Research Article

Is Risk Malignancy Index a Useful Tool for Predicting Malignant Ovarian Masses in Developing Countries?

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Introduction. Risk of Malignancy Index (RMI) is widely studied for prediction of malignant pelvic masses in Western population. However, little is known regarding its implication in the developing countries. The objective of this study is to determine how accurately the RMI can predict the malignant pelvic masses.

Materials and Methods. The study is a retrospective review of patients attending the gynecological clinic between January 2004 and December 2008 with adnexal masses. Information on demographic characteristics, ultrasound findings, menopausal status, CA125, and histopathology was collected. RMI score for each patient in the study group was calculated.

Results. The study group included a total of 283 patients. Analysis of the individual parameters of RMI revealed that ultrasound was the best predictor of malignancy with a sensitivity, specificity, and positive likelihood ratio of 78.3%, 81.5%, and 4.2, respectively. At a standard cut-off value of 250, RMI had a positive likelihood ratio of 8.1, while it was 6.8 at a cut-off of 200, albeit with comparable sensitivity and specificity.

Conclusion. RMI is a sensitive tool in predicting malignant adnexal masses. A cut-off of 200 may be suitable in developing countries for triaging and early referral to tertiary care centers.

1. Introduction

Ovarian masses are a frequent cause of gynecological consults and are often detected during imaging studies or exploratory surgery for evaluation of abdominal or pelvic pain syndromes. They occur across age groups and could result from benign or malignant disease. With more than 250,000 new cases reported every year, ovarian malignancies represent the fourth commonest cause of cancer deaths worldwide [1]. They also have the lowest 5-year survival rate (30–50%) among all gynecological cancers [2]. A recent report indicated an increasing incidence of ovarian cancers in the developing world, compared to the developed countries [3].

Early identification of ovarian carcinomas and referral to a gyneco-oncologist can facilitate accurate staging of the disease and optimal cytoreductive treatment, enhancing patient survival [4, 5]. Histopathology remains the diagnostic gold standard for this cancer, and a definitive biomarker has not been identified yet. Risk of Malignancy Index (RMI), which considers the serum CA125 level, menopausal status, and ultrasonographic findings in predicting malignant pelvic masses, is widely employed in the developed countries [6]. However, its utility in risk prediction in the developing countries is currently unknown.

The present study evaluated how accurately the RMI can predict the risk of malignant pelvic masses, among patients with an ovarian mass.

2. Material and Methods

After the approval of our institutional review board we conducted a retrospective review of the case files of patients with adnexal masses who attended the Gynecological Clinic at the Aga Khan University, Karachi, Pakistan, between January 2004 and December 2008. The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) criteria were used to identify adnexal masses. Patients with advanced disease were excluded from the study. We collected information on demographic characteristics, ultrasonographic findings, menopausal status, serum CA125 level, and histopathology. The RMI for each patient was calculated using the standard formula [6].
3. Results

3.1. Demographic Data. The study group consisted of a total of 283 patients. The age of the patients varied from 8 to 85 years (mean, 38.6 years). Premenopausal patients predominated in our study with 227 (80.8%) cases, while 54 (19.2%) of the affected patients were in the postmenopausal group.

3.2. Ultrasonography Findings. Two hundred and seven (73.7%) patients had a transabdominal ultrasonography for diagnosis, while transvaginal ultrasonography detected the disease in 74 (26.3%) cases. Table 1 shows the summary of ultrasound findings in our patients.

3.2.1. Laterality of Lesion. The investigation revealed a unilateral cyst in 252 (89.7%) cases, while 29 (10.3%) had bilateral cysts.

3.2.2. Loculation. The lesions were multilocular in 166 (59%) patients and unilocular in 115 (41%).

3.2.3. Echogenicity. Solid areas were absent in the lesions in 196 (69.8%) patients, while these were detected in 85 (30.2%) patients.

3.2.4. Evidence of Metastasis. The majority of patients (272, 96.8%) had no evidence of metastasis, while 9 (3.2%) had metastatic disease.

3.2.5. Presence of Ascites. Ascites was present in only 19 (6.8%) patients.

3.2.6. Ultrasound Score. We assigned scores of 0 (absence of specific findings), 1 (presence of one finding), or 3 (two or more findings) to the subjects, depending on the ultrasound findings. One hundred and nineteen (42.3%) cases had an ultrasound score of 1, while lesions of 88 (31.3%) and 74 (26.3%) patients were scored 0 and 3, respectively. Of the 207 (73.6%) patients with an ultrasound score 1, 196 (69.7%) had benign disease, while 8 (2.8%) and 3 (1%) had malignant and borderline disease, respectively. Seventy-four (26.3%) patients in our series had an ultrasound score of 3, and among them, 41 (14.5%) had benign, 29 (10.3%) had malignant, and 4 (1.4%) had borderline disease, respectively.

3.2.7. Ovarian Size. Ovarian size varied from 3 to 73 cm (mean, 10.5 cm).

3.3. Histopathology Findings. As shown in Table 2, 237 (84.3%) patients had benign lesions, while 37 (13.2%) had a malignant disease. Seven (2.5%) patients under 60 years of age had borderline lesions. One hundred and thirty-nine (49.4%) of the benign tumours occurred in patients aged 20 to 39 years, and 60 (21.3%) cases were in those aged 41–59 years. Patients aged ≤20 years and ≥60 years reported 24 (8.5%) and 14 (4.9%) cases of benign disease, respectively. Malignant disease peaked in the age group 40–59 years with 21 (7.4%) cases, while 10 (3.5%), 4 (1.4%), and 2 (0.7%) cases occurred among patients aged ≥60 years, 20–39 years, and ≤20 years, respectively. Three cases of borderline disease occurred in the age groups 21–39 and 40–59 years, and one (0.3%) case was in a woman aged ≤20 years, while such lesions were not detected in women ≥60 years. Two hundred and three (72.2%) of the 227 premenopausal patients had benign disease, while 18 (6.4%) had malignant, and 6 (2.1%) had borderline lesions. Among the 54 (19.2%) postmenopausal patients, 34 (12%) had benign disease, while 19 (6.7%) and 1 (0.3%) had malignant and borderline disease, respectively.

3.4. Serum CA125 Levels. The serum CA125 levels in the patients varied from 1.2 to 6803 U/mL (mean, 197 U/mL) (Table 2). One hundred and seventy-six (62.6%) patients had a serum CA125 level less than 35 U/mL, while the levels

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**Table 1: Summary of ultrasound findings in the study.**

| Frequency | Percentage (%) |
|-----------|----------------|
| Transabdominal scan | 207 | 73.7 |
| Transvaginal scan | 74 | 26.3 |
| Unilateral cyst | 252 | 89.7 |
| Bilateral cyst | 29 | 10.3 |
| Unilocular cyst | 115 | 41.0 |
| Multilocular cyst | 166 | 59.0 |
| Presence of solid areas | 85 | 30.2 |
| Absence of solid areas | 196 | 69.8 |
| Evidence of metastasis present | 9 | 3.2 |
| Evidence of metastasis absent | 272 | 96.8 |
| Presence of ascites | 19 | 6.8 |
| Absence of ascites | 262 | 93.2 |
| Ultrasound score 0 | 88 | 31.3 |
| Ultrasound score 1 | 119 | 42.3 |
| Ultrasound score 3 | 74 | 74 |

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**Table 2: Distribution of cases in the study.**

| Benign (%) | Borderline (%) | Malignant (%) | Total (%) |
|------------|---------------|--------------|-----------|
| Histopathology | 237 (84.3) | 7 (2.5) | 37 (13.2) | 281 |
| Age (years) | | | | |
| ≤20 | 24 (8.5) | 1 (0.3) | 2 (0.7) | 27 (9.6) |
| 20–39 | 139 (49.4) | 3 (1.0) | 4 (1.4) | 146 (51.9) |
| 40–59 | 60 (21.3) | 3 (1.0) | 21 (7.4) | 84 (29.8) |
| ≥60 | 14 (4.9) | 0 (0) | 10 (3.5) | 24 (8.5) |
| Premenopausal | 203 (72.2) | 6 (2.1) | 18 (6.4) | 227 (80.7) |
| Postmenopausal | 34 (12.0) | 1 (0.3) | 19 (6.7) | 54 (19.2) |
| Ultrasound score 1 | 196 (69.7) | 3 (1.0) | 8 (2.8) | 207 (73.6) |
| Ultrasound score 3 | 41 (14.5) | 4 (1.4) | 29 (10.3) | 74 (26.3) |
| CA125 ≥ 35 | 75 (26.6) | 4 (1.4) | 26 (9.2) | 105 (37.3) |
| CA125 < 35 | 162 (57.6) | 3 (1.0) | 11 (3.9) | 176 (62.6) |
| RMI groups | | | | |
| ≤25 | 117 (41.6) | 0 (0) | 3 (1.0) | 120 (42.7) |
| 25.1–249.9 | 106 (37.7) | 5 (1.7) | 14 (4.9) | 125 (44.4) |
| ≥250 | 14 (4.9) | 2 (0.7) | 20 (7.1) | 36 (12.8) |
we also compared the diagnostic performance of RMI scores ≥250 against CA125 levels >35 U/mL, ultrasound score of 3 and menopausal score of 3. Table 4 summarizes the findings from this analysis. Among the three criteria, an ultrasound score of 3 had the highest specificity (78.3%), while an RMI score ≥250 had the highest sensitivity (93.4%). The latter also had the highest positive predictive value of 55.5%, while negative predictive value was highest for an ultrasound score of 3 (96.1%). The positive likelihood ratio was highest for RMI score ≥250, while a score of 100 had the least negative likelihood ratio (0.39).

### 4. Discussion

About 10% of women undergo exploratory surgery for evaluation of ovarian masses during their lifetime [7]. Prompt identification of ovarian malignancies and referral to a gyneco-oncologist can enhance the patient survival rates [8], but a single method which can accurately predict ovarian malignancy is still unavailable. Herein we report that the multiparametric RMI score can be a useful tool in prediction of malignant ovarian disease, in low-resource settings.

The mean age of the patients with ovarian mass in our study was 36.87 years (range, 8 to 85 years). This is slightly higher than that reported in a similar study by Akdeniz et al. in 2009 [9].

In our study, 13.2% of the patients with an ovarian mass had malignant disease. Thirty-five percent of malignancies occurred in postmenopausal patients and 7.9% among the premenopausal patients. The data seem to agree with earlier reports of similar incidence rates and preponderance in postmenopausal patients [9–12].

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Table 3: Diagnostic performance of the different RMI cut-offs employed.

| RMI cut-off value | Sensitivity % | Specificity % | PPV (%) | NPV (%) | +LR ratio | −LR ratio |
|------------------|--------------|--------------|---------|---------|-----------|----------|
| 250              | 54.05 (20/37) | 93.4 (228/244) | 55.5 (20/36) | 93.06 (228/245) | 8.1 | 0.49 |
| 200              | 53.8 (21/39) | 92.2 (225/244) | 52.5 (21/40) | 92.5 (225/243) | 6.8 | 0.50 |
| 150              | 61.5 (24/39) | 89.3 (218/244) | 48.0 (24/50) | 93.5 (218/233) | 5.7 | 0.43 |
| 100              | 66.6 (26/39) | 84.0 (205/244) | 40.0 (26/65) | 94.0 (205/218) | 4.1 | 0.39 |

Table 4: Diagnostic performance of the criteria evaluated.

|                | Sensitivity % | Specificity % | PPV (%) | NPV (%) | +ve likelihood ratio | −ve likelihood ratio |
|----------------|--------------|--------------|---------|---------|---------------------|---------------------|
| RMI ≥ 250      | 54.05 (20/37) | 93.4 (228/244) | 55.5 (20/36) | 93.06 (228/245) | 8.1 | 0.49 |
| CA125 ≥ 35     | 70.2 (26/37) | 67.6 (165/244) | 24.7 (26/105) | 93.7 (165/176) | 2.1 | 0.44 |
| Ultrasound score 3 | 78.3 (29/37) | 81.5 (199/244) | 39.1 (29/74) | 96.1 (199/207) | 4.2 | 0.26 |
| Menopause score 3 | 51.3 (19/37) | 85.6 (209/244) | 35.1 (19/54) | 92.0 (209/227) | 3.5 | 0.56 |
Ultrasonography is widely appreciated as the best imaging method for evaluation of ovarian pathology. Several groups have reported higher sensitivity, specificity, and positive predictive values for this method (Agarwal et al., 2011, and references therein). In our study, an ultrasound score of 3 had the highest sensitivity (78.3%) and negative predictive value (96.1%) and the least negative likelihood ratio (0.26), among the parameters evaluated.

Several candidate biomarkers and their combinations have been employed in assessing the risk of ovarian malignancies, albeit with varying efficiency [13]. Serum CA125 level have been employed in assessing the risk of ovarian malignancies, and the parameter evaluated. The authors declare that there is no conflict of interests regarding the publication of this paper.

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We conclude that, in the absence of a definitive biomarker, the multiparametric Risk of Malignancy Index serves as a very useful tool for identification of malignant ovarian disease and their prompt triage and referral to expert care.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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