A new method to improve the pre-operative diagnosis of ovarian cancer based on ultrasound

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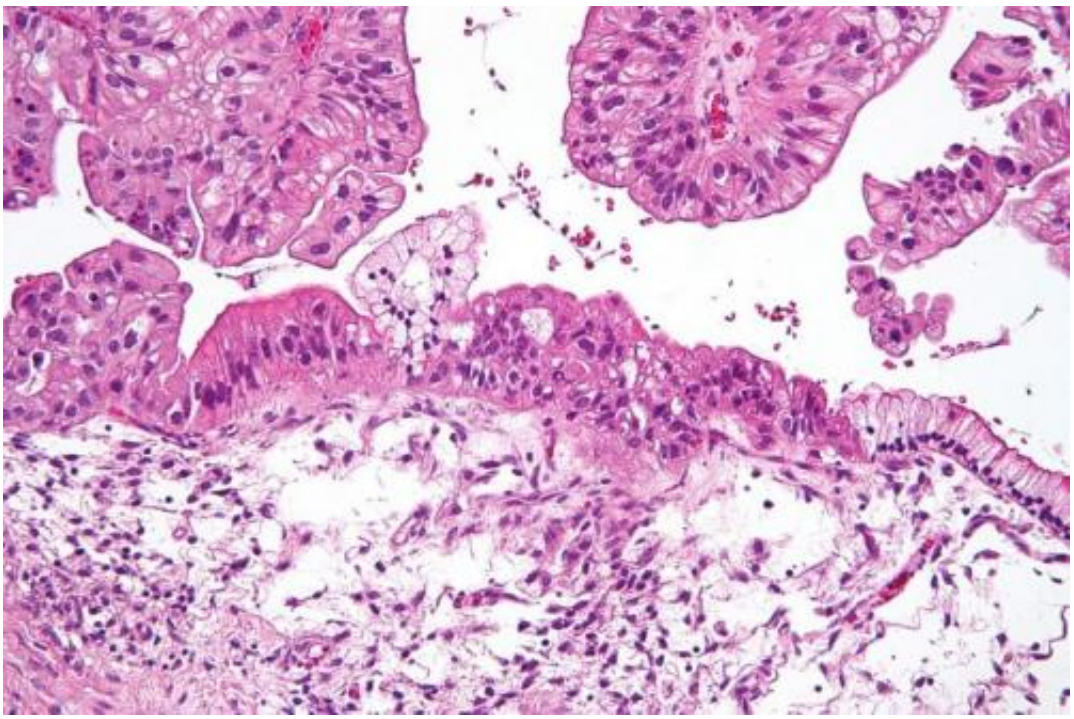

Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. H&E stain. The micrograph shows: Simple mucinous epithelium (right) and mucinous epithelium that pseudo-stratifies (left - diagnostic of a LMP tumour). Epithelium in a frond-like architecture is seen at the top of image. Credit: Nephron /Wikipedia. CC BY-SA 3.0

In a landmark study, investigators from Europe propose a new and

simple method to assess the risk of malignancy of women with an adnexal mass. The method identified between 89-99% of patients with ovarian cancer using the results of ultrasound examination, which can be obtained in referral and non-referral centers. The work is based on the "Simple Rules", criteria developed by the International Ovarian Tumor Analysis (IOTA) group to improve accurate diagnosis of ovarian cancer before surgery. Published in the *American Journal of Obstetrics and Gynecology*, this new approach has the potential to level and raise the playing field and put expert interpretation and improved diagnostic capability within reach of all practitioners.

While ovarian cancer is a common and potentially lethal disease, early detection and treatment improve survival. However, adnexal masses, ovarian masses or cysts that persist and become enlarged, often pose a diagnostic dilemma because preoperative tests to determine if they are benign or malignant are often inconclusive. The IOTA group developed a set of "Simple Rules" based on ultrasound images of the adnexal masses, which allows them to be classified as either benign or malignant.

Although the Simple Rules have been well-received by clinicians, an important question from patients and physicians has been whether it is possible to calculate the individual risk of malignancy for a particular patient. In this study published today, the IOTA group led by Professor Dirk Timmerman, MD, PhD, of the Department of Obstetrics and Gynecology, University Hospitals Leuven, Belgium, sought to develop and validate a model to predict the risk of malignancy in adnexal masses using the ultrasound features derived from the Simple Rules. This study represents the culmination of multiple consecutive multicenter studies involving 22 centers in 10 countries over 13 years (1999 to 2012) and approximately 5,000 patients with adnexal masses.

"The Simple Rules are intuitively attractive because of their ease of use, however, when used as originally suggested, they allow only a

categorization of tumors into three groups: benign, malignant, or inconclusive," explained Dr. Timmerman. "In this study we show that the Simple Rules can now be used to estimate the risk of malignancy in every adnexal mass and so can be used for individualized patient management."

In this study, the IOTA investigators examined patients before surgery, using a standardized examination technique and standardized terms and definitions to describe ultrasound findings. The predictions based on ultrasounds were subsequently compared with the histological findings after the tumor was examined by pathologists (gold standard to define if a tumor is benign or malignant). The risk of malignancy was calculated.

"We conclude that individual risk estimates can be derived from the five ultrasound features in the Simple Rules with performance similar to the best previously published algorithms," stated Dr. Timmerman. "A simple classification based on these risk estimates may form the basis of a clinical management approach. This will hopefully facilitate choosing optimal treatment for all patients presenting with adnexal masses."

Roberto Romero, MD, DMedSci, Editor-in-Chief for Obstetrics of the *American Journal of Obstetrics and Gynecology*, stated that "this is a major breakthrough and the culmination of a major effort by multiple investigators in Europe over more than 10 years. The investigators have addressed an important clinical challenge and provided a method that was validated rigorously and urgently needed by patients and physicians."

Beryl Benacerraf, MD, President of the American Institute of Ultrasound in Medicine (AIUM) and Clinical Professor of Radiology and OB GYN at Brigham and Women's Hospital, Harvard Medical School, Boston, commented in an editorial that "Although an earlier systematic review indicated that magnetic resonance imaging (MRI)

gives better results than ultrasound, Dr Timmerman and his colleagues have shown that the IOTA Simple Rules provide better results than ever before and support the notion that ultrasound is at least as accurate and likely better than MRI in distinguishing benign from malignant masses. The investigators publishing in AJOG have shown here that if we use the Simple Rules with the scoring instrument developed by the IOTA group, we will make the correct diagnosis more readily than ever before and this offers the advantage that most practitioners could adopt this approach successfully."

"I applaud this group for grappling with the challenging problem of the variability of ultrasound diagnoses of adnexal masses depending on the expertise of acquisition and interpretation, and succeeding in developing a simple, standardized, and scalable solution. By at once leveling and elevating the playing field, application of this method places expert interpretation and improved diagnostic ability within reach of all practitioners."

More information: "Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis (IOTA) group," by Dirk Timmerman, MD, PhD, Ben Van Calster, MSc, PhD, Antonia Testa, MD, PhD, Luca Savelli, MD, PhD, Daniela Fischerova, MD, PhD, Wouter Froyman, MD, Laure Wynants, MSc, Caroline Van Holsbeke, MD, PhD, Elisabeth Epstein, MD, PhD, Dorella Franchi, MD, Jeroen Kaijser, MD, PhD, Artur Czekierdowksi, MD, PhD, Stefano Guerriero, MD, PhD, Robert Fruscio, MD, PhD, Francesco PG Leone, MD, Alberto Rossi, MD, Chiara Landolfo, MD, Ignace Vergote, MD, PhD, Tom Bourne, MD, PhD, and Lil Valentin, MD, PhD, DOI: dx.doi.org/10.1016/j.ajog.2016.01.007.

"Ultrasonic diagnosis of ovarian masses: Can the playing field be leveled and raised at the same time?" by Beryl Benacerraf, MD, DOI: dx.doi.org/10.1016/j.ajog.2015.12.045.

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