Comparing Optimal Debulking Surgery Outcomes between Anemic and Non-Anemic Ovarian Cancer Patients at Dr. Hasan Sadikin General Hospital Bandung in 2022 – 2023

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Abstract
Objective: Ovarian cancer remains one of the most lethal gynecological malignancies. Optimal debulking surgery is one of the treatment options of ovarian cancer. Anemia was commonly observed in ovarian cancer patients, yet its association with the outcome of optimal debulking surgery remains unclear. This study aims to evaluate the association between preoperative anemia and the outcome of optimal debulking surgery.
Methods: A case-control analytical observational study was conducted on 87 ovarian cancer patients who had undergone optimal debulking surgery at Dr. Hasan Sadikin General Hospital in 2022-2023. Data were collected from medical records and was analyzed using Chi-square test.
Results: The majority of ovarian cancer patients at Dr. Hasan Sadikin General Hospital in 2022–2023 presented with mild to moderate anemia, accounting for 37,78% and 33,33% of cases, respectively. Only 24,44% had normal hemoglobin levels, while 4,44% had severe anemia. Optimal debulking was achieved in 76,7% of cases. No significant association was found between preoperative anemia and optimal debulking outcomes (p = 0,601; OR 1,21, 95% CI: 0,68–2,16).
Conclusion: Preoperative anemia was not associated with optimal debulking surgery outcomes.

Keywords: ovarian cancer; anemia; optimal debulking surgery

Perbandingan Keberhasilan *Optimal Debulking Surgery* antara Pasien Kanker Ovarium dengan Anemia dan Non-Anemia di RSUP Dr. Hasan Sadikin Bandung Tahun 2022 – 2023

Abstrak
Tujuan : Kanker ovarium merupakan salah satu keganasan ginekologi dengan angka kematian tertinggi. *Optimal debulking surgery* merupakan salah satu terapi utama pada pasien kanker ovarium. Anemia sering ditemukan pada pasien kanker ovarium. Namun, hubungan anemia dan keberhasilan *optimal debulking surgery* belum jelas. Penelitian ini bertujuan untuk mengevaluasi hubungan anemia preoperatif dan keberhasilan *optimal debulking surgery* pada pasien kanker ovarium.
Metode : Metode penelitian yang digunakan adalah studi observasional analitik dengan desain *case control* yang melibatkan pasien kanker ovarium yang menjalani *optimal debulking surgery* di RSUP Dr. Hasan Sadikin Bandung periode 2022 – 2023. Data diperoleh dari rekam medis dengan total 87 pasien yang memenuhi kriteria inklusi. Analisis hubungan anemia preoperatif dengan keberhasilan *optimal debulking surgery* dilakukan dengan uji *Chi square*.
Hasil : Mayoritas pasien kanker ovarium di RSUP Dr. Hasan Sadikin tahun 2022 – 2023 mengalami anemia ringan (37,78%) dan sedang (33,3%). Hanya 24,4% pasien memiliki kadar hemoglobin normal dengan 4,44% pasien mengalami anemia berat. *Optimal debulking surgery* berhasil dicapai pada 76,6%. Tidak ditemukan hubungan bermakna antara anemia preoperatif dan keberhasilan *optimal debulking surgery* (p = 0,601; OR 1,21; 95% CI : 0,68-2,16)
Kesimpulan : Hasil penelitian menunjukkan anemia preoperatif tidak berhubungan dengan keberhasilan *optimal debulking surgery* pada pasien kanker ovarium.

Kata kunci : Anemia; kanker ovarium; *optimal debulking surgery*

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Introduction

Ovarian cancer is one of the most lethal gynecological malignancies, with globally increasing incidences each year. It is characterized by the abnormal growth of cells in the ovaries. Globally, ovarian cancer is the eighth most common cancer and the fifth leading cause of cancer-related death among women. According to GLOBOCAN 2020, there were 314,000 new cases and 207,252 deaths.[1–3]with a focus on geographic variability across 20 world regions. There will be an estimated 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer In Indonesia, ovarian cancer is the third most common malignancy among women, with 14,896 new cases and 9,581 deaths reported in 2020.[4,5] Despite improvements in management over the past 30 years, the mortality rate remains high, with a 5-year survival rate of only 59,6% as of 2019.[6]

Histopathologically, ovarian cancer is classified into epithelial and non-epithelial types, which include further subtypes such as mucinous and non-mucinous. Associated risk factors include menopause, hormonal therapy, a family history of ovarian or breast cancer, obesity, and smoking.[7] Various therapeutic strategies have been developed to improve patient survival, including chemotherapy, targeted therapy, and surgery. One critical surgical approach is debulking surgery with the aim of removing as much of the tumor burden as possible. Debulking procedures are categorized as the removal of the majority of visible tumor tissue, leaving minimal or no macroscopic residual disease that is commonly defined as residual nodules ≤1 cm or even ≤0,5 cm, depending on institutional criteria. In contrast, suboptimal debulking surgeries leave behind tumor masses > 1 cm, often due to inaccessible tumor locations, risks to vital organs, or poor patient conditions precluding extensive surgical intervention.[8]

Serum cancer antigen 125 (CA 125) is a widely used biomarker in the treatment of ovarian cancer. Elevated CA 125 levels are often associated with the presence of ovarian malignancy, although they may also rise in benign conditions such as endometriosis, pelvic inflammatory disease, and menstruation. Preoperative CA 125 levels are useful in assessing the response to neoadjuvant chemotherapy and predicting the likelihood of successful debulking surgery. Additionally, computed tomography (CT) scans play an essential role in evaluating tumor size, location, and spread, guiding surgical planning by identifying potential involvement of other organs and the need for complex surgical procedures.[9] The combination of CA 125 assessment and CT imaging serves as a critical decision-making tool in ovarian cancer management, informing the timing and extent of debulking surgery. Together, these modalities enhance clinicians' ability to devise individualized treatment plans, thereby improving surgical outcomes and overall patient prognosis.[9] Research by Muniao et al. has highlighted the superior diagnostic performance of multi-biomarker panels in early detection of ovarian cancer beyond CA125. By combining various serum markers such as CA125, HE4, EGFR, G-CSF, Eotaxin, IL-2R, cVCAM, and MIF, diagnostic sensitivity and specificity reached 98,2% and 98,7%, respectively. These findings support the use of multi-biomarker strategies for early-stage disease detection, enabling timely treatment and potentially improving patient outcomes.[10]

Anemia is also commonly observed in patients with epithelial ovarian cancer. In China, the reported prevalence of anemia among EOC patients is 13,4%, while a study in Italy reported rates exceeding 30% even before surgical intervention. The anemia may result from paraneoplastic syndromes that suppress red blood cell production or increase their destruction. Elevated levels

of inflammatory cytokine particularly interleukin-6 (IL-6) can impair erythropoiesis, contributing to the development of anemia.[11]

Other hematologic abnormalities, such as leukocytosis and thrombocytosis, have been associated with advanced disease and worse prognosis in ovarian cancer. These elevations often reflect a tumor-induced chronic inflammatory state and may serve as markers of tumor aggressiveness. Hematocrit (Hct) levels can also be altered in these populations. A reduced Hct suggests anemia, while elevated values may be due to dehydration or other factors, which although unrelated to cancer itself, may still impact perioperative management. Preoperative anemia can complicate surgical treatment in ovarian cancer.[12,13] Patients with anemia often have poorer physical conditions, which may limit the ability to tolerate extensive surgery. Anemia is also linked to higher risk of surgical complications, including infections, bleeding, and delayed wound healing, all of which can reduce the likelihood of achieving optimal cytoreduction.[14] Anemia was indicated by fewer red blood cells and thus less oxygen delivered to body tissues. During surgery, especially extensive debulking surgery, the body's demand for oxygen increases. Preexisting anemia especially in ovarian cancer patients may compromise organ function, making patient less resilient to the stress of surgery and more prone to complications.[15]as well as its influence on postoperative outcomes, in 576 patients undergoing elective cardiac surgery (52.3% with cardiopulmonary bypass

Despite these concerns, few studies have specifically evaluated the impact of preoperative anemia on the success of debulking surgery in ovarian cancer. Most existing research, such as the study by Manning-Geist et al, has focused more broadly on outcomes related to perioperative blood transfusions. In their cohort of 270 patients undergoing interval debulking after neoadjuvant chemotherapy, 136 (50,4%) received perioperative packed red blood cell transfusions. The study found no significant differences in postoperative complications including infections, wound healing issues, or venous thromboembolism/ pulmonary embolism between patients who received transfusions and those who did not. Similarly, neither preoperative anemia nor surgical complexity significantly affected progression-free survival (PFS) or overall survival (0S).[16]

Given the limited data specifically addressing the relationship between preoperative anemia and optimal cytoreductive outcomes, this study aims to examine whether anemia prior to surgery influences the likelihood of achieving optimal debulking in ovarian cancer patients treated at Dr. Hasan Sadikin General Hospital.

Methods

This study is a quantitative observational analytical study using a retrospective case-control approach to evaluate the association between preoperative anemia and the outcome of debulking surgery in ovarian cancer patients from 2022 to 2023 at Dr. Hasan Sadikin General Hospital, with prior approval from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital, ethical exemption number DP.04.03/D.XIV.6.5/166/2024. The population for this study included all patients diagnosed with ovarian cancer who had undergone debulking surgery within the specified period. Total sampling method was applied for this study. Case groups were defined as patients who had successfully undergone optimal debulking surgery, while control groups comprised patients not successfully undergoing optimal debulking surgery. Ovarian cancer patients who did not undergo debulking surgery, patients who underwent debulking surgery for non-ovarian cancer, and patients with incomplete medical

records were excluded from this study.

Data were collected from medical records of eligible patients. The variables observed included preoperative anemia status and the outcome of optimal debulking surgeries. Preoperative hemoglobin levels were obtained from laboratory records, with measurements performed within 1-30 days prior to surgery. Preoperative anemia was stratified based on established clinical guidelines. The primary outcomes of the debulking surgeries were categorized as either optimal or suboptimal. Optimal debulking surgery was defined as the absence of any macroscopic residual tumor or the presence of residual tumor measuring less than 0.5 cm following the surgery. Suboptimal debulking surgery was defined as the presence of residual tumor measuring 0,5 cm or greater. The assessment of residual tumor was performed intraoperatively by the operating surgeon.

Descriptive statistics were used to characterize the basic demographics and clinical features of the study populations. A Chi-square test was conducted to assess the relationship between anemia and the outcome of debulking surgery. A p-value < 0,05 was considered statistically significant. All data analysis was performed using SPSS version 26.

Result

A total of 87 patients met the inclusion criteria consisting of 66 patients undergoing optimal debulking surgery and 21 patients undergoing sub optimal debulking surgery. Patients in both groups had mean ages of 54,33 ± 7,23 and 54,25 ± 7,40 years, respectively. **Table 1** shows the characteristics of ovarian cancer patients included in this study along with their preoperative anemia status and the outcomes of optimal debulking surgery.

The majority of ovarian cancer patients at Hasan Sadikin General Hospital from 2022-2023 presented with mild to moderate anemia. Specifically, 37,78% of patients had mild anemia, 33,3% had moderate anemia, and 4,44% suffered from severe anemia. Optimal debulking surgery was successfully achieved in the majority of the patients (76,67%). These findings suggest that despite the presence of anemia, a substantial proportion of patients were still able to undergo surgery with a favorable outcome.

Table 2 shows no significant association between preoperative anemia status and the outcome of debulking surgery in ovarian cancer patients (p value = 0,601). Although variations in the percentage of optimal debulking surgery were observed across

Table 1 Characteristics of the Study

Variables	Frequency (n)	Percentage (%)
Anemia		
- Normal (11 gr/dl)	22	24.44
- Mild anemia (9-10 gr/dl)	34	37.78
- Moderate anemia (7-8 gr/dl)	30	33.33
- Severe anemia (<7 gr/dl)	4	4.44
Debulking Surgery		
- Optimal	69	76.67
- Suboptimal	21	23.33

Table 2 Association between Preoperative Anemia and Optimal Debulking Surgery

	Debulking Surgery				Total	*P-value	OR (95% CI)
	Optimal		Suboptimal				
	N	%	N	%			
Anemia							
Normal	19	27,5	3	14,2	22	0,601	1,215 (0,683-2,161)
Mild	24	34,8	10	47,6	34		
Moderate	23	33.3	7	33,3	30		
Severe	3	4,3	1	4,7	4		

*Chi-square test

different anemia groups, these differences were not statistically significant.

Discussion

The majority of ovarian cancer patients in this study presented with mild to moderate anemia. This high prevalence of anemia is likely caused by paraneoplastic effects of the ovarian cancer itself, which can disrupt red blood cell production and increase their destruction. Paraneoplastic effects involve tumors releasing substances that interfere with normal bodily functions. In ovarian cancer, proinflammatory IL-6 can impair erythropoiesis in the bone marrow and accelerate red blood cell destruction in circulation. A previous study by Maccio et al. supports this finding, demonstrating a correlation between elevated IL-6 levels and reduced hemoglobin in ovarian cancer patients, highlighting the role of inflammation in cancer-related anemia.[11]

Our study revealed no significant association between preoperative anemia status and the outcome of debulking surgery in ovarian cancer patients. This finding suggests that the success of debulking surgery is primarily determined by surgical skills and the ability to achieve complete tumor resection rather than systemic conditions like anemia. Optimal debulking is more likely to be achieved when performed by specially trained gynecologic oncologists compared to general surgeons. The surgeon's expertise, experience in managing complex cases, and ability to plan appropriate surgical strategies play a crucial role in determining the success of debulking surgery in ovarian cancer patients. Interestingly, our findings are in contrast with two studies. A prospective study by Fowler et al. (2018) reported that moderate and severe preoperative anemia significantly increased the risk of postoperative complications and death.[17] A meta-analysis study by Fowler et al. (2015) found that preoperative anemia was strongly associated with increased mortality, kidney injury, infection, and the need for blood transfusion.[18]there are no evidence syntheses describing the impact of preoperative anaemia on postoperative outcomes. Methods A systematic review and meta-analysis of observational studies exploring associations between preoperative anaemia and postoperative outcomes was performed. Studies investigating trauma, burns, transplant, paediatric and obstetric populations were excluded. The primary outcome was 30-day or in-hospital mortality. Secondary outcomes were acute kidney injury, stroke and myocardial infarction. Predefined analyses were performed for the cardiac and non-cardiac surgery subgroups. A post hoc analysis was undertaken to evaluate the relationship between anaemia and infection. Data are presented as odds ratios

(ORs While these studies focused on general surgical populations rather than debulking surgery specifically, both highlight the need for further analysis to clarify the impact of preoperative anemia in ovarian cancer cytoreduction.

During surgery, local factors such as tumor vascularity, adhesions, and peritoneal tumor distribution exert a greater influence on whether optimal or suboptimal debulking is achieved. In this context, anemia does not appear to compromise the surgical team's ability to achieve optimal tumor removal. Furthermore, cancer patients often develop physiological adaptation to chronic anemia. Their bodies gradually adjust to lower hemoglobin levels, allowing them to tolerate major surgeries without significant impairment of vital organ function. These adaptations include the increased production of 2,3-bisphosphoglycerate within red blood cells, which enhances oxygen release to tissue. The role of pharmacological agents, such as erythropoietin, in stimulating erythropoiesis may also mitigate the impact of anemia. Erythropoietin boosts red blood cell production in the bone marrow, thereby improving hemoglobin levels and blood oxygen-carrying capacity.[19]

Moreover, the availability of advanced technology and facilities at the hospital plays a significant role. Our hospital where this study was conducted is equipped with excellent technological resources and facilities, supporting the successful execution of optimal debulking surgeries even in patients with anemia. The combination of expert surgical skills, cutting-edge technology, and adequate medical facilities enables precise preoperative assessment, accurate surgical intervention, and effective postoperative management, thereby enhancing the likelihood of optimal surgical outcomes.

It is crucial to understand that while preoperative anemia did not significantly impact the outcome of debulking surgery in our study, it has a more pronounced effect on postoperative outcomes. Anemia can influence recovery, increase the risk of complications, and prolong recovery time. Studies by Foley et al. have demonstrated a significant association between preoperative anemia and an increased incidence of postoperative complications in ovarian cancer patients undergoing surgery. Specifically, anemic patients showed increased odds of infectious complications (OR 1,16, 95% CI 1,07-1,26), suggesting that anemia may compromise the immune system, rendering the body more susceptible to infection during and after surgery due to suboptimal tissue oxygenation and impaired immune response. The risk of thromboembolic complications also rises with preoperative anemia (OR 1,39, 95% CI 1,15 – 1,68), possibly due to anemia-induced hypercoagulability. Furthermore, anemic patients have significantly higher odds of requiring blood transfusions intraoperatively or postoperatively (OR 5,78, 95% CI 5,34 – 6,26), which can introduce transfusions-related complications like reactions and blood-borne infections.[20]

In resource-limited settings, the findings of this study suggest that while correction of preoperative anemia remains important to reduce perioperative and postoperative morbidity, it should not delay cytoreductive surgery if patients are clinically stable. Surgical expertise and intraoperative strategies remain the primary determinants of achieving optimal debulking surgery. Therefore, health systems in low-resource settings may benefit more from investing in surgical training, multidisciplinary planning, and operative infrastructure.

Conclusion

Preoperative anemia was not associated with the outcomes of optimal debulking surgery. The success of optimal debulking surgery appears to be primarily influenced

by surgical expertise and the ability to achieve complete tumor resection rather than preoperative anemia status. Skilled gynecologic oncologists play a pivotal role in achieving optimal debulking. While not directly impacting surgical outcomes, preoperative anemia significantly affects postoperative morbidity, increasing the risk of complications, such as infection and thromboembolism, and prolonging recovery. Therefore, preoperative anemia treatments remain essential to improve overall surgical outcomes and patient recovery in ovarian cancer patients.

Limitation

This study has several limitations. Firstly, its retrospective design may introduce bias and limit our ability to account for all the influencing factors. Secondly, the relatively small sample size could affect the statistical power to detect subtle associations between anemia and surgical outcomes. Thirdly, this study only assessed intraoperative surgical outcomes (optimal vs suboptimal cytoreduction) without evaluating long-term endpoints such as progression-free survival, overall survival, or postoperative morbidity. Additionally, other potential confounding factors such as tumor stage, comorbidities, nutritional status, and intraoperative surgical complexity were not fully analyzed, which could also influence surgical outcomes. Finally, the study did not delve into the specific type or cause of anemia, which could provide further clinical insights. Future prospective studies with a larger sample size and comprehensive adjustment for confounding factors are needed to provide deeper understanding of the role of anemia in ovarian cancer surgery.

Declaration

Conflict of interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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