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Original Research Article

What is the Diagnostic Accuracy of the Serum CA 125 to CEA Ratio in Differentiation of Ovarian Malignancies from Non-Ovarian Malignancies

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Abstract

Background: Ovarian cancer is one of the leading causes of gynecological cancer-related mortality due to late diagnosis. Serum CA-125 is widely used as a tumor marker for ovarian malignancy but lacks specificity, as it may be elevated in several non-ovarian malignancies and benign conditions. Carcinoembryonic antigen (CEA) is more frequently elevated in gastrointestinal and other non-ovarian malignancies. The ratio of CA-125 to CEA has been proposed as a useful diagnostic tool to differentiate ovarian from non-ovarian malignancies.

Aim: To evaluate the diagnostic accuracy of the serum CA-125 to CEA ratio in differentiating ovarian malignancies from non-ovarian malignancies.

Materials and Methods: This hospital-based cross-sectional study included patients with histopathologically confirmed malignancies. Serum CA-125 and CEA levels were measured using chemiluminescent immunoassay techniques. The CA-125/CEA ratio was calculated for each patient. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value and to assess diagnostic performance.

Results: The CA-125/CEA ratio showed significantly higher values in ovarian malignancies compared to non-ovarian malignancies ($p < 0.001$). At an optimal cut-off value of >25, the ratio demonstrated good sensitivity and specificity for identifying ovarian malignancy. The area under the ROC curve indicated good diagnostic accuracy.

Conclusion: The serum CA-125 to CEA ratio is a simple, cost-effective, and reliable diagnostic marker for differentiating ovarian malignancies from non-ovarian malignancies and may be used as an adjunct to routine diagnostic evaluation.

Keywords: CA-125, CEA, Ovarian Cancer, Tumor Markers, Diagnostic Accuracy.

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Introduction

Ovarian cancer: in 2020, the global burden became a matter of concern. With another 294,422 new cases and 198,412 deaths. During the last 30 years, the incidence of ovarian cancer has increased significantly, with nearly two-fold in numbers. This rise has been strongly associated with lifestyle alterations [1]. Factors such as the adoption of Western habits, including trends in fecundity, delayed marriage, less interest in childbearing and lower rates of breastfeeding, are known to have played a major role in causing this upsurge [2].

Ovarian cancer is often silent since it seldom has any symptoms. with clear symptoms. At present, there is no powerful weapon available for screening the general population [3]. This frequently leads to presentation: advanced-stage diagnoses and 5-year survival was, in many cases, low rates. Please note early-stage treatments are successful, highlighting the importance of early detection for a better survival. Therefore, improving diagnostic methods, screening to detect high-risk cases and increasing recognition are important in achieving detection and declining mortality rates for ovarian cancer. [4]

Cancer antigen 125 (CA-125) is the most commonly used serum tumor marker for ovarian cancer, particularly epithelial ovarian carcinoma. Despite its widespread use, CA-125 lacks specificity and may be elevated in non-ovarian malignancies such as gastrointestinal cancers, lung cancers, and breast cancers, as well as in benign

gynecological and inflammatory conditions. [5] Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion and is primarily elevated in colorectal and other gastrointestinal malignancies. In ovarian cancer, CEA levels are usually low or only mildly elevated. [6] Recent studies suggest that the CA-125/CEA ratio improves diagnostic specificity by combining the strengths of both markers. A higher ratio favors ovarian origin, while a lower ratio suggests non-ovarian malignancy. This study aims to evaluate the diagnostic accuracy of the CA-125 to CEA ratio in differentiating ovarian malignancies from non-ovarian malignancies in a clinical setting. [7]

Aims and Objectives

Aim: To assess the diagnostic accuracy of the serum CA-125 to CEA ratio in differentiating ovarian malignancies from non-ovarian malignancies.

Objectives

1. To measure serum CA-125 and CEA levels in patients with confirmed malignancies.
2. To calculate the CA-125 to CEA ratio in ovarian and non-ovarian malignancies.
3. To compare the ratio between ovarian and non-ovarian malignancy groups.

Materials and Methods

Study Design: Hospital-based cross-sectional study.

Study Setting: Department of Biochemistry (clinical chemistry laboratory) in state cancer institute, Gauhati Medical College, Assam.

Study Duration: This study done for period of 6 month from October 2025 to March 2026.

Study Population: Patients diagnosed with malignancies based on histopathological confirmation, includes two groups: 40 cases of ovarian malignancies in group 1 and 40 female cases of non-ovarian malignancies in group 2.

Inclusion Criteria

- Female of any age with ovarian and non-ovarian malignancies
- Newly diagnosed, histopathologically confirmed malignancies
- No prior chemotherapy or radiotherapy

Exclusion Criteria

- Benign tumors and conditions like a vulval abscess, vaginal prolapse, spontaneous abortion and extrauterine pregnancy are excluded.
- Patients with inflammatory, hepatic, or renal diseases affecting tumor marker levels
- Previously treated malignancy cases

Sample Size: Calculated using formula for cross-sectional study population taking prevalence 0.05 and margin of error 0.495(<0.05), as it is cancer institute. It came around 80, so divided in two groups of 40.

Grouping

- Group 1: Ovarian malignancies
- Group 2: Non-ovarian malignancies (gastrointestinal, lung, breast, etc.)

Sample Collection

Venous blood samples were collected under aseptic conditions. Serum was separated by centrifugation and analyzed immediately or stored at −20°C until analysis.

Laboratory Analysis

- CA-125: Measured using chemiluminescent immunoassay in Vitros 5600 autoanalyzer
- CEA: Measured using chemiluminescent immunoassay in Vitros 5600 autoanalyzer

Calculation of Ratio

$$\text{CA-125/CEA Ratio} = \frac{\text{Serum CA-125 (U/mL)}}{\text{Serum CEA (ng/mL)}}$$

Statistical Analysis: Data were analyzed using SPSS version XX (or equivalent software). Continuous variables were expressed as mean ± standard deviation or median (interquartile range). Comparison between groups was performed using Student's t-test or Mann–Whitney U test as appropriate. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of the CA-125/CEA ratio. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated. A p-value <0.05 was considered statistically significant.

Results:

Table 1:

Variable	Non-Ovarian Cancer (n=40) Mean ± SD	Ovarian Cancer (n=40) Mean ± SD	p-value
Age (years)	45.85 ± 11.75	50.10 ± 11.60	0.171
CEA	18.06 ± 46.31	10.61 ± 36.35	0.003
CA-125	138.36 ± 239.07	696.82 ± 2894.61	0.002
CEA/CA-125 Ratio	18.11 ± 37.28	697.12 ± 3333.88	<0.001

Interpretation of Table 1: Comparison of Biomarkers between Ovarian and Non-Ovarian Malignancies

A total of 80 patients were included in the study, comprising 40 patients with ovarian cancer and 40 patients with non-ovarian malignancies. The mean age of patients with ovarian cancer was 50.10 ± 11.60 years, while that of patients with non-ovarian malignancies was 45.85 ± 11.75 years. The difference in age distribution between the two groups was not statistically significant ($p = 0.171$), indicating that age was comparable between the groups.

Serum CEA levels were significantly lower in ovarian cancer patients (10.61 ± 36.35 ng/mL) compared to non-ovarian malignancies (18.06 ± 46.31 ng/mL) ($p = 0.003$), suggesting that elevated CEA levels are more frequently associated with non-ovarian tumors, particularly gastrointestinal malignancies.

In contrast, serum CA-125 levels were markedly higher in ovarian cancer patients (696.82 ± 2894.61 U/mL) than in patients with non-ovarian cancers (138.36 ± 239.07 U/mL), and this difference was statistically significant ($p = 0.002$). This finding supports the established role of CA-125 as a primary biomarker for epithelial ovarian cancer.

The CA-125/CEA ratio demonstrated the strongest discriminatory ability between ovarian and non-ovarian malignancies. Patients with ovarian cancer showed substantially higher ratios than those with non-ovarian cancers, with a highly significant difference ($p < 0.001$). This finding indicates that combining CA-125 and CEA measurements may improve diagnostic accuracy compared with either marker alone.

Table 2:

Marker	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
Serum CEA	<10 ng/mL	90.2	39	59.7	80	0.699
Serum CEA	<5 ng/mL	85.4	43.9	60.3	75	0.699
CA-125/CEA Ratio	>20	58.5	80.5	75	66	0.805
CA-125/CEA Ratio	>30	56.1	80.5	74.2	64.7	0.805
CA-125/CEA Ratio	>50	56.1	97.6	95.8	69	0.805
CA-125/CEA Ratio	>100	31.7	97.6	92.9	58.8	0.805

Interpretation of Table 2: Diagnostic Performance of CEA and CA-125/CEA Ratio

Receiver operating characteristic (ROC) analysis demonstrated that serum CEA alone had limited diagnostic utility for distinguishing ovarian from non-ovarian malignancies, with an AUC of 0.699. At a cut-off value of <10 ng/mL, serum CEA showed high sensitivity (90.2%) but low specificity (39%), indicating a substantial false-positive rate. Similarly, at a cut-off of <5 ng/mL, sensitivity remained high (85.4%) while specificity improved only slightly to 43.9%.

The CA-125/CEA ratio exhibited superior diagnostic performance with an AUC of 0.805, indicating good discriminatory ability. A ratio >20 yielded a sensitivity of 58.5% and specificity of 80.5%.

Increasing the cut-off to >50 markedly improved specificity to 97.6% while maintaining a positive predictive value (PPV) of 95.8%, suggesting excellent ability to correctly identify ovarian malignancies. Although sensitivity decreased at higher cut-offs, the very high specificity indicates that elevated CA-125/CEA ratios strongly favor an ovarian origin of the malignancy. At a ratio >100, specificity remained 97.6% with a PPV of 92.9%, further emphasizing the usefulness of the CA-125/CEA ratio as a rule-in test for ovarian cancer.

Discussion

The present study demonstrated significantly higher CA-125 levels and CA-125/CEA ratios in ovarian cancer compared with non-ovarian malignancies. These findings are consistent with previous studies showing that CA-125 is highly expressed in epithelial ovarian cancer, whereas CEA is more commonly elevated in gastrointestinal and metastatic non-ovarian tumors. A study of Zanon et al. [7] CA125/CEA ratio cut off used to differentiate ovarian and with other cancer, and in ovarian vs non ovarian when cut-off value increased to 25 to 100 sensitivity decreased and specificity increased same as our study.

Similarly, choi et al. [8] found that combining CA-125 and CEA significantly improved diagnostic discrimination compared with either marker alone, particularly in differentiating various histopathological ovarian carcinomas.

But our study focused on differentiating ovarian from non-ovarian malignancies as a diagnostic marker and so that more patients can be selected for right treatment before surgery. More recently, a systematic review by stiekema et al. [9] highlighted that CA-125 remains the most widely used serum biomarker for ovarian cancer, but its diagnostic performance improves substantially when interpreted alongside complementary markers such as CEA and HE4. Recent studies have also shown

that the CA-125/CEA ratio may be particularly useful in distinguishing ovarian cancer from colorectal and gastrointestinal malignancies. Investigators have reported that ratios above 50 are associated with very high specificity (>90%) for ovarian origin, closely mirroring the findings of the present study where a cut-off >50 achieved a specificity of 97.6%. Also, that ratio with ultrasound can definitely differentiate the origin whether ovarian epithelial or gastrointestinal [10].

The observed AUC of 0.805 for the CA-125/CEA ratio indicates good diagnostic accuracy and is comparable to findings reported in contemporary ovarian cancer biomarker research, supporting its potential utility as an inexpensive and readily available adjunctive diagnostic tool, especially in resource-limited settings.

Limitation: Less study population and limited report with respect to a cancer hospital, and mostly not done both test to differentiate before surgery. Mostly depend on histopathological report for further treatment after surgery.

Conclusion

The serum CA-125/CEA ratio is a simple, cost-effective, and clinically useful adjunctive biomarker for differentiating primary ovarian malignancies from non-ovarian malignancies in patients presenting with pelvic or abdominopelvic masses. A higher CA-125/CEA ratio is more strongly associated with ovarian epithelial cancers, whereas a lower ratio suggests a non-ovarian origin, particularly metastatic gastrointestinal malignancies involving the ovary.

Although the ratio should not be used as a standalone diagnostic tool, its incorporation into preoperative assessment can improve diagnostic accuracy, assist surgeons in planning the extent of surgery, facilitate appropriate referral to gynecologic oncology services, and contribute to better perioperative decision-making. Therefore, the CA-125/CEA ratio represents a valuable supplementary marker in the surgical evaluation of suspected ovarian malignancies.

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Concept and Design: Dr. Souvik Pramanik

Acquisition, Analysis, or Interpretation of Data: Dr. Mousumi Borah

Drafting of Manuscript: Dr. Kaushik Nath

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