RESEARCH COMMUNICATION

Ultrasonography and Computed Tomography for Management of Adnexal Masses in Iranian Patients with Suspected Ovarian Cancer: Results of a Prospective Study

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Abstract

Background: To determine and compare the accuracy of sonographic and computerized tomography (CT) scan assessments in distinguishing between benign and malignant adnexal masses in an under-studied population of Iranian patients. Methods: Transabdominal sonography (TAS) and CT reports of 75 women with adnexal masses (34 malignant, and 41 benign) who were consecutive operated patients at a tertiary gynecology cancer center (Tehran, Iran) were examined. The sonography examinations were operated by a radiologist experienced in the gynecologic oncology field. Biomarkers were determined in blood samples. For CT and TAS, to classify masses as malignant or benign, receiver operating curves (ROC) were assessed and the areas under the curves were compared. Results: For TAS the sensitivity, specificity, positive predictive value and negative predictive value were 91%, 68%, 71% and 90%, respectively. For CT scans the results were 85%, 56 %, 62% and 83%, respectively. The AUC of sonography assessment to diagnose malignancy was significantly higher than that of CT scan (0.8 vs.0.71; $p<0.05$). Conclusion: TAS is a sensitive method for preoperative detection and staging of suspected ovarian cancer. Biomarkers and CT scan imaging add no additional findings for pre-operative characterization of ovarian masses.

Key Words: Ovarian mass - computerized tomography - ultrasonography - preoperative diagnosis

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Introduction

Inevitability of preoperative radiologic evaluation of adnexal masses is documented (Yazbek etal., 2008). The benefit of radiologic evaluation is the characterization of an adnexal mass, suggesting the probable etiology of the mass; and distinguishing between benign and malignant masses are often possible (Joshi et al.,2008). The results of radiologic assessments may preclude open surgical interventions(Goçmen et al.,2008), necessitate more elaborate preoperative diagnostic procedures (Henrich et al.,2007), assist interpretation of frozen sections, and help both surgeon and patient to plan and prepare for the operation (Funt et al.,2004). Overall, sonographic evaluation of adenexal mass is probably the most beneficial and inclusive diagnostic procedure.

The need for a second radiologic assessment by Computerized tumography (CT) or MRI is debatable. The sonography is traditionally known to be operative dependent (Yazbek etal., 2008) and the accuracy and perfectness of the sonograms are arguable in particular in developing countries. In our center, a tertiary referral teaching gynecology cancer center in Tehran (Iran), we routinely perform both sonographic and CT imaging evaluation before surgery of adnexal masses. However, the superiority of one of these assessments and the necessity of performing both procedures are indistinct to us. We have already documented some geographic and racial-dependent dissimilarity in clinico-pathological features of ovarian cancers in Iran (Ghaemmaghami et al., 2008). The current study assesses and compares the accuracy of transabdominal sonography (TAS) and CT scan of adenexal masses to identify the superior diagnostic modality to evaluate benign and malignant ovarian tumors and to indicate the implication of second radiologic examination.

Patients and Methods

The study population comprised 75 consecutive patients with adnexal mass who were admitted and operated from September 2007 in gynecology cancer centre of Valiasr hospital (Tehran, Iran), a teaching university hospital. Within one week before operation, a

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sonographic evaluation was performed, pelvic and abdominal CT scans were obtained, and blood samples were collected to determine biomarkers. All ultrasonographic examinations were performed by an attending radiologist experienced in the gynecology field. Pattern recognition was used to classify masses as benign, suspected benign, malignant, or suspected malignant. Serum CA-125 over the cutoff value of was regarded as positive (35 U/ml) (Goçmen et al., 2008). The patients were operated on by the attending gynecology surgeons. The demographic characteristics, reports of the sonographist, the CT scans, and the surgeons' findings were recorded. Pathologic proof of masses was obtained for all 75 patients. One year after the study opening date, the CT scans were delivered to the same radiologist, altogether and without identifications.

For comparison of subjects with malignant or benign masses Chi square analysis and Fisher exact test were used when appropriate for qualitative data and the t test were used for quantitative data. A series of multivariate binary logistic regression were used to examine the association of malignant masses with radiologic findings and positivity of serum biomarkers. The Receiver Operating Characteristic (ROC) curve of TAS, CT scan, and biomarkers were examined to determine malignancy; the areas under the curves were considered as a determinant of the appropriateness of the modality and the differences between AUC were analyzed employing STATA version 8. All other analyses were performed employing SPSS version 15 (SPSS Inc, Chicago, Illinois). A P value of 0.05 or less was accepted as significant.

Table 1. Types of Surgical Procedures and Preoperative Diagnosis with TAS

Pathology	Surgical procedures	Diagnosis with TAS
Benign (41)	TAH+BSO (11)	9 B in FS; with 4 M , 3 suspect B, and 2 B in TAS; 1 Derm in FS - B in TAS; 1 borderline in FS - suspect B in TAS
	TAH+BSO+O+L (7)	4 B in FS and suspect M in TAS; 2 M in FS, 1 M and 1 suspect M in TAS; 1 borderline in FS suspect M in TAS
	Cystectomy (10)	9 B, 5 B and 4 suspect B in TAS; 1 Derm in FS and benign in TAS
	Salpangoophonecoly (9)	7 B, 3 M and 4 suspect B; 2 Derm in FS, suspect B in TAS
	Myomectomy (4)	4 B in FS, 2 B and 2 suspect M in TAS
Cancer (30)	TAH+BSO (3)	1 B in FS, suspect B in TAS, 2 M in TS, suspect M in TAS
	TAH+BSO+O+L (24)	24 M in FS, 15 M, 5 suspect M, and 1 suspect B in TAS
	Salpangoophonecoly (1)	1 M in FS, suspect B in TAS
Malignant Germ Cell (4)		
	TAH+BSO+O+L (2)	2 M in FS and TAS
	Salpangoophonecoly(2)	2 M in FS and TAS

B, benign; FS, frozen section; M, malignant; TAH, ; BSO, ; OME, ; L,

Results

Out of 75 participants aged 40.7±10.7 years, 41 proved to have benign and 34 malignant masses. Those with malignant masses were older (mean age: 43.1±10.7 years as compared with 38.7±10.3 years); but the difference was statistically non-significant (p=0.07). Four subjects had germ cell tumors; these subjects were statistically younger (25.5 years) than subjects with epithelial malignant tumors (45.5 years; p<0.001). All the subjects had TAS and CT scan, but serum biomarker determination was missing in 3 subjects. The types of operative management of the tumors are shown in Table 1.

The findings of sonographic evaluation of benign and malignant masses are shown in Table 2. Malignant tumors were reported to have more frequent solid components compared to benign masses (36% vs. 22.7%; p<0.001). Internal septation, nodules, and vegetations were respectively found in 41.5%, 9.8%, and 2.4% cystic benign masses, and in 50%, 29.4, and 41.2% cystic malignant tumors. In malignant tumors sonographic evaluation found ascites in 18 subjects (52.9%), evidences of hepatic metastasis in 3 (8.8%), intestinal metastasis in 4 subjects (11.8%; including one report of suspected case), omental metastasis in 6 subjects (17.6%). Pelvic lymph node, para-aortic lymph node and pelvic wall involvement were reported in 2, one, and one subjects with malignant tumors, respectively. Three ascites, 1 suspicious hepatic metastasis and 1 pelvic wall involvement were incorrectly reported in benign tumors. Out of 34 malignant tumors, 8.8% were reported to be suspected benign, 20.6% were suspicious malignant, and the remaining 70.6% were malignant. No malignant tumor was classified to be benign. Classifying suspected malignant and suspected benign cases as correspondingly malignant and benign, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of sonographic assessment of adnexal masses was 91.2 %, 68.3 %, 70.5%, and 90.3%, respectively. The specificity of "benign" sonographic conclusion to exclude malignancy was 100%.

The findings of CT scan imaging of benign and malignant masses are compared in Table 2. Solid components were found in 41.5% of benign and in 91.2% of malignant tumors (p<0.001). Malignant tumors compared to benign masses were found to have more nodules (23.5 vs. 4.9; p<0.05), and vegetations (27.3 vs. 2.5; p<0.005). In malignant tumors CT scan imaging reviled, ascites in 17 subjects (50%), evidences of hepatic metastasis in 5 cases (14.7%; including one suspected case), intestinal metastasis in 5 cases (14.7%; including one suspected case), omental metastasis in 12 cases (35.3%), pelvic lymph node involvement in 8 cases (23.5%), para-aortic lymph node involvement in 7 cases (20.6%), and pelvic wall invasion in 4 cases (12.5%). Five ascites, 3 suspicious hepatic metastases and 2 suspicious intestinal metastases were incorrectly reported in benign tumors. Malignant tumors were reported as benign and

Table 2. Prevalence of Trans-abdominal Sonography (TAS) and CT scan(CTS) Examination in Pathologically Proven Benign and Malignant Masses

		Benign		Malignant	
		TAS	CTS	TAS	CTS
Type	Solid	24 (0.59)	2 (0.05)	7 (0.21)	6 (0.18)
	Cystic	8 (0.2)	24 (0.59)	9 (0.27)	3 (0.09)
	Both	9 (0.22)	15 (0.37)	18 (0.53)	25 (0.74)
Size	≤10cm	17 (0.42)	16 (0.39)	16 (0.47)	15 (0.44)
	>10cm	24 (0.59)	25 (0.61)	18 (0.53)	19 (0.56)
Septation	-	24 (0.59)	20 (0.49)	17 (0.50)	15 (0.44)
	+	17 (0.42)	21 (0.51)	17 (0.50)	19 (0.56)
Nodule	-	37 (0.90)	39 (0.95)	24 (0.71)	26 (0.77)
	+	4 (0.10)	2 (0.05)	10 (0.29)	8 (0.24)
Vegetation	-	40 (0.98)	39 (0.98)	20 (0.59)	24 (0.73)
	+	1 (0.02)	1 (0.03)	14 (0.41)	9 (0.27)
Cyst wall	-	26 (0.63)	26 (0.63)	15 (0.44)	15 (0.44)
thickening	+	15 (0.37)	15 (0.37)	19 (0.56)	19 (0.56)
Laterality	Uni-	39 (0.95)	39 (0.95)	30 (0.88)	30 (0.88)
	Bi-	2 (0.05)	2 (0.05)	4 (0.12)	4 (0.12)
Ascites	-	38 (0.93)	36 (0.88)	16 (0.47)	17 (0.50)
	+	3 (0.07)	5 (0.12)	18 (0.53)	17 (0.50)
Hepatic	-	40 (0.98)	38 (0.93)	31 (0.91)	29 (0.85)
metastasis	+	1 (0.02)	0 (0.00)	3 (0.09)	4 (0.12)
	Suspicious	0 (0.00)	3 (0.07)	0 (0.00)	1 (0.03)
Intestinal	-	41 (1.00)	39 (0.95)	30 (0.88)	29 (0.85)
Invasion	+	0 (0.00)	0 (0.00)	3 (0.09)	4 (0.12)
	Suspicious	0 (0.00)	2 (0.05)	0 (0.00)	1 (0.03)
Omental	-	41 (1.00)	41 (1.00)	28 (0.82)	22 (0.65)
metastasis	+	0 (0.00)	0 (0.00)	6 (0.18)	12 (0.35)
Pelvic	-	41 (1.00)	41 (1.00)	32 (0.94)	26 (0.77)
LAP	+	0 (0.00)	0 (0.00)	2 (0.06)	8 (0.24)
Paraaortic	-	41 (1.00)	40 (1.00)	32 (0.97)	27 (0.79)
LAP	+	0 (0.00)	0 (0.00)	1 (0.03)	7 (0.21)
Pelvic wall	-	40 (0.98)	37 (1.00)	33 (0.97)	28 (0.88)
	+	1 (0.02)	0 (0.00)	1 (0.03)	4 (0.13)

Data are numbers and proportions in parenthesis

suspected benign tumors in 2 (5.9%) and 3 (8.8%) cases, respectively. The sensitivity, specificity, PPV, and NPV of CT scan assessment of adnexal masses to diagnose benign and malignant tumors was 85.3 % 56.1%, 61.7%, and 82.1%, respectively.

Biomarker assays determined 29 positive serum CA-125; one case had pure alpha fetoprotein, and 5 subjects had positive CA-125 in combination with other markers. No positive serum CEA, CA19-9, and pure Beta HCG was determined. Serum biomarkers distinguished between benign and malignant tumors with sensitivity of 74.2%, specificity of 70.7%, PPV of 65.7%, and NPV of 78.4%.

The ROC curves of positive biomarkers, CT scans, and TAS examinations to classify benign and malignant masses are shown in figure 1 and the corresponding statistics are compared in table 3. Comparing the AUCs, conventional US evaluations were superior to CT imaging in diagnosis of malignant ovarian masses (0.80, CI: (0.69-0.90) vs. 0.71, CI: (0.59-0.83); p<0.05). Different binary logistic regression models were examined to predict benign versus malignant masses with TAS, CT, and positivity of biomarkers. In multivariate analysis the only independently associated assessment modality was found to be TAS, however, in bivariate models all three assessments were correlated with the final pathologic

Table 3. Comparison of Predictive Values of Different Preoperative Diagnostic Modalities to Discriminate Malignant and Benign Ovarian Tumors

	AUC	95% CI	P value	Sensitivity	Specificity
TAS	0.79	(0.69-0.9)	P<0.001	90.3	68.3
CTS	0.72	(0.6-0.84)	P<0.005	87.1	56.1
Biomarkers	0.72	(0.6-0.85)	P<0.005	74.2	70.7

AUC, area under the receiver operating characteristic curve; TAS: transabdominal sonography; CTS, computerized tomography scans; Biomarkers include CA-125, Alpha fetoprotein, and combination of beta HCG, Alpha fetoprotein, CA9-19 with CA-125

Table 4. Logistic Binary Regression Analysis of the Association of Preoperative Diagnosis of Adnexal Masses and Final Pathologically Proven Malignant and Benign Tumors

	Variable	β	(95%CI)	Significance
Univariate Model	TAS	22.3	(5.7-86.3)	<0.001
	CTS	7.4	(2.4-23)	<0.005
	Biomarkers	6.9	(2.4-19.8)	<0.001
Multivariate Model	TAS	2.9	(0.8-10)	0.9
	CTS	0.8	(0.1-7.9)	0.85
	Biomarkers	15.4	(1.6-149.4)	<0.05

β, Exponential beta. Multivariate model included the findings of transabdominal sonography (TAS) and CT scan (CTS), and positivity for biomarkers

diagnosis of the mass (Table 4).

Overall 47 TAH and BSO surgical procedures were performed including 33 omentectomies and lymphadenectomies; out of which 18 were conducted on pathologically proven benign masses. Frozen section wrongly diagnosed 3 of these benign masses as malignant and one as borderline tumor. One TAH and BSO were done in a subject with teratoma because of the surgical obligations or surgeon decisions. Out of 13 remaining unnecessary TAH and BSO operations 11 were done on benign masses not diagnosed by TAS as benign tumors. For malignant preoperative CT scans of benign masses, the figure of unnecessary TAH and BSO increased to 12 cases.

Discussion

We here found that transabdominal sonographic examination is an accurate and inclusive modality to distinguish between malignant and benign adnexal tumors before operation. TAS is fairly sensitive to detect malignant ovarian tumors (91%); this figure is considerably higher than that of CT scan (71%) and biomarker assays (%74). However, the positive predictive value of TAS (71%) is higher than that of CT examination (62%) and biomarker assays (66%), some superfluous major surgical procedures including omentectomy and lymphadenectomy may be a result of excessive confidence of surgical team on the false positive sonograms. We found that CT scan and biomarkers have no advantage on TAS and combining these modalities have minimal benefit for discriminating malignant and benign masses.

In the current study, 45% of adnexal masses were diagnosed to be ovarian cancers. This figure is higher than global prevalence of ovarian malignant tumors in adnexal

masses (20-30%). The plausible reason is that the study was conducted in a tertiary gynecologic oncology center and included patients who underwent surgical operations. In contrast to the final conclusion of TAS based on pattern recognition of benign and malignant tumors, solitary sonographic findings including size, solidity, wall thickening, vegetation, septation, laterality, and evidences of solid components, invasion, and metastasis were not sensitive measures of malignancy of the tumor; but evidences of metastasis excluding ascites and lymph node invasion were specific for malignant tumor (table 2). This account was true for the CT scan apart from that it showed high false positive evidences of hepatic metastasis and intestinal invasions reducing its specificity.

TAS showed high accuracy to determine malignancy than CT scan and biomarkers in regard to significant higher AUCs (Table3). In addition, CT and biomarkers showed minimal value to increase the productivity of TAS discriminating malignant and benign tumors (Table4). In view of limited financial resources in developing countries, routine CT examination of adnexal masses seems to be unsupported. Sonography examination, in particular trans-vaginally, is noninvasive credible method to distinguish malignant adnexal masses and to plan operations excluding specific cases(Liu et al.,2007). The specialist operated TAS in our center proved to be as valuable as in other centers in agreement with the results of Levine et al (Levine et al.,2008). Conversely, high reliance of surgical team on sonography and CT scan reports may cause some excessive extensive surgeries. In current study surgical teams has performed 4 omentectomy and lymphadenectomy surgeries on benign masses which were reported as "benign" in frozen sections but suspected malignancies in sonograms. CT scan reports had no beneficial value to reduce these potentially preventable extensive surgeries. These findings are in contrast with the results of some other studies(Kurtz et al.,1999; Badgwell and Bast .,2007; Schem et al.,2007).

Our study suffers of certain flaws. First, the subject of this study is behind the tide of new radiologic procedures including MRI, Doppler sonography, and PET scans. Nevertheless, this study is reporting the radiological features of ovarian cancers in an under studied area; and the results may prevent some implausible expenditures on pointless CT examinations. Second, we did not included subjects underwent non-operative management of adnexal masse. This cause overestimation of the frequency of caperous ovarian masses and may interfere with the observe sensitivity and specificity of studied modalities. Such patient enrolment was to facilitate collecting pathological prove of tumors.

In conclusion, TAS is a sensitive method for preoperative detection and staging of suspected ovarian cancer. Biomarkers and CT scan imaging add no additional findings for further pre-operative characterization of the ovarian masses.

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