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Short Communication

The risk of malignancy index (RMI) in women with adnexal masses in Wales

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ABSTRACT

Objective: To evaluate the accuracy of the risk of malignancy index (RMI) which combines serum CA-125 levels, ultrasound score, and menopausal state, in discriminating between benign and malignant adnexal masses in the Welsh population.
Materials and methods: Two hundred and forty-seven women with pelvic masses discussed consecutively at the South West Wales Gynaecological Oncology multidisciplinary meeting between January 2010 and June 2011 were included in this retrospective study. The main outcomes were surgical and pathological findings.
Results: The sensitivity and specificity of CA-125 at 35kU/L were 76% and 67%, respectively. CA-125 was found to be a relevant predictor of malignancy but the area under the receiver operating characteristic curve for each of the risk of malignancy indices was greater than the area for the CA-125 serum levels alone. Each of the RMIs has a different optimal threshold, however using a threshold of 200, RMI 1 had a sensitivity of 66% and a specificity of 91%; RMI 2 had a sensitivity of 74% and a specificity of 79%; and RMI 3 had a sensitivity of 68% and a specificity of 85%.
Conclusion: This is the first study in Wales to evaluate the RMI in triaging women with pelvic masses. Overall, RMI 1 and RMI 2 are better malignancy predictors than RMI 3. It would be recommended that RMI 1 and RMI 2 be compared in a head-to-head prospective study, although we suspect that RMI 1 is likely to be the overall best malignancy predictor.

Introduction

Ovarian cancer is a common gynaecological malignancy with a high mortality. In 2008, the disease was diagnosed in approximately 225,000 women worldwide, accounting for approximately 4% of all cancers diagnosed in women with corresponding 140,000 deaths [1]. In Wales, 373 women received a diagnosis of ovarian cancer in 2007, increasing by more than 5% in 2008 to 392 [2]. Ovarian cancer is more common in older women, with the highest incidence in those aged 75–79 years. [2]. Despite of advances in chemotherapy, ovarian cancer remains a lethal disease. This is because the disease is usually diagnosed at an advanced stage because most of the symptoms are nonspecific; hence, the difficulty in diagnosis at early stages. More than 60% of women presenting with ovarian cancer have Stage III or IV cancer when metastasis is already present, with 5-year relative survival of just 27% [3]. Only 15% of women present when the malignancy is still localized, with a 5-year relative survival of 92% [3].

Ovarian tumors present with a variety of symptoms, including abdominal pain, abdominal or adnexal mass, bloating, urinary urgency, and abnormal vaginal bleeding. Such clinical presentation could be caused by a number of different benign and malignant conditions. As a result, it usually poses a challenge to the gynecologist to distinguish between benign and malignant tumors. Consequently, there has been vigorous research into ovarian cancer screening methods and diagnostic tools. In 1990, Jacobs et al [4] developed the risk of malignancy index (RMI) after assessing how age, ultrasound score, menopausal status, clinical impression score, and serum CA-125 level could best distinguish between patients with benign and malignant pelvic masses. They noted that each criterion used alone provided statistically significant discrimination, with the most useful

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individual criteria being serum CA-125 level of 30 U/mL (sensitivity 81%, specificity 75%) and an ultrasound score of 2 (sensitivity 71%, specificity 83%) [4]. Jacobs et al therefore proposed that the combination of three criteria in an RMI is an effective tool to distinguish between cancer and benign lesions and is calculated using the product of the serum CA-125 level (U/mL), the ultrasound result (expressed as a score of 0, 1, or 3) and the menopausal status (1 if premenopausal and 3 if postmenopausal). By using an RMI cutoff level of 200, the sensitivity was 85% whereas the specificity was 97%, and patients with an RMI score of more than 200 had, on average, 42 times the background risk of cancer compared to 0.15 times the background risk in those with a lower score [4]. Tingulstad et al [5,6] developed modified RMI in 1996 (RMI 2) and 1999 (RMI 3), with differences mainly in scorings of ultrasound findings and menopausal status.

Although the Guideline Development Group of the National Institute for Health and Clinical Excellence (NICE) suggested that RMI 1 was the most useful index at identifying women with ovarian cancer compared to other malignancy indices in secondary care, it noted that current evidence did not indicate the optimum cutoff score to use for guiding management [7]. It therefore recommended that further research should be undertaken to determine the optimum threshold for RMI 1 that should be applied in secondary care to guide the management of women with suspected ovarian malignancy [7].

The purpose of this study is to evaluate the accuracy of the RMI, which combines serum CA-125 levels, ultrasound score, and menopausal state, in distinguishing between benign and malignant pelvic masses in the Welsh population. Although studies have validated the RMI in various populations [8–15], none has been done in Wales. This study is also aimed at determining the optimum threshold for the three RMIs. The long-term aim is to have a unified risk scoring system across Wales.

Materials and methods

The Abertawe Bro Morgannwg University Health Board is one of the largest health boards in Wales serving a population of approximately 600,000 covering the areas of Bridgend, Neath Port Talbot, and Swansea in South West Wales, United Kingdom. The Gynaecology Multidisciplinary Team (MDT) is based at the Singleton Hospital in Swansea, which is a 550-bed district general hospital. In addition to patients from Singleton Hospital, the Gynaecology MDT also discusses patients referred from seven other National Health Service (NHS) hospitals and many private clinics.

The Trust's database was used to identify women who had been referred to the gynecological oncology unit for management of pelvic mass and were discussed at the Multidisciplinary Meeting (MDM) over an 18-month period between January 2010 and June 2011. A total of 328 patients were identified in the database. Fifteen of the records were either incomplete or unavailable for review. Fifty-three of the remaining charts did not have an ultrasound examination and CA-125 was not recorded in six of the charts. Seven of the patients did not have both ultrasound examination and CA-125 recorded. Hence, a total of 247 patients were included in this retrospective review.

Three versions of RMI were compared, each incorporated serum CA-125 level, menopausal status, and ultrasound findings (Table 1). To calculate the RMI, the formula *serum CA-125 x M x U* is used. Serum CA-125 is the assayed level of the tumor marker expressed in kU/L, M refers to the menopausal status of the patient, and U is the ultrasound score.

In Singleton Hospital, CA-125 is considered normal if it is < 35 kU/L and it is commonly measured in women presenting with adnexal masses.

Table 1
The three versions of RMI compared in this study.

	M	U
RMI 1 [4]	1 if premenopausal 3 if postmenopausal	0 if no abnormality 1 if one abnormality 3 if ≥ 2 abnormalities
RMI 2 [5]	1 if premenopausal 4 if postmenopausal	1 if ≤ 1 abnormality 4 if ≥ 2 abnormalities
RMI 3 [6]	1 if premenopausal 3 if postmenopausal	1 if ≤ 1 abnormality 3 if ≥ 2 abnormalities

M = menopausal status; RMI = risk of malignancy index; U = ultrasound score.

Ultrasound score is computed based on the presence or absence of five features – multiloculated cyst, evidence of solid areas, bilateral lesions, presence of ascites, and evidence of metastases. In RMI 1, U = 0 if none of these features is present, 1 if one feature is present, and 3 if two or more features are present. For RMI 2, U = 1 if none or one feature is present and 4 if two or more features are present. In RMI 3, U = 1 if none or one feature is present and 3 if two or more features are present.

Surgical specimens are usually sent for histology and the results of patients included in this study were documented. In some cases where the lesion was considered benign from imaging review, resulting in no surgical intervention, the diagnosis was assumed to be correct (for example, ovarian cyst not otherwise specified).

The data were analyzed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago). A p-value of < 0.05 was considered statistically significant using Pearson Chi-square test. A receiver operating characteristic (ROC) curve was produced to show the relation between sensitivity and specificity of the RMI in distinguishing between benign and malignant masses. The closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test [16].

Results

Two hundred forty-seven women with adnexal masses were included in this retrospective study with a mean age of 58.09 years (range 19–95 years). One hundred sixty of the women had benign masses, whereas 87 women had malignant masses, giving a ratio of 2:1. Eighty patients were premenopausal, of whom 59 had benign masses and 21 had malignant masses. The number of postmenopausal women was 167 and of these, 101 had benign lesions whereas 66 had malignant neoplasm. The average age of women with benign lesions was 56.96 ± 17.991 years [95% confidence interval (CI), 54.15–59.77] and the average age for women with malignant masses was 60.16 ± 15.6 years (95% CI, 56.84–63.49). Postmenopausal women have a higher incidence of both benign and malignant lesions ($p = 0.041$). The 51–60 age group had the highest incidence of ovarian malignancy ($n = 23$).

The presence of ascites on ultrasound examination was significantly associated with a higher possibility of malignant adnexal mass ($p < 0.001$). There was no association between parity and pelvic mass ($p = 0.748$).

Of the 87 women in whom malignant masses were diagnosed, the International Federation of Gynecology and Obstetrics stage was not recorded in 13 patients. Most of the patients presented at Stage I ($n = 41$), four presented at Stage II, 17 presented at Stage III, and 12 presented at Stage 4 (Fig. 1). Most of the patients had Stage Ia malignant disease ($n = 25$), whereas 13 patients presented at Stage IIIc; 15 patients had Stage Ic malignant disease, whereas four patients presented with Stage IIb disease. Only one patient presented at Stage Ib and three presented at Stage IIIb. None presented at Stage IIa, IIc, or IIIa. In one patient, it was concluded that the