

# Time Intervals from the First Symptom to Surgery of Ovarian Malignancies in a Tertiary Government Hospital

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## ABSTRACT

**Objective.** This is a cross-sectional study aimed to determine the time intervals from the first symptom to surgery of 37 patients with ovarian malignancies who underwent surgery at a tertiary government hospital from June to October 2019.

**Methods.** Structured interviews of patients and chart reviews were conducted to identify the intervals and the reasons behind such. The data were analyzed using Stata/SE 14.1, with the time intervals presented as medians and the reasons as frequencies. Multinomial logistic regression analysis established the association of time intervals with the extent of surgery and final stage of ovarian malignancies.

**Results.** The median Total Time Interval from the first symptom to surgery was 214 days. The longest delay was the Total System Interval (from the first visit at the tertiary hospital to surgery) with a median of 70 days. This was followed closely by Patient Interval (from the first symptom to consult with the initial physician) with a median of 64 days. A distant third was the Initial Physician Interval (from the consult with the initial physician to the first visit at the tertiary hospital) with a median of 29 days. Most common reasons for the delays were the patients not acknowledging the gravity of their condition for the Patient Interval; choice to go to other hospitals, distance and laboratory works or diagnostics for the Initial Physician Interval; waiting for laboratory work-ups for the First System Interval; and waiting for other departments' clearance for the Second System Interval. The most common first symptom was abdominal enlargement. The length of interval and the final stage ( $p=0.056$  for Stage III and  $p=0.162$  for Stage IV)) as well as extent of surgery ( $p=0.093$ ) did not show significant association.

**Conclusion.** The time interval from first symptom to surgery showed a median of 214 days. The greatest delay is contributed by Total System Interval followed by Patient Interval due to varying reasons. Length of time intervals, however, was not found to be significantly associated with the extent of surgery and final stage.

**Key Words:** time intervals, diagnosis delay, treatment delay, gynecologic malignancies, ovarian malignancies

## INTRODUCTION

Ovarian cancer represents the fifth leading cause of deaths from cancer among women in the Philippines. The estimated age-standardized national incidence rate was 5.9 per 100,000 women. The estimated national standardized mortality rate was 3.9 per 100,000 women.<sup>1</sup> The first line of management generally involves surgery with the removal of the pathologic ovary and other foci of tumor and staging procedures.

The high mortality rate of ovarian cancer can be attributed to the fact that about 2/3 of these cases are diagnosed in advanced stage. One of the reasons for this is the lack of cost-effective screening tool for ovarian cancer. Studies on imaging and tumor markers have not resulted

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in a decrease in mortality for this disease (PLCO Trial).<sup>2</sup> Currently, there is no screening for early detection of ovarian cancer. Risk factors include family history of breast or ovarian cancer, endometriosis, pelvic inflammatory disease, polycystic ovarian syndrome, obesity, cigarette smoking, and no history of bilateral tubal ligation.<sup>3</sup>

Another reason why ovarian cancers are diagnosed late is because of failure to detect ovarian cancers early based on symptomatology. Patients would usually come in advanced disease because of late onset of significant symptoms or some symptoms were non-specific and were not attributed by patients to possible ovarian cancer. Most studies attribute the delay in treatment path as being primarily due to patient delay.<sup>4-6</sup>

There are only a few studies that cited the relationship between time intervals along the treatment pathway of ovarian malignancies and their outcome. Some studies show that prolonged intervals result to poorer outcomes.<sup>7-9</sup>

This is the first study in the local setting which looked at the time intervals from first symptom to the delivery of surgical management for cases of ovarian cancer.

Identification of time intervals from first symptom to surgery can give an idea of the efficiency of our health service delivery. It will aid in the development of directed efforts to improve the entire pathway, such as improving patient and general practitioner education and also the system process. Figure 1 depicts the conceptual framework of the study.

It is the objective of this study to determine the time intervals from the first symptom to surgery of patients with ovarian malignancies who are admitted for surgery at a tertiary hospital for a five-month period from June to October 2019. It also looked at the first symptoms as reported by patients and the reasons behind the time intervals. It also

identified the association between the time interval and the outcome as characterized by the stage of the malignancy and extent of surgery performed.

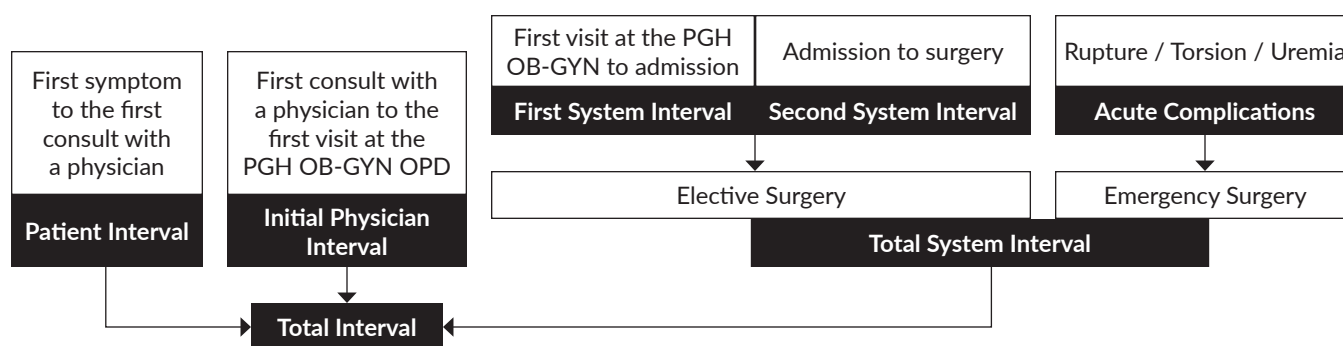
## METHODS

### Study Design

This is a cross-sectional study involving 37 patients with ovarian malignancies who underwent surgery for tissue diagnosis from June to October 2019 in the obstetrics and gynecology department of a tertiary government institution. There were structured interviews with patients and a review of their outpatient and admission charts. This study was approved by the institution's Research Ethics Board.

Women included were those admitted at the Gynecologic Wards and on their first or second post-operative day following their first surgery for ovarian cancer obtaining tissue diagnosis, elective or emergency. They must have undergone at least one outpatient or emergency consult for the present condition in the same institution. Their histopathologic result must have confirmed the ovarian malignancy. They have provided informed consent. Those who had previous surgery for tissue diagnosis and/or are undergoing neoadjuvant chemotherapy were excluded.

The structured interview questions were translated in the vernacular by the *Sentro ng Wikang Pambansa* of the University of the Philippines Manila. The interview was conducted by the principal investigator at bedside. In her absence, the trained research assistant took her place. The purpose of the interview was to determine the presence of risk factors, the first symptom, the patient interval and the initial physician interval. The interview also explored the reasons behind the Patient and Initial Physician Intervals.



**Figure 1. Total Intervals from first symptom to surgery.** The first symptom is the first manifestation felt by the patient that is related to the ovarian malignancy. The **Total Interval** refers to the overall calculated time from one phase of the patient's treatment pathway to the next. The **Patient Interval** is the time calculated from the first symptom to consult with the initial physician. The **Initial Physician Interval** is the time calculated from the consult with the initial physician to the first visit at the tertiary hospital. The **Total System Interval** is the time calculated from the first visit at the tertiary hospital to surgery. The **First System Interval** is the time calculated from the first visit at the tertiary hospital to admission while the **Second System Interval** is the time calculated from admission to surgery. Surgery is the actual procedure performed to obtain a tissue diagnosis for the ovarian malignancy, and may either be **Emergency surgery** if done on an emergency basis secondary to the patient developing acute complications, or **Elective surgery** if the surgery is done on an elective basis with the patient not having acute complications.

Review of the existing medical records (dates of imaging mostly from ultrasound, tumor marker results and referral letters) of the participants supplemented and attested to the accuracy of data gathered from the interview. Reviews were made by members of research team in compliance with the policies of the Medical Records Division of the institution which, in turn, complies with the Data Privacy Act of 2012. The subjects' medical charts from the Outpatient Department (if present) and from the present admission were reviewed to gather data, both on the actual time difference and the reasons for delays, on the system interval. The histopathology results of the recruited subjects were followed up two weeks after the surgery. The interventions done to the patients were determined by their respective residents-in-charge and did not affect the parameters measured in the study.

### Data Analysis

The data were encoded in Microsoft Excel and were analyzed using Stata/SE 14.1 (StataCorp Texas USA). The demographic data, clinical characteristics and first symptoms of the subjects were presented as frequencies. The time interval data were presented as medians. The reasons behind the time intervals were reported as frequencies. Multinomial logistic regression analysis was done to determine the association of time intervals with extent of surgery and final stage of ovarian malignancies. A  $p$ -value  $< 0.05$  was considered significant.

## RESULTS

A total of 37 patients with ovarian malignancies were included in this study. Table 1 shows the socio-demographic profile of the subjects included in the study.

The age ranged between 19 to 69 years old with a median of 53. Majority of the patients were married (48.65%) and high school graduates (59.46%). Only 21.62% had a gravidity or parity of 5. In terms of body mass index, 43.24% were obese.

The prevalence of risk factors in the 37 patients are as follows: three had family history of breast cancer (8.11%), three had current smoking (8.11%), two had family history of ovarian cancer (5.41%), two had  $>10$  years use of estrogen (5.41%), one had polycystic ovaries on sonography (2.70%) and none had endometriosis or PID (0.00%). No bilateral tubal ligation was done in 34 patients (91.9%).

The most common first symptom experienced was abdominal enlargement (45.95%) followed by pelvic heaviness (24.32%), pelvic pain (8.11%), bloatedness, abdominal mass, abnormal uterine bleeding (5.41%), constipation and incidental ultrasound finding (2.7%)

Table 2 describes the time intervals from the first symptom to surgery of patients with ovarian malignancies.

The total time interval, defined as the total time calculated from the first symptom to surgery, ranged between 16 to 922 days with a median of 214 days. Sub-intervals

**Table 1.** Demographic and clinical profile of patients with ovarian malignancies

N=37	
<b>Age (Median, Range)</b>	53, 19-69 years
<b>Civil Status</b>	
Single	12 (32.43)
Married	18 (48.65)
Widowed	6 (16.22)
Common law	1 (2.70)
<b>Educational attainment</b>	
None	0 (0.00)
Elementary	6 (16.22)
High school	22 (59.46)
College	6 (16.22)
Vocational	3 (8.11)
<b>Gravidity</b>	
$<5$	29 (78.38)
5+	8 (21.62)
<b>Parity</b>	
$<5$	29 (78.38)
5+	8 (21.62)
<b>BMI</b>	
Underweight	1 (2.70)
Normal	19 (51.35)
Overweight	1 (2.70)
Obese 1	12 (32.43)
Obese 2	4 (10.81)
<b>Kind of Surgery</b>	
Elective	36 (97.30)
Emergency	1 (2.70)
<b>Presence of Risk Factors</b>	
Family history of breast cancer	3 (8.11)
Family history of ovarian cancer	2 (5.41)
Endometriosis	0 (0.00)
PCOS	1 (2.70)
PID	0 (0.00)
Current smoking	3 (8.11)
Tubal ligation	3 (8.11)
Estrogen use, $>10$ years	2 (5.41)

**Table 2.** Time intervals from the first symptom to surgery of patients with ovarian malignancies

Time intervals (Median, Range)	
<b>Patient Interval</b>	64, 0-583 days
<b>Initial Physician Interval</b>	29, 0-411 days
<b>First System Interval</b>	66, 0-390 days
<b>Second System Interval</b>	4, 0-21 days
<b>Total time interval</b>	214, 16-922 days

showed a median of 64 days for the Patient Interval (from the first symptom to consult with the initial physician), 29 days for the Initial Physician Interval from the consult with the initial physician to the first visit at tertiary hospital), 70 days for the Total System Interval (from the first visit at the tertiary hospital to surgery), with 66 days for the First System Interval (from the first visit at the PGH Department of Obstetrics and Gynecology to admission) and 4 days for the Second System Interval (from admission to surgery).

The most common reason for the Patient Interval was the patients did not think that the symptom was serious (59.46%). In 8.11% of cases, the reasons for the delay included being busy with work or school, financial issues or other personal reasons (unsure if she would pursue work-up, visited a dead relative in the province).

In terms of the Physician Interval, the reasons for the interval were well-distributed. The most common reasons for the interval between the initial physician consult and the first consult at the tertiary hospital's Department of Obstetrics and Gynecology were choice to go to other hospitals first (13.51%), distance between home and hospital (13.51%), and facilitation of laboratory work-ups and diagnostics (13.51%). Another department has initially seen 13.51% of patients (10.81% by Surgery and 2.70% by General Medicine). In 10.81%, there seems to be no delay as their first consult was with the tertiary hospital's Department of Obstetrics and Gynecology.

The reported number of follow-ups to the Outpatient Department ranged between zero to eight, with a median of four times. For those who had no follow-ups, four cases (10.81%) went straight to the Admitting Section. Five cases (13.51%) were sent to the Admitting Section after being assessed as unstable at the Outpatient Department General Clinic when they presented during initial consult with abdominal tenderness, dyspnea and as a case of malignancy in a pregnant patient. In three cases (8.11%), they were sent to the Admitting Section after being assessed as unstable at the Admissions Clinic when they presented with dyspnea and pallor.

The median Total System Interval was 70 days. For the First System Interval, from the first visit at the tertiary hospital to admission, the most common reasons were waiting for necessary routine laboratory work-ups (59.46%), followed by waiting for routine medical clearance (37.84%). Clearances from other specializations were required in 24.32% and there were incomplete laboratory work and diagnostics in 13.51%.

For the Second System Interval, from admission to surgery, 43.24% of patients did not have delays in this sub-interval. In those with delays, the most common reasons were waiting for clearance from other departments (43.24%) and waiting for results of laboratory work-ups (35.13%). Stabilization of medical conditions (hypercalcemia, hypokalemia, pleural effusion, pneumonia, anemia, azotemia, hyperthyroidism and cellulitis) accounted for the interval in 29.73%. Additional diagnostics like 2D echocardiography, computed tomography scan and deep venous thrombosis screening were needed in 21.62%. There was also waiting for an available surgery schedule in 16.22%.

Full staging was done in 81.08% of patients, while advanced stages in 7% of patients precluded full staging and only allowed tissue biopsy. The most common histopathologic finding was mucinous carcinoma (21.62%) followed by high grade serous carcinoma (18.92%), borderline mucinous tumor (16.22%) serous borderline tumor (8.1%) and endometrioid

adenocarcinoma (2.7%). In terms of final staging, most had stage IA disease (24.32%) followed by stage IC1 (21.62%). Advanced stage diseases (stages III and IV) comprise 32.43%.

Multinomial logistic regression analysis was done to determine the association of time intervals with the extent of surgery and final stage of ovarian malignancies as depicted in Table 2. A p-value < 0.05 was considered significant. Length of time intervals was not found to be significantly associated with extent of surgery (p-value=0.093) and final stage of ovarian malignancies (p-value=0.056 for stage III and 0.162 for stage IV).

## DISCUSSION

### Symptoms of Ovarian Cancer

Di Saia, et al. state that progressive compression of the surrounding pelvic structures, causing vague abdominal discomfort, urinary frequency, and "pelvic pressure" may result from ovarian enlargement.<sup>3</sup> When its diameter becomes 10 to 15 cm, abdominal enlargement may already occur. Hence, vague symptoms may be present for several months before the diagnosis. Currently, there is no evidence available that CA-125 measurement and transvaginal sonography can be used effectively for widespread screening to reduce mortality from ovarian cancer or to decrease overall morbidity and mortality as shown in the largest trial evaluating the screening outcome for ovarian cancer (PLCO Trial).<sup>2</sup>

According to the American College of Obstetricians and Gynecologists, the following symptoms, especially if present for more than 12 days per month of new onset (less than 12 months duration), should prompt consult with a gynecologist or health care professional: bloating or an increase in abdominal size, pelvic or abdominal pain, difficulty eating or feeling full quickly, urinary symptoms (frequency and urgency), vaginal bleeding (especially post-menopausal) and change in bowel habits.<sup>10</sup> Women with these symptoms should have ovarian cancer included in their differential diagnosis. True enough, the most common first symptom experienced by the patients in the study was abdominal enlargement (45.95%) followed by pelvic heaviness (24.32%).

### Time Intervals from the First Symptom to Treatment

Andersen et al. proposed the General Model of Total Patient Delay wherein such delay can be divided into appraisal delay, illness delay, behavioral delay, scheduling delay and treatment delay.<sup>11</sup> This was supported by a review conducted by Walter et al, which demonstrated that there are recognizable stages between the recognition of a symptom, first presentation to a health care professional, subsequent diagnosis and initiation of treatment.<sup>12</sup> Moreover, the study stated that there was compelling proof to support the existence and importance of appraisal and treatment delay as defined in the Andersen Model, although treatment delay requires expansion. Coming from the initial framework set by Andersen et al, Evans et al. subcategorized Andersen's



fifth stage, treatment delays, into non-investigation of symptoms, treatment for non-cancer causes, lack of follow-up and referral and system delays.<sup>5,13</sup>

Hansen et al. studied the time intervals from first symptom to treatment of cancers in Denmark.<sup>6</sup> They computed for all cancer types and then for the ten most frequent cancers. They defined patient delay as the time from first perceived patient symptom until first presentation to the general practitioner, and system delay as the time from the start of the general practitioner-initiated investigation until the start of treatment.

Hansen et al. reported that the shortest delay seen among 2212 new cancer cases in Denmark from 2004 to 2005 was ovarian cancer patients, with a median of 60 days, ranging from 45 to 112 days ( $n=59$  out of 2212 cases or 2.7%).<sup>6</sup> This value is less than our Total Interval of 214 days. Similarly, most of the delays came from the system and the patient. However, both are shorter at 55 and 21 days, respectively, compared to our findings which are 70 and 64 days, respectively.

In a study by Allgar and Neal regarding delays in the diagnosis of six cancer types in the United Kingdom, they found out that ovarian cancer patients experienced the third shortest total delays with a mean of 90.3 days, following patients with breast cancer and lung cancer.<sup>4</sup> Still, this delay is shorter than our Total Interval of 214 days. Patient delay accounts for most of the delay in the treatment pathway, compared to our findings which showed Patient Interval to be the second cause of delay.

In this study, the median time interval from the first symptom to surgery was 214 days. Most of it was attributed to the First System Interval at median 66 days referring to the time from the first visit to the tertiary hospital to admission. The delays were due to performances of preoperative laboratories and seeking medical clearances. Following a close second at median 64 days is Patient Interval referring to the time from first symptom to the first physician consult. The delays were due to lack of knowledge of symptoms, lack of time to consult and finances. Our results are way much longer compared to studies done in the European countries like Denmark and the United Kingdom. Following Andersen's model, our delays are due to a combination of appraisal, behavioral, scheduling and treatment delays.

In a cohort study by Hansen et al, it was shown that a long patient delay implies the need to delve into patient awareness of cancers.<sup>6</sup> In the study of Evans et al. consisting of a total of 43 women interviewed, they mentioned that misattribution of symptoms to stress or menopause, misattribution of symptoms to a previous benign condition like bowel problems, etc., and non-recognition of symptoms as serious were the main reasons of patient interval in ovarian cancer diagnosis.<sup>13</sup> Consistently, these reasons were also stated in the review of Dobson et al.<sup>12</sup> The authors stated that misinterpretation or misattribution of symptoms to minor ailments, physical exertion, stress and ageing; fear of cancer diagnosis and treatment; embarrassment especially

when symptoms are located in private areas of the body; concern of appearing neurotic, hypochondriac; and wasting the doctor's time were the reasons cited for patient interval of diagnosis. They also added that prioritization of other life events affected the time of the health-seeking behaviors of the patients. Consistent with the results of the current study, the most common reason for patient interval was that the patients did not think that their symptoms are serious (59.46%). On the other hand, in the case study of Khorana & Bolwell, reasons of patient interval were that some patients chose to delay treatment because of preference for a specific physician, work-related issues or presence of prior family commitments.<sup>14</sup>

Initial Physician Interval can be attributed to different factors. The most common reason mentioned in studies is the occurrence of misdiagnosis. In the retrospective review of Kirwan et al. of 135 patients with epithelial ovarian cancer from 1992 to 1994, 73% of patients were referred directly to hospitals by their general practitioners within four weeks of presentation, where half were initially misdiagnosed to have irritable bowel syndrome.<sup>15</sup> Another reason that causes the initial physician delay is referral to other departments. In the same study by Kirwan et al, 44% of the patients were directly referred to gynecology department, 11% of which was for cancer investigation. However, the other 67% had delay in treatment due to referral to other departments first before to gynecologists. Moreover, Evans et al. also investigated the different factors that caused treatment delays among women with ovarian cancer.<sup>13</sup> Non-investigation of symptoms by general practitioner (e.g. relating it to hormonal problems), treatment given to non-cancer diseases (e.g. treating with antibiotics, pain killers, laxatives and other co-existing conditions), and referral delays (e.g. initially referring to other hospital services/ departments before going to gynecology) were the reasons mentioned in their study. In the current study, there were no delays in 10.81% because these patients did not consult other physicians but went directly to the tertiary hospital's Department of Obstetrics and Gynecology. However, in those who did not, the reasons for the delay included the choice to go to other hospitals first (13.51%), distance between home and hospital (13.51%), and facilitation of laboratory work-ups and diagnostics (13.51%). However, compared to the aforementioned study by Kirwan, only 13.51% were first seen by another department prior to referral to our department.

As mentioned earlier by Hansen et al, system intervals caused much of the total delays experienced by cancer patients.<sup>6</sup> The authors mentioned that logistics, waiting time and administrative procedures are some of the reasons of these delays. Consistent with the current study, the most common reasons were waiting for necessary routine laboratory work-ups (59.46%), followed by waiting for routine medical clearance (37.84%). Clearances from other specializations were required in 24.32% and there were incomplete laboratory work and diagnostics in 13.51%.

In addition, Evans et al. (2006) said that long waiting list for surgery also cause system delay.

To shorten the system interval, there has to be increased efficiency within the institution with scheduling of the necessary work-ups with the provision of more machines and more manpower. As for the medical clearances from other services, there has to be an expedited and efficient system for referrals for patients who will be undergoing surgeries. Also, it should be emphasized well to the patients that timely completion of their clearances and work-up are essential for them to be scheduled for surgery early so they will have more motivation for such. Sometimes, due to a longer time needed for surgery or treatment appointment; emergency management becomes necessary as the symptoms and stage of cancer worsens. In the study, however, only 2.7% required an emergency surgery for tumor rupture.

In the Optimal Care Pathway for Women with Ovarian Cancer by the Cancer Council of Australia, optimal timeframes to treatment were stated. Symptoms of more than four weeks and those that persist for more than a week after the initial treatment by the general practitioner should be investigated.<sup>16</sup> Results of the investigation should be available and be reviewed within one week. A specialist should be seen within two weeks of suspected diagnosis. The diagnostic workup should be complete within two weeks of specialist review. Results of the relevant laboratory examinations and diagnostics should be available for a multidisciplinary team discussion. Finally, surgery optimally has to be done within four weeks of diagnosis. These outlined ideal timeframes are very far from the actual intervals seen in the current study. These time frames must be set in the local institutions providing care for ovarian malignancies. There has to be a built-in evaluation system to check whether the time frames are met. Longer follow ups are warranted to look at more relevant outcomes related to ovarian cancer management including patient survival. The latter, however, is dependent on several other factors - related to the tumor behavior - aside from patient and health system factors.

### Associations between Time Intervals and Outcomes

Different results were reported by several studies regarding the effects (positive, negative and no association) of time intervals in ovarian cancer.<sup>17</sup>

In a study by Robinson, et al. among Danish women with endometrial and ovarian cancer, it was demonstrated that longer total delay was associated with reduced overall quality of life and appetite loss among ovarian cancer patients.<sup>18</sup> In addition, longer total delay was associated with decreased patient satisfaction. On the other hand, according to Tokuda et al, the longer interval was significantly associated with a lower likelihood of distant metastasis in ovarian cancer (OR= 0.97, 95% CI 0.96-0.99).<sup>19</sup>

According to Menczer, several weeks to several months of treatment delay among gynecological cancers do not have deleterious effects on its outcomes.<sup>20</sup> They stated that

late diagnosis or duration of treatment delay did not have a definite effect on outcome. More so, on the case control study of Nagle et al. done in Australia from 2002 to 2005 (n= 1463), it was seen that there were no significant differences in the time from the onset of symptoms to consultation with first medical practitioner (p-value= 0.19) or symptom onset to cancer diagnosis (p-value=0.64) among women with International Federation of Gynecology and Obstetrics (FIGO) stages I to IV.<sup>21</sup> No correlation was seen between the duration of the interval and the stage. Hence, they concluded that once ovarian cancer is symptomatic, reducing the time to diagnosis would not greatly alter stage of disease at diagnosis or survival. Consistent with the findings of the current study, the length of time intervals or delay were not significantly associated with tumor stage and extent of needed surgery. Likewise, in a study by Neal, et al. in United Kingdom, there was no difference in stage or survival in association with the referral interval.<sup>22</sup> Another study demonstrating that there is no association was done by Kirwan et al, (2002).<sup>14</sup>

Though studies have shown that delays in management of ovarian cancer have not resulted in better outcomes including survival, it is still imperative that centers providing ovarian cancer care should study ways on addressing the causes of delay. Patient-related delays may be addressed with patient education. Health system delays can be addressed by making more efficient pathways within the center including allotment of more doctors who could see patients at the Outpatient Department, provision of more machinery and manpower for earlier scheduling of work-up (CT scan/ MRI/ ultrasound/ laboratory tests), allocation of more beds for patients for elective surgery, provision of more operating rooms and more efficient operating room scheduling.

### CONCLUSION

The study depicts the time intervals from first symptom to surgical management of ovarian malignancies. The results are much longer compared to studies of the same nature conducted in centers in Europe. The delays are attributable to both System Interval and Patient Interval.

### Limitations and Recommendations

A strength of this study is the prospective nature of data collection wherein patients were followed-up through the course of the study. This enabled accurate measurement of time intervals starting from the initial consult in the institution until the eventual surgical management.

The findings of the current study are limited to patients with presumably low socioeconomic status who went to a tertiary government hospital for evaluation and management of their ovarian malignancies. These patients have lower access to health care and less resources to spend for check-ups and treatment. Hence, it may be expected that time intervals will be longer for these patients compared to the general population. A study involving patients under the

Pay Services may be done. Another limitation of this study is the sample size. Although derived from the number of ovarian malignancy patients operated on by the institution within a year (111 patients), this could have limited the power of the statistical tests which assessed the association of time intervals with extent of biopsy and final staging. Increasing the study length to increase the sample size is recommended. An increased sample size may also give insight if there are associations between the time intervals and the histopathology of the malignancies. Multi-center studies may also be performed.

### Statement of Authorship

Both authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising and approved the final version submitted.

### Author Disclosure

Both authors declared no conflicts of interest.

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### REFERENCES

- Laudico, A.V., Mirasol-Lumague, M., Medina, V. Mapua, C.A., Valenzuela, FG., Pukkala, E., Philippine Cancer Facts and Estimate [Internet]. 2015 [cited 2019 September]. Available from: [http://www.philcancer.org.ph/wp-content/uploads/2017/07/2015-PCS-Ca-Facts-Estimates\\_CAN090516.pdf](http://www.philcancer.org.ph/wp-content/uploads/2017/07/2015-PCS-Ca-Facts-Estimates_CAN090516.pdf).
- Temkin SM, Miller EA, Samimi G, Berg CD, Pinsky P, Minasian L. Outcomes from ovarian cancer screening in the PLCO trial: Histologic heterogeneity impacts detection, overdiagnosis and survival. *Eur J Cancer*. 2017 Dec; 87:182-8. doi: 10.1016/j.ejca.2017.10.015. Epub 2017 Nov 21. PMID: 29156299.
- DiSaia, P.J., Creasman, W.T., Mannel, R.S., Mcmeekin, D.S., Mutch, D.G. Clinical Gynecologic Oncology Ninth Edition. Philadelphia: Elsevier; 2018. pp 259
- Allgar VL, Neal RD. Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *Br J Cancer*. 2005 Jun 6;92(11):1959-70. doi: 10.1038/sj.bjc.6602587. PMID: 15870714; PMCID: PMC2361797.
- Evans J, Ziebland S, McPherson A. Minimizing delays in ovarian cancer diagnosis: an expansion of Andersen's model of 'total patient delay'. *Fam Pract*. 2007 Feb;24(1):48-55. doi: 10.1093/fampra/cml063. Epub 2006 Dec 7. PMID: 17158183.
- Hansen RP, Vedsted P, Sokolowski I, Søndergaard J, Olesen F. Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. *BMC Health Serv Res*. 2011 Oct 25; 11:284. doi: 10.1186/1472-6963-11-284. PM
- Richards MA. The National Awareness and Early Diagnosis Initiative in England: assembling the evidence. *Br J Cancer*. 2009 Dec 3;101 Suppl 2(Suppl 2): S1-4. doi: 10.1038/sj.bjc.6605382. PMID: 19956152; PMCID: PMC2790704.
- Risberg T, Sørbye SW, Norum J, Wist EA. Diagnostic delay causes more psychological distress in female than in male cancer patients. *Anticancer Res*. 1996 Mar-Apr;16(2):995-9. PMID: 8687166.
- Rutqvist, Lars. (2006). Waiting times for cancer patients - A "slippery slope" in oncology. *Acta oncologica* (Stockholm, Sweden). 45. 121-3. 10.1080/02841860600549204. ID: 22027084; PMCID: PMC3217887.
- The American College of Obstetricians and Gynecologists, ACOG Committee Opinion Number 716: The Role of the Obstetrician-Gynecologist in the Early Detection of Epithelial Ovarian Cancer in Women at Average Risk [Internet]. 2017 [cited 2019 September] Available from: <https://www.acog.org/-/media/Committee-Opinions/Committee-on-Gynecologic-Practice/co716.pdf?dmc=1&ts=20180415T0159100016>.
- Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol*. 1995 Mar;34 (Pt 1):33-52. doi: 10.1111/j.2044-8309.1995.tb01047.x. PMID: 7735731.
- Walter F, Webster A, Scott S, Emery J. The Andersen Model of Total Patient Delay: a systematic review of its application in cancer diagnosis. *J Health Serv Res Policy*. 2012 Apr;17(2):110-8. doi: 10.1258/jhsrp.2011.010113. Epub 2011 Oct 18. PMID: 22008712; PMCID: PMC3336942.
- Evans J, Ziebland S, McPherson A. Minimizing delays in ovarian cancer diagnosis: an expansion of Andersen's model of 'total patient delay'. *Fam Pract*. 2007 Feb;24(1):48-55. doi: 10.1093/fampra/cml063. Epub 2006 Dec 7. PMID: 17158183.
- Khorana, A., Bolwell, B., Reducing Time-to-Treatment for Newly Diagnosed Cancer Patients. [Internet]. 2019 [cited 2019 September]. Available from: [https://catalyst.nejm.org/time-to-treatment-cancer-patients/?fbclid=IwAR3d9okcivBRiDvVcl1v96b\\_yYhy1INxGH154j6LW2v9jZbJ2U3JdAK5zE](https://catalyst.nejm.org/time-to-treatment-cancer-patients/?fbclid=IwAR3d9okcivBRiDvVcl1v96b_yYhy1INxGH154j6LW2v9jZbJ2U3JdAK5zE).
- Kirwan JM, Tincello DG, Herod JJ, Frost O, Kingston RE. Effect of delays in primary care referral on survival of women with epithelial ovarian cancer: retrospective audit. *BMJ*. 2002 Jan 19;324(7330): 148-51. doi: 10.1136/bmj.324.7330.148. PMID: 11799032; PMCID: PMC64516.
- Cancer Council of Australia, Optimal Care Pathway for Women with Ovarian Cancer. [Internet]. 2007. [cited 2019 September]. Available from: <https://www.cancer.org.au/content/ocp/health/optimal-care-pathway-for-women-with-ovarian-cancer-june-2016.pdf>.
- Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. *Br J Cancer*. 2015 Mar 31;112 Suppl 1(Suppl 1): S92-107. doi: 10.1038/bjc.2015.48. PMID: 25734382; PMCID: PMC4385982.
- Robinson KM, Christensen KB, Ottesen B, Krasnik A. Diagnostic delay, quality of life and patient satisfaction among women diagnosed with endometrial or ovarian cancer: a nationwide Danish study. *Qual Life Res*. 2012 Nov;21(9):1519-25. doi: 10.1007/s11136-011-0077-3. Epub 2011 Dec 4. PMID: 22138966.
- Tokuda Y, Chinen K, Obara H, Joishy SK. Intervals between symptom onset and clinical presentation in cancer patients. *Intern Med*. 2009;48(11):899-905. doi: 10.2169/internalmedicine.48.1720. Epub 2009 Jun 1. PMID: 19483358.
- Menczer J. Diagnosis and treatment delay in gynecological malignancies. Does it affect outcome? *Int J Gynecol Cancer*. 2000 Mar;10(2):89-94. doi: 10.1046/j.1525-1438.2000.00020.x. PMID: 11240658.
- Nagle CM, Francis JE, Nelson AE, Zorbas H, Luxford K, de Fazio A, Fereday S, Bowtell DD, Green AC, Webb PM. Reducing time to diagnosis does not improve outcomes for women with symptomatic ovarian cancer: a report from the Australian Ovarian Cancer Study Group. *J Clin Oncol*. 2011 Jun 1;29(16):2253-8. doi: 10.1200/JCO.2010.32.2164. Epub 2011 May 2. PMID: 21537035.
- Neal RD, Allgar VL, Ali N, Leese B, Heywood P, Proctor G, Evans J. Stage, survival and delays in lung, colorectal, prostate and ovarian cancer: comparison between diagnostic routes. *Br J Gen Pract*. 2007 Mar;57(536):212-9. PMID: 17359608; PMCID: PMC2042569.

## APPENDIX

### Appendix A. Structured Interview Form

Patient Code Number \_\_\_\_\_ - \_\_\_\_\_

Date: \_\_\_\_\_

#### Risk Factors

	Oo	Hindi
Mayroon ba sa pamilya na may kanser sa suso?		
Mayroon ba sa pamilya na may kanser sa obaryo?		
Gumamit ka ba ng estrogen nang higit sa 10 taon?		
Nagkaroon kaba ng <i>pelvic inflammatory disease</i> o sakit na nakukuha sa pakikipagtalik na umakyat papunta sa matres, tubo o obaryo?		
Nagsisigarilyo ka ba sa ngayon?		
Natali na ba ang mga tubo mo?		

#### First Symptom

Ano ang unang sintomas na naramdaman mo patungkol sa iyong kanser sa obaryo?	
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#### Patient Interval (in weeks), to be supplemented by the dates in existing records (ultrasound results, tumor marker results, referral letters)

Gaano katagal ang lumipas mula sa unang sintomas na naramdaman mo patungkol sa iyong kanser sa obaryo hanggang sa unang nagpakonsulta ka sa doktor?	
Ano ang dahilan sa pagkaantala ng pagpapakonsulta sa unang doktor?	

#### Initial Physician Interval (in weeks), to be supplemented by the dates in existing records (ultrasound results, tumor marker results, referral letters)

Gaano katagal ang lumipas mula sa unang pagpapakonsulta mo sa doktor patungkol sa kanser sa obaryo hanggang sa una kang nagpunta sa PGH Department of Obstetrics and Gynecology?	
Ano ang dahilan sa pagkaantala ng pagpunta sa PGH Department of Obstetrics and Gynecology?	

#### System Delay, to be counterchecked with the chart review (in weeks)

Gaano katagal mula sa nakita ka ng doktor ng PGH hanggang sa ikaw ay naoperahan?	
Ano ang dahilan sa pagkaantala ng operasyon?	