Edessy ovarian cancer score (EOCS) in prediction of malignant ovarian masses

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Abstract: Background: recognizing cancer means that treatment is not delayed and appropriate staging can be carried out in specialized surgical centers. **Objective:** The aim of this study was to evaluate the risk factors of ovarian cancer and to find out an ovarian cancer score. **Methods:** This is a prospective study of 200 women admitted to the Department of Obstetrics and Gynecology of El Maadi Military Medical compound & Oncology institute after obtaining informed patients' consent for surgical exploration of pelvic masses. To diagnose malignant ovarian tumors and calculate Edessy ovarian cancer score for every case. **Results:** Using a cut-off level more than 5 to indicate malignancy, the suggested score gave sensitivity of 83%, specificity of 79.1%, PPV of 54.9%, and NPV of 93.8%, there were statistical significance increase in number of cases showed malignancy in cases with score more than 5 and significant increase in cases with benign lesions in those had score from 0 to 5. **Conclusion:** We concluded that the suggested score can be used for selection of cases for optimal therapy. This score is a simple technique that can be used even in less-specialized gynecology clinics to facilitate the selection of cases for referral to an oncology unit. Recommendations: Giving multiple score points for ultrasonographic features may significantly improves the results of next studies aiming to find out a good new score.
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1. Introduction

Ovarian cancer is the leading cause of death from gynecologic malignancy in the united states. Approximately 21,990 cases are diagnosed annually, and there are 15,460 deaths attributed to ovarian cancer each year *(Siegel R et al., 2011)*. Most patients present with advanced disease where the prognosis is poor. Although early-stage ovarian cancer is highly curable with conventional treatment, it is estimated that only 15% of patients have the disease confined to the ovary at the time of diagnosis*) Jelovac et al., 2011)*.

Most clinicians agree that the preliminary evaluation of a complex ovarian tumor should include a careful history, physical examination, laboratory studies including biomarker analysis, and appropriate imaging study *(Myers et al., 2006)*. Many investigators believe that in order to have a significant impact on reducing ovarian cancer mortality, we must place more emphasis on the development and testing of methods for early detection of the disease. It has been estimated, for example, that if 75% of ovarian cancer cases could be detected with stage I or II disease, the number of women dying of this cancer would be reduced by one half. One approach to early detection of ovarian cancer is to screen women at risk for the disease before the onset of symptoms*) Havrilesky et al., 2011)*.

The risk of malignancy index (RMI) in ovarian tumours is a validated clinical tool used for risk stratification of ovarian lesions, to guide further management *(Meys et al., 2016)*.

Mean survival time for women with ovarian malignancy is significantly improved when managed within a specialist gynaecological oncology service. Hence early diagnosis and referral is important. As the risk of malignancy increases, the appropriate location for management changes. Therefore, while women with a low risk of malignancy (RMI I less than 200) may be managed in a general gynaecology or cancer unit, those who are at higher risk (RMI I greater than or equal to 200 and suspicious CT findings) should be discussed by a multidisciplinary team *(Geomini et al., 2011)*.

The purpose of this study was to evaluate the risk factors of ovarian cancer and to evaluate the ability of the suggested score to discriminate a benign from a malignant pelvic mass and to evaluate its performance.

2. Materials and Methods

We conducted a prospective study of 200 women admitted to the Department of Obstetrics and Gynecology of El Maadi Military Medical compound & Oncology institute after obtaining informed patients' consent for surgical exploration of pelvic masses. between April 2013 and December 2015. The study was approved by the Ethics Committee of Faculty of Medicine, Al-Azhar university, Assuit. We included patients who met the following criteria; 1) age of 35 years or older 2) having adnexal mass diagnosed by an

ultrasound evaluation by either an abdominal transducer or a transvaginal probe 3) having preoperative measurement of serum levels of CA 125 by using a radioimmunoassay and 4) laparotomy for excision of ovarian mass and histopathology. The exclusion criteria were the patients with incomplete medical record, Any contraindication to operative interference or who already had histological diagnosis of malignant ovarian cancer.

Table 1 Edessy ovarian cancer score (EOCS)

Score Value / Parameter	Value = 0 (low risk)	Value = 1 (high risk)	Value =2 (very high risk)
Sonographic features (U)	Unilateral – Unilocular cyst	Unilateral - Multilocular cyst - Solid areas	Ascites or Bilateral lesions or Intra-abdominal metastases
Age (A)	35: 44 years	45: 55 years	56: 62 years
Serum CA 125 level (C)	35 U/ml>	35: 65 U/ml	65 U/ml >
BMI (B)	< 25 Kg /m2	25: 35 Kg /m2	> 35 Kg /m2
Parity (P)	3rd para or more	1st or 2nd para	Nullipara

Edessy ovarian cancer score (EOCS)was calculated for all patients together with the sensitivity, specificity and positive and negative predictive values of the suggested score. We used cut-off level of more than 5 for indicating malignancy. The methods for Edessy ovarian cancer score calculation were as follows: EOCS = U + A + C + B + P. The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 18.0. Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables in different groups. Reliability data were calculated using: Sensitivity, Specificity, Accuracy & positive predictive and negative predictive value. P value less than 0.05 was considered statistically significant. The histopathological diagnosis was considered as the gold standard for defining the outcomes. Tumors were classified according to World Health Organization definitions (1973).

3. Result

The suggested score had a good negative predictive value in comparison with its positive predictive value making this score to be used as a good negative test in prediction of ovarian cancer and improving preoperative diagnosis. In our study we found that the suggested score had a good sensitivity and specificity when compared with other scores. We think that malignancy risk indices is more reliable than the menopausal status, serum CA-125 levels, ultrasound features and tumor size separately in detecting malignancy.

There were 200 women included in the study. Table 2 shows patients' characteristics. For the histological examination, 47 of 200 patients (23.5%) had malignant, and 153 (76.5%) had benign disease. The distribution of histological diagnoses is shown in Table 3.

Table (2): Demographic data of the studied group:

Variable		(*n*=200)
Age	*35: 44 years N(%)*	77 (38.5%)
	45: 55 years N(%)	89 (44.5%)
	56: 62 years N(%)	34 (17%)
Residence	*Rural N(%)*	106 (53%)
	Urban N(%)	94 (47%)
Parity	*Nullipara N(%)*	108 (54%)
	1st or 2nd para N(%)	40 (20%)
	3rd para or more N(%)	52 (26%)
Smoking	*N(%)*	13 (6.5%)

Table (3): Pathology results among the studied group:

Variable	N (%)
Benign	(n=153)
Serous cyst adenoma	53(34.6%)
Mucinous cyst adenoma	24(15.7%)
Simple serous cyst	24(15.7%)
Endometriotic cyst	19(12.4%)
Dermoid cyst	9(5.9%)
Tubo-ovarian abcess	8(5.2%)
Retension cyst	8(5.2%)
Fibroma	3(2.0%)
Luteoma	3(2.0%)
Polycystic ovary	2(1.3%)
Malignant	(n=47)
Serous adenocarcinoma	21(44.7%)
Mucinous adenocarcinoma	16(34.0%)
Papillary cyst-adenocarcinoma	5(10.6%)
Undifferentiated carcinoma	2(4.3%)
Poorly differentiated serous adenocarcinoma	1(2.1%)
Clear cell carcinoma	1(2.1%)
Endometroid carcinoma	1(2.1%)

Univariate analysis showed that there were statistically significant differences between the benign,

and malignant group in these factors: Parity, BMI, and CA 125. The results of evaluation by EOCS are summarized in Table 4. By using a cut-off level more than 5 to indicate malignancy, the EOCS gave sensitivity of 83%, specificity of 79.1%, positive predictive value of 54.9%, and negative predictive value of 93.8% (Table 5). Table 6 shows after application of binary Logistic regression analysis for detection of significant risk factors of malignant ovarian lesions it was found that the significant risk factors were nulliparity, smoking, abdominal enlargement, CA 125 level more than 35 U/ml, ascites, lesions more than 10 cm, very high risk by US and score more than 5.

Table (4): Comparison between benign and malignant cases in studied parameters:

Variable		Total (n=200) N (%)	Benign (n=153) N (%)	Malignant (n=47) N (%)	P#
Age	35: 44 years	77 (38.5%)	65 (42.5%)	12 (25.5%)	0.04*
	45: 55 years	89 (44.5%)	64 (41.8%)	25 (53.2%)	0.17
	56: 62 years	34 (17%)	24 (15.7%)	10 (21.3%)	0.37
Residence	Rural	106 (53%)	87 (56.9%)	19 (40.4%)	0.04*
	Urban	94 (47%)	66 (43.1%)	28 (59.6%)	
Parity	Nulli-para	108 (54%)	72 (47.1%)	36 (76.6%)	<0.001**
	1st or 2nd para	40 (20%)	32 (20.9%)	8 (17.0%)	0.56
	3rd para or more	52 (26%)	49 (32.0%)	3 (6.4%)	<0.001**
Smoking		13 (6.5%)	3 (2.0%)	10 (21.3%)	<0.001**
History	Pelvic pain	112 (56%)	91(59.5%)	21(44.7%)	0.07
	Abdominal pain	75 (37.5%)	53(34.6%)	2(46.8%)2	0.13
	Abdominal bloating	110 (55%)	76(49.7%)	34(72.3%)	0.006**
	Menstrual irregularity	115 (57.5%)	83(54.2%)	32(68.1%)	0.09
	Constipation	67(33.5%)	51(33.3%)	16(34.0%)	0.93
	Dyspareunia	70 (35%)	52(34.0%)	18(38.3%)	0.59
	Abdominal enlargement	92 (46%)	59(38.6%)	33(70.2%)	<0.001**
Comorbidity	DM	23 (11.5%)	16 (10.5%)	7 (14.9%)	0.72
	HPT	42 (21%)	33 (21.6%)	9 (19.1%)	0.40
BMI	< 25 Kg /m2	82 (41%)	71 (46.4%)	11 (23.4%)	<0.001**
	25: 35 Kg /m2	77 (38.5%)	57 (37.3%)	20 (42.6%)	0.51
	> 35 Kg /m2	41 (20.5%)	25 (16.3%)	16 (34.0%)	<0.001**
Abdominal Mass		51 (25.5%)	33 (21.6%)	18 (38.3%)	0.02*
CA 125	< 35 U/ml	92 (46%)	81 (52.9%)	11 (23.4%)	<0.001**
	35: 65 U/ml	87 (43.5%)	63 (41.2%)	24 (51.1%)	0.23
	> 65 U/ml	21 (10.5%)	9 (5.9%)	12 (25.5%)	<0.001**
Sonograhic feature	Unilateral	133(66.5%)	120(78.4%	(27.7%)13	<0.001**
	Bilateral	67(33.5%)	33(21.6%)	(72.3%)34	
	Unilocular	45(22.5%)	40(26.1%)	5(10.6%)	0.03*
	Multilocular	155(77.5%)	113(73.9%)	42(89.4%)	
	Solid area	7 (3.5%)	4(2.6%)	3(6.4%)	0.22
	Ascities	9 (4.5%)	1(0.7%)	8(17%)	<0.001**
	Metastasis	2(1%)	0(0%)	2(4.3%)	0.04*
Size	< 6 cm	37(18.5%)	34(22.2%)	3(6.4%)	0.01*
	6: 10 cm	93(46.5%)	74(48.4%)	19(40.4%)	0.34
	> 10 cm	70(35%)	45(29.4%)	25(53.2%)	0.002**
Sonographic risk	Low risk	36 (18%)	34 (22.2%)	2 (4.3%)	0.005**
	High risk	93 (46.5%)	85 (55.6%)	8 (17.0%)	<0.001**
	Very high risk	71 (35.5%)	34 (22.2%)	37 (78.7%)	<0.001**
Score point	0 – 5 (n=129)	129 (64.5%)	121 (93.8%)	8 (6.2%)	<0.001**
	6 – 10 (n=71)	71 (35.5%)	32 (45.1%)	39 (54.9%)	

Table 5

Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC	P value
> 5	83	79.1	54.9	93.8	80	0.86	<0.001**

Table -6 Logistic regression analysis for detection of significant risk factor of malignant ovarian lesions:

Risk factor	B	S.E.	Wald	Sig.	Exp(B)	C.I.	
						Lower	Upper
Age(35-44 years)	0.06	0.44	0.98	0.19	1.05	0.63	4.15
Urban residence	0.70	0.53	1.73	0.19	2.02	0.71	5.74
Nullipara	1.32	0.65	4.13	0.04*	3.73	1.05	13.24
Smoking	3.12	0.86	13.07	<0.001**	22.73	4.18	123.61
Abdominal bloating	0.72	0.55	1.75	0.19	2.06	0.71	5.98
Abdominal enlargement	1.87	0.68	7.52	0.006**	6.48	1.70	24.6
BMI >25 Kg/m2	0.60	0.76	0.57	0.06	2.13	0.45	1.34
Abdominal mass	-0.35	0.67	0.28	0.56	0.70	0.19	2.59
CA 125 > 35 U/ml	3.01	0.69	12.14	0.01*	2.75	6.71	18.63
Bilateral lesion	-0.06	1.59	0.001	0.97	0.95	0.04	21.5
Multilocular lesion	0.58	0.84	0.47	0.5	1.78	0.34	9.22
Ascites	2.03	0.89	8.02	0.02*	6.95	2.70	24.6
Metastasis	0.75	0.57	1.85	0.09	2.4	0.74	4.08
Size > 10 cm	3.9	0.72	11.23	0.01*	2.98	8.90	20.5
Very high risk	3.6	0.67	4.41	0.01*	13.41	1.507	54.72
Score> 5	1.34	0.72	3.47	0.04*	3.83	2.933	15.7

4. Discussion

Correctly discriminating between benign or malignant adnexal masses is the essential starting point for optimal management. Most women with an adnexal mass do not have cancer (Menon et al., 2009).

Estimating the risk of malignancy is essential in the management of adnexal masses. An accurate differential diagnosis between benign and malignant masses will reduce morbidity and costs due to unnecessary operations, and will improve referral to a gynecologic oncologist for specialized cancer care, which improves outcome and overall survival *(Meys et al., 2015).*

Currently, the standard tools for detecting ovarian cancer are pelvic ultrasonography and measuring serum cancer antigen 125 (also called carbohydrate antigen 125; CA-125) levels, which could be combined with the menopausal status to calculate the risk malignancy index (RMI) and is considered a simple and affordable test *(Al-Musalhi et al., 2015).*

the present study aimed to evaluate the risk factors of ovarian cancer and to find out an ovarian cancer score. To achieve this target, we recruited 200 women presented with non-recurrent adnexal masses. They were subjected to careful history taking, thorough clinical examination, ultrasound examination, CA 125 assessment. We formulated a predictive score comprising ultrasound features, age, serum CA 125 levels, body mass index and parity.

In the current study, comparison between patients with benign and malignant tumors revealed that patients with malignant tumors are significantly older than patients with benign tumors. Also, they had higher frequency of BMI ≥ 35 kg/m2. In addition, they had higher frequency of nulliparity.

Also, we noted that patients with malignant tumors had significantly higher frequency of sonographic findings suggestive of malignancy when compared with patients with benign tumors.

The EOCS had a good sensitivity and specificity when compared with other scores. Also it had a good negative predictive value in comparison with its positive predictive value making this score to be used as a good negative test in prediction of ovarian cancer and improving preoperative diagnosis.

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