Preoperative Evaluation of Ovarian Masses: The Ovarian 'Crescent' Sign

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Abstract: Objective: The aim of the current study was to assess the validity of absent ovarian crescent sign in prediction of malignancy in women with an ovarian mass. **Methods:** A total of 100 consecutive women planned for surgical intervention for an ovarian mass, were included in the study. The "ovarian 'crescent' sign" was considered to be present when normal ovarian tissue was observed adjacent to the tumor. Risk of malignancy index (RMI) was calculated for each examined patient. Surgically removed specimens from all included women were histopathologically examined. **Results:** The mean age of included women was 35.1 ± 10.1 years (range 18 – 64 years). Of the included 100 women, 77 (77%) had benign ovarian tumors, while 23 (23%) had invasive ovarian malignancy. An absent ovarian crescent sign was significantly associated with almost 36-fold higher risk of ovarian malignancy [RR 35.71, 95% CI (8.93 to 142.86)], at a sensitivity of 91.3%, specificity of 97.4%; figures that were higher than the other two predictors (serum CA125 and the risk of malignancy index). **Conclusion:** In conclusion, absent ovarian crescent sign seems to be a promising sensitive preoperative marker for malignancy in women with ovarian malignancy with adequate specificity.

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1.Introduction:

Nearly 10% of women undergo surgery (whether open or laparoscopic) at some point during their lifetime for an ovarian mass. The risk of malignancy in an ovarian mass is remarkably variable ranging between 0.1 and 3 percent. This relatively wide range of malignancy risk is directly proportionate to the age and is significantly related to the postmenopausal status [1]. Preoperative differentiation between benign and malignant lesions seems imperative for several reasons including the extent of surgery performed (whether conservative or radical), proper counseling of the patient regarding the possibility of removal of one or both ovaries and/or the uterus, the approach of intervention (whether via laparoscopy or laparotomy and whether via a transverse or a midline incision) and lastly, whether to do the intervention at a primary center by a general gynecologist or at a tertiary center by a skilled surgeon with adequate oncological expertise. There are no, however, universally-accepted sonographic or laboratory criteria for distinguishing between benign and malignant nature of an ovarian mass [2]. Several scoring or classifying systems have been proposed including serum CA125 level, menopausal status, age, risk of malignancy index (RMI), morphological sonographic features (including tumor volume, solid components and papillary projections) as well as Doppler indices for the tumor blood supply [3-12]. None of these parameters had acceptable predictable validity in distinguishing benign from malignant ovarian masses. Presence of sonographically-detected normal ovarian tissue adjacent to the tumor tissue (the ovarian "crescent" sign) has been claimed to predict the nature of the lesion preoperatively [13]. The aim of the current work was to assess the validity of this sonographic sign as a preoperative predictor of malignancy in an ovarian mass.

2. Methods

The current study was a prospective observational study, conducted at two large hospitals in Cairo, Egypt: Ain-Shams University Maternity Hospital and Al-Agouza Police Hospital, during the period between May 2010 and November 2010. A total of 100 consecutive women planned for surgical intervention for an ovarian mass, were included in the study. Women who had adnexal masses of non-ovarian origin or who had complicated masses necessitating emergent intervention were not included in the study. Conventional preoperative assessment was made to all included women, including thorough history taking, general and local examination and preoperative anesthesia fitness assessment. In addition, serum CA125 level was checked for, using electroimmunoassay (ELECSYS® 2010, Roche, Germany). A serum CA125 level of 35 IU/ml was considered as the upper normal limit [13].Thorough transvaginal (at a frequency of 5 MHz) and transabdominal (at a frequency of 3.5 MHz) sonographic evaluation of the ovarian mass was made using Medison® (SonoAce® X4, Korea). The following sonographic findings regarding the mass

were reported in each examined patient: multilocular cystic lesions, solid areas, bilaterality, ascites and intra-abdominal metastases. In addition, the "ovarian 'crescent' sign" was considered to be present when normal ovarian tissue was observed adjacent to the tumor. Criteria to define this "ovarian crescent sign" were: presence of hypoechogenic tissue with or without ovarian follicles adjacent to the cyst wall; being not separated from the cyst by applying a moderate amount of pressure; and being enclosed within the ovarian capsule surrounding the mass [13].Risk of malignancy index (RMI) was calculated for each examined patient, according to the formula presented in box-1. A score of RMI above 200 was considered suggestive of malignancy [1]. Surgically removed specimens from all included women were histopathologically examined.

Box-1:Calculation of Risk of Malignancy Index (RMI)[1]

RMI = U x M x CA125

where U refers to ultrasound score, M to menopausal status and CA125 to its serum level.

Ultrasound Score:

Findings: multilocular cystic lesions – solid areas – bilateral lesions – ascites – intra-abdominal metastases

Each finding was scored 1 point

U = 0 (for an ultrasound score of 0)

U = 1 (for an ultrasound score of 1)

U = 3 (for an ultrasound score of 2-5)

Menopausal Status:

M = 1 if premenopausal; M = 3 if postmenopausal

Postmenopausal status was defined as women who had had no period for more than one year or women over the age of 50 or women who had a hysterectomy

CA125:

Serum CA125 level measured in IU/ml

Sample Size Justification:

Data from a recent previous study showed that the sensitivity of absent ovarian crescent sign in women with ovarian mass in prediction of malignancy was 96% [14]. The proportion of women who had malignant lesions among those who had ovarian mass necessitating surgical intervention was 24% in the same study. Calculation according to these values to have the least acceptable statistical figure produced a minimal sample size of 100. Therefore, 100 women planned for surgical intervention for ovarian mass were included in the study.

Statistical Methods:

Statistical analysis was performed using Microsoft® Excel® version 2010 and Statistical Package for Social Sciences (SPSS®) for Windows® version 15.0. Data were presented as range, mean and standard deviation (for numeric variables) or number and percentage (for categorical variables). Difference between two groups was estimated using independent student's *t*-test (for numeric variables) and chi-squared test (for categorical variables). Validity of measured parameters as predictors of malignancy was expressed in terms of sensitivity, specificity, positive predictive value, false positive and negative rates as well as positive likelihood ratio. Association between measured parameters and malignancy was expressed in terms of relative risk and its 95% confidence interval. Significance level was set <0.05.

3. Results

A total of 100 women presenting with ovarian mass were included in the study and sonographically examined preoperatively. The mean age of included women was 35.1 ± 10.1 years (range 18 – 64 years). Of the included 100 women, 63 (63%) were postmenopausal, while 37 (37%) were premenopausal. Of the included 100 women, 77 (77%) had benign ovarian tumors, while 23 (23%) had invasive ovarian malignancy. None of the specimens of included women showed borderline ovarian tumors. Table-1 shows histological features and staging of tumors in included women.

Table-1: shows histological features of ovarian tumors in included women. More than ¾ of the included women had benign lesions, while less than ¼ of the included women had malignant lesions. Nearly half of the included women had advanced stages (FIGO stages III/IV).

Table-1Histological Features of Ovarian Tumors in Included Women

Ovarian Tumors	
Benign Lesions	
Cystadenoma	
Mature Teratoma	77 (77%)
Endometrioma	42 (54.5%)
Inflammatory Mass	17 (22.1%)
Invasive Malignant	7 (9.1%)
Lesions	11 (14.3%)
Epithelial Malignant	
Lesions	23 (23%)
Non-Epithelial	22 (95.7%)
Malignant Lesions	1 (4.3%)
FIGO Stage I	8/23 (34.8%)
FIGO Stage II	4/23 (17.4%)
FIGO Stage III	10/23 (43.5%)
FIGO Stage IV	1/23 (4.3%)

FIGO International Federation of Gynecology and Obstetrics

Women who had invasive ovarian malignancy had a significantly higher mean age [45.1 ± 10.6 years vs. 33.6 ± 9.5 years, respectively, p=0.001] and a significantly higher proportion of being postmenopausal [19/23 (82.6%) vs. 44/77 (57.1%), respectively, p=0.026] when compared to women with benign ovarian lesions.

Serum CA125 above 35 IU/ml was significantly associated with almost 16-fold higher risk of ovarian malignancy. A score of RMI above 200 was significantly associated with almost 11-fold higher risk of ovarian malignancy. An absent ovarian crescent sign was significantly associated with almost 36-fold higher risk of ovarian; figures which were all better than the other two predictors (serum CA125 and RMI).Combined absence of ovarian crescent sign and a score of RMI above 200 were associated with a higher relative risk than each parameter individually [RR 59.48, 95% CI (8.4 to 500)], as well as a higher sensitivity (95.7%) and a lower FN (4.3%) (Table-2).

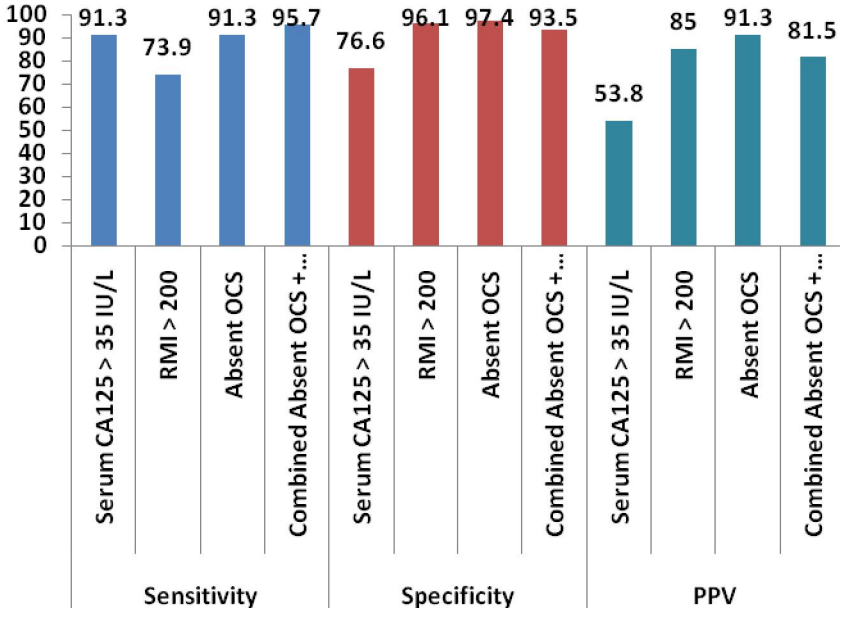
Table-2 shows the accuracy of serum CA125, RMI and absent ovarian crescent sign in prediction of ovarian malignancy. Absent ovarian crescent sign was the most specific by having the lowest false positive rate. Both serum CA125 and absent ovarian crescent sign have similar sensitivity and false negative rate.

Table-2:Validity of Serum CA125, RMI and Absent Ovarian Crescent Sign in Prediction of Ovarian Malignancy

Prediction of Invasive Ovarian Malignancy	Sensitivity	Specificity	PPV	FP	FN	LR+	RR (95% CI)
Serum CA125 > 35 IU/ml	91.3%	76.6%	53.8%	23.4%	8.7%	3.9	16.39 (4.08 to 66.67)
RMI > 200	73.9%	96.1%	85%	3.9%	26.1%	19.0	11.33 (5.12 to 25)
Absent OCS	91.3%	97.4%	91.3%	2.6%	8.7%	35.2	35.71 (8.93 to 142.86)
Combined Absent OCS + RMI > 200	95.7%	93.5%	81.5%	6.5%	4.3%	14.7	59.48 (8.4 to 500)

CA125 cancer antigen 125; RMI risk of malignancy index; OCS ovarian crescent sign;
PPV positive predictive value; FP false positive rate; FN false negative rate; LR+ positive likelihood ratio;
RR (95% CI) relative risk and its 95% confidence interval

Figure-1 shows the accuracy of serum CA125, RMI and absent ovarian crescent sign in prediction of ovarian malignancy. Absent ovarian crescent sign was the most specific by having the lowest false positive rate. Both serum CA125 and absent ovarian crescent sign have similar sensitivity and false negative rate.



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CA125 cancer antigen 125; RMI risk of malignancy index; OCS ovarian crescent sign;
PPV positive predictive value.

Figure-1. Bar-Chart showing Validity of Serum CA125, RMI and Absent Ovarian Crescent Sign in Prediction of Ovarian Malignancy

4. Discussion

The current study showed that absent ovarian crescent sign (i.e. absence of a sonographically-visible normal ovarian tissue adjacent to the adnexal tumor was strongly associated with malignancy. Serum CA125 showed a good sensitivity (91.3%) and a low false negative rate (8.7%), but a relatively low specificity (76.6%), PPV (53.8%), and a relatively high false positive rate (23.4%). On the other hand, a RMI above 200 showed a high specificity (96.1%) and PPV (85%) and a low false positive rate (3.9%), but a relatively low sensitivity (73.9%) and a relatively high false negative rate (26.1%). The absence of ovarian crescent sign, however, was associated with malignancy, with a sensitivity and false negative rates similar to those for serum CA125 (91.3% and 8.7%, respectively), and a specificity and PPV and false positive rates better than those for the RMI (97.4%, 91.3% and 2.6%, respectively). Absent ovarian crescent sign was, therefore, associated with the lowest false positive and negative rates, when compared to both serum CA125 and the RMI. When absent ovarian crescent sign was combined with a RMI score above 200, the false negative rate dropped to 4.3%.

In a similar study conducted by **Hillaby**[14], at King's College Hospital, UK, on 100 women with adnexal mass, 67 had benign ovarian tumors, 9 had borderline tumors while 24 had invasive malignant tumors. In this latter study, serum CA125 had slightly lower, yet comparable figures for sensitivity, specificity and PPV (88%, 66% and 45%). Absent ovarian crescent sign was predictor of invasive malignancy at a sensitivity, specificity, PPV of 96%, 76% and 56%, respectively; figures that were higher than those for serum CA125, yet quite different from those of the current study (higher sensitivity and lower both specificity and PPV). When both invasive malignant lesions and borderline lesions were categorized in one group, the figures were closer to those of the current study (91%, 84% and 73%). Hillaby et al. also examined the predictability of tumor volume ≥ 180 ml as well as Doppler ultrasound indices (pulsatility index [PI] and time-averaged maximum velocity [TAMXV]) and found that absent ovarian crescent sign was more sensitive [96% vs. 58% vs. 63%, respectively], but less specific [76% vs. 89% vs. 91%, respectively] than these Doppler ultrasound parameters, and was more sensitive and specific than tumor volume ≥ 180 ml [96% vs. 79% and 76% vs. 54%, respectively][14].

In another study conducted by **Kushtagi and Kulkarni** [13], at Kasturba Medical College, India, on 60 women with an adnexal mass, 11 (18.3%) had invasive malignant lesions. In this latter study, an absent ovarian crescent sign was compared to three different RMI systems [RMI 19, RMI 210 and RMI 311].The figures for sensitivity, specificity and PPV for absent ovarian crescent sign in prediction of invasive ovarian malignancy in this study were 90.9%, 77.6%, and 47.6%, respectively. The figures for RMI 1 (that was tested in the current study) were 72.7%, 89.9% and 61.5%, respectively. **Kushtagi and Kulkarni**(2) showed that absent ovarian crescent sign was more sensitive but less specific than RMI according to these three systems. In another study conducted by the same two authors on the same group of women, Kulkarni and Kushtagi compared the absent ovarian crescent sign to TAMXV, Doppler ultrasound indices (PI, resistance index [RI], peak systolic velocity [PSV]) as well as to scoring systems [Scoring systems of **DePriest** [4], **Granberg**[6], **Lerner** [7], Sassone [8] and multicenter scoring system [5]]. They concluded that absent ovarian crescent sign was more sensitive and specific than TAMXV and these Doppler ultrasound indices, and was more sensitive and specific than scoring systems proposed by **DePriest**[4] **and Granberg** [6], more sensitive but less specific than that proposed by Sassone et al. and the multicenter scoring system, and as specific but less sensitive than that proposed by Lerner[7] .

Absent ovarian crescent sign, therefore, seems, as shown by the results of the current and previous relevant studies, to be a valid preoperative predictor of ovarian malignancy in women with an adnexal mass. Positive features of this sonographic sign include non-invasiveness, relatively low cost, and that it does not need a high skill level of ultrasound imaging (regarding both the set and the sonographer), and it could be easily incorporated in the routine ultrasound assessment of an ovarian mass; in contrast to the Doppler ultrasound indices and the complex ultrasound features that require more advanced ultrasound sets and more expert sonographers and have relatively high inter-observer variation. There are, however, some drawbacks regarding this sign. Firstly, there was reported difficult detectability of such a sign in postmenopausal women (probably due to absent follicles which identify the normal ovarian tissue). In addition, in the presence of masses which are multicystic or heavily echogenic (such as fibromas, abscesses or endometriomas), this sign may be masked. In addition, the probability of failure to identify normal ovarian tissue in large ovarian lesions is to be considered. The ovarian crescent sign should, therefore, be evaluated and interpreted in the context of other clinical, sonographic and laboratory features. Moreover, the wide 95% confidence intervals for the RR for association between this sign and malignancy

may indicate an insufficient sample size. Thus, further larger and multicenter studies on this initially valuable sonographic sign should be conducted to validate the results of these studies.

In conclusion, absent ovarian crescent sign seems to be a promising sensitive preoperative marker for malignancy in women with ovarian malignancy with adequate specificity.

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