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Death of 43 Indonesian women with ovarian cancer: A case series

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ABSTRACT

BACKGROUND: Ovarian cancer is a gynecological cancer with a higher mortality than other gynecological cancers.
CASE REPORT: There were 43 cases of Indonesian women who died of ovarian cancer in 2015–2017. Patients were first diagnosed at the age of 40–59 years (65.11%), of which had normal BMI (62.72%) and mostly in stage III (39.53%). The histology was 88.3% epithelial ovarian cancer with the most subtypes of mucinous carcinoma (25.5%). The majority were referral patients (62.7%), but due to its malignancy, many died before receiving ovarian cancer treatment (40.74%). Of the 43 patients, 17 patients received chemotherapy, and 10 patients received a combination of surgical therapy and chemotherapy. Most of the deaths were caused by primary disease (69.77%). Patients with stages III and IV, as well as patients receiving surgery or chemotherapy alone had shorter survival times.
CONCLUSION: Most ovarian cancer patients are first diagnosed at stage III with the mucinous carcinoma subtype. Most deaths are caused by primary ovarian cancer. The therapy that provides the longest survival is a combination of surgery and chemotherapy.

1. Introduction

Ovarian cancer is the eighth most commonly occurring cancer, and the seventh leading cause of cancer-related death in women [1], with a morbidity rate of 6.1 per 100,000 women and a mortality rate of 4.3 per 100,000 [2]. An estimated 21,750 additional new ovarian cancer cases and 13,940 deaths are reported to occur in the U.S. each year [3]. In Indonesia, ovarian cancer is the third leading cause of cancer-related death in women [4]. This study reported cases of Indonesian women who died from ovarian cancer.

2. Method

This case series has been subject to physical approval based on the Declaration of Helsinki. It was reported that 43 Indonesian women died from ovarian cancer in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, in 2014–2017 which we used retrospective design. Patients were diagnosed using FIGO's Staging Classification [5] and the procedure for ovarian cancer therapy included surgery and chemotherapy based on the stage of ovarian cancer [6]. Participants were recorded regarding the prognosis of ovarian cancer. This case series is reported in line with the PROCESS guideline [7].

3. Results

Patients who died were in the age range of 20–62 years, with most patients being in the age range of 40–59 years (65.11%). Most patients had a good nutritional status with a BMI of 18.5–25 (62.79%). Most patients came from East Java, Indonesia (62.79%).

The result showing that most patients had stage-III ovarian cancer (39.53%) with a mean post-diagnosis survival age of 16 months (Fig. 1). Hispatology results showed that most patients had mucinous carcinoma (25.58%) and serous carsinoma (23.26%) (Fig. 2). There were 17 patients who experienced metastases that mostly occurred in the liver (47.06%). Detailed data on Indonesian woman with ovarian cancer could be seen in Table 1.

A total of 27 patients (62.79%) were referral patients from several hospitals, of which 40.74% of patients died before receiving therapy. The shedding mass could be seen in Fig. 3. A total of 33.33% referral patients underwent surgery, of which 18.52% were re-operated and died, while the rest underwent reoperation and chemotherapy. Most patients were identified died of ovarian cancer as many as 30 patients (69.77%), postoperative infections as many

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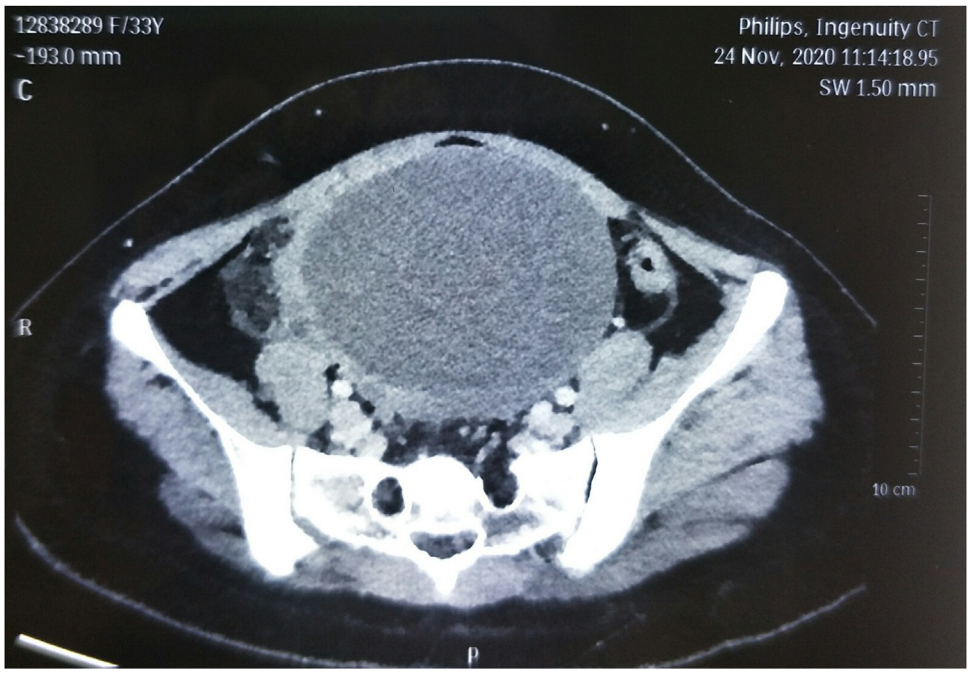

Fig. 1. CT-Scan of Patient with Ovarian Adenocarcinoma.

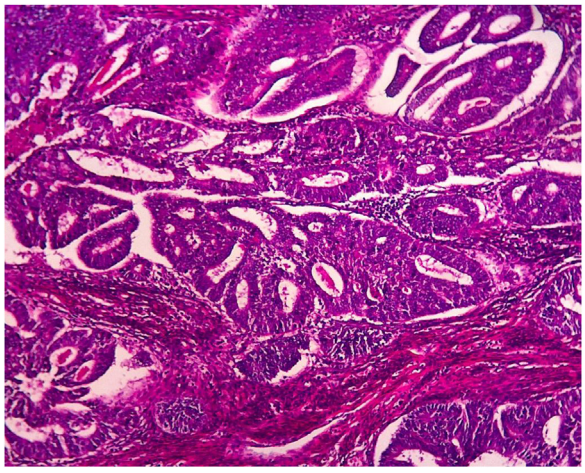

Fig. 2. Hispatology Results of Patient's Ovarian Carcinoma Tissue.

as 9 patients (20.93%), complications of chemotherapy as many as 2 patients (4.65%) and others.

4. Discussion

The average age of women diagnosed with ovarian cancer is 50–59 years, of which the number has increased at >65 years [8]. Recent studies have shown that ovarian cancer diagnoses have increased in women aged <50 years [9]. Age is a risk factor for ovarian cancer and usually occurs near or after menopause, with the average age at diagnosis approaching 60 years [8,10]. Some literatures stated that obesity significantly correlates with ovarian cancer, in which adults who have a BMI $\geq$ 30 have a higher risk of developing ovarian cancer [11,12].

It is estimated that 70–80% of new ovarian cancers are discovered after they have spread widely or have metastasized further so that the treatment results are not as expected. A study conducted by Torre LA et al. in America found that of all ovarian cancers, the largest incidence was found in stages III and IV. In epithelial ovarian cancer, only serous types are most commonly found in stages III and IV. This suggests the aggressiveness of high-grade serous carcinoma. The types of endometrioid, mucinous, clear cell carcinoma and nonepithelial ovarian cancer are generally diagnosed at stage I. The implication is that the 5-year survival rate in serous carcinoma is only 43%, compared to 82%, 71%, and 66% in endometrioid, mucinus, and clear carcinomas cell [13].

Epithelial ovarian cancer was most prevalent in this case report, with the most subtypes being serous carcinoma and mucinous carcinoma. The majority of ovarian cancers originate from epithelial cells (95%). Serous carcinoma is the most common subtype of epithelial ovarian cancer that usually occurs in women of older age [8]. In 2010–2014, while epithelial cancer was found mostly in all races and ethnicities (Hispanic, Asia/Pacific Islander, American Indian/Alaskan, non-Hispanic blacks and whites) in the United States, the disease was mostly found in non-racial white Hispanic [13].

In general, mucinous carcinoma is often found at an early stage and is still in a low-grade condition. As much as 83% of mucinous carcinomas were found to be stage I when first diagnosed, whereas Shimada et al. found 70% invasive mucinous carcinomas at stage I and II. The effect of histology on patient's survival depends on the stage suffered by the patient. In patients with stage I, the survival of patients with serous and mucinous carcinoma does not differ much. However, in patients with stage III, histological subtypes have a strong influence on patient survival. As much as 55% of patients with mucinous carcinoma died from the malignancy of the disease compared to patients with serous carcinoma. In stage-IV patients, the 5-year survival rate for serous carcinoma was almost double that of mucinous carcinoma (20.3% vs 10.2%) [14]. The disease severity is one of the factors that determines the patient's survival. Clinical stage is an important factor that can influence the prognosis of disease [15]. Ovarian cancer is a gynecological cancer which has the lowest 5-year survival rate (46%) compared to other gynecological cancers [16].

The cause of death of a disease can be traced ideally through an autopsy examination. However, autopsy is still not common in

Table 1
Detailed Data of Indonesian Women who died of Ovarian Cancer.

No	Age (years)	BMI	Stage	Patologi anatomy	Metastasis	Treatment		Cause of death	Note
						Chemotherapy	operative		
1	56	18.2	IIIC	clear cell carcinoma	–	√	√	Bleeding	–
2	38	14.8	IIIB	Serous carcinoma high grade. The tumor grows to the edge of the preparation	–	√	√	Primary disease	–
3	53	22.8	IIIC	Adenocarcinoma	–	–	√	Bleeding	–
4	48	25.2	IIIC	Serous carcinoma low grade. implantation into the peritoneum	Colon	–	√	Bleeding	–
5	47	24,5	IVB	papillary serous Adenocarcinoma grade 3	colon sigmoid	√	–	Comorbidities	–
6	46	20.1	IIIC	mucinous carcinoma	–	√	√	Intestinal bleeding and dilation	–
7	60	16.7	IIIB	Adenocarcinoma	Infiltration abdomen	–	√	Reoperation	–
8	39	20.2	IIIC	mucinous carcinoma ovarian grade 1	Liver and lung	–	√	Comorbidities	–
9	49	22.1	IIIC	undifferentiated carcinoma, the tumor grows to the edge of the operation	Liver	√	√	Primary disease	–
10	26	17.3	IVB	mucinous cyst adenocarcinoma ovarian grade 2	Bone and liver	√	–	Primary disease	–
11	36	17.7	IVA	Adenocarcinoma	Liver	–	√	Primary disease	–
12	36	22.7	IIIC	papillary mucinous moderate carcinoma	abdominal wall infiltration	–	√	Reoperation	–
13	20	19.8		mucinous cyst adenocarcinoma	–	–	√	Primary disease	–
14	50	15.73	IIIC	Serous carcinoma ovarian high grade	–	√	√	Reoperation	–
15	62	23.5		Adenocarcinoma ovarian well differentiated	–	√	–	Primary disease	–
16	40	32.8		Adult granulose cell tumor	–	√	–	Primary disease	–
17	52	19.47	IV A	Endometrioid adenocarcinoma ovarian grade 3	Colon sigmoid	√	–	Hypovolemic shock	–
18	45	23.4	IV B	Adenocarcinoma	liver	√	–	Comorbidities	–
19	43	24.6	IA	Squamous cell carcinoma arising in cyst adenocarcinoma	rectum	–	√	Primary disease	–
20	56	24.1		Serous cyst adenocarcinoma ovarian	–	–	–	Primary disease	Refusing therapy
21	34	22.6	IIIC	Papillary serous adenocarcinoma high grade	–	–	√	Primary disease	–
22	57	26	IC	Serous cyst adenocarcinoma ovarian	liver	–	–	Cardiogenic shock	Surgical optimiza-tion plan
23	44	21.6	IC	Endometrioid adenocarcinoma ovarian grade 2	–	–	–	Bleeding and ascites	Irregular medical consultation
24	43	21	IC	Cystic ovarian papilliferum carcinomatosis	lung	√	√	Comorbidities	–
25	60	16.8		Granuloma cell tumor	liver	–	–	Comorbidities	–
26	23	20.5	IV	Mucinous cyst adenocarcinoma carcinoma ovarian	liver	–	–	Primary disease	–
27	56	17.5	IIIC	Endometrioid carcinoma grade 3	–	√	√	Post-operative infection	–
28	41	35.5		papillary mucinous cyst adenocarcinoma well differentiated	–	√	–	Primary disease	–

Table 1 (*Continued*)

No	Age (years)	BMI	Stage	Patologi anatomy	Metastasis	Treatment		Cause of death	Note
						Chemotherapy	operative		
29	53	18.2	IIIC	Mucinous carcinoma	–	√	√	Primary disease	–
30	34	23.4	IIA	Adenocarcinoma	–	–	√	Wound dehiscence	–
31	55	19.6	IVB	Endometrial Carcinoma Ovarian	liver	√	–	Primary disease	–
32	55	20.2	IIIC	papillary mucinous cyst carcinoma	lung	–	–	Primary disease	Chemotherapy plan
33	58	23.7	IIIC	Endometrial Carcinoma Ovarian	liver	√	√	Comorbidities	–
34	51	17.1	IIIC	Mucinous cyst adenocarcinoma ovarian	–	–	–	Chemotherapy complications	Irregular chemotherapy
35	41	20.1	IIIC	Endometrioid adenocarcinoma grade 3 ovarian bilateral	–	√	√	Chemotherapy complications	
36	30	19.2		Malignant teratoma grade 3	–	–	√	Sepsis	
37	41	26.5		Serous adenocarcinoma ovarian	–	–	–	Primary disease	Without therapy
38	44	16.4	IIA	Undifferentiated carcinoma ovarian, discharge from the capsule and tubal infiltration	–	–	–	Primary disease	Without therapy
39	24	24.1		Choriocarcinoma	–	–	–	Primary disease	Without therapy
40	30	18.5		Mucinous cyst adenoma ovarian	–	–	–	Primary disease	Without therapy
41	57	23.9	IA	mucinous cyst adenocarcinoma	–	–	√	Primary disease	–
42	54	24.3		invasive serous carcinoma high grade	liver	–	–	Primary disease	Chemotherapy plan
43	41	19.4		serous papillary adenocarcinoma ovarian high grade	–	√	–	Primary disease	–

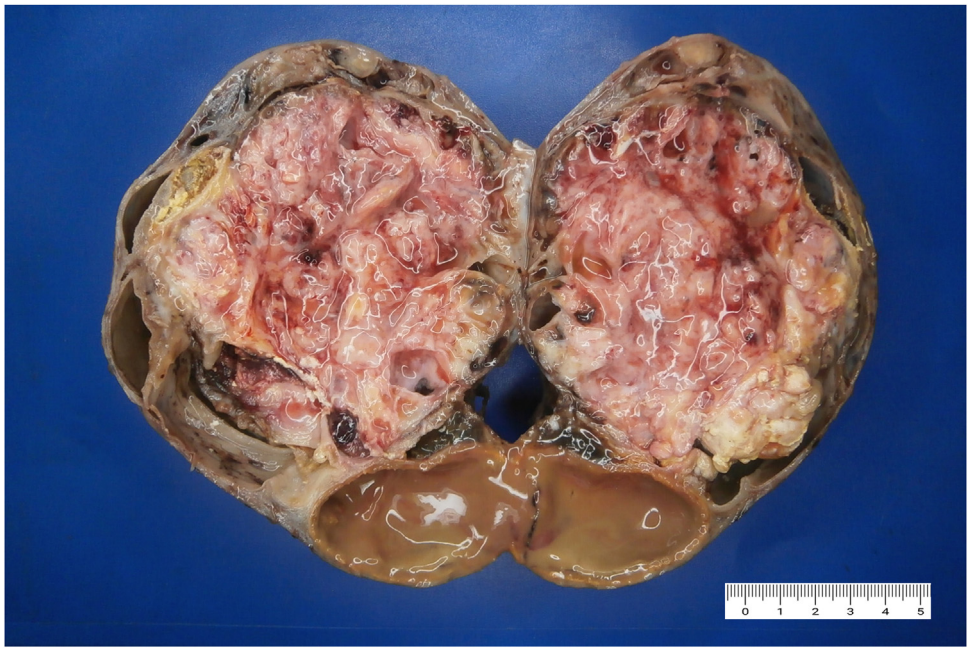

Fig. 3. The 3-kg Mass of Postoperative Carcinoma.

Indonesia since most people believe that disease is the destiny of God and those who died should be buried immediately. Based on the most recent literature, most ovarian cancer patients died of carcinomatosis. Aggressive cancer growth causes spread to the pelvis and abdomen, so that the patient experiences intestinal obstruction and failure of the surrounding organs, which ultimately results in the patient's death [17,18].

Management of ovarian cancer is ideally with primary cytoreduction surgery followed by administration of neoajuvan platinum chemotherapy. Primary cytoreduction surgery aims to obtain optimum cytoreduction results (residual mass <1 cm), which later becomes an important prognostic factor for determining the survival of epithelial ovarian cancer. As an alternative therapy in patients with advanced epithelial ovarian cancer, neoajuvan platinum chemotherapy can be given before surgery in order to reduce the tumor mass. Guidelines issued by the Society of Gynecologic Oncology (SGO) and the American Society for Clinical Oncology (ASCO) recommend administering neoajuvan platinum chemotherapy in patients with high perioperative risk and in patients who are less likely to undergo optimum cytoreduction surgery [19].

Patients with advanced epithelial ovarian cancer who have comorbid diseases or conditions that are less ideal for surgery, are at risk for postoperative complications so that they cannot tolerate postoperative chemotherapy. These patients consequently will only undergo surgery, so that it can reduce the patient's survival. As an alternative, neoajuvan chemotherapy may be given before surgery. After the patient received adjuvant chemotherapy, if the patient cannot tolerate primary cytoreduction surgery, at least the patient has received chemotherapy that provides better survival when compared to the patient who only received surgical therapy [20].

Increased survival rate can be achieved after receiving optimum ovarian cancer therapy, namely by a combination of chemotherapy and primary cytoreduction surgery. Unfortunately, this method is still difficult to implement in Indonesia because there are still limited health facilities capable of providing chemotherapy and surgical services performed by gynecological oncology doctors. Some private health facilities are able to provide chemotherapy but at a lot of cost.

5. Conclusion

Ovarian cancer patients are generally diagnosed at stage III and IV (55.7%), so that the success of treatment is very low. Most patients died of ovarian cancer had the subtypes of mucinous carcinoma (25.5%) and serous carcinoma (23.2%). The main cause of death in ovarian cancer patients is due to the primary ovarian cancer itself. Patients only receive chemotherapy or surgery, or a combination of surgery and chemotherapy. Patients with stage-III and IV ovarian cancer or who receive surgery or chemotherapy have lower survival rates. Early detection of ovarian cancer can increase the patient's survival rate so that the disease can be treated early by providing combination of chemotherapy and primary cytoreduction surgery.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Ethical approval

We have conducted an ethical approval base on Declaration of Helsinki at Ethical Committee in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Consent

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Author's contribution

All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Registration of research studies

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Guarantor

Pungky Mulawardhana is the person in charge for the publication of our manuscript.

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CRediT authorship contribution statement

Pungky Mulawardhana: Conceptualization, Formal analysis, Project administration, Writing - original draft, Writing - review & editing. **Poedjo Hartono:** Methodology, Resources. **Hari Nugroho:** Visualization, Investigation. **Atika Ayuningtyas:** Data curation, Supervision.

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