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Transvaginal colour Doppler in patients with ovarian endometriomas and pelvic pain

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BACKGROUND: The aim of this investigation was to correlate ovarian endometrioma vascularization with the presence of pelvic pain. METHODS: The presence of blood flow, peak systolic velocity (PSV, cm/s) and lowest pulsatility index (PI), assessed by transvaginal colour Doppler ultrasonography and CA-125 plasma concentrations, were retrospectively analysed in 74 patients who had undergone operations for cystic ovarian endometriosis. Fifty-two patients were asymptomatic (group A) and 22 presented with pelvic pain (group B). There were 56 endometriomas in group A and 26 in group B. RESULTS: Blood flow was found in 66.1 and 88.5% of endometriomas in groups A and B respectively ($P = 0.036$). PI was significantly lower ($P = 0.009$) and CA-125 concentration higher ($P = 0.0004$) in group B. There were no differences in PSV. CONCLUSIONS: We conclude that vascularization of ovarian endometriomas in patients presenting with pelvic pain is higher than in asymptomatic patients. This could be an indicator of endometriosis activity.

Key words: colour Doppler/ovarian endometriomas/vascularization

Introduction

The aetiology and natural history of endometriosis remains unclear. Mechanisms such as menstrual regurgitation and implantation or coelomic metaplasia have been implicated (Sampson, 1927; El-Mahgoub and Yaseen, 1980). It is not precisely known why ovarian endometriomas develop only in some patients. In addition, the precise mechanisms of the associated pelvic pain are not completely understood.

Fresh peritoneal implants may cause functional pain such as dysmenorrhoea, whereas deep infiltrating endometriosis and ovarian endometriomas are responsible for organic-type pain such as dyspareunia and chronic pelvic pain (Koninckx *et al*., 1991; Vercellini, 1997). These lesions have been found to be active, whereas intermediate infiltrating endometriosis has been shown to be mostly inactive (Cornillie *et al*., 1990). This 'activity' has been related to the vascularity of the lesion (Nisolle *et al*., 1993).

Angiogenesis appears as one of the processes involved in the pathogenesis of endometriosis (Donnez *et al*., 1998; Matsuzaki *et al*., 1998). Angiogenic factors are increased in the peritoneal fluid of patients with endometriosis (McLaren *et al*., 1996), in peritoneal endometriotic implants (Ferriani *et al*., 1993) and in ovarian endometriomas (Fujimoto *et al*., 1998).

Transvaginal sonography has a limited role in the diagnosis of superficial pelvic endometriosis. However, it is more efficient in the diagnosis of ovarian endometriomas (Kupfer *et al*., 1992; Mais *et al*., 1993). In addition, the use of transvaginal colour Doppler and colour Doppler energy allows the assessment of ovarian endometrioma vascularity (Kurjak and Kupesic, 1994; Aleem *et al*., 1995; Alcázar *et al*., 1997; Guerriero *et al*., 1998).

We speculated that ovarian endometriomas in patients presenting with pelvic pain would be more active than those in asymptomatic women and, therefore, their vascular features would be different. In the present study we aimed to compare vascularity patterns in ovarian endometriomas as assessed by transvaginal colour Doppler ultrasonography (TVCD) in asymptomatic patients and women with pelvic pain.

Materials and methods

Patients

This is a retrospective study. Clinical, surgical and sonographic data of a series of 74 consecutive patients with histologically proven ovarian endometriomas were reviewed. Bilateral endometriomas were found in eight patients. Patients' mean age was 34.1 years (SD: 8.4, range: 19–55). All patients were premenopausal.

Patients were divided into two groups according to clinical complaints. Group A included asymptomatic patients or patients presenting with mild or moderate dysmenorrhoea, but without dyspareunia or chronic pelvic pain ($n = 52$, 68.3%). Group B included patients presenting with severe dysmenorrhoea (no response to conventional analgesic treatment such as antiprostaglandins and requiring bed rest)

and/or dyspareunia (limiting pain during sexual intercourse) and/or chronic pelvic pain (pelvic pain throughout the menstrual cycle for >6 months). (n = 22, 31.7%).

All patients were surgically treated within one week after sonographic evaluation and definitive histological diagnosis of ovarian endometriosis was obtained. Operative findings were retrieved from surgical reports. The presence and type of pelvic adherences, revised American Fertility Society (rAFS) scores and stages were recorded (American Society for Reproductive Medicine, 1997). Information about the presence of other types of endometriotic lesions, such as red or white peritoneal lesions, could not be reliably retrieved and, therefore, were not used in this study. Fifty-five (67.1%) laparoscopic and 27 (32.9%) laparotomic surgical procedures were performed. Ovarian cystectomy was done in 41 cases (50%), oophorectomy in nine cases (11%), salpingo-oophorectomy in 17 cases (21%) and total abdominal hysterectomy with bilateral salpingo-oophorectomy in 15 cases (18%).

Ultrasound

All patients were evaluated by TVCD before surgery using a Philips P-700 SE (Philips Ultrasound, Santa Ana, CA, USA) or Toshiba SSA-370 A (Toshiba Co., Tokyo, Japan) device, both equipped with 6.0–6.5 MHz electronic phased array endovaginal probes and 5 MHz colour and pulsed Doppler systems. TVCD is routinely performed in the evaluation of any adnexal mass in our department; therefore, no institutional ethics approval was required.

On B-mode ultrasonography an ovarian endometrioma was suspected if the typical pattern of a 'round-shaped homogeneous hypoechoic mass of low-levels echoes' was detected (Alcázar *et al*., 1997; Guerriero *et al*., 1998). Endometrioma volume was calculated according to the prolate ellipsoid formula (height×length×width× 0.5233) and expressed in ml. Colour and pulsed Doppler were used to assess endometrioma vascularity. Colour Doppler examination methodology has been described in detail previously (Alcázar *et al*., 1997). Briefly, after morphological evaluation was performed, colour Doppler gate was activated to identify vessels within the mass. Pulsed Doppler was used to interrogate each colour signal identified and a flow velocity waveform (FVW) was obtained. Only arterial FVW were processed. The peak systolic velocity (PSV, in cm/s) and the pulsatility index (PI) were electronically computed. When multiple signals were obtained, the highest PSV and lowest PI were used for analytical purposes. Sample volume was set at 1.2–2.0 mm width. High-pass filter was set at 50 Hz. Spatial peak temporal average intensity was <80 mW/cm^2 in B-mode, colour Doppler and pulsed Doppler modes. Pulse repetition frequency was set at 1.5–25.0 kHz.

CA-125 Measurements

Blood samples from each patient were collected to measure CA-125 plasma concentration on the same day TVCD was performed. CA-125 measurements were analysed using an enzyme-immunoassay with a monoclonal antibody (Cobas-Core CA-125 II, Laboratories Roche, Basel, Switzerland). The sensitivity was <5 UI/ml. The intra- and interassay coefficients of variations were <5.3 and <7.5% respectively.

Statistics

Data are presented as mean and SD, and 95% confidence intervals (CI) are given where appropriate. The Kolmogorov–Smirnov test was used to compare data distribution of continuous variables. The Student's t- or Mann–Whitney U-tests were used to compare continuous variables. The χ^2 test was used to compare categorical variables, using the Kendall Tau-b test in cases of ordinal variables such as pelvic adherences or rAFS endometriosis stage. A P value $\leqslant 0.05$ was considered as statistically significant. All statistical analyses were performed using the Statistics Package for Social Sciences (SPSS) 9.0 for Windows® (SPSS Inc., Chicago, IL, USA).

Table I. Velocimetric parameters and CA-125 levels according to patient complaints. Data expressed as mean (95% CI)

	Group A	Group B
PSV (cm/s)[a]	21.4 (18.1–24.7)	20.9 (16.4–25.4)
PI[b]	1.5 (1.3–1.7)	1.1 (0.9–1.2)
CA-125 (UI/ml)[c]	39.5 (30.7–48.4)	63.6 (48.3–78.8)

[a]P = 0.848.
[b]P = 0.009.
[c]P = 0.004.
PSV = peak systolic velocity; PI = pulsatility index.

Results

The mean ages in group A (35.1 years, SD: 8.5) and B (31.8 years, SD: 7.8) were similar.

The sonographic appearance of endometriomas was similar in both groups. In group A it was as follows: 44 typical pattern (78.6%), seven cystic with heterogeneous echoes (12.5%), four anaechoic (7.1%) and one cystic with solid areas (1.8%). In group B, 19 had typical pattern (73.1%), four were cystic with heterogeneous echoes (15.4%), two were anaechoic (7.7%) and one was cystic with solid areas (3.8%).

The mean volume of the endometriomas in group A (99.1 ml, SD: 149.2) and group B (83.6 ml, SD: 75.4) were comparable.

The presence and type of pelvic adherences were not statistically different between groups. In group A, nine patients (17.3%) had no adherences, 29 (55.8%) had smooth adherences and 14 (26.9%) had dense adherences. In group B, three patients (13.6%) had no adherences, eight (36.4%) had smooth adherences and 11 (50%) had dense adherences.

Mean rAFS score in groups A and B were 31.6 (SD: 19.3) and 38.7 (SD: 19.8) respectively (P = 0.127). No differences in the distribution of rAFS stages were found: in group A, 10 patients (19.2%) were stage II, 28 (53.8%) were stage III and 14 (26.9%) were stage IV. In group B, one patient (4.5%) was stage II, 13 (59.1%) were stage III and eight (36.4%) were stage IV.

Blood flow was found in 37 (66.1%) endometriomas in group A and 23 (88.5%) in group B (P = 0.036). Mean PI was significantly lower (P = 0.009) and mean CA-125 significantly higher (P = 0.004) in group B, but no differences were found in PSV (Table I).

A trend towards a statistically significant difference in mean PI and CA-125 with regards to the type of adherence (Table II) and rAFS stage (Table III) was found.

Table II. Pulsatility index (PI) and CA-125 levels according to type of adherence. Data expressed as mean (95% CI)

	No or smooth adherences	Dense adherences
PI[a]	1.4 (1.2–1.6)	1.1 (0.9–1.3)
CA-125 (UI/ml)[b]	41.8 (32.8–50.8)	58.1 (42.4–73.8)

[a]$P = 0.065$.
[b]$P = 0.084$.

Table III. Pulsatility index (PI) and CA-125 according to revised American Fertility Society stages. Data expressed as mean (95% CI)

	PI[a]	CA-125[b]
Stage II	1.7 (1.1–2.2)	35.6 (15.5–55.6)
Stage III	1.3 (1.1–1.5)	50.6 (39.3–70.0)
Stage IV	1.1 (0.9–1.4)	47.8 (32.9–62.6)

[a]$P = 0.054$.
[b]$P = 0.404$.

The likelihood ratio for severe pain and/or dyspareunia in the presence of a PI $\leqslant$1.2 (upper 95% CI in the group B) was 3.5 (95% CI: 1.2–10.3).

Discussion

In this study we evaluated the role of TVCD in the assessment of ovarian endometrioma vascularization according to the clinical complaints of the patients.

The presence of ovarian cystic endometriosis is associated with pelvic pain in women suffering this disease (Vercellini, 1997). On the other hand, angiogenic factors have been found to be increased in ovarian endometriomas (Fujimoto, 1998). Angiogenesis is related to vascularization. Therefore, a correlation between vascularization and the presence of pelvic pain might be assumed.

Some studies assessing angiogenic 'activity' in endometriosis have used either morphometric or immunohistochemical techniques in endometriotic tissue (Ferriani *et al*., 1993; Nisolle *et al*., 1993; Fujimoto *et al*., 1998; Matsuzaki *et al*., 1998). Other studies have evaluated vascular activity measuring serum or peritoneal fluid concentrations of angiogenic factors, such as vascular endothelial growth factor (McLaren *et al*., 1996; Donnez *et al*., 1998).

TVCD allows non-invasive in-vivo assessment of ovarian endometrioma vascularization (Kurjak and Kupesic, 1994; Aleem *et al*., 1995; Alcázar *et al*., 1997; Guerriero *et al*., 1998). To the best of our knowledge, no other study has evaluated the relationship between clinical symptoms and the vascularization features, as assessed by TVCD, in patients with histologically proven ovarian endometrioma.

Our data indicate that endometrioma vascularization seems to be increased in patients presenting with pelvic pain as compared with those who are asymptomatic, suggesting a higher activity of the lesions. The rate of vascularized endometriomas in our study was 77.1%, which is similar to that found by other authors (Aleem *et al*., 1995). The percentage of vascularized ovarian endometriomas was higher in group B (88.6%) than in group A (66.1%). However, other authors have found a higher rate using colour Doppler energy (Guerriero *et al*., 1998). Hence, a possible bias regarding the vascularity detection by using conventional colour Doppler ultrasound should be born in mind. Notwithstanding, this finding would be in agreement with previous studies that found an increased angiogenic activity in patients with painful pelvic endometriosis (Cornillie *et al*., 1990; Nisolle *et al*., 1993; Donnez *et al*., 1998; Matsuzaki *et al*. 1998). Furthermore, in those cases with pelvic pain CA-125 levels were higher. This tumoural marker has also been related to deep infiltrating endometriosis (Koninckx *et al*., 1996).

In our study we have not attempted to correlate Doppler findings with immunohistochemical or morphometric vascular analysis. We are aware that this is a weakness and would be a valuable endeavour in further studies. If our results are confirmed in larger and prospective series in which this correlation is performed, our findings could be of clinical relevance, as we would have a non-invasive method to evaluate activity of endometriomas, which could lead to important implications in the management of these patients.

Another possible bias could be the presence and type of pelvic adherences and rAFS scores in both groups. However, we did not find any statistical difference in these parameters between both groups. These findings might highlight further the observations about vascular features assessed by colour Doppler ultrasound.

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