

Clinical value of the ultrasound Doppler index in determination of ovarian tumor malignancy

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Summary

Purpose of Investigation: Clinical evaluation of the newly created Doppler index (DS) in preoperative early differentiation of ovarian tumor malignancy.

Patients and Methods: The study involved data concerning 464 ovarian tumor examinations of women treated between 1994 and 2002. One hundred and sixty-five women had malignant ovarian tumors, and the other 299 tumors were benign on histopathology. Menopausal status of the studied women was also considered. Created ROC curves compare the diagnostic value of the suggested index. The number of vessels, their location and arrangement, shape of velocity waves as well as presence of the protodiastolic notch in the arterial vessels of the tumor were analyzed. Each of the mentioned features could acquire a point-value of 0 or 1.

Results: A cut-off point for the suggested Doppler index was determined at the level of 4 for the following prognostic values: sensitivity, specificity and accuracy which amounted to 86.7%; 93.3% and 90.9%, respectively. In the group of 101 postmenopausal women accuracy was higher – 94.1%, specificity and positive predictive value (PPV) was estimated as 100%.

Conclusions: The suggested Doppler index enables a precise prognosis of ovarian tumor malignancy and as a half-amount analysis helps in the decision making of the most effective therapeutic treatment.

Key words: Diagnostics; Doppler ultrasonography; Ovarian cancer; Ovarian tumors.

Introduction

Ultrasound examination, especially with the use of a high frequency transvaginal probe, is extremely important among early detection methods of ovarian tumors. Grey-scale ultrasonography has already unquestionable significance in this subject. Introduction of the morphological indices based on a combination of different tumor features makes it possible to achieve high levels of sensitivity and negative predictive values in malignancy prognosis [1-3]. Nevertheless specificity and positive predictive value are still rather low. Application of the Doppler technique makes the evaluation of vascularity in ovarian tumors possible in malignancy prognosis. Neoangiogenesis in malignant tumors lowers the flow indices (RI, PI, etc.) and can in this way be a marker of malignancy [4, 5]. Qualitative features of the flow also change and the objective estimation could be interesting and important in clinical application. The purpose of this study was to perform a clinical evaluation of the newly created Doppler index (DS) in the preoperative early differentiation of ovarian tumor malignancy.

Patients and Methods

The study involved data obtained in the evaluation of 464 ovarian tumor examinations of women treated at the Gynecology and Obstetric Hospital Clinic of Karol Marcinkowski University of Medical Sciences, Poznan, Poland in the years 1994-2002. As a result of histopathological examination, 165 women had malignant ovarian tumors detected, and another 299 were

found to suffer from benign tumors. Prognostic values among the scrutinized group of women were also analyzed in respect to their menopausal status by determining appropriate values for women before and after menopause. The obtained data allowed ROC curves to be drawn and the diagnostic value of the suggested index to be compared for the groups of patients under the scrutiny. Preoperatively clinical data were taken (history, physical examination and ultrasonography). Ultrasonographic examination was performed using a B&K Medical 3535 device and Aloka 2000 or 5500 equipment with a 5-6.5 MHz transvaginal probe and a 3.5-5 MHz abdominal probe as supplementary support. All the probes could perform a Doppler examination and the Aloka device was also equipped with a power-Doppler technique. First ultrasonographic morphological estimation was performed, and then a full Doppler examination was done. The analysis included Color flow mapping (CFM) and in some cases color Doppler energy (CDE) made it possible to demonstrate tumor vessels. Low frequency 50-100 Hz filters were used and an estimation was possible if the flow was bigger than 1 cm.

Doppler evaluation involved the number of vessels, their location and arrangement, and shape of velocity waves as well as presence of the protodiastolic notch in the arterial vessels of the tumor. Each of the mentioned features could acquire a point-value of 0 or 1 (Table 1). In creating our own new Doppler subjective (DS) index, half-amount vascularity features based on CFM were used. These elements are well known and accepted by many researchers [1, 4, 6, 7]. The Doppler index, calculated as the sum of all obtained points, with its cut-off level appointed with receiver operating characteristic curves (ROC), was used to predict the malignancy of the ovarian tumors. All data was analyzed statistically with the chi-square test. Sensitivity (SENS), specificity (SPEC), accuracy (ACC) as well as positive and negative predictive values (PPV & NPV) were calculated. To estimate the value of analyzed tests the area under ROC (AU

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Table 1. — Principles of grading scale in the Doppler Subjective (DS) index of ovarian tumors.

Point	Analyzed ovarian tumor Doppler ultrasonography features				
	Number of vessels	Location of vessels	Arrangement of vessels	Shape of velocity waves	Presence of protodiastolic notch
0	1 - 4	Peripheral	Regular	Sharp; high waveform amplitude	Present
1	≥ 5	In septae, in papillae or solid parts	Irregular, random	Smooth; low waveform amplitude	Absent

ROC) was worked out (GraphROC Software, Finland). Statistical significance was assumed as a p value below 0.05. All statistical analyses were performed with Statistica for Windows v. 5.0 (StatSoft, Poland).

Results

One hundred and sixty-five women had malignant and 299 benign ovarian tumors on histopathological examination. Mean and standard deviation for age in the subgroup of 363 women before menopause was 37.4 ± 9.7 years and for 101 patients after menopause 63.4 ± 8.7 years, respectively. The DS index was statistically significantly higher in the group of malignant tumors (chi-square = 305.96, p < 0.05).

A cut-off point for the suggested DS index was determined at the level of 4. Prognostic values obtained in the data analysis for all patients and subgroups are presented in Table 2. There were no statistically significant differences in the DS in subgroups of women before or after menopause for malignant and benign tumors (respectively, chi-square 9.04, p = 0.11; and chi-square 3.61, p = 0.6). Comparison of ROC curves for the DS index in early diagnosis of ovarian tumor malignancy in all groups of patients and in subgroups before and after menopause are presented in Figure 1.

Table 2. — Prognostic values of the half-amount estimation of tumor vascularity using the Doppler index (cut-off point DS ≥ 4).

Group of patients	SENS	95% CI	SPEC	95% CI	ACC	PPV	NPV
All patients n = 464	86.67	81.45-90.77	93.31	90.39-95.50	90.95	87.73	92.69
Women before menopause n = 363	82.42	74.43-88.61	92.65	89.45-95.05	90.08	78.95	94.03
Women after menopause n = 101	91.89	84.43-96.37	100	89.50-100	94.06	100	81.81

Discussion

The Color Doppler technique in the estimation of ovarian vascularity is still controversial as a useful tool in the differential diagnosis of adnexal mass malignancy. An early paper published by Kurjak *et al.* reports that in benign tumors flow could be evaluated only in 0.06% of cases and no flow was detected in normal ovaries [8].

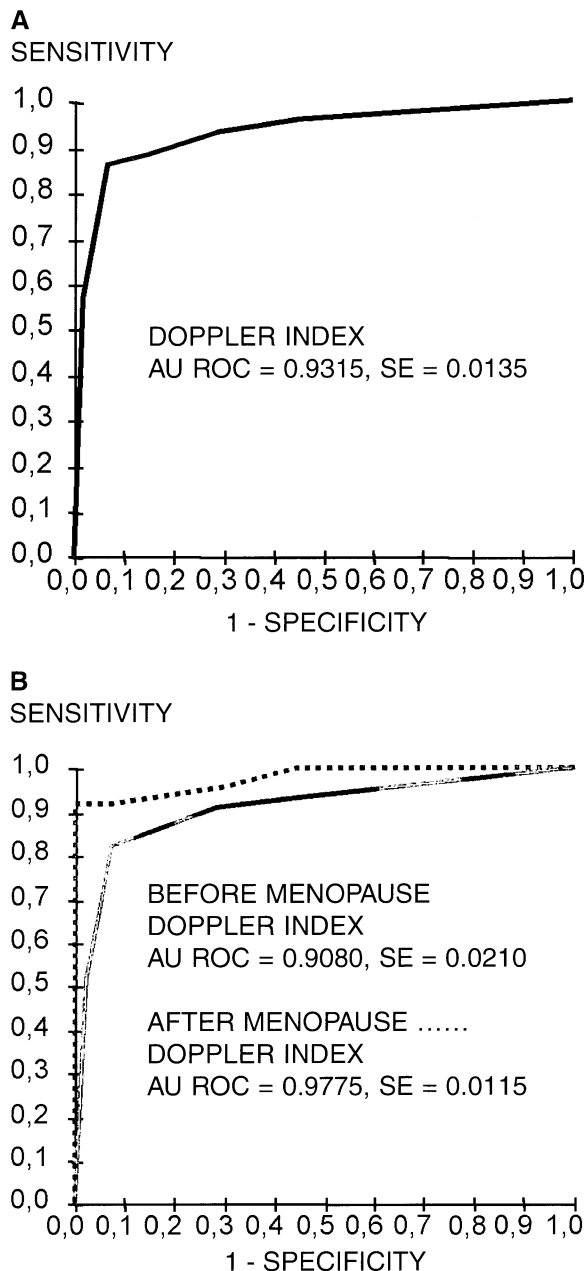


Figure 1. — Comparison of ROC curves for the Doppler Subjective (DS) index in early diagnosis of ovarian tumor malignancy in all groups of patients (A) and in subgroups before and after menopause (B).

Tepper *et al.* proved the presence of flow in 49.7% of benign and 65.8% of malignant ovarian tumors [9]. Guerriero *et al.* revealed an even higher index of vessel detection in adnexal masses [10]. They estimated flow in 100% of malignant and 94% of benign neoplasms using the CDE technique. In our study, using the Doppler technique, blood flow was revealed in all malignant tumors (n = 165) and 92% of benign masses. Similar results concerning level of blood vessel detection have been reported by Valentin [11]. They were reported as 100%

and 91% for malignant and benign masses, respectively. Estimation of an irregular network of vessels in tumors as a marker of malignancy using color Doppler ultrasonography concerns many researchers. It is well known that neoangiogenesis is more intensive in malignant masses. Folkman reports that increased angiogenesis can already be affirmed in very early stages of malignant neoplasms [12]. Consequently Doppler ultrasonography is supposed to be of great importance in the early diagnosis of ovarian masses. It is also essential that angiogenesis be present in several benign processes (e.g., inflammation, ectopic pregnancy, forming of a corpus luteum) [13]. Kurjak *et al.* in 1993 already took note of the usefulness of vascularisation assessment features for prognosis of tumor malignancy [4]. Location of vessels, their arrangement as well as shape of flow velocity waves were analyzed. The authors proved that a centralized location of tumor vessels in solid elements, septum or papilla and their irregularity, disseminated (multicentre) arrangement with typical low-resistant flow velocities statistically significantly more often are present in malignant ovarian tumors. A similar observation was reported by Prömpeler *et al.* [14]. For the reason that it is a quite new approach to the problem of ovarian tumor neoangiogenesis we created our own half-amount vascularisation index (DS). The foregoing results showed a high prognostic value of that index in the differential diagnosis of ovarian masses. Great benefit of half-amount Doppler estimation of neoangiogenesis in ovarian tumors diagnostics has also been confirmed by Caruso *et al.* [6]. Their study reports that color Doppler imaging has significantly ($p < 0.001$) higher specificity and positive predictive value than ultrasonographic estimation of ovarian tumor morphology and they are respectively, 96% vs 61-75% and 82% vs 35-48% [6]. Nevertheless, there are still many authors who believe that Doppler criteria are insufficient for choosing the best surgical approach for ovarian tumor treatment [11, 15, 16].

Conclusion

1. The suggested Doppler index enables a precise and easy way for the prognosis of ovarian tumor malignancy and as a half-amount analysis helps in the decision making of the most effective therapeutic treatment.
2. This method increases the specificity and positive predictive value of morphological indices.
3. The technique is a valuable second stage tool in early prognosis of ovarian tumor malignancy especially for women after menopause.

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