ORIGINAL ARTICLE

Evaluation of the diagnostic performance of the Malignant Risk Index II in women with adnexial mass diagnosis in a third level hospital

Evaluación del desempeño diagnóstico del Índice de Riesgo de Malignidad II en mujeres con diagnóstico de masa anexial en un hospital de tercer nivel

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Abstract

Objective*: Evaluate the usefulness of the Malignancy Risk Index II (MRI II) using diagnostic accuracy variables in 100 patients diagnosed with adnexal mass.* **Method:** *In a sample of 100 patients with a diagnosis of adnexal mass, demographic variables were quantified, and MRI II was applied. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were obtained using a 2 x 2 table and compared with the histopathological result.* **Results:** *MRI II with a positive result was presented in 73.1% (52 patients) with malignant histopathological result and in 26.9% of patients with benign histopathological result. It presents a sensitivity in the test of 73.1%, a specificity of 70.8%, positive and negative predictive value of 73.2 and 70.8%, respectively. Diagnostic accuracy of 72%.* **Conclusions***: MRI II is a screening tool with acceptable diagnostic performance to regulate behavior, such as referring to a specialized center or requesting more specific studies in patients diagnosed with adnexal mass due to suspected malignancy.*

Keywords: *Adnexal mass; Antigen CA-125; Ovarian cancer.*

Resumen

Objetivo: *Evaluar la exactitud diagnóstica del Índice de Riesgo de Malignidad II (IRM II) en 100 pacientes con diagnóstico de masa anexial.* **Método:** *En una muestra de 100 pacientes con diagnóstico de masa anexial se cuantificaron variables demográficas y se aplicó el IRM II. Mediante una tabla 2 × 2 se obtuvieron la sensibilidad, la especificidad, el valor predictivo positivo, el valor predictivo negativo y la exactitud diagnóstica, y se compararon con el resultado histopatológico.* **Resultados:** *El IRM II con resultado positivo se presentó en el 73.1% (52 pacientes) de los casos con resultado histopatológico maligno y en el 26.9% de aquellos con resultado histopatológico benigno. Presenta una sensibilidad en la prueba del 73.1%, una especificidad del 70.8%, un valor predictivo positivo del 73.2% y un valor predictivo negativo del 70.8%. La exactitud diagnóstica es del 72%.* **Conclusiones:** *El IRM II es una herramienta de cribaje con aceptable desempeño*

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diagnóstico para normar la conducta, como referir a un centro especializado o solicitar estudios más específicos en pacientes con diagnóstico de masa anexial por sospecha de malignidad.

Palabras clave: *Masa anexial. Antígeno CA-125. Cáncer de ovario.*

Introduction

Adnexal masses (tumors of the ovary, uterine tubes, and tissue adjacent to adnexa) are a common gynecological problem that can occur at all ages. In the United States of America, a 5-10% risk of developing an adnexal mass in the course of a woman's life is estimated[1]. An observational study of 335 asymptomatic women aged 25 to 40 years, an adnexal mass prevalence of 7.8% was found[2]. In another series of 8,794 asymptomatic postmenopausal women, 2.5% had a simple unilocular cyst[3].

Adnexal mass approach focuses on determining probable etiology based on anatomical location, age, and reproductive status. These masses can be symptomatic or not, and the importance of their study at all ages is to determine if it is a pathology that requires urgent care (ectopic pregnancy or twisted ovarian cyst) or ruling out the presence of a malignant tumor. In this situation, an appropriate approach becomes important, since ovarian cancer is currently a disease with a growing incidence in the world and of high lethality, since the clinical manifestations that motivate the search for medical attention occur at advanced stages.

Ovarian cancer is one of the neoplasms with the highest incidence in women. Worldwide, it continues to rank fifth, and third in Mexico, corresponding to 3.9%. By age groups, it ranks first in females younger than 19 and between 20 and 29 years of age, to then drop to third place at 30-69 years of age. Worldwide, it is the most common cause of cancer death in women[4]. Currently, according to statistics from the International Agency for Research on Cancer (IARC) reported in 2018 (GLOBOCAN), ovarian cancer in Mexico accounts for 2.5% (4,759 cases) of new cases, and for 3.3% of cancer deaths (2,765 deaths) in Mexico[5].

According to the National Cancerology Institute of Mexico, during the 2000-2004 period, ovarian cancer accounted for 3.9% of malignant neoplasms in women, only preceded by breast (17.5%) and cervical (14.7%) cancers[6,7].

In Oaxaca, according to reports by the National Institute of Statistics, Geography and Information (INEGI – *Instituto Nacional de Estadística Geografía e Información*), in 2009 there were 1,691 deaths from epithelial ovarian cancer (2.4% of total cancer deaths)[8].

Most women with ovarian cancer do not have any associated risk factors or symptoms at early stages. Currently, screening interventions are limited and do not show a sustainable level of evidence to be applied to the general population. Since epithelial ovarian cancer is the most common histological lineage, in up to 95% of cases[9], much of the research focuses on the development of markers or screening methods that enable detecting it at early stages or confined to the pelvis. Different low sensitivity and specificity markers are available, but tools have been developed that combine various biochemical markers, as well as risk factors, which increase overall sensitivity and specificity[10]. The Risk of Malignancy Index (RMI II) is a scale that allows to raise malignancy suspicion in adnexal masses through transvaginal ultrasound findings, cancer antigen 125 (CA-125) serum concentration and patient menopausal status (Table 1). This index is conventionally used in the European population (National Institute for Health and Care Excellence guidelines), but there are only few studies on its usefulness in the Mexican population.

Method

A retrospective, cross-sectional, analytical, diagnostic test-type study was carried out in 100 women diagnosed with adnexal mass between January 2015 and January 2017.

For the development of the study, demographic data, menopausal status, laboratory (serum CA-125 concentrations) and ultrasonography results (mass size) and adnexal mass histopathological analysis findings (standard) were obtained.

A descriptive analysis of variables was performed with RMI II results sensitivity, specificity, positive predictive value, negative predictive value and diagnostic test accuracy measurement in comparison with the standard (adnexal mass histopathology result) in a 2 x 2 table (Table 2).

Table 1. Risk of Malignancy Index II

Parameter	Value
CA-125	CA-125 serum concentration=CA-125 U/mL
Menopausal status (M) (amenorrhea>1 year)	Premenopausal M=1 Postmenopausal M=4
Ultrasound evaluation (U)	Multilocularity Presence of solid areas Bilaterality Ascites Extra-ovarian tumors One point is given for each If there are 2 or more points, U=4 If there are less than 2 points, U=1
Risk of malignancy index=CA-125 x M x U	
A value > 200 is an indication for referral to a tertiary care center	

Adapted from Tingulstad *et al*.[20]

Table 2. 2 x 2 table

RMI II pathology report	Positive	Negative	Total
Positive	38	14	52
Negative	14	34	48
Total	52	48	100
Sensitivity	73%		
Specificity	70.8%		
Positive predictive value	73%		
Negative predictive value	70%		
Diagnostic accuracy	72%		

Results

One hundred women diagnosed with adnexal mass over a 2-year period in a tertiary care hospital were analyzed. Regarding demographic variables, median age was 48.6 ± 17.5 years. The most common initial symptom in 57% of patients was abdominal pain, followed by abdominal perimeter increase in 28% (Table 3). Tumor mean longest diameter was directly proportional to histopathological malignancy result, with a mean of 70.9 mm for malignant results and 43 mm for benign histopathological reports.

Diagnostic performance of the test in our population yielded a sensitivity of 73.1%, specificity of 70.8%, a positive predictive value of 73.2% and a negative predictive value of 70.8%. Diagnostic accuracy was 72% (Table 2).

Table 3. Results

Variable	Result*
Age, years	48.6 ± 17.5
Body mass index	26.7 ± 8.1
Menarche	13.2 ± 1.5
Age at sexual activity initiation	17.6 ± 6.0
Pregnancies, median (IQR)	2.0 (1.0-4.0)
Menopause, n (%)	60 (60)
Initial symptom, n (%)	
Pain	57%
Abdominal perimeter increase	28%
Uterine bleeding	10%
Largest tumor size, median (IQR)	14.0 (8.8-78.0)
Smallest tumor size, median (IQR)	55.0 (15.8-296.0)
RMI, median (IQR)	209.0 (54.6-1752.0)

RMI: Risk of Malignancy Index; IQR: interquartile range.
*Variables expressed as means±standard deviation, except where otherwise specified.

Discussion

It has been estimated that 1-2% of women will develop ovarian cancer throughout their lives[11,12], but the lethality associated with this disease is high. Symptoms appear at advanced stages and are non-specific; up to 75% of cases have been reported to be diagnosed at advanced stages[13]. The approach for ruling out malignancy is carried out in two sequential steps: clinical suspicion established by screening measures and surgical exploration that offers a definitive diagnosis[14]. Clinical suspicion is established by imaging studies, age, menopausal status, risk factors and biochemical tests[15]. Separately, each of these approaches has a low sensitivity and specificity, which do not offer advantages that improve clinical suspicion, which is why current research is focused on obtaining a tool that has sufficient diagnostic accuracy to be able to raise the suspicion of malignancy in women who present with an adnexal mass based on different available biochemical, clinical and imaging markers[16].

In 1990, Jacobs et al.[17,18] designed the RMI, a screening method that evaluates patient menopausal status, ultrasound findings, and CA-125 serum concentration[17,18]. Subsequently, in an effort to improve its sensitivity and specificity, Tingulstad et al.[19] created a new version, RMI II (Table 1), in which the score obtained by ultrasound images was modified, which produce a total of 4 points when at least two characteristics

by this method are present. When the multiplication result is ≥ 200, the suspicion that the adnexal mass is of malignant origin is very high and the patient should be referred to a specialized center for early approach and treatment. There are already different series in the world on the use of this malignancy index, which award it with sensitivity rates ranging from 89% to 96% depending on the investigated population, and specificity rates ranging from 86.2% to 91% (slightly higher than that obtained in our study)[20-23].

In Mexico, the evidence on the use of this index and its usefulness for adnexal masses discrimination is scarce and most of it originates from retrospective studies, as it is the case of this work. In this sense, it is worth mentioning the retrospective study carried out by Treviño-Báez et al.[24], in which they found a sensitivity of 86.7% and a specificity of 94.9%, with a diagnostic accuracy of 81.9% for detecting patients with a malignant adnexal neoplasm. In 2009, Yamamoto et al.[25] linked the tumor size to the risk of malignancy, and found a directly proportional relationship. In our study, a mean of 43 mm for tumor longest diameter was found for a benign histopathological result and a mean of 70.9 for a malignant pathological result.

Clinical and cost-benefit advantages are evident, and this opens the possibility to implement systematic use of this index in emergency services and outpatient clinics in order to identify patients who require specialized evaluation, since in some populations, RMI II has been observed to have satisfactory efficiency for classifying postmenopausal women with adnexal tumors, both benign and malignant, and thus enable offering some of the minimally-invasive treatment modalities, which is safe and with better results[26].

Conclusions

Ovarian cancer is a major threat to the health of women in the State of Oaxaca, Mexico, and all over the world due to its high incidence and prevalence, as well as associated complications and diagnostic delay due to its non-specific signs and symptoms, which generate high costs for the country and are deleterious for health indicators.

The present study allows us to know that RMI II, as a tool for discriminating malignant and benign adnexal masses, is better in precision than many clinical or imaging or laboratory parameters alone, simple to apply, low-cost, and available at any secondary and tertiary care center. The RMI II has a sensitivity, a specificity, a negative predictive value, a positive predictive value and a diagnostic accuracy that, although lower than those obtained by Jacobs et al.[17,18], are acceptable (diagnostic accuracy of 72%) in our patients, which is why its regular use can be put into practice in our unit for patients diagnosed with adnexal masses.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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