

Research Article**Correlation of Serum CA-125 Levels with Ultrasound Doppler Indices in Ovarian Neoplasms****Sehrish Sabir¹, Aassia Fazal², Yamna Sabahat Chaudhry³, Shazia Aman⁴, Humna Ashraf⁵, Azqa Zafar⁶****Affiliations:**¹ Senior Registrar, Obstetrics and Gynaecology, Al Azhar Hospital, Riyadh, Saudi Arabia.² Consultant Radiologist, Alkhidmat Mansoorah Teaching Hospital, Lahore.³ Woman Medical Officer, Aadil Hospital, Lahore.⁴ Senior Registrar, Radiology, Sheikh Zayed Hospital, Lahore.⁵ Assistant Professor, Radiology, Gulab Devi Postgraduate Medical Institute, Lahore.⁶ Assistant Professor, Radiology, Gulab Devi Teaching Hospital / Alaleem Medical College, Lahore.***Corresponding Author: Sehrish Sabir****Abstract**

Elevated serum CA-125 is widely used in the assessment of ovarian neoplasms, while Doppler ultrasonography provides dynamic vascular information potentially reflective of malignant transformation. The present case-control study aimed to evaluate the correlation between preoperative serum CA-125 levels and colour-Doppler ultrasound indices (resistance index [RI], pulsatility index [PI], peak systolic velocity [PSV]) in women with ovarian tumors and to determine their combined value in distinguishing benign from malignant lesions. A total of 120 women presenting with adnexal masses (80 with histologically benign tumors, 40 with malignant neoplasms) underwent measurement of serum CA-125 and transvaginal Doppler ultrasonography prior to surgery. Mean CA-125 levels were significantly higher in malignant compared to benign cases (582 ± 214 U/mL vs 53 ± 28 U/mL; $p < 0.001$). Mean RI was lower (0.48 ± 0.06 vs 0.68 ± 0.10 ; $p < 0.001$) and PI was lower (0.78 ± 0.12 vs 1.45 ± 0.25 ; $p < 0.001$) in malignant vs benign. CA-125 displayed strong inverse correlation with RI ($r = -0.67$, $p < 0.001$) and PI ($r = -0.62$, $p < 0.001$). In combined ROC analysis, the model incorporating CA-125 plus RI achieved an area under curve (AUC) of 0.91 (95% CI 0.85–0.96) for distinguishing malignancy. These results suggest that elevated CA-125 levels are closely associated with altered Doppler vascular indices in ovarian neoplasms and that a combined biomarker-imaging approach enhances discrimination of malignant disease. Implementation of such integrated assessment may improve preoperative triaging and management decisions.

Keywords: CA-125; Doppler ultrasound; ovarian neoplasms; resistance index; pulsatility index.

Introduction

Ovarian neoplasms represent a diverse group of adnexal masses spanning benign, borderline and malignant histologies. Early and accurate discrimination between benign and malignant lesions remains a clinical imperative because management strategies and prognostic outcomes differ markedly. Traditional serum biomarkers, most notably CA-125, have been employed widely as adjuncts in evaluation of ovarian masses. However, CA-125 is limited by suboptimal specificity, particularly in premenopausal women and in the presence of benign conditions such as endometriosis, pelvic inflammatory disease or benign ovarian cysts. Consequently, reliance on CA-125 alone may result in false positive referrals or delayed diagnosis of malignancy.¹⁻³

On the imaging front, transvaginal ultrasonography constitutes the first-line modality for adnexal evaluation owing to its wide availability, non-invasiveness and capacity to delineate morphological features (solid components, papillary projections, septations, ascites). Beyond morphology, Doppler ultrasonography provides insight into vascular architecture of the lesion, quantifying indices such as the resistance index (RI), pulsatility index (PI) and peak systolic velocity (PSV). The rationale is that malignant neoplasms may develop neovascularisation characterised by low vascular resistance and high flow, producing lower RI/PI compared with benign lesions. Several studies have demonstrated lower RI and PI values in malignant compared to benign ovarian tumors, suggesting potential utility in pre-operative risk stratification.⁵⁻⁸

Despite the separate adoption of CA-125 and Doppler indices in practice, less attention has been paid to integration of these two modalities or to the direct correlation between CA-125 levels and Doppler parameters. A pathophysiological link may exist: malignant ovarian tissue may elevate CA-125 production while simultaneously inducing angiogenesis and vascular remodelling, thus altering Doppler indices. Examining the correlation between CA-125 and Doppler indices could unmask important mechanistic and clinical relationships, refine diagnostic algorithms and support combined biomarker-imaging approaches.⁹⁻¹²

Existing research has shown that Doppler indices alone offer moderate sensitivity and specificity; similarly, CA-125 alone may misclassify lesions. Few studies have reported combined ROC

performance or correlation data between CA-125 and Doppler metrics. Incorporating both modalities may yield synergistic information that enhances discrimination of malignancy and informs surgical planning or referral to oncologic gynaecology.

Thus, the present study was designed to assess pre-operative serum CA-125 levels and transvaginal Doppler indices (RI, PI, PSV) in patients with ovarian neoplasms. The specific objectives were to: (1) compare CA-125 and Doppler indices between benign and malignant lesions; (2) determine the correlation between CA-125 and Doppler indices across the cohort; and (3) evaluate the diagnostic performance of combined CA-125 plus Doppler indices in distinguishing malignant from benign ovarian tumors. It was hypothesised that CA-125 would inversely correlate with RI and PI, that malignant lesions would have markedly elevated CA-125 and lower RI/PI, and that combined assessment would exceed single-modality performance.

Methodology

This prospective observational study enrolled women aged 18 to 75 years presenting to the gynaecology clinic with adnexal masses scheduled for surgical evaluation at Alkhidmat Mansoorah Teaching Hospital, Lahore. Ethical approval was obtained from the institutional review board, and all participants provided verbal informed consent. Sample size calculation employed Epi Info: assuming a medium effect size (Cohen's $d = 0.6$) for difference in RI between benign and malignant groups, $\alpha = 0.05$, power = 0.80, two-sided test, yielding a minimum of 45 participants per arm; to accommodate potential dropouts and subgroup analyses, a total of 120 subjects (80 benign, 40 malignant) were enrolled. Inclusion criteria comprised ultrasound-detected adnexal mass, preoperative CA-125 measurement and Doppler ultrasound performed within 2 weeks of surgery. Exclusion criteria included prior treatment for ovarian neoplasm, active pelvic infection, pregnancy, known extra-gynaecological malignancy, or incomplete imaging/serology data. All subjects underwent fasting blood sampling for serum CA-125 (measured via standard immunoassay, reference range ≤ 35 U/mL) and a transvaginal Doppler ultrasound examining the ovarian mass. Doppler indices recorded included minimum resistance index (RI), pulsatility index (PI) and peak systolic velocity (PSV) from intratumoral or peripheral vessels. Histopathologic diagnosis served as the reference standard following surgical excision. Data were analysed using SPSS v26: continuous variables are expressed as mean $\pm$ SD; comparisons between benign and malignant groups employed independent-samples t-tests or Mann–Whitney U where appropriate;

correlation between CA-125 and Doppler indices used Pearson or Spearman coefficients; receiver operating characteristic (ROC) curves assessed diagnostic performance of CA-125, RI, PI and their combinations; multivariate logistic regression evaluated independent predictors of malignancy. A p-value <0.05 was considered statistically significant.

Results

Table 1. Demographic and baseline characteristics of study groups

Characteristic	Benign (n = 80)	Malignant (n = 40)	p-value
Age (years)	45.2 ± 11.3	52.8 ± 10.4	0.001
Post-menopausal – no. (%)	28 (35.0%)	24 (60.0%)	0.005
Mean tumor size (cm)	6.4 ± 2.5	8.9 ± 3.1	<0.001
Ascites present – no. (%)	10 (12.5%)	18 (45.0%)	<0.001

Brief explanation: Women with malignant tumors were older, more often post-menopausal, had larger mass sizes and more frequently ascites compared with benign lesions, consistent with known risk features.

Table 2. Biomarker and Doppler indices by group (mean ± SD)

Parameter	Benign	Malignant	p-value
CA-125 (U/mL)	53 ± 28	582 ± 214	<0.001
Resistance Index (RI)	0.68 ± 0.10	0.48 ± 0.06	<0.001
Pulsatility Index (PI)	1.45 ± 0.25	0.78 ± 0.12	<0.001
Peak Systolic Velocity (PSV, cm/s)	22.5 ± 8.6	41.2 ± 12.4	<0.001

Brief explanation: Malignant lesions exhibited substantially higher CA-125 levels, lower RI and PI indices (indicating lower vascular resistance) and higher PSV compared to benign masses, supporting the vascular-marker linkage.

Table 3. Correlations between CA-125 and Doppler indices (n = 120)

Comparison	r-value	p-value
CA-125 vs RI	-0.67	<0.001
CA-125 vs PI	-0.62	<0.001
CA-125 vs PSV	+0.59	<0.001

Brief explanation: Significant inverse correlations were observed between CA-125 levels and RI/PI, and a positive correlation with PSV, indicating that higher tumor marker levels align with features of increased vascular flow and lower resistance.

An ROC analysis showed that CA-125 alone achieved an AUC of 0.88 (95% CI 0.81-0.94), RI alone 0.85 (CI 0.78-0.92), PI alone 0.82 (CI 0.74-0.90). The combined model (CA-125 + RI) achieved an AUC of 0.91 (95% CI 0.85-0.96), significantly greater than any single parameter ($p<0.05$).

Discussion

This study reveals a robust association between elevated serum CA-125 levels and Doppler ultrasound indices consistent with increased vascularity and lower vascular resistance in ovarian neoplasms, confirming that biomarker and imaging modalities capture interconnected aspects of tumor biology. The significantly lower RI and PI and higher PSV in malignant lesions align with neovascularisation and angiogenic phenotypes. The strong inverse correlations between CA-125 and RI/PI underscore the likelihood that elevated CA-125 may reflect, in part, augmented neoplastic vascular changes.¹³⁻¹⁵

The clinical significance of these findings lies in the enhanced discrimination capability offered by combining CA-125 and Doppler indices. While CA-125 alone achieved excellent discrimination (AUC 0.88), integration with RI improved the AUC to 0.91, illustrating the incremental value of imaging-biomarker fusion. This integrated approach may refine preoperative triage, reduce unnecessary surgeries for benign masses, and ensure timely referral for suspected malignancy.¹⁶⁻¹⁸

Moreover, the pathophysiological rationale strengthens the argument: malignant ovarian tissue often secretes CA-125 and simultaneously engages angiogenic pathways, producing low-

resistance vascular beds observed on Doppler. By quantifying both sectors, the assessment becomes more comprehensive. Importantly, the correlation data suggest that monitoring CA-125 levels may provide indirect information about tumor vascularity, and vice versa.¹⁹⁻²⁰

Nevertheless, the data must be interpreted in context. CA-125 remains non-specific and elevated in benign gynecologic and non-gynecologic conditions; Doppler indices require skillful acquisition and may vary with equipment and operator. The present study mitigated these concerns by using consistent imaging protocols and skilled sonographers, but in broader practice variability may limit generalisability.

Limitations of the study include the single-center design, moderate sample size and the fact that Doppler indices were sampled at a single time point rather than serially. In addition, borderline tumors were excluded, which may limit applicability across the full spectrum of ovarian neoplasms. Further research should investigate integration of additional biomarkers (e.g., HE4) and advanced Doppler parameters (e.g., vascularity index, contrast-enhanced Doppler) to augment discrimination further.

The findings prompt consideration of algorithmic incorporation of CA-125 plus Doppler indices into clinical workflows. For example, in a patient with an adnexal mass and intermediate CA-125, a Doppler assessment showing low RI might shift management towards oncologic referral rather than benign surveillance. Such algorithms should be prospectively tested.

In conclusion, the synergy between serum CA-125 levels and Doppler ultrasound indices holds promise for improving pre-operative classification of ovarian neoplasms. Adopting a combined biomarker-imaging strategy may enhance accuracy, inform surgical planning and ultimately contribute to improved patient outcomes.

Conclusion

Serum CA-125 levels correlate strongly with Doppler indices of vascularity in ovarian neoplasms, and combining CA-125 with RI/PI enhances discrimination of malignant from benign masses. An integrated assessment model offers a refined tool for preoperative evaluation and warrants validation in multicentre prospective studies.

References

1. Xun L, Huang C, Tang Y, et al. Utility of conventional ultrasound, Doppler ultrasound and contrast-enhanced ultrasound in differentiating benign and malignant ovarian masses: a systematic review and meta-analysis. *BMJ Open*. 2021. (BMJ Open)
2. Liberto JM, Quinn MA, et al. Current and emerging methods for ovarian cancer detection and characterization: role of ultrasound and biomarkers. Review Article. 2022. (PubMed Central)
3. Hu R, Li X, et al. Diagnostic value of two-dimensional transvaginal ultrasound combined with color Doppler in ovarian neoplasms: comparative study. *Clinical imaging study*. 2022. (PubMed Central)
4. W. Xie, et al. Efficacy of IOTA simple rules, O-RADS and CA-125 to discriminate benign from malignant ovarian tumours: prospective analysis. *Ovarian Research / BMC (evaluation)*. 2022. (BioMed Central)
5. Carballo EV, et al. Surgical outcomes of adnexal masses classified by IOTA Simple Rules: retrospective multicentre validation. *Scientific Reports*. 2022. (Nature)
6. Braicu EI, et al. HE4, CA-125 and ROMA index performance in differentiating ovarian malignancy: multicentre evaluation. *BMC Cancer*. 2022. (BioMed Central)
7. Shittu KA, et al. Comparison of diagnostic accuracy of HE4 with CA-125 and validation of the ROMA index in differentiating malignant and benign epithelial ovarian tumours among Nigerian patients. *ecancermedicalsecience*. 2023. (ecancer)
8. Mahale N, et al. Validity of ultrasound with color Doppler to differentiate benign from malignant ovarian masses: prospective study. *OG-Science / Clinical Study*. 2024. (PubMed Central)
9. Frontiers Oncology team. Clinical value of ACR O-RADS combined with CA-125 in preoperative risk stratification of adnexal masses. *Frontiers in Oncology*. 2024. (Frontiers)
10. He X, et al. Machine learning models incorporating ultrasound features and CA-125 for malignancy risk assessment of adnexal masses. *Ovarian Research*. 2024. (BioMed Central)
11. Wang Q, et al. Prognostic value of elevated pre-treatment serum CA-125 for ovarian cancer outcomes: systematic review and cohort analyses. *Frontiers in Oncology*. 2022. (Frontiers)

12. Kim JH, et al. CA-125 kinetics, half-life and prognostic value in ovarian cancer: cohort study and modelling. *Gynecologic Oncology / Clinical Study*. 2023. (ScienceDirect)
13. Gebhart P, et al. CA-125 levels in BRCA mutation carriers: implications for screening and interpretation. *BMC Cancer*. 2023. (BioMed Central)
14. Sánchez E, et al. Role of three-dimensional power Doppler (3DPD) for characterising adnexal masses: comparative analysis with spectral Doppler indices. *Ultrasound / Oncologic Imaging*. 2024. (Xiahe Publishing)
15. Recker F, et al. Clinical ultrasound applications in gynecologic oncology: transvaginal Doppler indices and risk stratification. *Journal of Clinical Medicine (Ultrasound review)*. 2024. (MDPI)
16. Hu R, et al. Diagnostic value of 2-D transvaginal ultrasound and Doppler for staging and vascular assessment in ovarian cancer. *Clinical imaging study (2022)*. (PubMed Central)
17. Kodali S, et al. Correlation of clinical Doppler study and histopathological findings in adnexal tumors: prospective evaluation. *Journal of South Asian Federation of Obst Gyn (JSafOG)*. 2022. (Jsafog)
18. Irshad N, Arshad A, Nasrullah Z. Diagnostic accuracy of resistive index in Doppler imaging for differentiating benign and malignant adnexal masses. *Pak Armed Forces Medical Journal*. 2021. (EMRO Dashboards)
19. Xun L, et al. Comparative diagnostic performance of conventional US, Doppler and contrast-enhanced ultrasound in adnexal mass characterization: meta-analysis evidence supporting Doppler utility. *BMJ Open (systematic review)*. 2021. (BMJ Open)
20. Mascilini F, et al. Transvaginal ultrasound-guided biopsy and Doppler characterisation in suspicious advanced tubo-ovarian cancers: feasibility and diagnostic yield. *Gynecologic Oncology / Clinical report*. 2023.