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# Correlation between IOTA Simple Ultrasound Rules and Histopathological Findings in Adnexal Masses: A Tertiary Hospital-Based Study from Bangladesh

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## Abstract

**Background:** Preoperative differentiation of benign vs malignant adnexal masses is essential for timely oncology referral and avoiding unnecessary surgery. We evaluated the diagnostic accuracy of the International Ovarian Tumor Analysis (IOTA) Simple Rules (SRs) in a tertiary oncology center in Bangladesh. **Methods:** In this prospective study, 94 consecutive patients underwent standardized transvaginal/transabdominal ultrasonography and subsequent surgery with histopathology as reference. Masses were classified per IOTA SRs as benign, malignant, or indeterminate. Diagnostic metrics were calculated for conclusive SR classifications. **Results:** Of 94 analyzable cases, histopathology showed 53 benign (56.4%) and 41 malignant (43.6%). SR categorization yielded 48 benign (51.1%), 38 malignant (40.4%), and 8 indeterminate (8.5%). For conclusive cases (n = 86), IOTA SRs achieved sensitivity 84.2% (95% CI 68.8 - 94.0), specificity 87.2% (74.3 - 95.1), PPV 84.2%, NPV 87.2%, and overall accuracy 85.9% (76.6 - 92.5). The most frequent malignant features were M1 (irregular solid tumor) and M5 (very strong Doppler flow). **Conclusion:** IOTA SRs demonstrated robust, low-cost diagnostic performance in this tertiary oncology setting. Slightly lower estimates than some multicenter series likely reflect single-center design, higher malignancy prevalence, and operator variability. Larger multicenter studies in LMICs are warranted for broader validation.

**Keywords**

Adnexal Masses, IOTA Simple Rules, Ultrasonography, Diagnostic Accuracy, Bangladesh

## 1. Introduction

Adnexal masses are a frequent diagnostic and therapeutic challenge in gynecology, encompassing conditions ranging from functional cysts to malignant ovarian neoplasms. Globally, ovarian cancer is the most lethal gynecological malignancy, accounting for over 295,000 new cases and 185,000 deaths annually, with five-year survival rates below 30% in many low- and middle-income countries. Early differentiation of malignant from benign adnexal masses is therefore pivotal to expedite referral to gynecologic oncology for malignancy and avoid unnecessary radical procedures for benign disease [1]-[5].

Over the last three decades, multiple strategies have been explored to improve preoperative diagnosis. Tumor markers such as CA-125, while widely used, have limited specificity, particularly in premenopausal women [6]-[8]. Risk algorithms such as the Risk of Malignancy Index (RMI) and the OVA1 test combine CA-125, menopausal status and imaging, but are either too resource-intensive or inconsistently validated outside high-income settings [9]-[11]. In contrast, ultrasonography remains the first-line modality for adnexal mass evaluation due to its accessibility, non-invasiveness and affordability. However, its diagnostic reliability has traditionally been undermined by operator dependence and lack of standardized interpretation criteria.

To address these limitations, the International Ovarian Tumor Analysis (IOTA) group developed standardized ultrasound terminology and the widely used IOTA Simple Rules (SRs) comprising five benign (B) and five malignant (M) features. In a large multicenter prospective validation (~2,000 patients, 19 centers), SRs showed excellent discrimination (sensitivity 92%, specificity 96%) with conclusive results for ~77% of masses; adding expert judgment for inconclusive cases maintained strong performance (91% sensitivity, 93% specificity) [12] [13]. As the IOTA framework matured, the three-step strategy—simple descriptors → SRs → expert review—enabled non-expert sonographers to classify ~84% of masses using the first two steps, achieving sensitivity 95.2%, specificity 97.7%, and accuracy 97.2% on external validation; a recent meta-analysis similarly reported pooled sensitivity and specificity near 94% [14] [15].

Regional evidence from Asia supports clinical utility. A large Indian study found that IOTA SR and the ADNEX model achieved high diagnostic accuracy (~91%) and outperformed RMI 4; O-RADS showed the highest sensitivity (98%) while ADNEX provided the highest specificity (93%) [16].

According to GLOBOCAN 2022, Bangladesh recorded an estimated 2,846 new ovarian cancer cases and 1,857 deaths, underscoring the need for accurate, low-cost triage tools such as the IOTA Simple Rules [17] [18]. Preliminary national data from Chittagong Medical College Hospital (n = 45) showed IOTA SRs outperforming RMI 4 (accuracy 93.3% vs 73.3%) [19] [20].

Taken together, global validation, Asian data, and early Bangladeshi experience highlight the diagnostic accuracy and feasibility of IOTA SRs. Yet adequately powered, tertiary oncology–based Bangladeshi studies remain scarce, particularly regarding the indeterminate group that challenges decision-making. Therefore, this study evaluated the diagnostic accuracy of IOTA Simple Ultrasound Rules against histopathology in a tertiary oncology hospital in Bangladesh, estimating sensitivity, specificity, PPV, NPV, and outcomes of inconclusive cases, and describing the histopathological spectrum of adnexal masses in this cohort.

## 2. Materials and Methods

### 2.1. Study Settings

This study was conducted at the Department of Gynecologic Oncology, Bangladesh Medical University, Shahbagh, Dhaka. Patients presenting with suspected adnexal masses to the outpatient and inpatient departments of Gynecologic Oncology and Obstetrics & Gynaecology units were included.

### 2.2. Study Design

A prospective, cross-sectional study design was employed to evaluate the diagnostic performance of the IOTA Simple Ultrasound Rules in distinguishing benign from malignant adnexal masses, using histopathological diagnosis as the reference standard.

### 2.3. Study Procedure

Ethical approval was obtained from the Institutional Review Board (IRB) of Bangladesh Medical University before commencing the study. A total of 94 consecutive patients with clinically suspected adnexal masses, fulfilling inclusion criteria, were recruited from outpatient and inpatient departments. Written informed consent was obtained after explaining the study objectives, procedures, and voluntary participation.

Each participant underwent transvaginal ultrasonography (TVS) using either a Voluson P8 or Philips ultrasound machine. Ultrasound examinations followed the standardized guidelines of the IOTA group (Timmerman *et al.*, 2008). When TVS was insufficient due to mass size or position, transabdominal ultrasonography was performed.

The IOTA Simple Ultrasound Rules were applied to classify adnexal masses based on specific sonographic features. A mass was classified as benign if one or more benign features were present without any malignant features, malignant if one or more malignant features were present without benign features, and inconclusive if both benign and malignant features coexisted or if none of the defined features were identified.

Malignant features (M-Rules) included: irregular solid tumors (M1), ascites (M2), four or more papillary projections (M3), irregular multilocular solid tumors ≥100 mm (M4), and very strong blood flow (color score 4, M5). Benign features (B-Rules) included: unilocular cysts (B1), solid components <7 mm (B2), acoustic shadows (B3), smooth multilocular tumors <100 mm (B4), and absent detectable blood flow (color score 1, B5).

All participants underwent surgical removal of the adnexal mass within 120 days of ultrasound assessment. The surgical approach—laparoscopy or laparotomy—was based on clinical indications. Excised specimens were examined histopathologically, serving as the definitive diagnostic reference. Ultrasound evaluations and interpretations were completed before surgery and before histopathological results were available to avoid bias.

## 2.4. Sample Size

The sample size of 94 was calculated based on the estimated prevalence of adnexal masses, anticipated sensitivity and specificity of the IOTA rules, desired precision, and confidence levels, providing adequate power to evaluate diagnostic accuracy.

## 2.5. Data Collection

Data were collected using a structured questionnaire capturing demographic details, clinical history, sonographic findings, serum CA-125 levels, and histopathological outcomes. Investigators conducted patient interviews and reviewed medical records. Confidentiality was maintained by assigning unique identification numbers, with data accessible only to the research team and used solely for this study.

## 2.6. Data Analysis

Data were entered and analyzed using SPSS version 24. Quantitative variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Diagnostic performance metrics—sensitivity, specificity, PPV, and NPV—were calculated against histopathological diagnosis. The proportion of inconclusive cases by IOTA and their histopathological outcomes were recorded. The distribution of final histopathological diagnoses was analyzed. Statistical significance was set at $p < 0.05$ with 95% confidence intervals.

## 2.7. Ethical Considerations

The study adhered to the Declaration of Helsinki (1964) and its amendments. Written informed consent was obtained after explaining the objectives, methods, risks, and benefits. No experimental drugs or procedures beyond standard clinical care were used. Confidentiality and anonymity were rigorously maintained via unique identifiers, with data access restricted to the research team. The study posed no additional risks or burdens beyond routine clinical management. No conflicts of interest were declared.

# 3. Results

## 3.1. Age and Menopausal Distribution

Table 1 summarizes malignancy increased with age, from 32–39% in younger groups to 63% among women older than 50 years. Postmenopausal women show higher malignancy (43.9%) than premenopausal (37%), highlighting increased risk after menopause.

**Table 1.** Age and menopausal distribution of respondents in benign and malignant tumor. (n = 94)

| Characteristics | Benign (%) | Malignant (%) |
|---|---|---|
| Age Group (in Years) | | |
| 10 - 30 years | 23 (67.6%) | 11 (32.4%) |
| 30 - 50 years | 20 (60.6%) | 13 (39.4%) |
| >50 years | 10 (37.0%) | 17 (63.0%) |
| Menopausal status (n = 84) | | |
| Premenopausal | 17 (63.0%) | 10 (37.0%) |
| Postmenopausal | 32 (56.1%) | 25 (43.9%) |

## 3.2. Sonographic Categorization of Adnexal Masses

The sonographic assessment of adnexal masses using the IOTA Simple Ultrasound Rules classified the masses into three categories. Among the 94 cases, 48 (51.1%) were categorized as benign, 38 (40.4%) as malignant, and 8 (8.5%) were inconclusive or indeterminate (**Figure 1**).

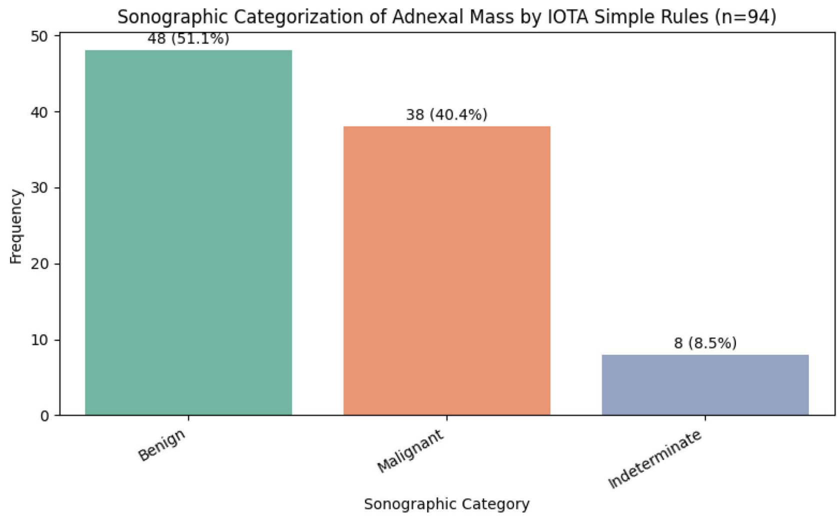


**Figure 1.** Sonographic categorization of adnexal mass by IOTA simple rules.

## 3.3. Association of the Sonographic Findings and IOTA Classification

The majority of adnexal masses were unilateral across all histopathological groups, found in 95.9% of benign, 97.4% of malignant, and all (100%) indeterminate cases, with no statistically significant difference (p = 0.8). Bilateral involvement was rare. A significant association was observed in terms of locularity (p < 0.001): unilocular cysts were most frequently seen in benign cases (89.8%), while multilocular morphology predominated among malignant masses (71.1%). Regarding consistency, cystic structures were dominant in benign tumors (79.6%), whereas malignant lesions more often exhibited mixed (50.0%) or solid (13.2%) components (p < 0.001). The presence of free fluid was another strongly discriminating feature, significantly more common in malignant cases (71.1%) compared to benign (8.2%) and indeterminate groups (25.0%) (p < 0.001) (**Table 2**).

**Table 2.** Association of the sonographic findings and IOTA classification among the participants. (n = 94)

| Characteristics | Benign (n = 48) | Malignant (n = 38) | Indeterminate (n = 8) | p-value |
|---|---|---|---|---|
| Number | | | | |
| Unilateral | 47 (95.9%) | 37 (97.4%) | 8 (100.0%) | 0.8 |
| Bilateral | 1 (2.0%) | 1 (2.6%) | 0 (0.0%) | |
| Locularity | | | | |
| Unilocular | 44 (89.8%) | 11 (28.9%) | 6 (75.0%) | <0.001 |
| Multilocular | 4 (8.2%) | 27 (71.1%) | 2 (25.0%) | |
| Consistency | | | | |
| Cystic | 39 (79.6%) | 14 (36.8%) | 4 (50.0%) | <0.001 |
| Mixed | 8 (16.3%) | 19 (50.0%) | 2 (25.0%) | |
| Solid | 1 (2.0%) | 5 (13.2%) | 2 (25.0%) | |
| Free Fluid | | | | |
| Yes | 4 (8.2%) | 27 (71.1%) | 2 (25.0%) | <0.001 |
| No | 43 (87.8%) | 11 (28.9%) | 6 (75.0%) | |

## 3.4. IOTA Sonography Diagnostic Performance

The IOTA Simple Sonographic categorization demonstrated high diagnostic accuracy in differentiating benign and malignant adnexal masses when compared to histopathological diagnosis, with a sensitivity of 84.21% and specificity of 87.23%. The positive predictive value (PPV) was 84.21%, while the negative predictive value (NPV) was 87.23%, resulting in an overall accuracy of 85.88% (**Table 3**).

**Table 3.** Diagnostic accuracy of sonographic categorization compared to histopathological diagnosis. (n = 86)

| **Diagnosis Test** | **Sensitivity (%)** | **Specificity (%)** | **PPV (%)** | **NPV (%)** | **Accuracy (%)** |
|---|---|---|---|---|---|
| Sonography vs Histopathology | 84.21 (68.75, 93.98) | 87.23 (74.26, 95.12) | 84.21 (68.75, 93.98) | 87.23 (74.26, 95.12) | 85.88 (76.64, 92.49) |

## 3.5. Distribution of IOTA Ultrasound Features

Among malignant features, M1 (Irregular solid tumor) was the most frequently observed, comprising 38.9% of malignant findings, followed by M5 (Very strong blood flow) at 27.8%. For benign features, B1 (Unilocular cyst) and B5 (No detectable blood flow (color score 1) were the predominant findings, each accounting for 32.9% of benign feature occurrences (**Figure 2**).

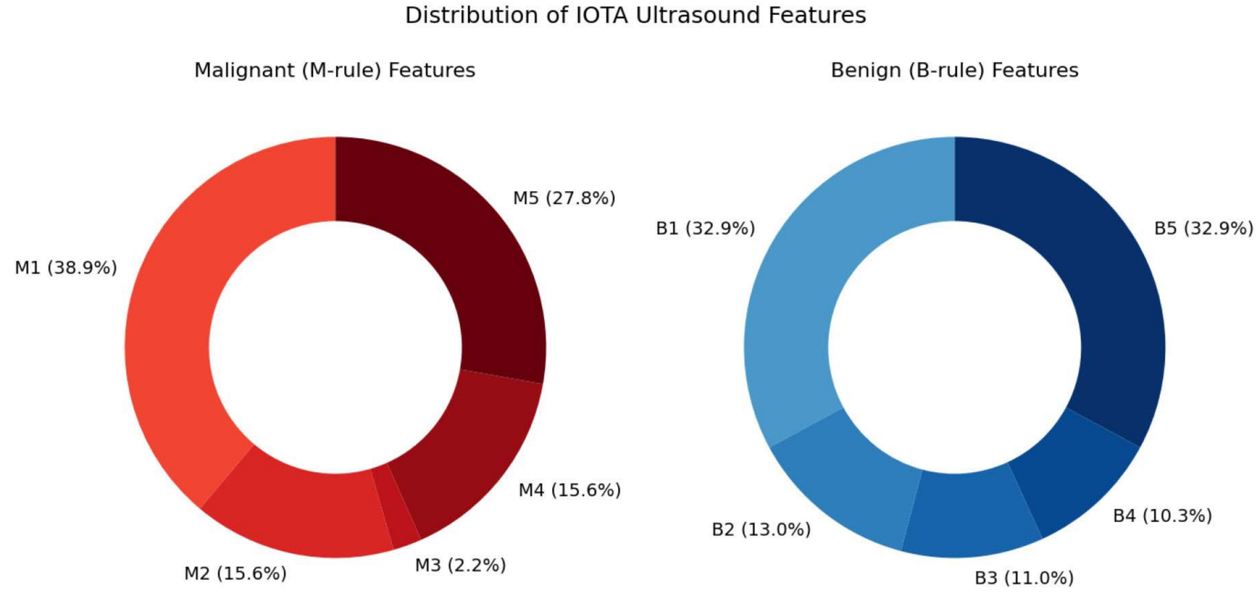


**Figure 2.** Distribution of IOTA ultrasound features. (n = 94)

### 3.6. Association between Sonographic Categorization and Histopathological Diagnosis

There was a statistically significant association between IOTA Simple Rules and histopathology ($p < 0.001$). Of sonographically malignant masses, 84.2% were malignant histologically; of sonographically benign, 87.2% were benign. Indeterminate cases (n = 8) showed 37.5% malignant and 62.5% benign outcomes (**Table 4**).

**Table 4.** Association between sonographic categorization and histopathological diagnosis. (n = 94)

| Sonographic Categorization | Malignant n (%) | Benign n (%) | Total | p-value |
|---|---|---|---|---|
| Malignant | 32 (84.2) | 6 (15.8) | 38 | <0.001 |
| Benign | 6 (12.8) | 41 (87.2) | 47 | |
| Indeterminate | 3 (37.5) | 5 (62.5) | 8 | |
| Total | 41 | 53 | 94 | |

### 3.7. Distribution of Histopathological Diagnoses

Among the 94 participants included in the study, the distribution of histopathological diagnoses revealed that the majority of adnexal masses were benign. Specifically, 53 cases (56.4%) were histologically confirmed as benign tumors, whereas 41 cases (43.6%) were diagnosed as malignant (**Figure 3**).

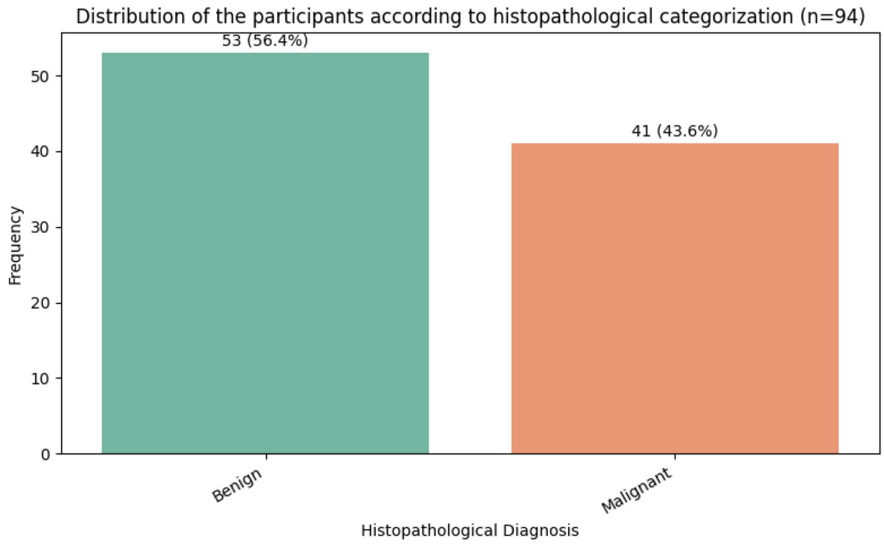


**Figure 3.** Histological classification of Adnexal Mass. (n = 94)

### 3.8. Sonographic Pattern Analysis of Inconclusive Cases

**Table 5** details the specific sonographic rule combinations observed among the 8 cases categorized as indeterminate by IOTA and their corresponding histopathological outcomes. The most frequently observed combination was M2 + B2, found in 3 cases, two of which were benign and one malignant. Two cases exhibited the pattern B3 + M4 + M5 (acoustic shadows with irregular multilocular solid tumors and very strong blood flow), and three cases showed B3 + M4, both patterns also resulting in benign histopathological diagnoses.

**Table 5.** Comparison between sonographic and histopathological findings of inconclusive cases. (n = 8)

| Sonographic findings (IOTA rules) | Frequency | Histopathology | |
|---|---|---|---|
| | | Benign | Malignant |
| M2 + B2 | 3 | 2 | 1 |
| B3 + M4 + M5 | 2 | | **2** |
| B3 + M4 | 3 | 3 | |

### 3.9. Prevalence and Diagnostic Accuracy of Benign Sonographic Features

**Table 6** summarizes benign ultrasound features (n = 57) and their diagnostic yield, where "Predicted" denotes correctly identified benign cases and "Result" the total instances of each feature. B2 (solid components <7 mm) was most frequent (13 cases) and most predictive (92.3%). B1 (unilocular cyst) and B3 (acoustic shadows) each appeared in 12 cases, with predictive values of 75.0% and 83.6%, respectively. B5 (absent blood flow, color score 1) occurred in 12 cases with a 75.0% predictive value. B4 (smooth multilocular tumors <100 mm) was least predictive at 50.0% (8 cases).

**Table 6.** Prevalence and predictive power of benign factors. (n = 57)

| Benign | Predicted | Result | Percentage % |
|---|---|---|---|
| B1 | 9 | 12 | 75. 0 |
| B2 | 12 | 13 | 92.3 |
| B3 | 10 | 12 | 83.6 |
| B4 | 4 | 8 | 50.0 |
| B5 | 9 | 12 | 75.0 |

**Table 7** summarizes the distribution and predictive accuracy of malignant ultrasound features. Among these, M5 (very strong blood flow, color score 4) was the most commonly observed malignant criterion, found in 16 cases with a predictive accuracy of 91.2%. M1 (irregular solid tumor) and M4 (irregular multilocular solid tumors ≥100 mm) were also frequent, observed in 9 and 7 cases respectively, with predictive accuracies of approximately 79% and 94%. Features such as M2 (ascites) showed strong predictive value exceeding 90%. Although M3 (presence of four or more papillary projections) was rare in this cohort (1 case), it achieved perfect predictive accuracy of 100%.

**Table 7.** Prevalence and predictive power of malignant factors. (n = 38)

| Malignant | Predicted | Results | Percentage % |
|---|---|---|---|
| M1 | 7 | 9 | 78.9 |
| M2 | 4 | 5 | 92.9 |
| M3 | 1 | 1 | 100 |
| M4 | 6 | 7 | 94.4 |
| M5 | 14 | 16 | 91.2 |

**Table 8** presents the frequency and diagnostic distribution of combined benign and malignant ultrasound features per IOTA Simple Rules in adnexal masses. Among the 94 cases analyzed, benign features B1 (unilocular cyst), B2 (solid component <7 mm), B3 (acoustic shadows), B4 (smooth multilocular tumors <100 mm), and B5 (absent blood flow, color score 1) were recorded alongside malignant features M1–M5. The most frequent benign features were B2 (13 cases) and B1/B3 (12 each), while malignant features M5 (16) and M4 (7) were most common. Overall, 53/94 (56.4%) cases were benign and 41/94 (43.6%) were malignant.

**Table 8.** Observed combinations of benign and malignant ultrasound features of IOTA simple rules ranked by frequency (n = 94).

| | Applicable B factors | | | | | Applicable M factors | | | | | FREQ | Benign | Malignant | Rate of Malignancy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SN | B1 | B2 | B3 | B4 | B5 | M1 | M2 | M3 | M4 | M5 | | | | |
| | 12 | 13 | 12 | 8 | 12 | 9 | 5 | 1 | 7 | 16 | | 53 | 41 | 43.6% |

## 4. Discussion

The study's findings indicate that applying the IOTA Simple Ultrasound Rules (SR) for diagnosing adnexal masses is a credible and effective method, aligning accurately with the histopathological results. Our findings indicate that IOTA SR is useful for differentiating benign from malignant adnexal masses and will help to manage these patients, especially in Bangladesh, a country with limited access to advanced diagnostic tools. The correlation between the ultrasound features and the histopathology findings underscores the opportunity for ultrasound to be a non-invasive, low-cost option for early diagnosis and pre-operative assessment.

In this tertiary oncology cohort, IOTA Simple Rules (SRs) showed robust diagnostic performance (sensitivity 84.2%, specificity 87.2%, accuracy 85.9%) with an indeterminate rate of 8.5%. Malignancy prevalence was high (43.6%), consistent with referral-center case mix. As high disease prevalence increases the proportion of true malignant cases, it can mathematically lower the negative predictive value (NPV), meaning even a negative test result carries a relatively higher residual risk of malignancy in such settings. Feature-level trends were coherent: multilocularity, mixed/solid composition, and free fluid associated with malignancy, whereas unilocular and cystic morphology favored benign disease. Among single features, B2 (solid components <7 mm) and B3 (acoustic shadows) were strongly predictive of benignity, while M1 (irregular solid tumor) and M5 (very strong Doppler flow) dominated malignant findings.

Our accuracy sits at the lower end of seminal IOTA validations (typically sensitivity/specificity ~90 - 96%) but remains clinically robust [12] [14] [15].The indeterminate proportion (8.5%) closely matches large external validations reporting ~7 - 11% [12] [14] [15]. Consistent with IOTA descriptors, acoustic shadows (B3) were benign-leaning—commonly seen in fibromas or dermoids—while ascites and solid/multilocular-solid architecture tracked with malignancy [12] [15] [21].

Head-to-head and synthesis studies from Asia report comparable or slightly higher performance for SRs and related models. Indian and regional cohorts have shown mid-80s to mid-90s sensitivities/specificities for SRs and ADNEX, even with non-expert examiners [16] [21] [22]. In particular, Khastgir *et al.* found SRs and ADNEX to outperform RMI 4 overall; O-RADS tended to maximize sensitivity but sometimes at the expense of specificity—an effect echoed in systematic comparisons [16] [21] [23]. Against this backdrop, our point estimates are plausible for a high-prevalence oncology setting and align with the directionality of feature-outcome associations reported elsewhere [12] [14]-[16] [21] [23] [24].

Several context factors likely explain the modestly lower sensitivity/specificity than multicenter benchmarks: (i) case mix/prevalence—our malignancy rate of 43.6% can depress NPV and alter decision thresholds; (ii) operator variability—features such as papillary projections (M3), vascular flow scoring (M5), and the recognition of subtle solid components or septations are particularly prone to subjective interpretation, affecting SR accuracy; (iii) equipment and protocol heterogeneity—different platforms and the need to alternate TVS/TAS in large or high-rising masses; and (iv) time to surgery (≤120 days)—interval change in lesion characteristics can introduce verification drift. These factors are typical in LMIC oncology pathways and likely account for part of the gap from idealized multicenter conditions [12] [14] [15] [22].

Indeterminate SR classifications were uncommon (8/94) yet clinically important. In our series, mixed patterns yielded mixed outcomes (e.g., M2 + B2 occurred in three cases, two benign and one malignant), whereas B3 + M4 + M5 skewed malignant and B3+M4 skewed benign. This reinforces standard escalation: apply SRs first; if indeterminate, proceed to a secondary risk tool (e.g., ADNEX) or expert review, as recommended in the IOTA three-step strategy to reduce indeterminacy while preserving specificity [14] [15] [22]. In resource-constrained settings, this tiered approach can focus on oncologic referrals and limit unnecessary laparotomies.

Adnexal masses, particularly ovarian tumors, are a significant clinical challenge because of the difficulty in early diagnosis and the potential for malignancy, especially in low-resource settings like Bangladesh. Many patients present with advanced-stage disease, which is often associated with poorer prognosis and survival rates. For Bangladesh and similar contexts, SRs offer a low-cost, teachable framework with performance that compares favorably to biomarker-heavy indices. Our data echo prior Bangladeshi experience where SRs outperformed RMI 4 against histopathology [20]. Given the high malignancy prevalence in oncology centers, emphasizing structured SR acquisition, Doppler standardization, and brief upskilling on feature recognition could lift sensitivity without sacrificing specificity. Embedding a protocolized fallback (ADNEX or expert adjudication) for indeterminate scans would further streamline triage.

Stratified analyses by menopausal status and histotype, plus decision-curve evaluation, would clarify where SRs add the most net clinical benefit and how to operationalize them across referral tiers.

Considering future research, IOTA SR should be evaluated alongside other indicators like serum CA-125 and contrast-enhanced ultrasound to further improve the ability to differentiate benign from malignant masses. In addition, larger prospective multicenter studies with varied demographics would help validate IOTA SR across different clinical situations and its use in detecting early-stage malignancies. Finally, a review of borderline and uncommon malignancies would help refine the rules and enhance the specificity of the system.

## 5. Strengths and Limitations

This study has several strengths. Its prospective design with histopathology as the gold standard ensured a reliable assessment of diagnostic accuracy. The comprehensive evaluation of all IOTA Simple Rule features, including indeterminate cases, allowed detailed feature-level analysis. Conducted in a tertiary oncology center, the study captured a clinically relevant spectrum of adnexal masses and provides contextually relevant evidence for Bangladesh and other LMIC settings, addressing a critical regional knowledge gap. However, there are notable limitations. The single-center design and relatively small sample size may limit the generalizability of findings. Operator dependence of ultrasound, despite adherence to

IOTA protocols, could introduce variability in feature detection. Referral bias toward complex or high-risk cases may have led to an overrepresentation of malignant lesions, influencing sensitivity and specificity estimates. While the IOTA Simple Ultrasound Rules demonstrated robust diagnostic performance in our cohort, the observed sensitivity (84.2%) and specificity (87.2%) were slightly lower than the ranges reported in large multicenter validations (92 - 96%). This difference may reflect several factors, including the relatively small sample size, single-center design, and operator experience variability. Additionally, as a tertiary oncology center, our cohort likely included a higher proportion of complex or advanced masses, which could affect the performance metrics. These considerations should be considered when interpreting the results and underscore the need for larger, multicenter studies in Bangladesh to confirm generalizability.

## 6. Conclusion

The IOTA Simple Ultrasound Rules demonstrated strong diagnostic performance in differentiating benign and malignant adnexal masses in a tertiary oncology setting in Bangladesh, with high sensitivity, specificity, and overall accuracy. Feature-level analysis confirmed that key sonographic markers such as multilocularity, solid components, and ascites effectively discriminate malignancy, while indeterminate cases highlight the need for careful evaluation. These findings support the feasibility and clinical utility of implementing IOTA protocols in LMIC contexts, potentially improving early detection, guiding appropriate referrals, and reducing unnecessary surgical interventions. However, further large-scale, multicenter studies are warranted to validate these results and ensure broader applicability across diverse healthcare settings.

## Author Contributions

All authors contributed to the development of this work.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Phinyo, P., Patumanond, J., Saenrungmuaeng, P., Chirdchim, W., Pipanmekaporn, T., Tantraworasin, A., *et al.* (2020) Early-Stage Ovarian Malignancy Score versus Risk of Malignancy Indices: Accuracy and Clinical Utility for Preoperative Diagnosis of Women with Adnexal Masses. *Medicina*, **56**, Article No. 702. https://doi.org/10.3390/medicina56120702

[2] Gui, J. (2025) Analysis of Global Ovarian Cancer Disease Burden and Its Changing Trend from 1990 to 2021. *BMC Women's Health*, **25**, Article No. 352. https://doi.org/10.1186/s12905-025-03904-y

[3] Yoeli-Bik, R., Longman, R.E., Wroblewski, K., Weigert, M., Abramowicz, J.S. and Lengyel, E. (2023) Diagnostic Performance of Ultrasonography-Based Risk Models in Differentiating between Benign and Malignant Ovarian Tumors in a US Cohort.

*JAMA Network Open*, **6**, e2323289.
https://doi.org/10.1001/jamanetworkopen.2023.23289

[4] Koirala, P., Moon, A.S. and Chuang, L. (2020) Clinical Utility of Preoperative Assessment in Ovarian Cancer Cytoreduction. *Diagnostics*, **10**, Article No. 568.
https://doi.org/10.3390/diagnostics10080568

[5] Reinert, T., Nogueira-Rodrigues, A., Kestelman, F.P., Ashton-Prolla, P., Graudenz, M.S. and Bines, J. (2018) The Challenge of Evaluating Adnexal Masses in Patients with Breast Cancer. *Clinical Breast Cancer*, **18**, e587-e594.
https://doi.org/10.1016/j.clbc.2018.03.006

[6] Charkhchi, P., Cybulski, C., Gronwald, J., Wong, F.O., Narod, S.A. and Akbari, M.R. (2020) CA125 and Ovarian Cancer: A Comprehensive Review. *Cancers*, **12**, Article No. 3730. https://doi.org/10.3390/cancers12123730

[7] Al Musalhi, K., Al Kindi, M., Al Aisary, F., Ramadhan, F., Al Rawahi, T., Al Hatali, K., *et al.* (2016) Evaluation of HE4, CA-125, Risk of Ovarian Malignancy Algorithm (ROMA) and Risk of Malignancy Index (RMI) in the Preoperative Assessment of Patients with Adnexal Mass. *Oman Medical Journal*, **31**, 336-344.
https://doi.org/10.5001/omj.2016.68

[8] Shin, K., Kim, H., Kwon, B.S., Suh, D.S., Joo, J.K. and Kim, K.H. (2020) Clinical Usefulness of Cancer Antigen (CA) 125, Human Epididymis 4, and CA72-4 Levels and Risk of Ovarian Malignancy Algorithm Values for Diagnosing Ovarian Tumors in Korean Patients with and without Endometriosis. *Annals of Laboratory Medicine*, **40**, 40-47. https://doi.org/10.3343/alm.2020.40.1.40

[9] Moolthiya, W. and Yuenyao, P. (2009) The Risk of Malignancy Index (RMI) in Diagnosis of Ovarian Malignancy. *Asian Pacific Journal of Cancer Prevention: APJCP*, **10**, 865-868.

[10] Tantipalakorn, C., Tinnangwattana, D., Lerthiranwong, T., Luewan, S. and Tongsong, T. (2023) Comparisons of Effectiveness in Differentiating Benign from Malignant Ovarian Masses between Conventional and Modified Risk of Malignancy Index (RMI). *International Journal of Environmental Research and Public Health*, **20**, Article No. 888. https://doi.org/10.3390/ijerph20010888

[11] Stephens, A.N., Hobbs, S.J., Kang, S., Bilandzic, M., Rainczuk, A., Oehler, M.K., *et al.* (2023) A Novel Predictive Multi-Marker Test for the Pre-Surgical Identification of Ovarian Cancer. *Cancers*, **15**, Article No. 5267.
https://doi.org/10.3390/cancers15215267

[12] Timmerman, D., Ameye, L., Fischerova, D., Epstein, E., Melis, G.B., Guerriero, S., *et al.* (2010) Simple Ultrasound Rules to Distinguish between Benign and Malignant Adnexal Masses before Surgery: Prospective Validation by IOTA Group. *BMJ*, **341**, c6839. https://doi.org/10.1136/bmj.c6839

[13] Xie, W.T., Wang, Y.Q., Xiang, Z.S., Du, Z.S., Huang, S.X., Chen, Y.J., *et al.* (2022) Efficacy of IOTA Simple Rules, O-RADS, and CA125 to Distinguish Benign and Malignant Adnexal Masses. *Journal of Ovarian Research*, **15**, Article No. 15.
https://doi.org/10.1186/s13048-022-00947-9

[14] Alcázar, J.L., Vargas, F., Boscá, G., Salazar, B., Aguilar, J.C., Catalan, C., *et al.* (2025) IOTA Three-Step Strategy for Classifying Adnexal Masses: A Systematic Review and Meta-Analysis. *Onco*, **5**, Article No. 22. https://doi.org/10.3390/onco5020022

[15] Hidalgo, J.J., Ros, F., Aubá, M., Errasti, T., Olartecoechea, B., Ruiz-Zambrana, Á., *et al.* (2019) Prospective External Validation of IOTA Three-Step Strategy for Characterizing and Classifying Adnexal Masses and Retrospective Assessment of Alternative Two-Step Strategy Using Simple-Rules Risk. *Ultrasound in Obstetrics & Gynecology*,

**53**, 693-700. https://doi.org/10.1002/uog.20163

[16] Khastgir, G., Siwatch, S., Singh, T., Jain, V., Sikka, P. and Srinivasan, R. (2025) Beyond the Image: Performance of O-RADS, ADNEX, IOTA Simple Rules & RMI 4 in Differentiating Benign and Malignant Adnexal Masses—An Indian Perspective. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, **313**, Article ID: 114585. https://doi.org/10.1016/j.ejogrb.2025.114585

[17] IARC. Bangladesh Fact Sheet. https://gco.iarc.who.int/media/globocan/factsheets/populations/50-bangladesh-fact-sheet.pdf?utm_source=chatgpt.com

[18] Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R.L., Soerjomataram, I., *et al.* (2024) Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA*: *A Cancer Journal for Clinicians*, **74**, 229-263. https://doi.org/10.3322/caac.21834

[19] American Cancer Society. Global Cancer Facts & Figures 5.

[20] Jabin, I., *et al.* (2022) Diagnostic Performance of IOTA-SRs and RMI 4 for Diagnosis of Malignancy in Ovarian Masses: Comparison with Histopathology. *Journal of Chittagong Medical College Teachers' Association*, **33**, 30-36.

[21] Solanki, V., Singh, P., Sharma, C., Ghuman, N., Sureka, B., Shekhar, S., *et al.* (2020) Predicting Malignancy in Adnexal Masses by the International Ovarian Tumor Analysis-Simple Rules. *Journal of Mid-life Health*, **11**, 217-223. https://doi.org/10.4103/jmh.jmh_103_20

[22] Chankrachang, A., Lattiwongsakorn, W., Tantipalakorn, C. and Tongsong, T. (2025) Diagnostic Performance of ADNEX Model and IOTA Simple Rules in Differentiating Malignant from Benign Adnexal Masses When Assessed by Non-Expert Examiners. *Journal of Clinical Medicine*, **14**, Article No. 2776. https://doi.org/10.3390/jcm14082776

[23] Han, J., Wen, J. and Hu, W. (2024) Comparison of O-RADS with the ADNEX Model and IOTA SR for Risk Stratification of Adnexal Lesions: A Systematic Review and Meta-Analysis. *Frontiers in Oncology*, **14**, Article ID: 1354837. https://doi.org/10.3389/fonc.2024.1354837

[24] Su, N., Yang, Y., Liu, Z., Gao, L., Dai, Q., Li, J., *et al.* (2023) Validation of the Diagnostic Efficacy of O-RADS in Adnexal Masses. *Scientific Reports*, **13**, Article No. 15667. https://doi.org/10.1038/s41598-023-42836-1