Ultrasound as a Diagnostic Tool for Preoperative Prediction of Adnexal Masses Nature

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Abstract
Proper oncological treatment of patients with adnexal masses depends on appropriate preoperative discrimination between benign and malignant ovarian tumors. There are suggestions that appropriate malignancy risk estimation could be achieved by ultrasound assessment of adnexal mass echomorphology by an experienced sonographer. Evaluating morphologic characteristics of the adnexal masses, in so called pattern recognition, features like presence of mixed consistency or multilocular components, septa or excrescence could differentiate benign from malignant neoplasms. Doppler examination of intratumoral blood flow velocity waveforms, with resistance and pulsatility indexes determination, raises confidence in achieving the correct diagnosis. Therefore, detailed ultrasonographic examination with Doppler scan should always be performed in all patients with adnexal masses. For more accurate preoperative triage calculation of RMI is advisable.

Keywords: Ultrasound; Doppler; RMI; Adnexal masses

Introduction
Proper oncological treatment of patients with adnexal masses depends on appropriate preoperative discrimination between benign and malignant ovarian tumors [1]. It is well known that malignant ovarian tumors are associated with highest mortality rate of all gynecological cancers [2]. Ovarian cancer presents late as early symptoms are often vague. Sixty per cent of women are diagnosed at an advanced stage, which has a 5-year survival as low as 10%. On the other hand early diagnosis provides the 5-year survival of up to 90% [3]. However, it may be difficult to preoperatively determine the nature of adnexal tumors.

No single diagnostic tool (ultrasonography - US, magnetic resonance imaging - MRI, computerized tomography - CT and radioimmunoscintigraphy - RS) is good enough in this determination. There are suggestions that appropriate malignancy risk estimation could be achieved by ultrasound assessment of adnexal mass echomorphology by an experienced sonographer [1]. As ultrasound scan depicts the mass, its characterization can be performed during the same examination. Additionally, this examination is not expensive, easily accessible, and without any harm to the patient. Therefore, ultrasonography is nowadays accepted as the primary imaging modality in the evaluation of an ovarian mass and the main triage method prior to treatment [4].

The greater use of transvaginal ultrasound scanning in everyday practice for the investigation of different gynecological symptoms and conditions leads to an increasing number of ovarian cysts and other tumors that come to the attention of gynecologists. The risk of ovarian cancer in these cysts is low, but much unnecessary anxiety can be caused and unnecessary intervention undertaken if a wrong diagnosis is made [3]. Conversely, misjudging the malignant tumor can have grave prognosis, which once again points out the the importance of expert transvaginal ultrasound diagnosis of adnexal masses.

Ultrasound examination of the adnexal masses is based on detecting changes in size and architecture of the adnexal structures that might precede the manifestation of the disease [2]. Emphasizing morphologic characteristics of the adnexal masses, in so called pattern recognition, features like presence of mixed consistency or multilocular components, septa or excrescence could differentiate benign from malignant neoplasms [5-7]. This pattern recognition of adnexal masses reach a sensitivity of 86% and specificity of 80% when is performed by non-expert ultrasound examiner, and when performed by experienced one it has sensitivity of 90% and specificity of 93% [7]. Nevertheless, the optimal US diagnostic criteria to use when characterizing a suspected ovarian neoplasm still remain controversial [4]. The usual ultrasound classification of ovarian cysts regards them as bilateral or unilateral unilocular, unilocular solid, multilocular, multilocular solid or solid. The sonographer also examines the existence and number of papillae (none, one to five or more than five). Ovaries should be visualized in both longitudinal and transverse planes. The size of ovary and the tumor should be evaluated and the volume calculated by the formula: length \times width \times depth \times 0.5233 [3]. In premenopausal women ovarian volume should not exceed 20 cm$^3$ and 10 cm$^3$ in postmenopausal women [8]. Furthermore, the presence of ascites and metastases must be registered.

In most studies, failure to visualize the ovary is regarded as a negative screen. Still, some researchers feel that in order to minimize the chance of missing an abnormal ovary, sonographers should be requested to demonstrate a 3-cm length of a clearly defined iliac vein in the pelvic side wall if the ovary was not visualized, and a minimum time of 5 min must be spent to identify each ovary [3].

To improve diagnostic performance of ultrasound serum CA-125 test and menopausal status are added in algorithm of Risk of Malignancy Index (RMI). RMI is categorized as RMI≤25: low risk (risk of cancer <3%), RMI 25 – 250: moderate risk (risk of cancer 20%) and RMI>250: high risk (risk of cancer 75%). Using an RMI cut-off level of 250, the sensitivity for ovarian cancer is 85% and the specificity 97%. The index was validated in numerous studies and proven as the most accurate algorithms for predicting the nature of adnexal masses so far. RMI is a reliable factor for differentiation of benign from malignant adnexal masses both in pre- and postmenopausal patients [9]. Therefore, it is...
the most widely used algorithm which should be calculated for every patient with adnexal masses.

Beside MRI other scoring systems and logistic regression models were also developed to predict ovarian malignancy risk estimation [10]. Researchers have made several scoring systems that could give a better prognostic value in comparison to judgement of adnexal masses nature based only on its characteristics, which is a subjective method. These algorithms score inner wall structure (smooth or with papillae), wall thickness (thin ≤ 3; thick >3), presence of septa (no, thin, thick) and echogenicity (from sonolucent to solid) of the ovarian cysts [11,12]. Some algorithms went further and also allow corrections for typical dermoids and hemorrhagic corpora lutea, which has given the best accuracy in estimation of tumors nature (84%) [13]. A large multicentered study examined more than 50 variables (demographic, clinical, tumor markers and ultrasound characteristics), and logistic regression of 12 variables was used to calculate the risk of malignancy of adnexal masses [14]. Some logistic regression models used to determine the optimal ultrasound variables for the prediction of malignancy show that only papillary projection score and time-averaged maximum velocity contributed significantly to the prediction of malignancy [3]. However, all these new models for malignancy prediction have yet to be confirmed in future studies. Therefore, the most common approach to estimate the likelihood of ovarian malignancy in daily practice is still the use of ultrasound examination as a first-stage, and the serum CA-125 combined with HE4 as a second-stage tool [6,15].

Doppler ultrasound examination is usually added on grayscale imaging mostly with intention to more correctly predict malignancy. Intratumoral blood flow velocity waveforms are obtained to determine the resistance index (RI) and Pulsatility Index (PI). It has been shown that evaluation of gray-scale ultrasound morphology with color Doppler findings of an ovarian mass by experienced examiner is highly accurate in predicting the nature of adnexal tumors [16]. Doppler examination raises confidence in achieving the correct diagnosis mostly in stage I ovarian carcinoma (83%) [17]. The degree of vascularization or blood flow velocities may not be sufficient enough in discriminating between different types of malignancies, since most of them are well vascularized. However, advanced epithelial ovarian malignancy has more solid tissue making it more patterns recognizable on the gray scale and more vascularized at color Doppler ultrasound examination [18]. They show increased flow signals both at the periphery and in the central parts of the mass as well as in septa and in the solid areas [19]. Moreover, the power Doppler vascularity index (quantification of the number of pixels in a defined region of interest obtained using customized color quantifying software) has high diagnostic value in discriminating between benign and malignant adnexal masses [20-21]. Therefore, optimal ovarian lesion characterization might be obtained through the combination of gray-scale US morphology and color Doppler flow imaging evaluation.

In conclusion ultrasound parameters are proven as good predictors of tumors nature. Therefore, detailed ultrasonographic examination with Doppler scan should always be performed in all patients with adnexal masses. For more accurate preoperative triage calculation of RMI is advisable.

References