

Research Article

CA-125 Examination as a Predictor the Resectability of Advanced Stage of Ovarian Cancer

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Abstract

Objective: To determine serum CA-125 examination as predictor in predicting the resectability of advanced ovarian cancer at dr. M. Djamil Padang

Methods: The research sample was obtained using a consecutive sampling technique, wherein samples were collected one by one within the specified timeframe until the required sample size was achieved.

Results: The mean CA-125 level among respondents was 589.66 U/mL with a standard deviation of 841.55 U/mL. The study also revealed that a CA-125 cutoff value of 337.5 U/mL demonstrated high sensitivity (92.31%) and specificity (90.90%) in predicting the resectability of ovarian cancer.

Conclusion: Serum CA-125 examination shows a promising result in predicting the resectability of advanced ovarian cancer at dr. M. Djamil Padang

Keywords: CA-125, consecutive sampling technique, ovarian cancer.

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INTRODUCTION

For women everywhere, ovarian cancer is the number one gynecological cancer killer. Ovarian cancer is the fifth leading cause of death among women globally.¹ Globally, 204,000 women are diagnosed with ovarian cancer, and it causes 125,000 deaths each year.² In the United States, although ovarian cancer ranks as the eighth most common cancer in women, the number of deaths is far greater than the total number of deaths from gynecological cancer in that country. Every year in the United States, it is estimated that as many as 21,650 new cases are found, and 15,520 women die from ovarian cancer. The 2018 Indonesian Society of Gynecologic Oncology stated that ovarian cancer ranks third in Indonesia

after cervical cancer and corpus uterine cancer.³

The exact number of cases of ovarian cancer in Indonesia is still unknown, the incidence of ovarian cancer in Indonesia is predicted to be around 537 patients, with a patient mortality rate of 126 cases.⁴ At RSUP Dr. M. Djamil, ovarian cancer constitutes the most common malignancy in the Obstetrics and Gynecology department. Ovarian cancer is often asymptomatic, with only a few patients exhibiting specific symptoms. Consequently, about 70% of cases are diagnosed at an advanced stage, with a survival rate below 30%. Conversely, early detection at stage I significantly increases the chances of survival to 90%.⁵ However, patients typically present at stages II-IV, resulting in low treatment success rates. Given this context, the author aims to

investigate "the role of CA-125 as a predictor of the resectability of advanced-stage ovarian cancer at Dr. M. Djamil Padang."

METHODS

The is a cross-sectional study, specifically focusing on diagnostic tests. The results were presented in the form of sensitivity output and the area under the curve (AUC) output of CA-125 as a predictor of the resectability of ovarian cancer, utilizing CA-125 levels as a diagnostic test tool. Researchers utilized a consecutive sampling method, collecting samples one by one throughout the study period until an adequate sample size was achieved. Inclusion and exclusion criteria were applied to select the sample for this investigation.

RESULTS

The research aimed to assess the utility of CA-125 examination in predicting the resectability of advanced ovarian cancer at RSUP Dr. M. Djamil Padang. The study involved 35 patients and commenced in August 2021, continuing until the desired sample size was attained at the Obstetrics and Gynecology Department of Dr. M. Djamil Padang Central General Hospital. Among the 35 patients included in the study, the mean CA-125 level was found to be 589.66 U/ml, with a standard deviation of 841.55 U/ml. This result indicates a significantly elevated CA-125 level in advanced-stage ovarian cancer cases.

Table 1. Description of CA-125 Levels at Dr. M. Djamil Hospital Padang

Variable	Advanced ovarian cancer (n=35)
	Mean ± SD
CA-125 Levels	589.66 ± 841.55

The research also found that a CA-125 cutoff value of 337.5 U/mL was highly sensitive (92.31%) and specific (90.90%) for predicting whether or not ovarian cancer could be resected.

Table 2. Description of Mass Resectability of Advance Ovarian Cancer at Dr. M. Djamil Hospital Padang

Variable	Advanced ovarian cancer (n=35)
	f (%)
Resectable	13 (37.1)
Non Resectable	22 (62.9)

Interpretation: Most of advance ovarian cancer are non resectable mass about 22 people (62%).

The results of the analysis show several cut-off points for CA-125 levels. To explain the appropriate cut-off points for this study, researchers used the cut-off point graph in Figure 1 to determine sensitivity and specificity. The results showed that the cut point for CA-125 levels was ≤ 337.50 U/mL (resectable) and > 337.51 U/ml (not resectable) with a specificity of 90.9% and a specificity of 92.3%.

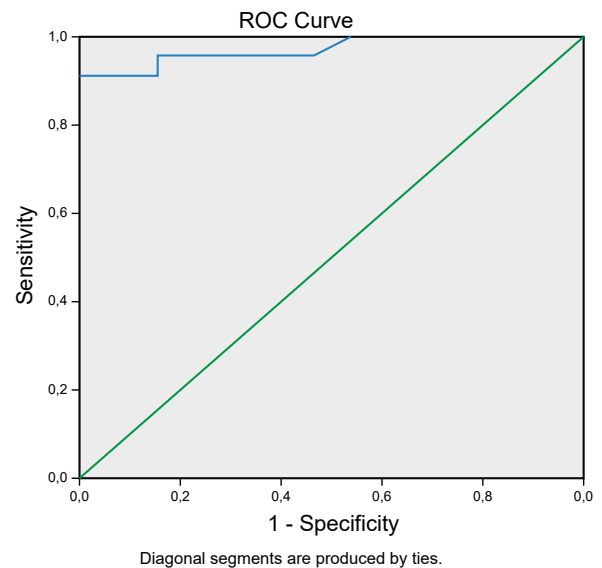


Figure 1. Receiver Operating Curve (ROC) for CA 125 and Resectability

Table 3. Sensitivity and Specificity Data of CA-125 cut-off point as Resectability Predictor of Advanced Ovarian Cancer

Variable	Resectability	
	(Resectable)	(Unresectable)
CA – 125 (≤ 337.5 U/mL)	12 (85.7)	2 (14.3)
(> 337.5 U/mL)	1 (4.8)	20 (95.2)
Total	13	22

From 35 patients, 12 patients had COP < 337.5 U/ml (resectable), 2 patients had COP < 337.5 U/ml (not resectable), 1 patient had COP > 337.5 U/ml (resectable), and 20 patients COP > 337.5 U/ml (not resectable). The results of the analysis showed that the sensitivity (92.31%), specificity (90.90%), positive predictive value (85.71%), negative predictive value (95.24%) were very good. All these values are considered good if ≥ 70%.

DISCUSSION

CA-125 Levels in Ovarian Cancer Patients

CA-125, a glycoprotein with a high molecular mass, is produced by both ovarian cancer cells

and normal cells in coelomic epithelial tissue. It serves as a crucial marker for monitoring tumor activity in patients with established ovarian cancer. CA-125 levels are routinely monitored to assess how well a patient is responding to therapy and to detect any signs of cancer recurrence after treatment. In approximately 90% of patients with epithelial ovarian cancer, changes in blood CA-125 levels are closely associated with disease remission and progression. Over the past two decades, CA-125 has been regarded as the gold standard tumor marker in medicine, playing a pivotal role in tracking treatment effectiveness and identifying potential cancer recurrence.⁶

Serum CA-125 levels before surgery may help rule out patients as candidates for primary cytoreduction and laparotomy. In order to identify patients who might benefit from decreased suboptimal cytoreduction, they employed a preoperative blood CA-125 level of 500 U/ml or above as a cutoff criterion.⁷ Based on the research results it is known that the mean CA-125 level of respondents is equal to 589.66 U/ml with a standard deviation of 841.55 U/ml. Patients who had resectability of a non-resectable tumor mass (>1 cm), which was 62.9%, were higher than those who had resectable tumors (<1 cm), which was 37.1%. In women with histologically confirmed ovarian cancer, serum CA-125 levels exceed 35 U/ml in over 80% of cases. CA-125 testing can detect 85% of clinically severe ovarian cancer cases. However, it's important to note that elevated CA-125 levels can also be observed in various other malignancies besides ovarian cancer, including lung, bladder, gastric, hepatic, and pancreatic cancers, as well as leukemia, non-Hodgkin's lymphoma, and mediastinal teratomas. The CA-125 mucin is considered the most reliable marker for epithelial ovarian cancer, with a normal range typically falling between 0-35 kU/L. However, in premenopausal women, normal CA-125 levels may reach up to 100 kU/L or higher, particularly during menstruation. Over the past two decades, CA-125 has consistently demonstrated its efficacy as the primary tumor marker for clinical applications in medicine.⁶

Sensitivity, Specificity, Positive and Negative Predictive Value, and Cut-Off Point Rate CA-125 as a Resectability Predictor of Ovarian Cancer

Malignancy prediction in ovarian tumor patients necessitates a comprehensive assessment

that incorporates not only the patient's medical history and physical examination but also the utilization of tumor markers, such as CA-125. Preoperatively, CA-125 is widely employed to evaluate the severity of epithelial ovarian cancers. In particular, serum CA-125 has shown the strongest association with a borderline diagnosis or malignancy among ovarian mucinous tumors. The diagnostic efficacy of serum CA-125 is thus maximized in these cases.⁸

Ovarian cancer is frequently diagnosed at an advanced stage because patients often do not experience symptoms until the disease has progressed significantly. Only about a quarter of ovarian cancer cases are detected early. In ovarian cancer management, CA-125 is utilized as a predictor of recurrence and assesses resectability. Approximately 80% of ovarian cancer patients will exhibit elevated CA-125 levels before any recurrence is evident on clinical examination or imaging studies.⁹ The CA-125 test may be used to analyze, monitor, and assess the response to treatment in ovarian cancer, despite the fact that it is not specific for the diagnosis of ovarian cancer itself. A decrease in CA-125 levels over time indicates that the treatment is effective. Moreover, CA-125 expression is typically much higher in serous type epithelial ovarian cancer compared to other forms of epithelial ovarian cancer.¹⁰

Some epidemiologists have established a minimum positive predictive value of 10% for early detection tests of ovarian cancer, requiring a sensitivity of at least 75% and a specificity of better than 99.6%. In the study, the Area Under the Curve (AUC) value was found to be 97%, with a p-value of 0.0001. This indicates that CA-125 can serve as a reliable predictor in forecasting the resectability of advanced ovarian cancer, as assessed by the Receiver Operating Characteristic (ROC) curve. The ROC curve evaluates the performance of tumor markers by correlating the sensitivity and specificity of the diagnostic test. The AUC obtained from this study's findings surpassed the AUC value reported in a study, which utilized ultrasonography to predict hip carcinoma with an AUC value of 89%. The CA-125 predictor exhibited a 78% positive predictive value and a 73% negative predictive value.¹¹

The research also identified a CA-125 cutoff value of 337.5 U/mL, which exhibited high sensitivity (92.31%) and specificity (90.90%) in predicting the resectability of ovarian cancer. These findings align with previous studies, which

demonstrated that preoperative IL-6 and CA-125 levels were associated with surgical outcomes (suboptimal and optimal cytoreduction), with a cutoff point of 418.5 U/mL, yielding a sensitivity value of 88.9% and a specificity value of 77.2%. Furthermore, another study revealed that a CA-125 cutoff value of 248.55 U/mL had a sensitivity of 73.2%, specificity of 73.6%, and accuracy of 73.3% ($p=0.0001$) in predicting cytoreduction for epithelial ovarian cancer. Additionally, a CA-125 cutoff of 100 U/mL was shown to have a sensitivity of 72% and a specificity of 73% for predicting inadequate cytoreduction surgery in stage III ovarian cancer patients.¹²

Determining a cutoff point for assessing a predictor involves establishing normal and abnormal limit values, also known as the threshold values for positive and negative test results. A test result is considered positive if it surpasses the threshold value, while it is deemed negative if it falls below this threshold. The findings of this investigation, with a sensitivity of 78% and a specificity of 73%, are consistent with previous reports suggesting that optimal cytoreduction success decreases beyond certain CA-125 levels.¹¹

CA-125 expression in ovarian cancer masses is attributed to its lubrication and hydration properties, which create a protective and anti-adhesive barrier, facilitating mass development. In a study by Mani et al. (2007), high CA-125 levels were observed in 90% of ovarian cancer cases, with an initial rise detected in 34% of cases and a median CA-125 level of 1,733 U/ml. Given its excellent sensitivity and specificity, CA-125 testing continues to be advocated for in the diagnosis of ovarian cancer.¹³

CONCLUSIONS

The CA-125 examination yielded highly promising results as a predictor for forecasting the resectability of advanced ovarian cancer at RSUP Dr. M. Djamil Padang, particularly with a Cutoff Point (COP) 337.5 U/mL for the resectability of advanced ovarian cancer at RSUP dr. M. Djamil Padang.

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