Role of Color Doppler Ultrasonography in Benign and Malignant Adnexal Masses: A Systematic review.

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Abstract

Introduction: An adnexal mass is a mass in tissue of the adnexa of uterus such as the ovaries, fallopian tubes, or any of the surrounding connective tissue. Adnexal masses can be benign, premalignant and malignant. They can be further divided into simple or complex masses. In women, before menopause, adnexal masses are of large variety including ovarian cysts, ectopic pregnancy, non-cancerous and cancerous tumors, endometriomas and polycystic ovaries. In such women causes include follicular cysts, corpus luteum cysts and abscesses. Prevalence of malignant ovarian cancer is high in young women. After menopause, cancer, fibroids, fibromas or diverticular abscesses are potential causes. **Purpose:** The key purpose of the study was the role of color Doppler ultrasonography in diagnosis of benign and malignant adnexal masses in women. The data used in this study is based on previous existing studies. **Method:** The Literature (google Scholar, science Direct, PUBMED) was searched using keywords adnexal masses, color Doppler ultrasonography. Found articles were a combination of retrospective and prospective studies and only prospective studies were selected from 1992 to 2012. Only relevant articles were assessed and selected. **Results:** Most Studies are of the opinion that color Doppler ultrasonography (Abdominal or transvaginal) has better accuracy than grey scale ultrasonography due to the evaluation of blood flow in center or periphery of the adnexal mass. **Conclusion:** Color Doppler ultrasound is a better choice for initial evaluation and screening of adnexal masses because it is widely available, relatively cheaper than other investigations and is non-invasive.

Keywords: Doppler Ultrasonography, Adnexal Masses

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Introduction:

Most of the adnexal masses in women of reproductive age are benign cysts. Only 10% are malignant and ratio of malignancy in women under 30 years is lower. Most common of the adnexal growths are endometriomas and adult cystic teratomas. The remainder is functional cysts or serous or mucinous cystadenomas. Regardless of the age group physicians must consider the possibilities of structural deformities and uterine masses. In all premenopausal women, pregnancy-related adnexal masses such as ectopic pregnancy, corpus luteum cysts, theca lutein cysts, and luteomas should be thought of.

Availability of both gray scale and color Doppler ultrasonography can help both patient and the physician to identify, evaluate and treat adnexal masses in time. It is possible to identify whether a mass is malignant or benign from its features. Most of the malignant adnexal masses can be suspected on gray scale ultrasonography and suspicious masses can undergo color Doppler sonography to detect whether the blood flow is mainly in central or peripheral region of the mass and then confirm at MRI, Cancer markers and histopathology. The purpose of this review is to focus on color Doppler ultrasonography mainly.

Method:

Search strategy:

Literatures like Google Scholar, science Direct, PubMed were used and key words like adnexal masses, color Doppler sonography, Adnexal cancer were used.

Study Selection:

Multiple retrospective, prospective, cross sectional studies were reviewed and additional methodological filters were used for paper selection and selected papers published from 1992 to 2012 were assessed and selected. Articles on adnexal masses and role of color Doppler ultrasonography in adnexal masses were included.

Results:

A total of 16 original papers were examined that discussed the role of color Doppler sonography in benign and malignant adnexal masses.

In 2003 Juan Luis Alcázar conducted a prospective study in two parts in a tertiary care university hospital to develop a new sonographic scoring system for differentiation between benign and malignant adnexal masses. In the first part morphologic and Doppler sonographic data of 705 adnexal masses in 665 patients who were diagnosed and treated from January 1995 to June 2001 was collected. The scoring system was designed to use the parameters which are independent predictors of malignancy. Between July 2001 and March 2002, the results of 90 adnexal masses in 86 participants were cross validated prospectively in the second part. Multivariate logistic regression analysis showed that thick papillary predictions, solid areas, central flow, and velocimetric features with high velocity and low resistance were the only independent predictor parameters. The cross validation showed that the new scoring system had better diagnostic performance when compared with previous scoring system [1].

In 2005, Stefano Guerriero conducted a study of 453 pelvic masses that went ultrasonography before surgery. Masses that showed typical benignity on B-Mode underwent laparoscopy whereas masses that were beyond umbilicus were considered high risk and underwent laparotomy. Remaining masses were assessed by power Doppler. Masses with central vascularization went laparotomy and masses with peripheral vascularity underwent laparoscopy. Among 284 very low-risk, 32 low-risk, 46 high-risk, 91 very high-risk masses, the rate of malignant masses were 0%, 0%, 52%, and 78%, respectively. The diagnostic accuracy of B-mode ultrasonography in diagnosing adnexal malignancies can be increased because of higher specificity [2] .

In 2005, S.A. Sohaib did a prospective study to find the accuracy of Ultrasonography and MRI in adnexal masses to determine which patients will benefit from MRI. 72 women (mean age 53 years, range 19 to 86 years) with clinically suspected adnexal masses were scanned with gray scale ultrasound transabdominally and transvaginally and color Doppler examination was done. MRI was done then before and after transfusing gadolinium injection. The masses were categorized on the basis of images details without knowledge of clinical details and compared with surgical and histopathological findings. The sensitivity, specificity and accuracy of MRI were 96.6%, 83.7% and 88.9%, respectively, and of US were 100%, 39.5% and 63.9%, respectively for malignant lesions. 19(26%) patients who on US were thought malignant were benign on MRI [3].

Stefano Guerriero MD in 2002 with collaboration of three universities departments of obstetrics and gynecology conducted a prospective study of 826 complex pelvic masses that were undergone transvaginal ultrasonography and CA-125 was performed before surgery. A gray scale ultrasonogram was done first and then a color Doppler sonogram was performed and the masses were checked for vascularity. Blood flow shown within the excrescences or solid areas was considered malignant and masses with no flow were considered benign. Color Doppler sonography was more accurate than gray scale sonography because of higher specificity (0.94 versus 0.84; $P < .001$)[4].

Study conducted as a collaborated work in 2010 by Stefano Guerriero, MD in two European university departments of obstetrics and gynecology between 1997 and 2007. A total of 2148 adnexal masses in 1997 women were undergone transvaginal sonography before surgical exploration. A mass was first studied with grey scale ultrasonography and upon having features of malignancy, was then studied with color Doppler ultrasonography. A cystic mass which didn't have the features of benignity was considered malignant and all the solid masses were graded malignant or benign on the basis of blood flow presence in central or peripheral zone of the mass. Malignant masses had central flow and benign masses had peripheral flow. Four hundred and sixty eight masses were malignant. Color Doppler sonography was more accurate comparing with grey scale ultrasonography in terms of higher specificity (94% vs 89%, $P = 0.001$) and similar sensitivity (95% vs 98%, $P = 0.44$). With color Doppler ultrasonographic evaluation the pretest probability rose from 22% to 82%. The accuracy of diagnosing adnexal masses increases when evaluated in terms of vessel distribution by color Doppler ultrasonography [5].

A prospective study was done by S M Stein in 1995 on the usefulness of color Doppler, spectral Doppler and gray scale ultrasonography to differentiate benign from malignant masses. A total of 170 masses in 161 participants were classified as benign or malignant on the basis of gray scale, color Doppler ultrasonography (internal flow, peripheral flow or no flow)and spectral Doppler ultrasonography (threshold of PI and RI 1.0 and 0.4 respectively). 123 masses were declared benign and 46 were malignant out of 170 on basis of surgical pathology. 46 of the 47 masses were suggestive of malignancy and 76 of the 123 benign masses were not suggestive of malignancy (sensitivity, 98%; specificity, 62%; negative predictive value [NPV], 99%; and positive predictive value [PPV], 50%). As a predictor of malignancy internal flow showed sensitivity of 77%, a specificity of 69%, an NPV of 89%, and a PPV of 49%. In malignant masses the values of PI and RI were lower as compared with benign masses. For a PI of less than 1.0, sensitivity was 67%, specificity was 66%, NPV was 83%, and PPV was 46%. For an RI of less than 0.4, sensitivity was 24%, specificity was 90%, NPV was 73%, and PPV was 50%.Gray scale ultrasonography was reliable for benign adnexal masses and unreliable for malignant adnexal masses. Since no central or peripheral blood flow suggested benignity, 17 masses had no flow whatsoever. Spectral Doppler analysis with RI and PI was not useful[6].

U M Hamper in 1993 studied 31 adnexal masses to assess the characteristics of blood flow before surgical excision to assess whether color flow Doppler sonography can help distinguish benign from malignant adnexal masses. The PI and RI were calculated from waveforms generated from blood flow to ovaries via transvaginal ultrasonography. Out of 31 masses 25 were benign and 06 were malignant on histopathology. Benign tumors and cysts showed higher pulsatility index (mean, 1.93 +/- 1.02; range, 0.23-3.99) and resistive index (mean, 0.77 +/- 0.22; range, 0.2-1.0) as compared to malignant tumors (pulsatility index: mean, 0.77 +/- 0.33; range, 0.31-1.09; resistive index: mean, 0.5 +/- 0.17; range, 0.27-0.67)[7].

In 1997 Angela Reles MD published an investigation to check the predictive value of blood flow velocity by transvaginal color Doppler sonography and conventional ultrasound criteria to assess adnexal masses preoperatively. 98 patients, suspicious of having adnexal masses were admitted in hospital and underwent transvaginal color Doppler ultrasonography and CDS. The PI of waveforms generated by blood flow velocity evaluated by CDS was compared with preexisting sonographic criteria to differentiate between benign from malignant adnexal masses. TVS had sensitivity of 91% and a specificity of 84% in detecting malignant ovarian tumors compared with CDS with a sensitivity of 90% and a specificity of 74%, using 1.1 as a cut-off value for the pulsatility index. The specificity of CDS was higher in postmenopausal (88%) than in premenopausal (63%) patients. The sensitivity and specificity of diagnosing malignant ovarian tumours could be elevated to 95 percent and 86 percent using TVS and CDS combined[8].

In 1994 S Salem conducted a study to see whether color Doppler sonography PI (pulsatility index) had an impact on the diagnosis of benign or malignant adnexal masses. Over the 18 months 102 masses in 99 patients underwent color and pulsed Doppler ultrasonography after they had undergone conventional sonography. The PI was calculated on the basis of waveforms generated from central flow, peripheral flow, and flow within or immediately adjacent to the mass. Each lesion was categorized benign/malignant according to its gray scale ultrasound morphologic features. Of the 102 adnexal masses, 89 were benign and 13 were malignant. Among seven of the 89 benign lesions, no flow was detected and were excluded from study. Sixty five among eighty two showed PI equal to or greater than 1.0 and remaining seventeen were below 1.0. Ten of the thirteen malignant masses showed PI less than 1.0. Benign masses showed positive predictive value of 96% and 37% for malignant masses. Benign masses show a higher positive predictive value of high impedance flow and low positive predictive value for malignant masses. Overlap between benign and malignant masses showed severe limitations in differentiating benign from malignant adnexal masses[9].

The prospective study done in 1999 by Dr D. Timmerman was to evaluate the subjective assessment of benign from malignant adnexal masses. Initially one sonographer assessed three participants with adnexal masses and images were taken and then reassessed by five different sonographers with different experiences. The clinical data of participants was shared with sonographers and opinions were compared with the initial examiner. It was found that the initial examiner and the most experienced sonographer obtained an accuracy of 92%. The least experienced observer obtained lesser accuracy varying from 82% to 87%. It was discovered that experience played vital role in detection of benign and malignant adnexal masses and accuracy is correlated with experience[10].

In 1996 A. CARUSO evaluated flow waveforms from ovarian tumors with color Doppler ultrasonography to predict malignancy to compare with some morphologic scoring systems. 122 patients were performed ultrasonography before surgery based on vascular characteristics and on Doppler RI, a vascular score was calculated. One hundred one women had benign and 21 had malignant tumors on histopathology. Color Doppler

detected vascular patterns on all malignant tumors but only 43% of benign masses showed vascularity. Malignant masses showed greater vascular score than benign masses. Doppler ultrasonography achieved better specificity and PPV when compared to morphological scores (96% vs 61–75% and 82% vs 35–48%). In the presurgical characterization of ovarian neoplasms, colour Doppler ultrasonography of ovarian tumours seems to be a comprehensive tool[11].

The prospective study by A Kurjak in 1992 was aimed to develop a new scoring system using transvaginal color Doppler and pulsed doppler ultrasonography for characterization of ovarian lesions. 812 women were screened with ultrasonography and 174 masses were found and analyzed. Tumors were categorized benign or malignant. Scoring system results were compared with histopathology. 38 malignant and 136 benign masses were found and then confirmed. The color Doppler scoring system showed a sensitivity of 97.3% and a specificity of 100%, compared with the morphological scoring system's sensitivity of 92.1% and specificity of 94.8%. Data shows new color Doppler scoring system maximizes the ability to discriminate between benign and malignant entities[12].

J N Buy in 1996 prospectively evaluated one hundred and fifteen women with 132 adnexal masses (98 benign, 03 borderline and 31 malignant) with color Doppler (transabdominal in all and transvaginal in 111) and conventional sonography to compare the results with spectral Doppler separately. Three methods differentiated benign from borderline and malignant masses. In the first, conventional sonography was used. In the second, conventional sonography was combined with color Doppler. The presence of color flow in an echogenic portion classified as malignant by conventional sonography indicated malignancy; the absence of color flow in an echogenic portion classified as malignant at conventional sonography indicated benignancy; the presence or absence of color flow in a regular wall or septum indicated benignancy. The third method used spectral Doppler analysis. Malignancy was indicated by a resistive index (RI) less than or equal to 0.4, a pulsatility index (PI) less than or equal to 1, or a peak systolic velocity (PSV) greater than or equal to 15 cm/sec. Using conventional sonography alone, accuracy was 83%, sensitivity was 88%, and specificity was 82%. Using conventional sonography and color Doppler, accuracy was 95%, sensitivity was 88%, and specificity was 97%. Using spectral Doppler analysis and an RI less than or equal to 0.4, accuracy was 77%, sensitivity was 18%, and specificity was 98%. For a PI less than or equal to 1, accuracy was 68%, sensitivity was 71%, and specificity was 67%. For a PSV greater than or equal to 15 cm/sec, accuracy was 72%, sensitivity was 47%, and specificity was 81%. Adding color Doppler to conventional sonography produced a specificity and positive predictive value higher than those of conventional sonography alone. Specificity increased from 82% to 97% ($p < .001$), and positive predictive value increased from 63% to 91%. RI, PI, and PSV were of limited value[13].

To differentiate benign from malignant ovarian tumors preoperatively Gerardo Zanetta in 1994 designed a study to compare the sensitivity and specificity of transvaginal color Doppler ultrasonography with CA 125 levels, conventional ultrasound and histopathologic findings. The study comprised of Forty-seven benign, 29 malignant and four borderline masses. Mean PI and RI were higher in benign than in malignant masses but an overlap was observed. Sensitivity, specificity and accuracy of color Doppler in predicting malignancy were 85%, 91% and 89% by using a cut-off value of 0.56 for resistance index and 97%, 87%, 91% by using a cut-off value of 1.0 for pulsatility index. The accuracy of both indexes in differentiating benign from malignant tumors was superior to that obtained by using conventional ultrasound and CA 125[14].

In 2012 ToonVan Gorp published a study which was done From August, 2005 to March, 2009 to assess the diagnostic accuracy of ROMA (risk of ovarian malignancy assay) and compare with two most widely used ultrasound methods, namely the risk of malignancy index (RMI) and subjective assessment by ultrasound. 432 women with a pelvic mass were enrolled in a single-centre prospective cohort study. Ultrasound was performed initially and preoperative CA125 and HE4 serum levels were measured. Once the final surgical pathology reports were obtained, the diagnostic accuracy and performance indices of ROMA, RMI and subjective assessment were calculated. Subjective assessment had the highest area under the receiver operator characteristic curve (AUC) (0.968, 95% CI: 0.945–0.984), followed by the RMI (0.931, 95% CI: 0.901–0.955). The subjective assessment and RMI both had significantly higher AUCs than the ROMA (0.893, 95% CI: 0.857–0.922; $P < 0.0001$ and $P = 0.0030$, respectively)[15].

IN 2010 Dirk Timmerman conducted a prospective study on a large scale participating 1938 women with adnexal masses who underwent ultrasonography at 19 ultrasound centers in eight countries. This study mainly focused to assess the diagnostic performance of simple ultrasound rules to predict benignity/malignancy in an adnexal mass and to test the performance of the risk of malignancy index, two logistic regression models, and subjective assessment of ultrasonic findings by an experienced ultrasound examiner in adnexal masses for which the simple rules yield an inconclusive result. The results were then cross matched with histopathology for the confirmation of diagnosis. Out of 1938 72% had benign tumors, 19.2 % had primary invasive tumors, 5.7% had

borderline malignant tumors, and 3% had metastatic tumors in the ovary. The simple rules yielded a conclusive result in 77% masses, for which they resulted in a sensitivity of 92% and a specificity of 96%. The corresponding sensitivity and specificity of subjective assessment were 91% and 96%. In the 357 masses for which the simple rules yielded an inconclusive result and with available results of CA-125 measurements, the sensitivities were 89% for subjective assessment, 50% for the risk of malignancy index, 89% for logistic regression model 1, and 82% for logistic regression model 2; the corresponding specificities were 78%, 84%, 44% and 48%. In adnexal masses subjective assessment of ultrasonic findings by an experienced ultrasound examiner was the most accurate diagnostic test; the risk of malignancy index and the two regression models were not useful [16].

Discussion:

Keeping in view the results of studies mentioned above, it is clear that the importance of ultrasonography as a diagnostic modality cannot be ignored and has the tendency to reveal vital information to reach a diagnosis. Though, it cannot be used as a gold standard for the diagnosis of benign or malignant adnexal masses; it can help sonographers and physician to go in the right direction. Few points come in handy when scanning adnexal masses with ultrasonography which includes the location, size, shape, the presence of blood flow patterns whether central, marginal or peripheral, the pulsatility index, resistive index, and most important of all the experience of a sonographer play vital role in screening. According to studies; the accuracy, sensitivity and specificity of the color doppler ultrasound varies in different adnexal masses in terms of blood flow, Pi and Ri. Histopathology and cancer markers remain gold standard but features of ultrasound such as wide availability, cost effectiveness and being non invasive are beneficial for both patients and physicians.

Conclusion:

Color Doppler ultrasonography helps screen suspicious masses but is not gold standard for confirmation. When it comes to comparison between Gray scale ultrasound and color Doppler ultrasound, the accuracy, specificity and sensitivities are far better than grey scale ultrasonography.

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