

RESEARCH ARTICLE

Ovarian Malignancy Probability Score (OMPS) for Appropriate Referral of Adnexal Masses

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Abstract

Background: Ovarian cancer is the most common cancer cause of gynecologic cancer deaths. In order to increase the likelihood of patient survival through primary operation by gynecologic oncologists, an appropriate algorithm for referral is considered here. **Materials and Methods:** Suspicious adnexal mass cases including ovarian malignancy probability score-1 (OMPS1) scores between 2.3-3.65 are re-evaluated by OMPS2. Sensitivity and specificity of each score were determined. **Results:** Sensitivity and specificity with a 3.82 score of OMPS2 in the studied subgroup (OMPS1 scores between 2.3-3.65) were 64% and 76.9% respectively. **Conclusions:** Management of OMPS1 scores of below 2.3 with sensitivity of 100% and above 3.65 with specificity of 72.9% is clear. In the subgroup of cases with OMPS1 score between 2.3-3.65, OMPS2 is helpful for triage with a cutoff score of 3.82.

Keywords: Ovarian cancer - adnexal mass - probability score - centralized care - prediction

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Introduction

Ovarian cancer is the fifth cancer cause of female cancer death. Due to its high fatality, ovarian cancer is the most common cause of gynecologic cancer deaths (Eltabbakh, 2004; Le et al., 2009; Arab et al., 2014). First visit of women with pelvic masses is usually by a general gynecologist or surgeon. Benign and malignant conditions are probable in adnexal mass cases, which are definitely diagnosed and treated just by surgery. Primary surgery of the ovarian cancer is the most critical part of treatment to increase survival (Arikan et al., 2014).

Most studies confirm that in case the operation of ovarian cancer is done by a Gynecologic oncologist, the best survival shall be achieved (Eisenkop et al., 1992; Mayer et al., 1992; Le et al., 1997). On the one hand, adnexal mass patients' referral to Gynecologic oncologists might bring them stress of travel and difficulty for doing follow-ups in relation with the operation. Referral of pelvic mass cases are challenging for gynecologists and general surgeons.

Optimal arrangement would be referral of all ovarian cancer cases and then few benign cases are operated by Gynecologic oncologists (McGowan, 1993).

So, differentiation between benign and malignant ovarian tumors is the main decision to make. Measuring serum CA125 is the most effective single test which enables to predict malignancy of ovarian tumors (Gadducci et al., 1992). In 80% of advanced ovarian cancer cases, serum CA125 increases, while it increases just in 50-60% of early stage cases (Posadas et al., 2004).

Also, serum CA125 increases in some benign conditions in younger patients (Lewandowski, 2003; Moss et al., 2005). In this regard, just serum CA125 measurement is not enough to distinguish which adnexal masses are candidates for referral, particularly in young women (Moss et al., 2005).

Some of the guidelines suggest using serum CA125 level and other items in order to properly discriminate benign from malignant cases (Jacobs et al., 1990). Many studies, as mentioned above, have reported better survival of ovarian cancer patients if operated in primary surgery by a gynecologic oncologist, who is the most qualified person to do staging and cyto-reduction. "MC Gowan" reported the chance for complete staging to be 97% when done by Gynecologic oncologists, as compared with 50% chance by gynecologists and 35% by general surgeons (McGowan, 1993). Optimal debulking increases survival chance for advanced stage patients by 30-40% in comparison to 0-15% increase by suboptimal debulking (Bristow et al., 2002).

"Risk of malignancy index" (RMI1) is a simple schema, revised as RMI2 (with little changes), which was reported by Jacobs et al. (1990), has a sensitivity of 85.4% and specificity of 96.9%. Items of RMI include serum CA125 level, menopausal status and sonographic findings. Five parameters of sonographic findings in favor of malignancy which take score of (U) are as follows: multiloculation, solid area, bilaterality, ascitis and metastasis clue. All of patients with RMI above 200 are recommended for referral.

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$$RMI = U \times M \times \text{Serum CA125}$$

RMI₂ Score is more sensitive compared to RMI₁, with specificity of 89-92% and positive predictive value (PPV) of 80% (Gadducci et al., 1992).

An OMPS1 is constructed based on a multi-center study of 3303 operated Ovarian masses. OMPS is calculated in the following way (Arab et al., 2012):

Age × 0.062 + tumor size (cm) × 0.012 + 1.172 (if solid) + 1.289 (if ascites) + 0.758 (if bilateral) with the score number of 3.65 as cut off value of malignancy prediction by OMPS1, the sensitivity of 77.9% and specificity of 72.9% are achieved (Arab et al., 2012). Revised OMPS1, called as OMPS2, is calculated in the following way (Arab et al., 2012):

OMPS₁ + 1.444 (if CA125=36-200) or 3.842 (if CA125>200)

Guidelines of SGO and ACOG (ACOG, 2002) for adnexal mass referral are presented in the following two groups: *i*) Premenopausal (below 50 years old) including: CA125>200 U/ml; Ascites; Metastasis clue (clinical or image- based); History of breast or ovarian cancer in first degree family members. *ii*) Postmenopausal (equal or above 50 years old) including: CA125>35 U/ml; Ascites; Nodularity or fixed tumor; Metastasis clue (clinical or image- based); History of breast or ovarian cancer in first degree family members.

As it was mentioned above, most of adnexal mass malignancy prediction and referral guides have some error. So, if all adnexal masses are operated by tertiary medical centers and gynecologic oncologists as recommended by National Comprehensive Cancer Network (NCCN) guides (du Bois et al., 2005, Earle et al., 2006, Giede et al., 2005), these centers might be crowded by patients in the waiting list for surgery. Referral and prediction of malignancy criteria based on the region of practice is mentioned (Yavuzcan et al., 2013). If the idea of referral for selected cases based on sonographic and CA125 findings is accepted, as recommended by Society of Gynecology-Oncologists (SGO) and American College of Obstetrics & Gynecologists (ACOG) (Le et al., 2009), some malignant cases might be mismanaged by less expert surgeons.

The present study is to suggest a proper algorithm to triage for referral of adnexal mass cases. Thus, low risk cases are not referred and each case is decided based on triage algorithm.

Materials and Methods

In the present study, triage algorithm is constructed based on OMPS1 scores of high sensitivity (100%) in the first step to rule out malignancy (Arab et al., 2012). High specificity is used in the next step to accurately predict malignancy. Cases with intermediate scores that are between 2.3-3.65 which are reevaluated and decided on the basis of OMPS2 score, which is more specific (Arab et al., 2012).

In this regard in a new data-set of 430 operated adnexal masses, selected cases based on OMPS1 (scores between 2.3-3.65) are separated to be included in determination of sensitivity and specificity of each score in this subgroup.

Results

In the subgroup of 123 out of 430 adnexal mass cases with OMPS1 scores between 2.3-3.65, sensitivity and specificity of malignancy prediction is calculated for each score of OMPS2 separately (Table 1).

Table 1. Sensitivity and Specificity of OMPS2 Scores in Intermediate Risk Patients (OMPS1=2.3 -3.65)

OMPS2 score	Sensitivity (%)	Specificity (%)
2.3	100	0
2.4	94.1	4.4
2.5	94.1	10.6
2.6	94.1	13.8
2.63	94.1	16.9
2.7	88.2	20
2.8	88.2	26.3
2.9	88.2	35.6
3	82.4	43.1
3.1	70.6	49.4
3.2	70.6	57.5
3.3	70.6	61.3
3.4	70.6	68.1
3.51	64.7	71.3
3.67	64.7	75
3.77	64.7	75.6
3.82	64.7	76.9
3.9	58.8	76.9
4	58.8	78.1
4.1	58.8	79.4
4.2	58.8	82.5
4.3	58.8	86.3
4.43	47.1	88.8
4.52	41.2	91.3
4.62	41.2	94.4
4.7	35.3	95
4.8	29.4	96.9
5.59	29.4	98.1
6.5	11.8	98.1

*OMPS: Ovarian Malignancy Probability Score

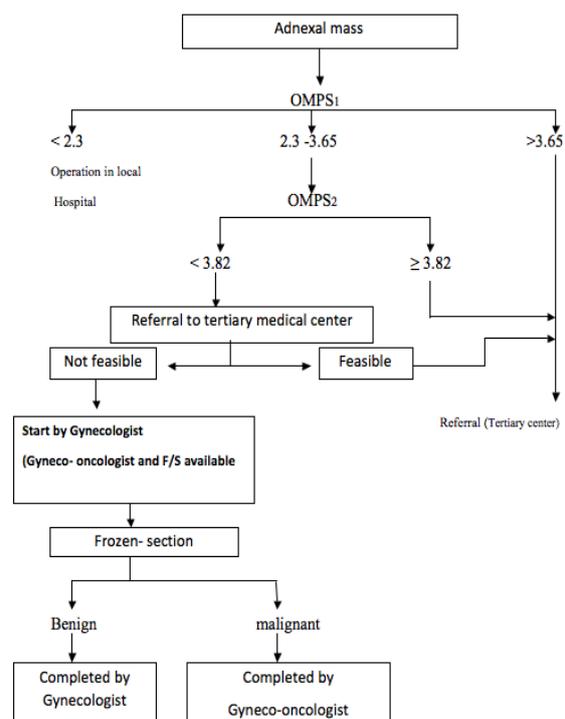


Figure 1. Algorithm1- Referral Guideline in Adnexal Masses Based on OMPS₁ and OMPS₂

In the present study, in the subgroup of intermediate risk patients based on their OMPS1 (between 2.3 -3.65), if their OMPS2 has a score of 3.82, then sensitivity and specificity will be 64% and 76.9%, in prediction of malignancy respectively (Table 1).

Discussion

Based on NCCN, 2013, recommendation is referral of all adnexal mass patients to gynecologic oncologists (du Bois et al., 2005; Giede et al., 2005; Earle et al., 2006). Referral of all cases of adnexal mass takes high cost due to travel of many patients in order to be operated by Gynecologic oncologists in far or near tertiary medical centers.

In addition, their treatment is done while they are away from their family. Sometimes they spend a long time waiting to be operated in tertiary medical centers.

On the other hand, to make decision to refer selected patients on the basis of SGO or ACOG guides or RMI1 or RMI2 has the risk of some error.

Some limitations of RMI model are mentioned hereunder: *i)* They are qualitative models; for instance, regardless of their exact age, all of menopausal patients receive similar scores (Le et al., 2009). *ii)* All five sonographic findings are considered as equal; while sonographic finding of solid area is a more significant predictor of malignancy in comparison to other findings (Le et al., 2009). *iii)* The size of tumor is not considered in the model. *iv)* Sonography - as a sensitive test (Jacobs et al., 1990) - and serum CA125 measurement - as a specific test (Jacobs et al., 1990) - are combined in prediction of malignancy; while in referral prediction for triage aims, a sensitive test is needed in the first step and a specific one in the next step.

In OMPS1 model, the above mentioned limitations are not observed. Due to its being based on regression analysis, the value of each parameter such as every year of increasing age or every centimeter of increasing size or value of any different sonographic finding is calculated exactly. In OMPS2 model, serum CA125 measurement is added to OMPS1.

SGO and ACOG referral guides for adnexal mass are made on the basis of CA125 above 200 in premenopausal and 35 in postmenopausal women, ascites, evidence of abdominal metastasis and family history (Le et al., 2009). However, menopausal status is considered instead of age. This limitation was present in RMI, as well, in which some of significant findings of sonography such as solid area, bilateral mass and size of mass are not regarded. It seems to be accurate in referral of very advanced cases.

OMPS model does not have such limitations. Guidelines of SGO and ACOG for correct referral of adnexal mass sort out 70% of premenopausal and 94% of postmenopausal ovarian cancers, with PPV of 33.8% and 59.5%, respectively. That is while the negative predictive value of SGO and ACOG in both subgroups of old and young age was above 90% (Le et al., 1997).

Construction of algorithm for referral: OMPS1 score of less than 2.3 showed 100% sensitivity in prediction of malignancy. So, patients with score of less than 2.3 might be operated in the local hospital of the patients' hometown.

In contrast, patients with OMPS1 score of above 3.65 are high risk for malignancy with specificity of 72.9% and should be referred to tertiary care medical centers where frozen section and Gynecologic oncologist are available.

In the intermediate group of patients with OMPS1 scores between 2.3- 3.65, using OMPS2 as a more specific model, adding CA125 level is helpful in triage.

In these intermediate cases, OMPS2 score would be used to divide patients into two groups according to their score, one group having scores of equal or above 3.82 are considered as high risk and the other group having scores of below 3.82 are considered as intermediate risk. As shown in table 1, as for OMPS2 scores above 3.82, specificity of malignancy prediction is about 76.9% and they are managed similar to OMPS1 score above 3.65. As concerns OMPS2 score below 3.82, there are two alternative management routes: either to be referred similar to the previous group or to be operated by a gynecologist in a medical center if only access to gynecologic oncologist and frozen-section is possible, if necessary. In this group, a gynecologist might start the operation, and if the frozen section reveals malignancy, a gynecologic oncologist is invited to the operation field to complete the surgery besides the gynecologist (algorithm 1).

In conclusion, first triage is suggested to be done by OMPS1 as a sensitive model. In suspicious cases (scores above 3.65), referral to tertiary medical center is recommended; and, in benign cases (scores below 2.3), operation in local hospitals is recommended. In scores between 2.3- 3.65, OMPS2 model as more specific one is used to decide for referral. If the OMPS2 score is above 3.82, the patients are managed similar to OMPS1 score above 3.65. In case the OMPS2 score is below 3.82, they might be referred if feasible or operated by Gynecologist, only when frozen section and gynecologic oncologist are available. In case of malignant result of frozen-section, the operation is completed by a Gynecologic oncologist.

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