An ultrasonographic morphological index for prediction of ovarian tumor malignancy

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Summary

Purpose of investigation: A newly created ultrasonographic scale called the Poznan index as well as scales already well known (introduced by Sassone, De Priest and Lerner) were compared in our group of patients.

Method: A morphological index was based on seven sonographic ovarian tumor features. Examinations on 686 patients were evaluated. Comparison of prognostic values of the Poznan index with other applied morphological indices in our group of patients was based on the area under receiver operating characteristic (ROC) curves.

Results: The cut-off level of the new index is 8 points. The new morphological index has a specificity of 77.0%, and negative and positive predictive values of 90.7% and 69.1%, respectively. It has a sensitivity of 86.7% and accuracy of 80.6%. The Poznan index proved its usefulness and superiority (AU ROC = 0.89).

Conclusion: Using this morphological index it is possible to make a precise prognosis of ovarian tumor malignancy. It also makes it possible to make the right decision concerning the manner of surgical treatment.

Key words: Cancer; Diagnostics; Morphological index; Ovarian tumor; Ultrasonography.

Introduction

Gynecological malignancy is an important subject in women's healthcare all over the world. Today ovarian cancer is in fourth position among others neoplasm localizations in Poland with a percentage of 6.2. The morbidity of malignant ovarian tumors concerns one-fourth of gynecological neoplasms but mortality affects almost half of them. The reason for this situation is the late diagnosis and difficult treatment of this disease. It is also very important to distinguish between malignant and benign ovarian tumors and introduce proper treatment on this basis.

There is no doubt about the fact that transvaginal ultrasonography and created morphological indices are very useful and can support decision making in these cases. On the other hand a variety of publicized indices and lack of consensus show that there is still no perfect method of early and precise ultrasonographic differentiation between malignant and benign lesions. This led us to create a new scoring scale and compare it with other well known methods [1, 2].

Materials and Methods

We examined a group of 686 women diagnosed and surgically treated because of ovarian masses in the Gynecological and Obstetrical Teaching Hospital of Karol Marcinkowski University of Medical Sciences in Poznan, Poland during the years 1994-2002. Of the ovarian tumors 255 were malignant on histopathology. Preoperative diagnostics comprised gynecological examination and ultrasonographic evaluation. Ultrasonograpy was performed with a B&K Medical device (type 3535) and Aloka devices (models 2000 and 5500) using 5.0-6.5 MHz endovaginal probes. In some rare situations, e.g., if there was a huge tumor or in virgins, we also used transabdominal 3.5-5 MHz transducers. Tumor volume, its morphology as well as ascites were analyzed. Based on our experience, the literature and logistic analyses we created a new morphological index consisting of seven ultrasonographic examination features (Table 1). The type of tumor was verified by the results of postoperative pathological examination. Borderline tumors and metastases to the gonads qualified as malignant ovarian tumors. The results of the examinations were statistically analyzed. The grouping of patients was also estimated using three other morphological indices proposed by: DePriest, Sassone and Lerner [3, 5, 9]. Analysis was also performed in subgroups of premenopausal and postmenopausal patients. All prognostic values (sensitivity, specificity, negative and positive predictive values and accuracy) for all indices were calculated. These values were used to construct receiver operating characteristic (ROC) curves. The area under each curve was also calculated using GraphROC for Windows (GraphROC Software, Turku, Finland). The cut-off value was calculated on the basis of ROC analysis. To evaluate differences of analyzed areas under ROC we used the method described by Hanley and McNeil and included it in the applied software [3]. In our study we assumed a concluding error risk of 5% and (connected with the risk) significance level of $p < 0.05$ indicating statistically significant differences. Statistical analyses were carried out using data analysis software system Statistica (StatSoft, Inc. 2001, version 6).

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Table 1. — *Ultrasonographic morphological index created for early prediction of ovarian tumor malignancy (cut-off level Poznan index ≥ 8).*

Points	Ultrasonographic variables						
	Volume of ovary	Wall structure	Wall thickness	Septa	Echogenicity	Localization	Ascites
0	Before menopause After menopause	Smooth	Thin ≤ 3 mm	No septa	No echo	Unilateral	No ascites
1	Before menopause After menopause	Irregular ≤ 3 mm	Thick > 3 mm	Thin ≤ 3 mm	Low echogenicity	Bilateral	
2	> 50-200 cm^3	Papilla > 3 mm	Solid tumor	Thick > 3 mm	Low echogenicity + central hyperechogenic		Ascites present
3	> 200-500 cm^3	Solid tumor			Mixed echogenicity		
4	> 500 cm^3				High echogenicity		

Results

Mean age of the examined 686 patients was 42.7 ± 14.7 years (range: 11-80). Final pathological examination confirmed malignancy in 255 cases (37.2%). The other 62.8% of tumors were benign. There were 159 (23.2%) postmenopausal patients in our group of patients.

The analyses of ROC curves revealed that for grouping all patients the best cut-off level of the Poznan index was eight points. Subgroup evaluation showed slightly different values of the best prediction level for the morphological index. It was nine points for premenopausal patients and 7 points for postmenopausal. Prognostic values for these cut-off levels are shown in Table 2.

We compared prognostic values of all analyzed morphological indices in Tables 3-5. Cut-off levels were applied in accordance with the rules shown in original papers. Analyses were conducted in all groups of patients and also in subgroups of women before and after menopause.

Constructed ROC curves are shown in Figures 1-3. Different lines correspond to all indices analyzed in our group of women and also in the premenopausal and postmenopausal subgroups. Statistical analysis of area under the ROC revealed significant differences between our Poznan index as well as the Lerner index compared with the others ($p < 0.05$). These differences were also significant for the premenopausal and postmenopausal subgroups. The highest area under ROC for all patients was

Fig. 1

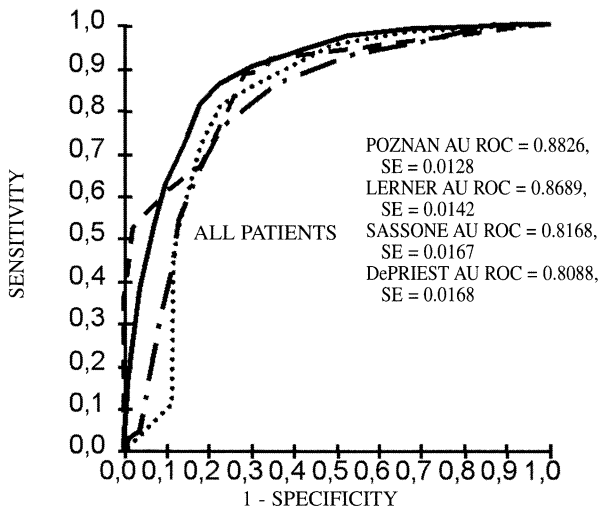

Fig. 2

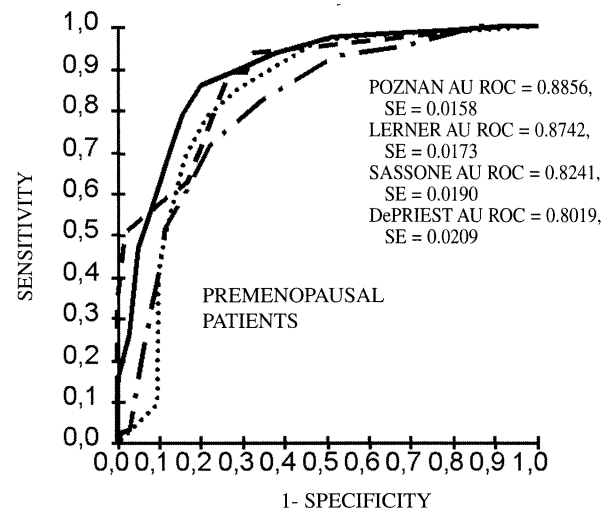

Fig. 3

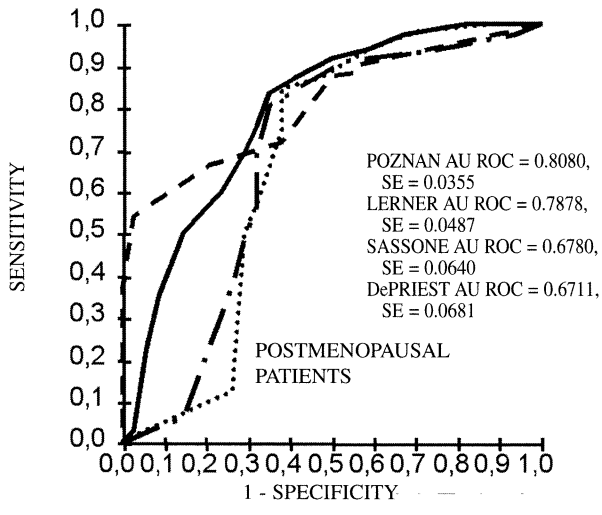

Figure 1. — Comparision of ROC curves for analyzed morphological indices for grouping of all patients (POZNAN INDEX - _____ ; Sassone index ·····; Lerner index -·-·-; De Priest index -·-·-).

Figure 2. — Comparision of ROC curves for analyzed morphological indices for premenopausal patients (POZNAN INDEX - _____ ; Sassone index ·····; Lerner index ----; De Priest index -·-·-).

Figure 3. — Comparision of ROC curves for analyzed morphological indices for postmenopausal patients (POZNAN INDEX - _____ ; Sassone index ·····; Lerner index ----; De Priest index -·-·-).

Table 2. — *Prognostic values of ultrasonographic morphological index (POZNAN INDEX) in differentiating between malignant and benign ovarian tumors.*

Group of patients	Cut-off level of Poznan Index	SENS [%]	95% CI [%]	SPEC [%]	95% CI [%]	ACC [%]	PPV [%]	NPV [%]
Premenopausal n = 527	9	79.2	72.5-84.9	83.3	80.0-86.4	82.4	61.0	92.5
Postmenopausal n = 159	7	92.0	86.7-95.6	50.0	34.9-65.1	83.0	87.1	63.0
All patients n = 686	8	86.7	82.6-90.0	77.0	73.4-80.3	80.6	69.1	90.7

Table 3. — *Prognostic values of analyzed morphological indices in prediction of ovarian tumor malignancy.*

Index (cut-off)	SENS [%]	95% CI [%]	SPEC [%]	95% CI [%]	ACC [%]	PPV [%]	NPV [%]
Poznan Index (8)	86.7	82.6-90.0	77.0	73.4-80.3	80.6	69.1	90.7
DePriest (5)	86.7	82.6-90.0	64.0	60.0-67.9	72.4	58.8	89.0
Sassone (9)	81.6	77.1-85.5	77.0	73.4-80.3	78.7	67.8	87.6
Lerner (3)	89.0	85.2-92.1	67.1	63.1-70.8	75.2	61.5	91.2

Table 4. — *Prognostic values of analyzed morphological indices in prediction of ovarian tumor malignancy for premenopausal women.*

Index (cut-off)	SENS [%]	95% CI [%]	SPEC [%]	95% CI [%]	ACC [%]	PPV [%]	NPV [%]
Poznan Index (8)	86.2	80.1-90.8	78.6	74.9-81.9	80.5	56.9	94.6
DePriest (5)	82.3	75.8-87.6	65.5	61.4-69.4	69.6	43.9	91.9
Sassone (9)	78.5	71.6-84.2	78.3	74.6-81.7	78.4	54.3	91.7
Lerner (3)	89.2	83.6-93.3	69.0	65.0-72.8	74.0	48.5	95.1

Table 5. — *Prognostic values of analyzed morphological indices in prediction of ovarian tumor malignancy for postmenopausal women.*

Index (cut-off)	SENS [%]	95% CI [%]	SPEC [%]	95% CI [%]	ACC [%]	PPV [%]	NPV [%]
Poznan Index (8)	87.2	81.1-91.8	58.8	43.2-73.1	81.1	88.6	55.6
DePriest (5)	91.2	85.8-95.0	47.1	32.2-62.4	81.8	86.4	59.3
Sassone (9)	84.8	78.4-89.8	61.8	46.1-75.7	79.9	89.1	52.5
Lerner (3)	88.8	83.0-93.1	44.1	29.5-59.6	79.2	85.4	51.7

Table 6. — *Comparison of accuracy between the Poznan index and three others morphological indices* (McNemar test).

Group of patients		Morphological index			
		Poznan index ≥ 8	Sassone ≥ 9	DePriest ≥ 5	Lerner ≥ 3
All patients	accuracy [%]	80.6	78.7	72.4	75.2
	p value		0.02	< 0.001	< 0.001
tumors	accuracy [%]	86.1	82.4	80.6	78.2
≤ 5 cm	p value		0.04	0.03	< 0.001
FIGO	accuracy [%]	76.0	73.9	65.6	68.1
Stage I	p value		0.01	< 0.001	< 0.001

from the Poznan index – 0.88; Other values of area under ROC are presented in Figures 1-3. For postmenopausal women the highest AU ROC was 0.80 for the Lerner index and 0.79 for our morphological Poznan index. Results of analyzed index accuracy comparison for all tumors and for small (≤ 5 cm) changes as well as early (I) FIGO stages are presented in Table 6. According to McNemar's test we proved statistically significant differences between these parameters for our new index and the others.

Accuracy of the Poznan index for tumor diameter ≤ 5 cm was 86.1%. Sensitivity and specificity were 86.4% and 88.4%, respectively, and positive and negative predictive values were 43.3% and 95.6%, respectively. Accuracy of the Poznan index for early FIGO stage was 76%. Sensitivity and specificity were 71.1% and 77%, respectively, while positive and negative predictive values were 39.3% and 92.7%, respectively.

Discussion

Ultrasonographic examination of ovarian masses can by very subjective and vary depending on observer skill and experience. Results of such analysis can also be very difficult to compare. Ultrasonography is nevertheless unquestionably useful in early diagnosis of ovarian tumors and malignancy. Many authors report that the specificity of this method is much lower than the sensitivity [1, 4, 5]. The need for an objective tool and possibility of quantitative presentation of the results confirms the usefulness of the creation of morphological indices. It is also important to popularize and verify them [5, 6]. Based on our large number of patients we generated new morphological index characteristics for the analyzed population. Prospective estimation of created indices is also very important and can be quite different from results presented in original papers. We applied three other well known indices in our population and also got much lower levels of prognostic values [5-7]. The explanation for this has already been described in the literature. It may be due to the difficulty of proper popularization of guidelines concerning different ultrasonographic methods and the manner of points given [8]. Mistakes can be caused by subtle misunderstandings and also by differences between teaching populations used to create an index, and prospectively estimated groups of women.

The index presented by Sassone *et al.* [6], has, for example, high sensitivity and specificity – 100% and 83%, respectively, but it has low positive predictive value – 37%. Adding estimation of tumor volume and ascites allows us to achieve a much higher value of PPV - 69.1%. However there are also opinions that tumor volume estimation lowers index specificity because of an existing group of large benign ovarian cysts [6]. Our results do not confirm this opinion. It is still a very rare situation when malignant tumors at the moment of diagnosis are smaller then 10-20 cm^3 [2, 5, 9].

Some benign ovarian pathologies, e.g. mature teratoma, can produce false-positive results of tumor estimation based on the morphological index. In these cases it is very important to analyze the characteristic ultrasonographic picture based on expert clinical experience. Tubo-ovarian abscesses can also simulate malignant masses but in this case some other clinical findings can be very helpful in identifying false-positive results of the morphological index [10]. In some difficult and unclear cases it is important to add Doppler flow estimation as well as biochemical marker assessment. In the presented research we affirm that for analyses of a large population

of women our newly created morphological index is better than the three other indices [5-7]. It also has statistically significant superiority in diagnosis of small tumors and early stages of disease [10]. Popularization of vaginal ultrasonography is crucial for early diagnosis of ovarian malignancy. Proper morphological index applications can make this estimation easier and more reproducible.

Conclusions

1. Ultrasonography together with a precise ovarian tumor morphological index makes an accurate prognosis possible and helps in determining the best treatment.

2. Our newly created index has shown superiority in diagnosing the analyzed population of women with ovarian masses.

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