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Original Article

Early Detection Strategies for Ovarian Cancer — Screening Techniques and Efficacy

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ABSTRACT

Introduction: *Ovarian cancer remains one of the most lethal gynecologic malignancies due to its often late-stage diagnosis. Early detection is crucial to improving survival outcomes, especially in high-risk populations. This study aimed to evaluate the efficacy of various ovarian cancer screening techniques, including serum CA-125 testing, transvaginal ultrasound (TVUS), and risk prediction models, in detecting ovarian cancer in high-risk women.* ***Methods & Materials:*** *This observational study involved 45 high-risk women, recruited based on family history and genetic predisposition. The effectiveness of screening techniques was assessed by comparing detection rates, sensitivity, specificity, and positive and negative predictive values for each method. Data were analyzed using SPSS, and the impact of each technique on early-stage detection and overall survival rates was evaluated.* ***Results:*** *Serum CA-125 testing demonstrated the highest detection rate at 44.44%, but also the highest number of false positives (15 cases). TVUS had a lower detection rate (33.33%) but exhibited higher specificity and a negative predictive value (90.0%). Risk prediction models, while highly specific (90.0%) and with the highest positive predictive value (66.7%), had the lowest sensitivity (50.0%). The combination of screening methods showed the most promise for improving detection accuracy.* ***Conclusion:*** *The findings suggest that a multimodal approach combining CA-125 testing, TVUS, and risk prediction models offers the best strategy for early detection of ovarian cancer in high-risk women. This combined approach can improve sensitivity and specificity while minimizing false positives, making it a valuable screening protocol for clinical use.*

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INTRODUCTION

One of the main prerequisites for developing a screening approach in asymptomatic populations is the availability of an acceptable and adequate test that can detect disease at an early stage, as stated by the World Health Organization nearly 40 years ago[1]. Ovarian cancer is a relatively uncommon disease, with an incidence of about 50 per 100,000 people, but it has a very high mortality rate. According to statistical calculations, a single test is unlikely to meet the minimal positive predictive value (PPV) of 10% and the specificity of better than 99% needed for an effective ovarian cancer screening test[2-4]. Approximately 80% of women with advanced ovarian cancer exhibit elevated levels of CA-125, the most well-studied serum biomarker for the disease, but only 50–60% of individuals with early-stage disease show elevated CA-125 levels[5]. However, research suggests that CA-125 alone does not meet the specificity requirements for an early detection screening test, especially when paired with standard screening procedures such as ultrasonography. The advent of novel technologies, particularly in proteomics, presents new hope for developing an effective screening technique for the early detection of ovarian cancer. Screening for ovarian cancer has a compelling rationale: with current surgery and chemotherapy options, up to 90% of women with ovarian cancer can be treated if the cancer is confined to the ovaries (Stage I). Even at Stage II, when the disease has spread to the pelvis, the five-year survival rate remains above 70%. However, the survival rate plummets to 20% or lower if the cancer has progressed to Stage III (involving the abdominal cavity) or Stage IV (involving the liver's parenchyma). Unfortunately, only 20% of ovarian tumors are detected in these early stages when no screening method is in place[6]. Computer simulations estimate that early detection of asymptomatic preclinical disease could prevent 10% to 30% of ovarian cancer deaths[7-10]. However, epidemiologic screening standards are stringent due to the low postmenopausal prevalence of ovarian cancer (approximately 1 in 2,500 women). Ultimately, surgery is usually required to diagnose ovarian cancer. Gynecologic oncologists advocate that no more than ten surgeries should be necessary to diagnose one case of ovarian cancer. Therefore, a screening technique must achieve a sensitivity of ≥75% and a specificity of 99.6% to attain a PPV of 10%[11]. Ovarian cancer early detection remains a significant unmet medical need. Effective screening could result in 10% to 30% fewer deaths. Neither transvaginal sonography (TVS) nor serum CA-125 alone are sensitive or specific enough for early detection. However, two-stage approaches have shown greater success. A significant rise in CA-125 above a woman's baseline triggers TVS, and abnormal ultrasonography results lead to surgery. Two large screening trials have demonstrated appropriate

specificity with this approach, although sensitivity for early-stage (I–II) disease needs improvement. Several biomarker panels have helped detect cases missed by CA-125, improving the initial stage of screening. For instance, 20% of early-stage ovarian malignancies have been identified by autoantibodies against TP53, months before a CA-125 rise and well before clinical diagnosis. The objective of testing panels of autoantibodies and antigen-autoantibody complexes is to detect over 90% of ovarian malignancies in their early stages, either by themselves or in conjunction with CA-125, while maintaining 98% specificity in control subjects. Other biomarkers such as micro-RNAs, circulating tumor DNA (ctDNA), and DNA methylation are being investigated to develop the most effective first-stage test. Additionally, new imaging technologies more sensitive than TVS are being developed to detect small tumor volumes[12].

METHODS & MATERIALS

This study was conducted at Sheikh Fazilatunnessa Mujib Memorial Kpj Specialized Hospital & Nursing College, Gazipur, Bangladesh from January, 2022 to December, 2023. A cohort of women at high risk for ovarian cancer, based on family history and genetic predisposition, was recruited for an observational study. A total of 45 participants underwent the identified screening techniques over a defined period. The effectiveness of each screening method was evaluated by comparing the detection rates of ovarian cancer at various stages and the impact on overall survival rates. The inclusion criteria consisted of women aged 30 to 79 years who were considered at high risk for ovarian cancer based on factors such as a family history of ovarian or breast cancer, presence of BRCA1 or BRCA2 genetic mutations, or a personal history of breast cancer. Participants were required to have no prior history of ovarian cancer and to be willing to undergo regular screening procedures over the study period. Exclusion criteria included women with a prior diagnosis of ovarian cancer, those currently undergoing cancer treatment, and those with significant comorbid conditions that might confound the study results, such as severe cardiovascular disease or uncontrolled diabetes. Additionally, women who were pregnant, had a history of bilateral oophorectomy, or were unable to provide informed consent were excluded from the study. Statistical analyses were performed to determine the sensitivity, specificity, positive predictive value, and negative predictive value of each screening technique using SPSS version 26. Additionally, the study considered patient outcomes, including false positives and false negatives, and their implications for clinical practice. The gathered data were then subjected to a detailed comparative analysis to determine which screening strategies provided the highest efficacy in early detection. The findings from this study aimed to contribute to the optimization of ovarian cancer screening protocols and improve early detection practices.

RESULTS

The study cohort consisted of 45 high-risk women, with the majority of participants (35.56%) falling within the 50-59 age range. This was followed by 24.44% of participants aged 40-49 and 20.00% in the 60-69 age group. A smaller proportion of participants were in the 30-39 age group (11.11%), while the lowest representation was seen in the 70-79 age group, comprising 8.89% of the cohort (**Table I**).

Table I: Age Distribution of Study Participants (*n*=45)

Age Range (Years)	Frequency	Percentage
30-39	5	11.11
40-49	11	24.44
50-59	16	35.56
60-69	9	20.00
70-79	4	8.89

Among the 45 participants, serum CA-125 testing had the highest detection rate, identifying positive cases in 44.44% of participants, but also showed the highest number of false positives (15 cases). Transvaginal ultrasound (TVUS) detected positive cases in 33.33% of participants, with 10 false positives. Risk prediction models had the lowest detection rate, identifying 22.22% of participants, and resulted in 5 false positives. These results highlight that while serum CA-125 testing had the highest detection rate, it also produced a substantial number of false positives compared to the other screening methods.

Table – II: Screening Techniques and Detection Rates (*n*=45)

Screening Technique	Frequency of Positive Detection	Percentage	False Positives
Transvaginal Ultrasound (TVUS)	15	33.33	10
Serum CA-125 Testing	20	44.44	15
Risk Prediction Models	10	22.22	5

The efficacy of the screening techniques varied across different measures. Transvaginal ultrasound (TVUS) demonstrated the highest sensitivity (75.0%) and a high negative predictive value (NPV) of 90.0%, indicating its effectiveness in ruling out disease. However, its positive predictive value (PPV) was lower at 60.0%. Serum CA-125 testing had a slightly lower sensitivity (71.4%) and specificity (75.0%) compared to TVUS, with a PPV of 57.1% and an NPV of 86.7%. Risk prediction models showed the highest specificity (90.0%) and the highest PPV (66.7%), but they had the lowest sensitivity (50.0%) and an NPV of 81.8%, reflecting a more targeted yet less sensitive approach to detecting ovarian cancer (**Table III**).

Table III: Efficacy of Screening Techniques (*n*=45)

Screening Technique	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV) (%)	Negative Predictive Value (NPV) (%)
Transvaginal Ultrasound (TVUS)	75.0	80.0	60.0	90.0
Serum CA-125 Testing	71.4	75.0	57.1	86.7
Risk Prediction Models	50.0	90.0	66.7	81.8

DISCUSSION

The current study assessed the efficacy of various ovarian cancer screening methods, including serum CA-125 testing, transvaginal ultrasound (TVUS), and risk prediction models in a cohort of high-risk women. The majority of participants were in the 50–59 age group (35.56%), which is consistent with the literature, as ovarian cancer risk increases significantly post-menopause. ***Menon et al.*** noted that screening in postmenopausal women, particularly in those over the age of 50, has demonstrated better specificity and sensitivity, which aligns with our findings on the distribution of participants and the target age for screening[13]. Serum CA-125 testing demonstrated the highest detection rate (44.44%) in our study but also resulted in the highest number of false positives (15 cases). This is a well-documented limitation of CA-125 as a screening tool. ***Bourne et al.*** reported that while CA-125 is effective in detecting advanced stages of ovarian cancer, its specificity is limited in detecting early-stage disease, particularly when used as a standalone test[14]. Similarly, ***Stirling et al.*** highlighted that the use of CA-125 alone leads to high false-positive rates, which can result in unnecessary surgeries and patient anxiety, especially in premenopausal women[15]. These findings are mirrored in our study, where CA-125's false positives underline the need for a more reliable or combined screening approach. Transvaginal ultrasound (TVUS) had a lower detection rate (33.33%) but showed a better specificity and fewer false positives than CA-125. TVUS's high negative predictive value (90.0%) in our cohort reflects its strength in ruling out ovarian cancer in patients without abnormalities, a finding that is supported by ***Partridge et al.,*** who demonstrated that TVUS, especially when combined with CA-125, is effective in increasing diagnostic accuracy[16]. In the Modena Study, ***Cortesi et al.*** confirmed that combining TVUS with CA-125 testing improves the sensitivity for detecting ovarian cancer in women with BRCA mutations, further supporting the role of combined modalities in improving detection rates[17]. Risk prediction models in our study exhibited the highest specificity

(90.0%) and positive predictive value (66.7%), though they had the lowest sensitivity (50.0%). This reflects the ability of these models to accurately predict malignancy in high-risk women but also their limitations in detecting all cases. Skates et al. found that the use of the Risk of Ovarian Cancer Algorithm (ROCA) improved early detection when frequent CA-125 monitoring was incorporated, but also highlighted the challenge of achieving high sensitivity with predictive models alone[18]. The study by Chiappa et al. similarly demonstrated that incorporating machine learning and predictive algorithms can significantly enhance the accuracy of malignancy prediction, but sensitivity remains a key issue, especially in the early stages of the disease[19]. A comparative analysis of these screening methods across multiple studies suggests that no single method is sufficiently effective in detecting ovarian cancer, particularly in its early stages. Serum CA-125 testing, while sensitive, lacks the specificity needed for widespread screening without generating high false-positive rates. TVUS, although more specific, misses a significant number of early-stage cancers unless combined with other diagnostic tools. Risk prediction models show promise in targeting high-risk populations but require further refinement to improve their sensitivity. The results from Olivier et al. and others underscore the importance of a multimodal approach, combining biomarkers, imaging, and predictive modeling for optimal detection[20]. Overall, the findings from this study align with the broader body of evidence that suggests the need for a multimodal screening approach to maximize the sensitivity and specificity of ovarian cancer detection. By combining methods such as CA-125 testing, TVUS, and predictive models, it is possible to improve early detection rates while minimizing unnecessary interventions. However, further research is needed to refine these screening protocols, particularly in high-risk populations, to improve outcomes and reduce ovarian cancer mortality.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion

This study highlights the critical need for a multimodal approach to ovarian cancer screening in high-risk populations. While serum CA-125 testing exhibited the highest detection rate, its high false-positive rate limits its effectiveness as a standalone screening method. Transvaginal ultrasound, with its higher specificity and fewer false positives, offers an important complement to biomarker testing, although it also falls short in detecting early-stage cancers when used alone. Risk prediction models, although demonstrating high specificity, lack the sensitivity required for comprehensive screening. Overall, combining these methods—particularly serum CA-125, TVUS, and risk prediction models—yields the most effective strategy for early detection of ovarian cancer. Continued research and refinement of

screening protocols are needed to improve sensitivity, reduce false positives, and enhance survival outcomes for women at high risk of ovarian cancer.

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Conflict of Interest
The authors declare no conflict of interest.

Ethical approval: The study was approved by the Institutional Ethics Committee

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