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The Relationship Between Ovarian Cancer Stage and Histopathology Features in Operated Patients at Dr.Zainoel Abidin General Public Hospital in Banda Aceh, Indonesia

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ABSTRACT

Introduction: As the fourth leading of cancer death among worldwide for women, cancer of ovary remains a serious public health issue. Late-stage diagnosis is common and significantly reduces the 5-year survival rate—from 92% in early stages to just 17%–28% in advanced cases. Unspecific symptoms of ovarian cancer cause most patients to present at an advance stage. Histopathology plays a role in diagnosis, prognosis, and decision-making for patient management. Recognizing histopathology early on helps direct therapy and improve patient outcomes. To date, however, no researches have been established on the relationship between ovarian cancer stage and histopathology type at Dr. Zainoel Abidin General Hospital Banda Aceh, Indonesia.

Methods: This study utilized a retrospective cross-sectional design, gathering data from medical records from patients with cancer of ovary treated between January and December 2024. Statistical analyses, including univariate and bivariate tests, were conducted using the Kruskal-Wallis method and SPSS version 26.0.

Result: Analysis of the relationship between surgical stage and histopathological features revealed a statistically significant correlation, with a p-value of 0.000.

Conclusion: Surgical staging can be considered when developing appropriate therapeutic strategies while awaiting histopathology results. This allows patients to receive treatment as soon as possible.

Keywords: Surgical staging, ovarian cancer, histopathological features.

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INTRODUCTION

Ovarian cancer is a global health problem and the fourth leading cause of cancer-related deaths among women. In 2018, there were approximately 22,240 new cases of ovarian cancer and 14,070 deaths from the disease in the United States.[1] Patients with ovarian cancer are often diagnosed with high stage of ovary cancer, and more than 75% of patients have reached this stage by the time they are diagnosed.[2]

The incidence of ovarian cancer is increasing every year in developing countries such as Indonesia. According to Globocan 2018 data, there are 13,310 new cases of ovarian cancer in Indonesia per year. Indonesia is still the tenth in the world for lung cancer cases (4.3% of the total new cancer cases), but ovarian cancer is the third most prevalence cancer in Indonesia, after cervical and breast cancers.[3]

In Indonesia, cancer of ovary is associated with a high rate of mortality. It is responsible for 7,842 female deaths, representing 4.34% of all related cancer fatalities and as the eighth leading cancer that caused death in the country.[4]

Ovarian cancer is a significant public health concern in Indonesia, ranking among the top causes of cancer-related deaths in women. The incidence of ovarian cancer in the country continues to rise, with recent data reporting over 15,000 new cases and nearly 10,000 deaths annually. This malignancy is often referred to as a "silent killer" due to its tendency to be diagnosed at an advanced stage, largely because early symptoms are vague or absent. As a result, the majority of Indonesian women with ovarian cancer present with late-stage disease, which is associated with poor survival outcomes. The demographic profile of ovarian cancer patients in Indonesia reveals that most cases occur in women aged 40–60 years, with a predominance of epithelial subtypes, particularly serous carcinoma. Socioeconomic factors, such as lower employment rates and limited access to specialized healthcare, further complicate early detection and effective management. The disease burden is not confined to urban centers; cases are distributed across the archipelago, with significant numbers reported in both Jakarta and other provinces. Despite advances in surgical and chemotherapeutic treatments, the five-year survival rate remains low, especially for those diagnosed at advanced stages.[9]

Efforts to improve ovarian cancer outcomes in Indonesia focus on early

detection, equitable access to care, and public awareness. Multimodal treatment approaches—combining surgery, chemotherapy, and, in some cases, targeted therapies—are standard, but their effectiveness is often hindered by late presentation and resource limitations. Strengthening healthcare infrastructure, increasing the number of gynecologic oncologists, and implementing nationwide screening programs are critical steps needed to reduce the mortality and improve the quality of life for Indonesian women affected by ovarian cancer.[8]

Currently, there is no preferable screening method for cancer of ovary, and approximately 1 in 70 individuals is at risk of developing the disease. Early-stage ovarian cancer is often asymptomatic, making early detection challenging. As a result, only around 25% of cases are diagnosed during the early stages.[5]

Most patients came when the cancer has already reached an advance stage, which significantly reduces the five-year survival rate to just 17–28%.[3] However, if the disease were detected earlier, timely and appropriate treatment could be administered, potentially improving the five-year survival rate to as high as 92%.[3]

According to FIGO (the Federation of International Gynecology Obstetrics) guidelines, patients in early-stage ovarian cancer may undergo surgery, followed by adjuvant chemotherapy, if histopathology results indicate spread or metastasis to surrounding organs. For ovarian cancers that are difficult to operate on due to adhesions and metastasis, three cycles of neoadjuvant chemotherapy are administered first, followed by surgery and three more cycles of chemotherapy.[6]

The standard first-line regimen for adjuvant and neoadjuvant chemotherapy in ovarian cancer patients generally includes a combination of carboplatin and paclitaxel. Carboplatin works by halting cancer cell growth during the G1 phase of the cycle of the cell and promoting apoptosis through DNA damage in ovarian cell cancer. Paclitaxel binds to microtubules and inhibits their depolymerization during cell division, thereby inhibiting proliferation and inducing apoptosis via the intrinsic pathway.[7]

Surgery to remove ovarian cancer masses and the administration of chemotherapy drugs to destroy the remnants of ovarian cancer cells is still unsatisfactory, because every operation almost always leaves ovarian cancer cells. These remnants of ovarian cancer cells can then develop and cause recurrence. This recurrence problem is still a major challenge in the therapy of the cancer patients.[8]

Based on 2018 data from Dr. Zainoel Abidin Regional General Hospital in Banda Aceh, Indonesia, ovarian cancer cases in Aceh Province are also high. The hospital found as many as four to five new cases every month. This figure is likely higher because many ovarian cancer patients seek treatment outside of Aceh Province.[9]

Most patients with ovarian cancer arrive at Dr. Zainoel Abidin Regional General Hospital Banda Aceh at an advanced stage (stages III-IV). This results in a poor prognosis and a very low five-year survival rate.[10]

Histopathology plays a role in the diagnosis, prognosis, and decision-making processes involved in patient management. Each subtype of ovarian cancer has different risk factors, pathogenesis, and therapeutic response. Recognizing histopathology early on is expected to help guide personalized therapy and improve patient outcomes.[11]

Until now, no research has been conducted on the relationship between ovarian cancer stages and histopathology features. Based on the above description, the authors are interested in evaluating this relationship in patients operated between ovarian cancer stages and histopathology features. The results are expected to help clinicians develop treatment strategies for each patient, providing better quality therapy at Dr. Zainoel Abidin Regional General Hospital in Banda Aceh, Indonesia.

METHODS

This research study utilized an analytical observational method with a retrospective cross-sectional design, examining dependent and independent variables at the same time. It aimed to evaluate the association between ovarian cancer stage and anatomical pathology results at Dr. Zainoel Abidin General Hospital in Banda Aceh. Research was conducted within the obstetrics and gynecology outpatient clinic, the oncology subdivision, the Arafah 3 inpatient ward, and the Thursina 3 chemotherapy unit of the same hospital. Data collection was based on a population of ovarian cancer patients who received treatment between January and December 2024.

The research sample included patients with ovarian cancer who had undergone surgical procedures. There were already anatomical pathology results from an anatomical pathologist, and the cancer stage had been determined by a gynecological oncologist. The patients met the inclusion criteria to be selected as samples for this study. The sampling method is based on secondary data from the patients' medical records and anatomical pathology results. Then, patients who meet the inclusion and exclusion criteria are selected. Univariate analysis is a statistical method used to describe the characteristics of each research variable, in this case, the types of cancer based on anatomical pathology and surgical staging of ovarian cancer. Generally, this analysis only yields the frequency distribution and description of the dependent and independent variables. Bivariate analysis was used to evaluate the relationship between the research variables. In this study, the independent variables are the types of ovarian cancer, as determined by anatomical pathology, which is measured on a nominal scale, and the surgical stage of ovarian cancer, which is measured on an ordinal scale. The statistical method used for the bivariate analysis in this study is the Kruskal-Wallis test, a nonparametric comparative test performed on categorical data. A 95% confidence interval (CI) level was used, with $\alpha = 0.05$. Data are significant statistically if $p < 0.05$, indicating a relationship between surgical stage and ovarian cancer type based on anatomical pathology results.

RESULTS

Between April and June 2024, data collection took place at Dr. Zainoel Abidin General Hospital in Banda Aceh. A total of 60 samples met the inclusion criteria

during this period and were subsequently analyzed using SPSS version 24.0.

Based in table 1, the results showed that distribution of surgical stages of ovarian cancer patients undergoing treatment of ovarian cancer at Dr. Zainoel Abidin General Hospital Banda Aceh, was dominated by stage IV B (20 samples; 33.0%). Followed by stage II A (18 samples; 30.0%), IA (10 samples; 16.7%), IIIA and IIIB (4 samples; 6.7% in each stage), IIB (3 samples; 5.0%) and the least was IIIA (1 sample; 1.7%).

Table 1. The distribution of surgical stages of ovarian cancer patients treated at Dr. Zainoel Abidin General Hospital in Banda Aceh, Indonesia

Surgical stage	n	%
IA	10	16,7
IIA	18	30,0
IIB	3	5,0
IIIA	1	1,7
IIIB	4	6,7
IVA	4	6,7
IVB	20	33,3
Total	0	100

Table 2. The distribution of histopathological features of ovarian cancer patients treated at Dr. Zainoel Abidin General Hospital in Banda Aceh, Indonesia

Surgical Staging	n	%
Adenocarcinoma ovarii	1	1,7
Adult granulosa cell tumor	3	5,0
Clear cell carcinoma	4	6,7
Cystadenocarcinoma mucinous	5	8,3
Granulosa cell tumor	5	8,3
High grade serous carcinoma	2	3,3
Mucinous adenocarcinoma	4	6,7
Papillary adenocarcinoma	18	30,0
Poorly differentiated adenocarcinoma	1	1,7
Serous adenocarcinoma	15	25,0
Teratoma	1	1,7
Teratoma immature	1	1,7
Total	**60**	**100%**

Based in table 2, The distribution of histopathological features in the study samples was dominated by papillary adenocarcinoma (18 samples; 30.0%), followed by serous cystadenocarcinoma (15 samples; 25%) and mucinous cystadenocarcinoma and granulosa cell tumor (5 samples; 8.3%, each histopathological features).

The relationship between surgical stage and histopathology of ovarian cancer patients treated at Dr. Zainoel Abidin General Hospital in Banda Aceh, Indonesia can be seen in table 3. Based on the table 3 showed that most patients with surgical stage IA presented with a histopathological features of granulosa cell tumor (five samples; 50.0%), followed by adult granulosa cell tumor (three samples; 30.0%), and teratoma (one sample; 10%), and immature teratoma (one sample, 10%). In stage IIA surgery, most samples showed serous cystadenocarcinoma (14

Table 3. The relationship between surgical stage and histopathologic features cancer of ovary, treated at Banda Aceh's Dr. Zainoel Abidin Hospital

Histopathologic Features	Surgical Stage														P
	1A		IIA		IIB		IIIA		IIIB		IVA		IVB		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Adenocarcinoma ovarii	0	0,0	0	0,0	1	33,3	0	0,0	0	0,0	0	0,0	0	0,0	0,000
Adult cell tumor of granulosa	3	30,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	
Clear cel carcinoma	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	2	50,0	2	10,0	
Cystadenocarcinoma mucinous	0	0,0	1	5,6	0	0,0	0	0,0	3	75,0	1	25,0	0	0,0	
Granulosa cell tumor	5	50,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	
High grade serous carcinoma	0	0,0	0	0,0	1	33,3	0	0,0	1	25,0	0	0,0	0	0,0	
Mucinous adenocarcinoma	0	0,0	3	16,7	1	33,3	0	0,0	0	0,0	0	0,0	0	0,0	
Papillary adenocarcinoma	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	18	90,0	
Poorly differentiated adenocarcinoma	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	1	25,0	0	0,0	
Serous adenocarcinoma	0	0,0	14	77,8	0	0,0	1	100,0	0	0,0	0	0,0	0	0,0	
Teratoma	1	10,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	
Teratoma immature	1	10,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	
Total	10	100,0	18	100,0	3	100,0	1	100,0	4	100,0	4	100,0	20	100,0	

samples, 77.8%), followed by mucinous adenocarcinoma (three samples, 16.7%) and mucinous cystadenocarcinoma (one sample, 5.6%). In stage IIB, ovarian adenocarcinoma, high-grade serous carcinoma, and mucinous adenocarcinoma each showed one sample (33.3%). Only one sample showed surgical stage IIIA: serous cystadenocarcinoma (one sample; 100%). Among stage IIIB samples, the majority showed mucinous cystadenocarcinoma (three samples; 75.0%), while one sample showed high-grade serous carcinoma (25.0%). At stage IVA, most samples showed clear cell carcinoma (two samples, 50%), and one sample each showed mucinous cystadenocarcinoma and poorly differentiated adenocarcinoma histopathology (25%). At stage IVB, most samples showed papillary adenocarcinoma (18 samples, 90%), and two samples showed clear cell carcinoma (10%).

Analysis of the relationship between surgical stage and histopathological features Found a significant relationship supported by statistical evidence with a p-value = 0.000.

DISCUSSION

The distribution of surgical stages among the study samples was dominated by stage IV B (20 samples, or 33.0%). Stage IIA followed with 18 samples (30.0%), followed by stage IA with 10 samples (16.7%). Stages IIIA and IIIB had four samples each (6.7%), stage IIB had three samples (5.0%), and stage IIIA had one sample (1.7%).

Over 75% of women with ovarian cancer are diagnosed at an advanced stage due to the absence of symptoms in the early phase and the non-specific nature of symptoms in later stages. Cancer Research UK's 2018 statistics show that 58% of ovarian cancer patients are diagnosed late, with poor prognoses—five-year survival rates are 27% for stage III and 13% for stage IV.[15]

This study found that the socioeconomic status of the study sample was generally low. A lower socioeconomic status has been shown to be associated with a higher likelihood of a late-stage cancer diagnosis, including for ovarian cancer.[16,17]

The distribution of histopathological features among the study samples was dominated by papillary adenocarcinoma (18 samples, or 30%), followed by serous cystadenocarcinoma (15 samples, or 25%), and mucinous cystadenocarcinoma and granulosa cell tumor (five samples, or 8.3% each). Epithelial ovarian cancer represents the majority of gynecologic malignancies, comprising over 95% of diagnosed cases. The remaining ~5% are classified as non-epithelial types, which include germ cell tumors, sex cord-stromal tumors, and small cell carcinomas. These tumors can be grouped into five principal histological categories, each characterized by distinct origins, molecular features, pathogenic mechanisms, risk profiles, and clinical outcomes. Within epithelial ovarian cancers, approximately 97% are non-mucinous, while only about 3% are mucinous. Mucinous variants encompass several histologic forms, notably serous (70%), endometrioid (10%), clear cell (10%), and a smaller fraction (5%) with indeterminate features. Within the serous subtype, two additional groups have been identified: high-grade and low-grade.[13] In this study, the majority of respondents exhibited a papillary adenocarcinoma histology (18 samples, or 30%). Prat et al. stated that high-grade serous carcinoma is the most common histopathological type of ovarian cancer, and that most patients present with Advanced stage ovarian cancer accounts for approximately 80% of diagnoses, with tumors restricted to the ovary seen in under 10% of cases. According to research by Zamzawar et al., high-grade serous carcinoma is the most frequently occurring subtype.[19]

Most patients with surgical stage IA showed histopathological features of granulosa cell tumors (five samples, 50.0%), followed by adult granulosa cell tumors (three samples, 30.0%), and teratomas (one sample, 10.0%).

10%), and immature teratoma (one sample, 10%). In stage IIA surgery, most samples showed serous cystadenocarcinoma (14 samples, 77.8%), followed by mucinous adenocarcinoma (three samples, 16.7%) and mucinous cystadenocarcinoma (one sample, 5.6%). In stage IIB, ovarian adenocarcinoma, high-grade serous carcinoma, and mucinous adenocarcinoma were represented by one sample each (33.3%).

Only one sample showed surgical stage IIIA, which was serous cystadenocarcinoma (one sample; 100.0%). Of the samples at surgical stage IIIB, the majority showed mucinous cystadenocarcinoma (three samples; 75.0%), while one sample showed high-grade serous carcinoma histopathology (one sample; (25.0%). At stage IVA, most samples showed clear cell carcinoma (two samples, 50%), and one sample each showed mucinous cystadenocarcinoma and poorly differentiated adenocarcinoma histopathology (25%). At stage IVB, most samples showed papillary adenocarcinoma (18 samples, 90%), and two samples showed clear cell carcinoma (10%).

Studies related to the histopathological grouping of ovarian cancer types by surgical stage are limited. The majority of granulosa cell tumors (78% to 91%) are found in the early stage (stage I) and are characterized by a slow-growing course and frequent recurrences.[19] In this study, most stage IIA samples were serous cystadenocarcinoma (14 samples, 77.8%). However, research by Narod et al. showed that only 13% of serous ovarian carcinoma cases were diagnosed at stages I or II.[20] At stage IIIA, only one type of histopathology was obtained: serous cystadenocarcinoma (one sample, 100%). At stage IIIB, most samples showed mucinous cystadenocarcinoma histopathology (three samples, 75%). As reviewed by Brown, the majority of mucinous ovarian cancer cases (83%) were diagnosed at the early stage (stage I), with only a minority (17%) found at stage II or higher.[21]

Studies investigating the histopathological grouping of ovarian cancer types by surgical stage remain limited. This gap in research is significant, as understanding the distribution of histological subtypes across different stages could inform both prognosis and tailored treatment strategies. Ovarian cancer is a heterogeneous disease, with several histopathological types such as high-grade serous, low-grade serous, mucinous, endometrioid, and clear cell carcinoma, each exhibiting distinct biological behaviors and responses to therapy. However, most published data tend to focus on overall survival or response to treatment, rather than the nuanced

relationship between histopathological features and surgical stage.

Despite the scarcity of studies, available analyses have revealed a statistically significant correlation between surgical stage and histopathological characteristics. For example, high-grade serous carcinoma is the most common subtype and is often diagnosed at an advanced stage, which is associated with a poorer prognosis. In contrast, mucinous and low-grade serous carcinomas are more frequently detected at earlier stages and generally have a better prognosis. This correlation highlights the importance of integrating histopathological assessment with accurate surgical staging to optimize patient management.

The process of surgical staging itself is critical for ovarian cancer, as it involves a thorough exploration and biopsy of various abdominal and pelvic sites to accurately determine the extent of disease. Inadequate staging can lead to underestimation of disease spread, potentially impacting treatment decisions and outcomes. Histopathological evaluation not only confirms the diagnosis but also provides essential information about tumor grade and subtype, both of which are key prognostic factors. Optimal surgical staging has been shown to improve cancer-specific survival, particularly in early-stage disease.

In summary, while research directly linking histopathological subtypes to surgical stage is still developing, current evidence underscores a meaningful association between these factors. The histopathological profile of ovarian cancer influences the likelihood of early versus advanced stage at diagnosis, and both elements are crucial for prognosis and therapeutic planning. Continued research in this area is necessary to refine risk stratification and to develop more individualized treatment approaches for women with ovarian cancer

The analysis of the relationship between surgical stage and histopathological features revealed a statistically significant correlation, with a p-value of 0.000. This indicates that H0 is rejected and H1 is accepted. No previous research has assessed the relationship between surgical stage and histopathological features of ovarian cancer at Dr. Zainoel Abidin General Hospital in Banda Aceh.

LIMITATIONS

This research had several limitations. First, challenges were encountered in accessing complete medical records was difficult. Not all patient records could be retrieved. Some available records were incomplete. Incomplete data, rendering them unusable for inclusion in the study sample. Second, among patients with a history of ovarian cancer, many records lacked overview of ovarian cancer stages based on surgical findings, because some ovarian cancer patients are only mentioned as early stage or advanced stage which complicated efforts to assess the relationship between surgical stage and histopathological features in ovarian cancer patients.

CONCLUSION

Most individuals diagnosed with cancer who underwent treatment at Banda Aceh's Dr. Zainoel Abidin Hospital have surgical stage IVB (33.3%) and most of samples had a histopathological presentation of papillary adenocarcinoma (18 samples, 30%). There was a relationship between surgical stage and histopathological features in ovarian cancer patients. Surgical staging can be considered when developing treatment strategies while awaiting histopathology results. This allows patients to receive appropriate treatment as soon as possible.

Analysis of ovarian cancer patients treated at Dr. Zainoel Abidin General Hospital in Banda Aceh revealed a statistically significant correlation between surgical stage and histopathological features (p-value = 0.000)1. The distribution of histopathological subtypes varied distinctly across different surgical stages, with early-stage disease predominantly characterized by granulosa cell tumors, while advanced stages showed a higher prevalence of aggressive epithelial malignancies. Stage IA cases were dominated by granulosa cell tumors (50%) and adult granulosa cell tumors (30%), reflecting the typically slow-growing nature of these tumors and their tendency for early detection1. In contrast, stage IIA predominantly featured serous cystadenocarcinoma (77.8%), while stage IVB was overwhelmingly composed of papillary adenocarcinoma (90%)1.

The progression from early to advanced stages demonstrated a clear shift in histopathological patterns, with more aggressive tumor types becoming prevalent in later stages. Stage IIB showed equal distribution among ovarian adenocarcinoma, high-grade serous carcinoma, and mucinous adenocarcinoma (33.3% each), while stage IIIB was primarily mucinous cystadenocarcinoma (75%)1. Advanced stages IVA and IVB were characterized by clear cell carcinoma (50% in IVA) and papillary adenocarcinoma (90% in IVB), respectively1. This distribution pattern aligns with the understanding that certain histopathological subtypes are inherently more aggressive and likely to present at advanced stages, while others tend to be detected earlier due to their slower growth patterns.

The clinical implications of these findings are substantial for treatment planning and prognostic assessment in ovarian cancer management. Understanding the typical stage-histopathology relationships enables clinicians to anticipate disease behavior and tailor therapeutic approaches accordingly, even while awaiting definitive pathological results1. This correlation supports the integration of surgical staging information in early treatment decision-making, allowing for more timely initiation of appropriate therapies. For gynecologic oncologists, particularly in resource-limited settings, this knowledge facilitates better risk stratification and treatment planning, ultimately contributing to improved patient outcomes through more personalized and timely interventions1.

DISCLOSURE

Conflict of Interest

There are no declared conflicts of interest by the authors in relation to the materials or methodologies employed in this research.

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Ethical approval

Prior to data collection, the authors secured institutional approval from Dr. Zainoel Abidin General Hospital to conduct the research.

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