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The diagnosis of endometriomas using colour Doppler energy imaging

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We studied the role of colour Doppler energy (CDE) (or power Doppler) imaging in the differentiation between endometriomas and other adnexal masses in premenopausal non-pregnant women. A total of 170 consecutive patients with persistent adnexal masses was submitted to B-mode transvaginal ultrasonography associated with CDE imaging evaluation. Plasma concentrations of CA125 were measured before surgery. Using CDE imaging evaluation of vessel distribution, the occurrence of one of the following findings was considered to indicate the likely presence of endometrioma: (i) a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes without papillary proliferations associated with 'poor' vascularization; (ii) a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes with an echogenic portion in which no flow was detected. The overall agreement between the test result and the actual outcome was calculated using the k index. The CDE imaging evaluation was more accurate in the diagnosis of endometriomas compared with B-mode ultrasonography alone (k = 0.88 and 0.80 respectively). According to the logistic regression equation obtained, the probability of the presence of endometrioma varied between a minimum of 1.4% for patients with no risk factors to a maximum of 95.6% for patients with two risk factors (CDE result and value of CA125 >25 IU/ml).

Key words: CA125/colour Doppler energy imaging/cystic ovarian diseases/endometrioma/transvaginal ultrasound

Introduction

Sonography has been widely used in the diagnosis of endometrioma, but to our knowledge only two studies have evaluated the specificity and sensitivity of transvaginal colour Doppler in the differential diagnosis of this kind of cyst from other types of adnexal mass (Kurjak and Kupesic, 1994; Alcàzar *et al.*, 1997), with differing results. Using an overall combined score of clinical and biochemical parameters in addition to B-mode, colour Doppler and pulsed Doppler, Kurjak and Kupesic (1994) obtained improved accuracy of transvaginal ultrasonography in the diagnosis of endometrioma. However, Alcàzar and colleagues (1997) found no improvement in the diagnostic accuracy of B-mode transvaginal ultrasonography with the addition of transvaginal colour Doppler. Several authors (Tekay and Jouppila, 1992; Timor-Tritsch *et al.*, 1993; Chou *et al.*, 1994; Aleem *et al.*, 1995; Anandakumar *et al.*, 1996) have reported a low rate of presence of arterial blood flow in endometriomas (ranging from 41 to 78%), and only Kurjak and Kupesic (1994) and Tekay and Jouppila (1995) found a higher detection rate. This lack of information about the vascularity of these benign adnexal masses may interfere with the preoperative diagnosis, reducing the reproducibility of the studies (Kurjak, 1995). For these reasons, an increase in the sensitivity of the Doppler equipment used for Doppler measurements is required. Recently, another method of flow detection has become available: a variation of conventional colour Doppler imaging (CDI) using the amplitude ('energy' or 'power') of the Doppler signal (Kremkau, 1995). Because background noise is of low energy, colour Doppler energy (CDE) imaging (or power Doppler imaging) represents this by a uniformly coloured background that is easily distinguishable from true flow. Thus, CDE imaging has the ability to image areas of low blood flow which are currently undetectable by frequency-based techniques (Weskott, 1997). By using this method, it is theoretically possible to detect and characterize blood flow in all adnexal masses.

The aim of this prospective study was to compare the accuracy of transvaginal ultrasonography alone and combined with CDE imaging and the measurement of plasma CA125 in the diagnosis of endometrioma in a premenopausal population with persistent adnexal mass. The k statistic was calculated and used to evaluate the extent of agreement between test results and actual findings (Fleiss, 1981). The influence of different parameters was also studied using a stepwise logistic regression (Tomlinson *et al.*, 1996).

Materials and methods

Subjects

This study has been reviewed and approved by the ethical committee of the Department of Obstetrics and Gynaecology of the University of Cagliari. The candidates for this study were 245 consecutive premenopausal non-pregnant women under observation between April 1995 and October 1997. All the patients were referred with a diagnosis of adnexal mass based on palpation or ultrasound imaging. After a 1–3 month follow-up, 170 adnexal masses in 153 women persisted and were submitted to laparoscopy (n = 123) or laparotomy (n = 30). The average age of the study population was 33.4 ± 9.2 years (mean ± SD), ranging from 14 to 54 years. Women who had undergone previous bilateral salpingo–oophorectomy, or with endometrial or cervical carcinoma, were excluded from the study.

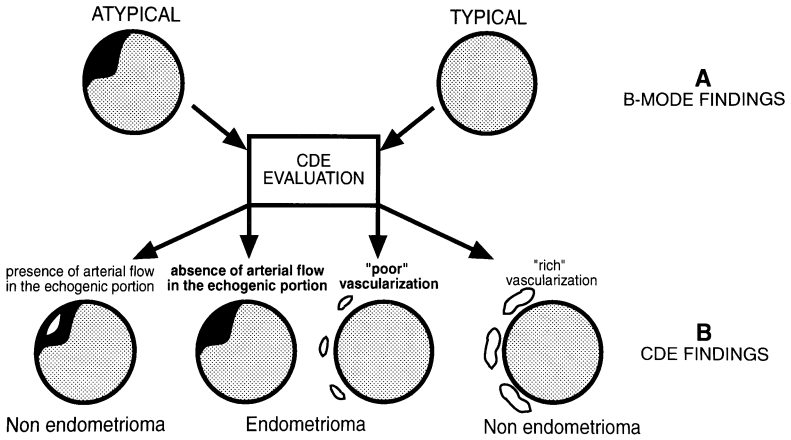

Figure 1. Proposed diagnostic algorithm for persistent adnexal masses. Using B-mode ultrasonography an endometrioma was diagnosed when a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes without papillary proliferations was visualized (**A**, typical findings). After this evaluation, the colour Doppler energy (CDE) imaging evaluation (**B**) was performed and an endometrioma was diagnosed when either typical B-mode findings associated with 'poor' vascularization or B-mode findings with an echogenic portion without arterial flow were visualized.

Methods

Within the 15 days prior to surgery, all patients with a persistent mass underwent a transvaginal ultrasonography with an Acuson 128 XP/10 ultrasound system equipped with a 7 MHz endovaginal probe (Acuson Inc., Mountain View, CA, USA). The unit was equipped with a colour pulsed Doppler ultrasonography system upgraded with CDE. All scans were performed by the same physician (S.G.), who was blinded to the patient's history, in the follicular phase to avoid the risk of measuring the low impedance flow present during menses or late luteal phase (Kupesic and Kurjak, 1994).

Using B-mode ultrasonography, an endometrioma was diagnosed when a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes without papillary proliferations and with a clear demarcation from the ovarian parenchyma (typical findings) was visualized (Mais *et al.*, 1993) (Figure 1A).

All scans were completed by transvaginal CDE imaging. To avoid the risks of bias, conventional colour Doppler imaging evaluation was not performed, either before or after CDE imaging evaluation. The machine settings were fixed at the following parameters: log compression (dynamic range of energy signal) 35–40 dB, mix 4 (= most transparent), CDE post-processing 6, power <500, pre-processing 1, persistence 3 (= medium amount of smoothing), filter 3, gate setting 2. To initiate the Doppler study, colour signals were looked for along the wall and within the septa. When detected, the pulsed Doppler gate was superimposed, and the pulsatility index (PI) and resistance index (RI) were electronically computed. When multiple signals were obtained from the same mass, the lowest PI and RI values were used for the statistical analysis. The intra-observer coefficient of variation was determined by analysing three sets of five consecutive waveforms from the vessel with the lowest PI and RI in the first 10 masses studied. The intra-observer variabilities for RI and PI were 3 and 4% respectively.

Using CDE imaging (evaluation of vessel distribution), the occurrence of one of the following findings was considered to indicate the likely presence of endometrioma: (i) a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes without papillary proliferations associated with 'poor' vascularization (Aleem *et al.*, 1995); (ii) a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes with an echogenic portion in which no flow was detected (atypical findings) (Figure 1B). A cyst was defined as 'poorly' vascularized when only two to four small colour signals were visualized along the wall. We evaluated also the distribution of vessels (central, periphery and ovarian hilus) (Kurjak and Kupesic, 1994; Alcàzar *et al.*, 1997) and the intensity of CDE signal ('poor' vascularization or 'rich' vascularization) (Aleem *et al.*, 1995).

Blood samples were collected on the same day from all patients to measure serum concentrations of CA125. The CA125 measurements were performed with an immunoradiometric assay method which used two monoclonal antibodies (CIS Bio International, Gif sur Yvette, France). The intra-assay and inter-assay coefficients of variation were 3.9 and 4.2% respectively; the sensitivity was <0.5 IU/ml. A CA125 cut-off value of 25 IU/ml, previously defined as the best cut-off in the diagnosis of endometrioma when associated with transvaginal ultrasound, was considered (Guerriero *et al.*, 1996a,b).

At surgery, all ovaries were carefully observed by two of the authors (V.M. and G.B.M.) and all ovarian masses were enucleated from the ovary or removed together with the ovary. The ultrasonographic impressions and the CA125 values were then compared with the final histopathological diagnosis.

Statistics

For comparison of different percentages of distribution of vessels and the intensity of CDE signals in endometriotic and non-endometriotic cysts, the χ^2 statistic was used. The sensitivity, specificity, and positive and negative predictive values of transvaginal ultrasonography and all combined methods were calculated for each adnexal mass (Mais *et al.*, 1993; Guerriero *et al.*, 1996a,b). To evaluate the overall agreement between a test result and the actual outcome, the k index was calculated according to Fleiss (1981). k values ranging between 0.40 and 0.75 were assumed to indicate a strong agreement. The influence of different sonographic findings and biochemical parameters was studied by stepwise logistic regression using the Statistical Package for the Social Sciences for Macintosh, version 6.1.1 (SPSS Inc., Chicago, IL, USA). The model of best fit that adequately described the data was chosen (Tomlinson *et al.*, 1996).

Results

Of the 153 subjects with persistent adnexal masses, 58 were found to have one or two endometriomas confirmed by pathology (prevalence 34%). The prevalence of different histotypes, the patients' ages and the mean diameters of masses are reported in Table I. The median PI value for endometriotic

Table I. Characteristics of the study population

Histotype	Number of masses (% of total)	Patient's age (years)[a]	Diameter of the mass (mm)[a]	Serum CA125 concentration (IU/ml)[b]	Lowest PI[b]	Lowest RI[b]
Endometrioma	58 (34)	31.8 ± 6.5	40.8 ± 16.7	51.6 (9–1000)	0.88 (0.36–2.28)	0.57 (0.33–0.96)
Serous cyst	27 (16)	33.7 ± 10.4	58.5 ± 24.2	17.0 (3.4–34.6)	1.07 (0.48–4.01)	0.61 (0.40–1.0)
Haemorrhagic cyst	24 (14)	34.1 ± 8.6	47.3 ± 24.4	26.1 (8.9–277)	0.80 (0.31–3.32)	0.54 (0.25–0.83)
Dermoid cyst	24 (14)	31.4 ± 10.5	57.4 ± 28.5	18.0 (3.4–113)	1.06 (0.48–4.21)	0.61 (0.39–0.91)
Hydrosalpinx	9 (5)	31.8 ± 11.4	41.5 ± 11.0	55.6 (12.1–500)	1.44 (0.43–2.90)	0.71 (0.33–0.91)
Ovarian cancer	9 (5)	41.0 ± 10.1	81.8 ± 38.1	123.9 (15.7–710)	0.71 (0.30–1.33)	0.47 (0.25–0.73)
Serous cystadenoma	6 (4)	34.0 ± 9.6	57.3 ± 20.2	15.2 (9.5–18.6)	1.16 (0.93–3.50)	0.66 (0.59–1.05)
Mucinous cystadenoma	6 (4)	39.5 ± 6.2	70.0 ± 29.9	14.1 (6.4–39.1)	0.53 (0.44–0.56)	0.40 (0.33–0.43)
Miscellaneous[c]	7 (4)	37.0 ± 12.4	49.9 ± 23.1	18.5 (7.3–63.6)	0.92 (0.49–2.42)	0.59 (0.33–0.86)

[a]Values are mean ± SD.
[b]Values are median (ranges in parentheses).
[c]Parovarian cyst, $n = 2$; tubo-ovarian complex, $n = 3$; pedunculated fibroid, $n = 2$.
PI = pulsatility index; RI = resistance index.

cysts was 0.88 (range: 0.36–2.28) and 0.90 in non-endometriotic benign cysts (range: 0.31–4.21). The median RI value for endometriotic cysts was 0.57 (range: 0.33–0.96) and 0.52 in non-endometriotic benign cysts (range: 0.25–1.05). The median serum CA125 values in patients with endometriotic cysts were 51.6 IU/ml (range: 9–1000 IU/ml) and 17.9 IU/ml in patients with non-endometriotic benign cysts (range: 3.4–500 IU/ml). Table I shows the median values of PI, RI and CA125 for different histotypes.

Intratumoral arterial blood flow could be readily detected by CDE imaging in all malignant tumours and in 94% of the benign ovarian tumours. No arterial flow was detected in two serous cystadenomas, two cystic teratomas, two parovarian cysts, one serous cyst, one tubo–ovarian complex and one endometrioma. Intratumoral arterial blood was visualized in 98% (57/58) of endometriomas. The analysis of vessel distribution showed the presence of a typical colour appearance of endometriomas, the 'hilus sign' (Kurjak and Kupesic, 1994; Alcàzar *et al*., 1997) (presence of vessels at the level of ovarian hilus) in 50% (29/58) of these endometriomas but only in 4% (4/112) of non-endometriotic cysts ($P < 0.0001$). We did not find 'high vascularization' in any endometrioma, but it was present in 20% (23/112) of non-endometriotic cysts ($P < 0.0002$). Colour was present in the periphery of the mass in 88% (51/58) of endometriomas and in 78% (87/112) of non-endometriotic cysts ($P = 0.1$).

Of the 51 endometriomas following by B-mode transvaginal ultrasonography, 47 were confirmed by pathology as were 108 of 119 non-endometriotic cysts. The ultrasonographic findings of the four false-positive cases were similar to findings considered characteristic for endometrioma, but pathological work-up revealed two serous cysts (mean diameter: 32 mm and 110 mm), one haemorrhagic cyst (mean diameter: 54 mm) and a mucinous cystadenoma (mean diameter: 34 mm). The 11 false negative cases following B-mode ultrasonography were adnexal masses with anechoic content at ultrasonography (3/10) or ipoechoic mass with irregular walls or an echogenic portion (8/10) (Figure 2A). The sensitivity, specificity, positive and negative predictive values, and k index of B-mode transvaginal ultrasonography in differentiating endometrioma from other adnexal masses are shown in Table II. The k index of 0.80 suggests good agreement between results of B-mode transvaginal ultrasonography and those of surgery.

The combined use of transvaginal ultrasonography and CDE imaging demonstrates increased accuracy in the diagnosis of endometrioma in comparison with B-mode transvaginal ultrasonography alone (values of k: 0.88 and 0.80 respectively) (Table II). The three false positive cases observed using CDE imaging were two serous cysts and a haemorrhagic cyst. The six false negative cases following CDE imaging were endometriomas with anechoic or partially anechoic content (3/6) or with an atypical ultrasonographic appearance due to an irregular vascularized wall or a vascularized echogenic portion in a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes (3/6) (Figure 2B). Also, the use of 'hilus sign' alone or combined with B-mode findings gave a lower value of k index (Table II).

A logistic regression analysis was performed to identify prognostic factors. Four parameters (B-mode findings, presence of 'hilus sign', CDE imaging evaluation, CA125 >25 IU/ml) were entered sequentially into the model. The best fit model was obtained and is displayed in Table III. The significant variables were: CDE imaging combined approach ($P < 0.01$), CA125 >25 IU/ml ($P < 0.05$; Table III). The equation that describes the probability of the presence of an endometrioma according to the significant variables is the following: $1/\{1+\exp[-4.2705 + 5.2917\times(\text{CDE imaging combined approach}) + 2.0618\times(\text{CA125} > 25\ \text{IU/ml})]\}$. According to this formula, the probability of the presence of an endometrioma ranged between a minimum of 1.4% for patients with no risk factors to a maximum of 95.6% for patients with two risk factors.

Discussion

The present study suggests that CDE imaging should be considered as a useful 'secondary test' after B-mode evaluation in the diagnosis of endometrioma in a premenopausal population. This group of patients, characterized by a high incidence of endometriomas and functional cysts but a low incidence of ovarian cancer (Guerriero *et al.*, 1997a,b), must be considered separately from the postmenopausal population. In fact, among

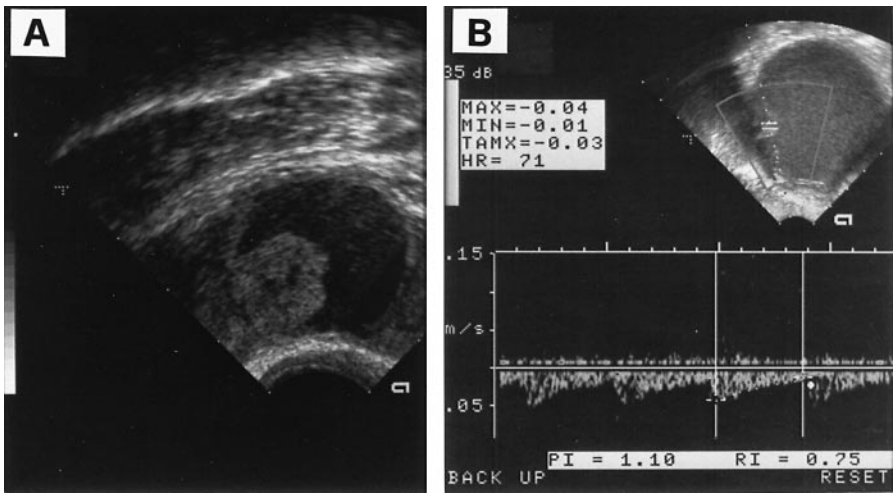

Figure 2. Examples of true positive and false negative cases of colour Doppler energy (CDE) imaging in the diagnosis of endometrioma. (**A**) With B-mode ultrasonography, the echogenic portion was seen against the inner wall of a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes. On CDE imaging evaluation, no flow was detected in this echogenic portion; the mass was suspected to be an endometrioma, and pathology confirmed the diagnosis (true positive case). (**B**) On CDE imaging evaluation, a small echogenic portion with arterial flow inside was seen against the inner wall of a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes; the mass was suspected to be a non-endometriotic cyst, but an endometrioma was found at pathology (false negative case).

Table II. The diagnostic accuracy of ultrasonographic findings in the diagnosis of endometrioma

	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	k value
CDE[a]	97	90	95	95	0.88
B-mode	96	81	92	91	0.80
Presence of 'hilus sign'	96	47	87	78	0.48
B-mode and/or 'hilus sign'	95	83	89	91	0.79
B-mode and 'hilus sign'	98	45	93	77	0.49

[a]CDE, colour Doppler imaging evaluation of vessel distribution.

Table III. Relationship between the most significant explanatory variables and presence of endometrioma analysed by logistic regression model (χ^2 = 149.915; df = 2; P = 0.0001)

Independent variable	Coefficient	SE	*P*-value	Odds ratio	95% CI
CDE	5.2917	0.717	0.0000	198.67	48.70–810.44
CA125 >25 IU/ml	2.0618	0.808	0.0107	7.86	1.61–38.29
Intercept = –4.2705 (SE = 0.8061)					

CDE = colour Doppler energy.

women of reproductive age, the main ultrasonographic criterion to be assessed is the persistence of the mass for 1–3 months (Osmers *et al.*, 1996; Pascual *et al.*, 1997) because this follow-up can reduce the number of functional cysts submitted to surgery (Nezhat *et al.*, 1996). Like other benign ovarian masses (Mais *et al.*, 1993; Guerriero *et al.*, 1996a,b, 1997a,b; Osmers *et al.*, 1996; Pascual *et al.*, 1997), endometriotic cysts are characterized by simple ultrasonographic findings. When a typical ultrasonographic aspect is present, the use of colour Doppler may confirm the presence of 'poor vascularity', characteristic of endometriomas (Kurjak and Kupesic, 1994; Aleem *et al.*, 1995), while in cases with atypical or suspicious findings, a very sensitive method for detecting blood flow should be used to characterize the distribution of vessels. When the B-mode is inconclusive for the presence of an echogenic portion in a round-shaped homogeneous hypoechoic 'tissue' of low-level echoes, only the addition of a new approach such as CDE imaging can reduce the number of false negative findings in the diagnosis of endometrioma.

The present study confirms the high detection rate of arterial flow using CDE imaging. Unfortunately, this high detection rate for endometriomas (98%) is associated with a considerable overlap of values of PI and RI between endometrioma and other benign adnexal masses, as previously shown by other authors (Kurjak and Kupesic, 1994; Aleem *et al.*, 1995; Alcàzar *et al.*, 1997). This finding can interfere with the possibility of defining a useful cut-off value for the diagnosis of ovarian endometrioma. Alcàzar and colleagues (1997) failed to obtain

an improvement in the diagnostic accuracy of B-mode transvaginal ultrasonography because of a low detection rate of arterial flow in endometriotic and non-endometriotic benign adnexal masses. However, this group used a different colour Doppler approach based on 'hilus sign' only. On the contrary, our simple CDE imaging flow-chart (Figure 1), based on the localization of vessels and intensity of arterial flow, permits exclusion of ipoechoic masses with 'rich vascularization' frequently associated with the presence of corpus luteum cysts or mucinous cystadenoma. Otherwise, the use of this method as a secondary test permits inclusion of atypical endometriomas in which no flow is detected in the echogenic portion due to the presence of a clot and enables them to be differentiated from an intracystic vegetation. When CDE imaging evaluation is positive and serum CA125 concentration is >25 IU/ml, the probability of the presence of an endometrioma is high (95.6%) and medical treatment should be excluded. In these cases, the use of operative laparoscopy is suggested to confirm the diagnosis, and to remove the cystic wall and the adhesions frequently associated with the presence of ovarian endometriosis, leading to reduced postoperative pain, shorter hospital stay and faster recovery (Mais *et al.*, 1996). As derived by logistic regression, the absence of the ultrasonographic and biochemical factors reduces the possibility of the presence of ovarian endometrioma to 1.4%. These patients, in the absence of pelvic pain or findings suggestive of ovarian cancer and dermoid cysts, can postpone operative laparoscopy and undergo a longer follow-up to reduce further the risk of unnecessary surgery due to functional cysts.

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