals which led to reduced outpatient. "The State of Emergency" impacted healthcare but major decrease in surgery was not observed. Patients did not report advanced cancer states, but careful observation is required.

INTRODUCTION

More than a year has passed since coronavirus disease 2019 (COVID-19) was first identified and spread globally, and as of April 1, 2021, more than 129 million people have been infected and 2.8 million people have succumbed to COVID [1]. In Japan, more than 470,000 people have been infected since the first case was reported on January 14, 2020 [2], and more than 9,200 people have died as of April 1, 2021 [3].

As infectious diseases become more prevalent, hospitals are forced to focus on the treatment of these diseases, and other patients tend to refrain from visiting the doctors to avoid the risk of infection. The natural history of malignant diseases shows that they worsen over time and become rather life-threatening. There is a trade-off between the risk of dying from infection and avoiding treatment for malignant diseases. In the midst of an infectious disease pandemic, when patients, medical personnel, and medical facilities are all restricted, the clinical challenge is to set up patient priority criteria while simultaneously managing COVID-19 and cancer treatment. Many organizations dealing with gynecologic malignancies have suggested some priority guidelines [4].

In Japan, clinicians are facing similar challenges in providing treatment to patients with gynecological malignancies. By March 2021, three epidemic peaks had occurred in Japan: the first wave was during April–May 2020, the second wave during August–September, and the third wave is from November to the present time. Fortunately, the prevalence of infections and COVID-based mortality in Japan had remained low compared to the United States and other developed countries in Europe. The social situation and the restrictive measures being enforced in different countries may not necessarily be similar. The Ministry of Health, Labour and Welfare of the Japanese Government sets the general policy for assigning hospital functions; however, actual designation and implementation of these policies are performed by the prefectural governments. Other countries have also taken measures to separate COVID-19 specialty hospitals from other hospitals [5]. However, in Japan, most prefectures did not identify and designate separate facilities for COVID-19 treatment. This led to high-functioning medical centers providing simultaneous treatment for malignancy as well as for COVID-19 infected patients.

For the development of optimal clinical strategies in the future, assessing the clinical conditions of patients with gynecological malignancies and constrains in their treatment during the COVID-19 pandemic in 2020 is pertinent. In this study, the findings of a

nationwide survey conducted by the COVID-19 task force of the Japan Society of Gynecologic Oncology (JSGO), a leading Japanese medical association for gynecologic oncologists, have been reported.

MATERIALS AND METHODS

We interviewed 265 designated training facilities that provide training to formally certify gynecologic oncologists about the state of their clinical practice from the time period between March and December 2020. These training facilities have been recognized by the JSGO. The requirements for certification is presented in **Table S1**. All facilities should have been general hospitals providing multidisciplinary care, and recognized as regional centers of excellence eligible for receiving patient referrals.

We asked the facility doctors in charge to fill out a web-based form (Google Forms) by email or postal mail during January–March 2021. The questionnaire was designed by JSGO COVID-19 task force members. The questionnaires were completed using the name of the facility. Duplicate responses were removed through inquiries.

Information about the following was obtained: facility demographics, COVID-19 treatment status, restrictions on treatment, changes in the number of treatments, main reasons for changes, and the number of patient cases with progressive stages of cervical cancer including cervical intraepithelial neoplasia, endometrial cancer, and ovarian cancer (including fallopian tube cancer and primary peritoneal cancer). The staging systems used included International Federation of Gynecology and Obstetrics (FIGO) 2008 for cervical cancer, FIGO 2008 for endometrial cancer, and FIGO 2014 for ovarian cancer. In context of hospital visits and treatments, we surveyed the change in frequency of the visits and the underlying reasons for such changes. In case of surgeries, the change in frequency of the surgeries was noted and the actual number of surgeries conducted in 2019 was used as control data. Any difference in these data were examined statistically.

The “Prefectures operating under special safety precautions” designates prefectures of particular concern as identified by the Japanese Government during “the State of Emergency” between April 7 and May 25, 2020, which includes Hokkaido, Ibaraki, Saitama, Chiba, Tokyo, Kanagawa, Aichi, Ishikawa, Gifu, Kyoto, Osaka, Hyogo, and Fukuoka [6]. The prefectural government designated medical facilities as “Priority medical institutions for accepting COVID-19” and “Cooperating medical institutions for accepting COVID-19,” respectively, and requested them to accept patients infected with COVID-19.

In this study, only the data regarding the number of treatments was collected. This part of the data was collected completely independent to the patient demographics and patients' personal information and was exempt from review by the ethics committee. The χ^2 test, Kruskal-Wallis test, and Mann-Whitney U test were performed using the GraphPad Prism 9 (GraphPad Software, Inc., La Jolla, CA, USA) software for statistical analysis.

RESULTS

A total of 232 facilities (87.5%) responded out of the 265 facilities that had been contacted.

Table 1. Characteristics of the medical facilities

Number of all responding facilities	Value (n=232)
Priority medical institutions accepting COVID-19	194 (83.6)
Collaborative institutions accepting suspected patients with COVID-19	18 (7.8)
Others	20 (8.6)
Facilities in "Prefectures operating under special safety precautions"	151 (65.1)
Facilities in normally operating prefectures	81 (34.9)
Facilities not experiencing restrictions	61 (26.2)
Facilities with a period of restriction	171 (73.7)
To allocate manpower for COVID-19	67 (28.9)
To build a system for infection control	53 (22.8)
Due to event of nosocomial infection/s	42 (18.1)
Others	9 (3.9)

Values are presented as number (%).
COVID-19, coronavirus disease 2019.

1. Characteristics of the facilities

The number of facilities designated by prefectures as the "Priority medical institutions for accepting COVID-19" and "Cooperating medical institutions for accepting COVID-19" were 194 (83.6%) and 18 (7.8%), respectively, and 98.7% of the facilities actually treated COVID-19 patients, including the suspected cases.

Almost all of the facilities provided COVID-19 care. Due to the maelstrom in the early days of the spread of the infection, 171 facilities (73.7%) experienced restrictions in the gynecology department or the entire hospital. The underlying reasons attributed to the restrictions imposed on the medical facilities have been tabulated in **Table 1**.

2. Changes in the number of treatments

In order to get insight into the status of the medical practice during the pandemic, the questions were designed separately for the period from March to July 2020, which represents the first wave of "the State of Emergency," and for the period from August to December 2020.

The designated training facilities review and summarize their own clinical performance (see condition 11 in **Table S1**), thus the respondent answered the number of outpatients and surgeries based on their database. The change observed may be attributed to the subjectivity of the survey respondents. However, it is worthwhile to note that during the 2020 pandemic situation in Japan, the public transport was not suspended and no curfew was imposed by the government. The government recommended the residents to refrain from going out unnecessarily, but it was clearly stated that hospital visits were excluded from the suggested recommendation. Therefore, excluding the case when a shutdown of the outpatient services in a hospital occurred to curb chances of nosocomial infections or other reasons, no external factors may have prevented patients from visiting a hospital. We also consider it reasonable to assume that a postponed appointment meant the patient's request.

Fig. 1 shows the changes in the number of outpatient visits and surgeries and the underlying factors contributing to the change in numbers based off the perception of the survey participants. Of the 232 facilities that responded to the questionnaire for the time period of March 2020–July 2020, a total of 184 facilities (79.3%) responded that there was a decrease, 5 facilities (2.2%) responded that there was an increase, and 43 facilities (18.5%) responded that there was no change. Of the 184 facilities that answered that there was a decrease, 70 facilities attributed the decrease to the functional restriction of hospital and 99 facilities provided patient request as the reason. Regarding the period between August 2020–

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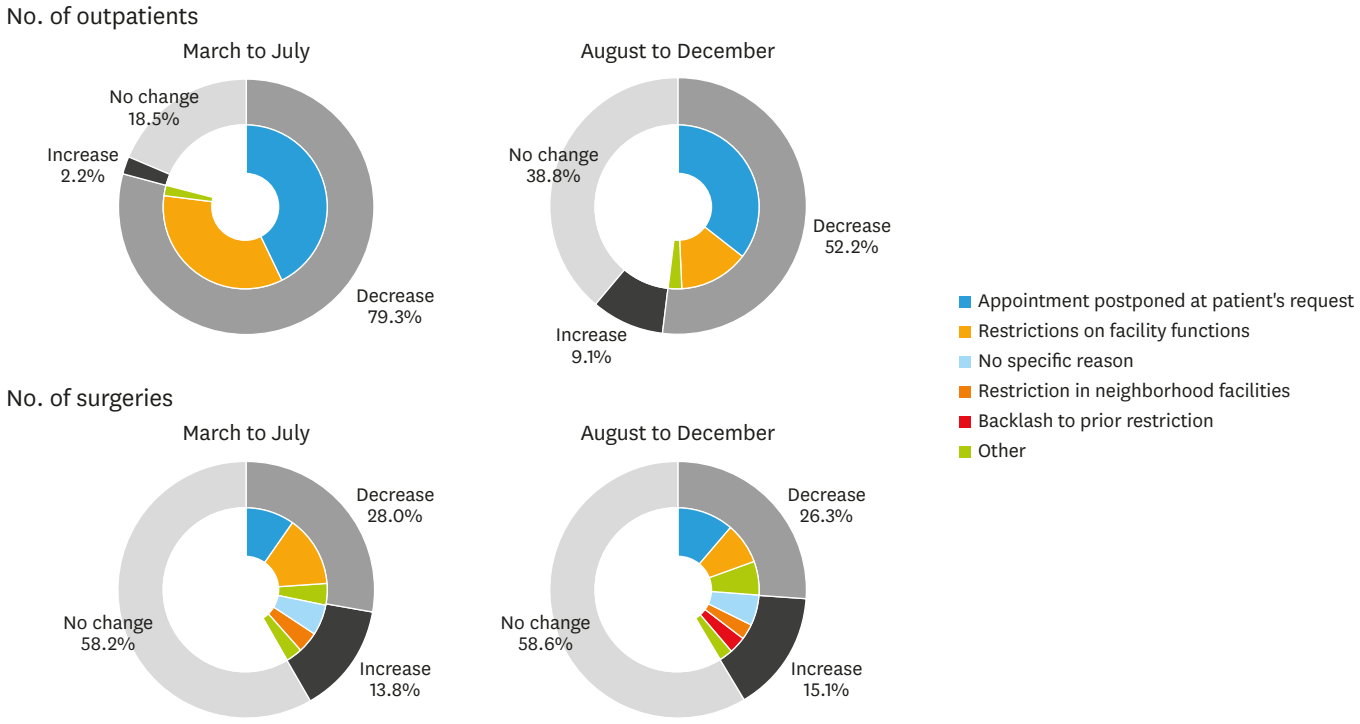

Fig. 1. The percentage of the response with regard to the change in the number of outpatient visits and surgeries and the underlying factors contributing to the change based off the perception of the survey participants.

December 2020, 121 facilities (52.2%) answered that there was a decrease, 21 facilities (9.1%) answered that there was an increase, and 90 facilities (38.8%) answered that there was no change. Of the 121 facilities that responded that there was a decrease, 29 facilities attributed the decrease to the functional restrictions of the hospital and 82 facilities provided patient request as the reason. The major reason attributed to the decrease in the outpatient visits was reluctance of patients to visit medical facilities during the pandemic rather than restrictions in the treatment available.

About 30% of the facilities reported a decrease in the number of surgeries, the reasons being restrictions and patients' requests to postpone invasive medical procedures. In contrast, about 15% of the medical facilities responded to the survey noting an increase in the number of surgeries. Some of these changes were attributed to the increase in restrictions in the neighborhood facilities. There were also responses of backlash to prior restriction during the period from August to December.

The number of chemotherapy and radiotherapy-based procedures were also noted in the survey, and approximately 80% of the facilities responded that there was no change in the frequency of the procedures. An increase in the number of advanced cases opting for these procedures as an alternative to surgery was also expected, but only 6 centers (2.6%) cited these as reasons for the increase.

3. Change of actual number of surgeries

The change in the trend of the actual number of surgeries has been shown in **Table 2**. Compared to 2019, there was an overall decrease of 3.9% was observed. A total of fifty-nine facilities reported that the number of surgeries decreased by 10 or more in absolute number

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Table 2. Actual number of surgeries for gynecological malignancies

	March to July	August to December	Total		March to July	August to December	Total	p-value*
All								
2019	10,839	10,839	21,605					
2020	10,576	10,187	20,763					
Ratio (%)	−2.4	−6	−3.9					
Facilities in "Prefectures operating under special safety precautions"				vs.	Facilities in normally operating prefectures			
2019	7,343	7,498	14,841		3,295	3,268	6,563	
2020	7,102	6,940	14,042		3,304	3,247	6,551	
Ratio (%)	−3.3	−7.4	−5.4		0.3	−0.6	−0.2	0.011
Facilities with a period of restriction				vs.	Facilities not experiencing restrictions			
2019	8,004	7,891	15,895		2,835	2,875	5,710	
2020	7,495	7,314	14,809		3,081	2,873	5,954	
Ratio (%)	−6.4	−7.3	−6.8		8.7	−0.1	4.3	<0.001

*χ^2 test.

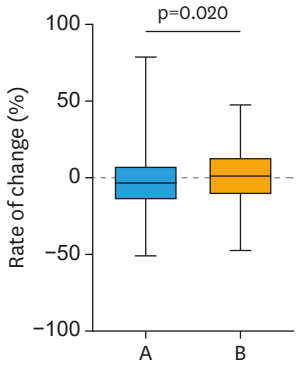


Fig. 2. The rate of change in the number of surgeries of each facility were categorized as: (A) Facilities in "Prefectures operating under special safety precautions", and (B) Facilities in normally operating prefectures. There was a significant difference in distribution as calculated by Mann-Whitney U test.

and 10% or more in percentage. A total of thirty-nine facilities reported that the number of surgeries increased by 10 or more in absolute number and 10% or more in percentage. A significant difference was observed when the responses of all facilities were sub-classified into "Prefectures operating under special safety precautions" (a decrease by 5.4% was observed) or normally operating prefectures (the decrease was by 0.2%). A clear difference was observed when the responses of all facilities were categorized based on whether they experienced COVID-19-based functional restrictions (decrease by 6.8%) or not (increase by 4.3%). The rate of change for each facility was plotted in **Fig. 2**. More facilities in the "Prefectures operating under special safety precautions" tended to have a statistically significant decrease in the number of surgeries conducted. The decrease in the total was attributed to overall decrease in almost all facilities rather than substantial decrease in a few facilities.

4. Delay in medical consultation and treatment and its impact

The **Table 3** shows the response of the participants to the survey question regarding their experience about cases who were intentionally avoiding a visit to the doctor due to fear of infection, and, as well as cases who were refused an appointment at the hospital since they resided in areas with high COVID-19 prevalence. The data on delay in treatment after initial visit was also recorded. The data represents the impact on treatment and prognosis due to delay in consultation as perceived by clinicians.

Table 3. Delay in medical consultation and treatment and its impact

Whether or not patients refrained from visiting the doctor based on their own judgment
Yes, 162 (69.8)
No, 70 (30.2)
Whether or not there were visiting restrictions due to stay in certain prevalent areas
Yes, 83 (35.8)
No, 149 (64.2)
Whether or not doctors felt medical management/prognosis were impacted due to delays in medical visits
Yes, 79 (34.1)
No, 153 (65.9)
Delay in treatment (March to July vs. August to December)
Significant delay (5 vs.3)
Treatment postponed at patients' request (4 vs. 2)
Restrictions on facility functions (1 vs. 1)
A few weeks delay (54 vs. 26)
Treatment postponed at patients' request (10 vs. 5)
Restrictions on facility functions (33 vs. 16)
COVID-19 infection (11 vs. 5)
No delay (173 vs.203)

Values are presented as number (%).
COVID-19, coronavirus disease 2019.

5. Distribution of cancer stages

The trend of the actual number of treatments by cancer type and stage is shown in **Fig. 3**. It was feared that the proportion of advanced cancers would increase due to patients refraining from screening and consultation. The number of patients treated was categorized by stage and compared with the distribution of past data in Japan. Past data as control was extracted from the annual reports of the Committee on Gynecologic Oncology of the Japan Society of Obstetrics and Gynecology (JSOG) [7-9]. There was no increase in the rate of advanced stages in the three major cancer types.

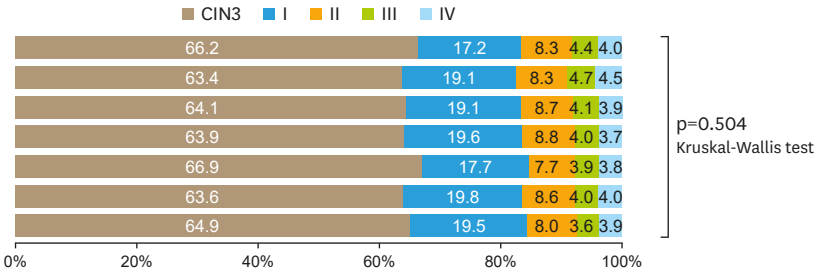
This comparison did not compare the same population of facilities. The data surveyed in this study was collected from 232 facilities and the JSOG data used as control data was collected from about 450 facilities. The JSOG data is the largest database in Japan and the 232 facilities included in this survey are part of the JSOG database (see condition 12 on **Table S1**). The number of treatments reported in this survey data were equivalent to 70% to 80% of annual JSOG data for all cancer types, although the number of the facilities was half of the total and the data was collected for a period of 10 months only. This means that these 232 facilities are a group of high-volume centers that are representative of the current oncology-based clinical situation in Japan. Considering that a high-function hospital can provide intensive care in all of these 232 facilities, it can be assumed that advanced cancers would be concentrated there. If there is no increase in advanced cancers in the group of facilities reported in this study, it is reasonable to assume that there is no overall increase.

DISCUSSION

This is the first report examining the clinical overload in high-functioning facilities in Japan, which now have to balance their resources for simultaneous administration of treatment for COVID-19 as well as gynecological malignancy. Similar studies have been reported from other countries and are web-based with anonymous questionnaires, having response rates ranging from 40% to 70% of the intended population [5,10,11]. The response rate amongst gynecological oncologists in Japan was rather high due to their high sensitivity and

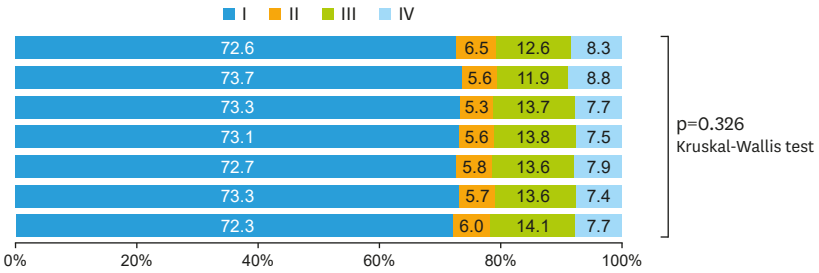
Cervical cancer

	CIN3	I	II	III	IV	Total
2020.8–12	4,814	1,248	603	318	292	7,275
2020.3–7	4,621	1,389	608	344	328	7,290
2019	13,049	3,893	1,775	843	793	20,353
2018	13,621	4,179	1,882	851	798	21,331
2017	15,734	4,164	1,804	917	899	23,518
2016	13,172	4,107	1,782	820	820	20,701
2015	13,757	4,138	1,705	757	836	21,193



Endometrial cancer

	I	II	III	IV	Total
2020.8–12	2,913	260	506	331	4,010
2020.3–7	3,124	237	506	374	4,241
2019	8,237	591	1,535	867	11,230
2018	8,134	619	1,536	831	11,120
2017	8,056	644	1,506	879	11,085
2016	7,417	578	1,374	750	10,119
2015	6,991	576	1,365	741	9,673



Ovarian cancer (including fallopian tube cancer and primary peritoneal cancer)

	I	II	III	IV	NAC	Total
2020.8–12	1,241	205	918	426	-	2,790
2020.3–7	1,245	256	974	463	-	2,938
2019	3,035	585	1,500	428	1,457	7,005
2018	3,085	586	1,519	483	1,332	7,005
2017	2,875	617	1,639	460	1,140	6,731
2016	2,728	570	1,626	482	1,018	6,424
2015	2,565	539	1,635	429	749	5,917

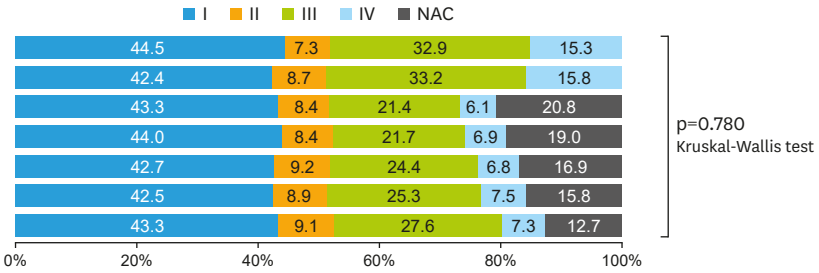


Fig. 3. Distribution of stages in three major types of gynecological cancer based on current survey data and Japan Society of Obstetrics and Gynecology database. Based on the Kruskal-Wallis test, the distribution in this survey had no significant difference compared to past data as the control for all cancer types. CIN, cervical intraepithelial neoplasia; NAC, neoadjuvant chemotherapy.

willingness to cooperate in data generation. It was assumed that the current situation has been assessed more accurately.

In terms of the change in the number of infected people reported daily, the second wave was more prevalent than the first wave. In spite of the appalling situation during the period between August and December, a lower percentage of facilities reported a decrease in the number of outpatient visits compared to the period between March and July. The reduction in doctor visits attributed to pandemic-based restrictions was lower. It may be assumed that the concerted efforts of each institution led to the establishment of a viable treatment strategy which effectively balanced malignancy care and COVID-19 care. Contrary to this result, the number of facilities that cited patient preference as the reason for the decrease in outpatients did not decrease significantly (99 facilities compared to 82 facilities). Refraining from visiting a doctor based on the patient's own judgment may be expected to be an issue in the future. Hence, it is important for clinicians to focus on prevention of nosocomial infections, which may encourage patients to visit hospitals on schedule.

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In Japan, a substantial decrease in the treatment of patients with thoracic ailments including lung and heart surgery was reported [12]; however, gynecologic malignancy surgery decreased by less than 4%. This might be due to the limited use of ICU in gynecologic oncology surgery and the efforts of gynecologic oncologists to maintain continuous treatment regimens. However, the data suggested that facilities that had restrictions due to COVID-19 were faced with greater clinical challenges than those that did not.

There have been some reports from other countries that investigated changes in treatment strategies [10,11]. These studies have revealed the negative impact of COVID-19 pandemic on the choice of cancer treatment strategies with clinicians choosing radiation or chemotherapy as an alternative to surgery. Our survey also investigated the trends and underlying reasons for changes in chemotherapy and radiation-based therapeutic regimens. Limited number of facilities reported change in therapeutic strategy to circumvent surgical procedure, suggesting that the COVID-19 pandemic forced few clinicians to alter their treatment options. These instances in Japan were far fewer than those reported overseas.

In terms of the simple distribution of stages, no significant increase in the number of advanced cancer cases was observed. However, it was difficult to measure the impact of delay in visitations to the clinic or delay in treatment with the help of data encompassing a year. Assuming that the delay in diagnosis might contribute to the increase in advanced cancers and adversely affecting a patient's prognosis [13], it would be likely that the increase in advanced cancers would not become apparent until after the pandemic is over. A total of 34.1% survey participants responded that they perceived the delay in consultation and treatment affected disease management and prognosis. We believe that the effect of COVID-19 on gynecological malignancy treatment cannot be ignored.

There were several limitations in this study. The first limitation of this study is the simplicity of the survey questionnaire. When detailed questions are part of a questionnaire, the data resolution becomes high and the accuracy of the interpretation increases, but complex questions take more time and effort to answer reducing the chances of individuals participating in the survey. Since we were concerned that a complex questionnaire would lead to a low response rate, we developed a relatively simplified set of questions. This is a preliminary study which did not aim to explore the patient dynamics in-depth to keep the data set rather straightforward. For instance, in terms of the number of outpatient visits, classifying the data further into new patients and follow-up patients would increase the complexity of study and may yield different results after all. Similarly, the number of surgeries performed was accounted for but the details of the surgical procedures were not explored. Considering the reports from other countries [14], it is possible that the number of laparoscopic surgery and highly invasive surgeries such as lymph node dissection and gastrointestinal resection may be affected, but we did not attempt to sub classify the data. Secondly, the data surveyed in this study and the JSOG data used as control data were based on reports from designated facilities only. Including data from all hospitals in Japan may increase the overall accuracy of the results reported here.

In addition, it did not include the variance attributed to annual changes. Based on JSOG data and Cancer Statistics by National Cancer Center Japan [15], the number of gynecological cancers diagnosed and treated had increased over the years. If this was taken into account, the decline in the treatments may be greater than what is evident in the current study.

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In conclusion, the healthcare system in Japan in the midst of a pandemic in 2020 remained relatively unaffected; however, the impact, if any, was due to the government's designation of "Prefectures operating under special safety precautions" and restrictions on hospitals' functioning during the pandemic. The decrease in the number of visits appears to be influenced more by patients' voluntary refrainment from availing hospital-based treatments rather than by healthcare facility-based restrictions. The COVID-19 pandemic is not yet under control; hence, we need to continue to balance COVID-19 and cancer-based treatment. It is imperative to focus on enforcing preventative efforts to reduce nosocomial infections and alleviate the clinical problems associated with limited availability of hospital-based patient care, which will eventually reduce patients' reluctance to avail timely and appropriate clinical care.

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SUPPLEMENTARY MATERIAL

Table S1

List of requirements set by the Japanese Society of Gynecologic Oncology for certification of designated training facilities

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