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The use of ultrasound-based 'soft markers' for the prediction of pelvic pathology in women with chronic pelvic pain—can we reduce the need for laparoscopy?

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Objective To assess the accuracy of new transvaginal ultrasound-scan-based markers and to compare them to conventional ultrasound methods used in the detection of common pelvic pathology in women with chronic pelvic pain (CPP).

Design A prospective observational study.

Setting Teaching hospital.

Population A total of 120 consecutive women with CPP undergoing transvaginal ultrasonography before either diagnostic or operative laparoscopy.

Methods Anatomical abnormalities, e.g. endometrioma or hydrosalpinx (hard markers), were documented. The woman was then assessed for the presence or absence of 'soft markers' (reduced ovarian mobility and site-specific pelvic tenderness).

Main outcome measure Presence or absence of pelvic pathology noted during laparoscopy.

Results Seventy women had pelvic pathology, of whom 51 had endometriosis alone, 7 both endometriosis and pelvic adhesions, 6 pelvic adhesions, 1 hydrosalpinx with endometriosis and 5 hydrosalpinx and pelvic adhesions. The likelihood ratio for the hard markers was infinity (specificity was 100%), for the soft makers 1.9 (95% CI 1.2–3.1) and for a 'normal' ultrasound 0.18 (0.09–0.34). The pre-test probability of pelvic disease in our population of women with CPP was 58%, and this probability of disease was raised to 100% with the presence of hard markers and to 73% with the presence of soft markers. The pre-test probability of 58% fell to 20% when ultrasound finding was found to be normal.

Conclusion This new approach improves the detection and exclusion of significant pathology in women with CPP and may lead to a reduction in the number of unnecessary laparoscopies carried out on women with CPP.

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Introduction

The aetiology of chronic pelvic pain (CPP) is diverse, poorly understood, and often presents a perplexing clinical problem.[1,2] There is no universally accepted definition of CPP; hence, it is difficult to compare the results of studies in the literature.

Mathias *et al.*[3] conducted a telephone survey of 5263 women aged 18–50 years who were randomly selected from the general US population. The prevalence of CPP, defined as pelvic pain of at least 6-month duration and with pain having occurred in the past 3 months, was 14.7%. Another postal questionnaire survey by Zondervan *et al.*[4] in the UK involving 4000 women aged 18–49 reported a prevalence of 24%. Both these studies confirm that CPP is a common problem in the general population.

CPP accounts for 10% of gynaecological visits[5] and 50% of all diagnostic laparoscopies.[6] Gynaecologists use laparoscopy liberally as the 'gold standard' in the assessment of women with CPP.[6] The most common findings at laparoscopy are pelvic endometriosis and adhesions.[7] However, in up to 40% of women with CPP, laparoscopy fails to identify any obvious cause for the pain.[7] In the UK alone, the annual direct

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treatment cost for women with CPP is estimated at £152 million, with indirect costs of £24 million.[8] In 1992, it was estimated that the cost to the NHS for negative laparoscopies carried out in women with CPP was £182 million.[8] An improvement in the selection of women for laparoscopic procedures would clearly be of benefit to both patients and the wider NHS.

Conventionally, an ultrasound scan will report the presence or absence of pathology such as ovarian cysts or hydrosalpinges. However, more subtle information is available about the state of the pelvis based on the degree of ovarian and uterine mobility as well as tenderness. We have given these pelvic findings the term *soft markers* for the presence or absence of pelvic pathology. These subjective findings are usually not reported during routine scans. However, they have the potential to improve the diagnostic yield from transvaginal ultrasound scan (TVS).

The aim of this study was to prospectively evaluate these TVS-based soft markers for the detection of common pelvic pathology (endometriosis and pelvic adhesions) in women undergoing diagnostic laparoscopy for CPP.

Patients and methods

Between February 2001 and October 2002, 120 consecutive, premenopausal nonpregnant women with CPP booked for diagnostic or operative laparoscopy (adhesiolysis or excision/coagulation of endometriosis) were included in this study. The women were undergoing surgery for CPP, they were included if they met the following criteria: pain in the lower abdomen or pelvis, of at least 6-month duration, occurring continuously or intermittently, not associated exclusively with menstruation or sexual intercourse. The exclusion criteria were pregnancy and acute pelvic infection. The women filled out a questionnaire recording basic demographic data and the duration of pain. Visual analogue scores (1–100) were used to assess the severity of the pain. All the women had TVS 1–2 weeks before their surgical procedure as part of the routine management protocol for the unit. All the scans were performed by a single gynaecologist (E.O.) with substantial experience of transvaginal ultrasonography (over 7000 scans). An Aloka SSD 2000 or 4000 with a 5-MHz vaginal probe was used in all cases (Keymed, Southend on Sea, UK, and Aloka Co., Tokyo, Japan). Longitudinal and transverse views of the uterus and adnexa were obtained. The scan result was initially reported as normal or abnormal based on conventional findings (the presence or absence of hard markers for pelvic pathology). A hard marker was defined as a structural abnormality, e.g. an endometrioma or hydrosalpinx. If one or more hard markers were present, the scan was described as abnormal and in the absence of any hard markers, the scan was described as normal. The final ultrasound report placed in the patient's notes was based on these findings. The pelvis was also assessed for the presence or absence of the following soft markers.

1. Site-specific pelvic tenderness.
2. Ovarian mobility.
3. Presence of loculated peritoneal fluid in the pelvis.

Site-specific tenderness was chosen because tenderness over specific structures, e.g. the uterosacral ligaments, may be associated with the presence of endometriosis. Also, in women with endometriosis or pelvic adhesions, the ovary is frequently found to be adherent to the pelvic sidewall or the uterus at the time of laparoscopy. Loculated peritoneal fluid can be identified by TVS[9] and may be an indirect marker of pelvic pathology. The aim of this study was to see if this information could be obtained using TVS, and in combination with hard markers used to improve diagnostic confidence.

Site-specific pelvic tenderness was assessed by means of a verbal analogue score (1–10), the patient was asked to indicate any points of tenderness during the scan, which were noted on a data sheet. The presence of tenderness on TVS was described as positive. Ovarian mobility was assessed by gentle pressure with the transvaginal probe. When the uterus is anteverted, the ovary is usually situated over the internal iliac vessels and should glide freely when gentle pressure is applied to it. This was defined as 'freely mobile'. If the ovary did not glide freely when pressure was applied with the probe, it was defined as fixed. The location of the ovary was also noted, e.g. attached to the pelvic sidewall or the uterus. Ovarian mobility was thus scored as either freely mobile or fixed. The presence of loculated fluid in either the adnexa or the pouch of Douglas was recorded. The scan was described as abnormal if one or more of the soft markers were present and normal if there were no soft markers present. The assessment of TVS-based soft markers is subjective; we compared the inter-observer variation in 38 women between an expert sonographer and an experienced sonographer. The kappa between the two observers was moderate at 0.47.

All women had endocervical swabs taken for *Chlamydia* (DNA analysis; BDProbetec™, Sparks, MD, USA) and for microscopy and culture.

All women underwent a routine laparoscopy under general anaesthesia, and all procedures were uncomplicated. Either T.B. or another senior gynaecologist supervised all the cases. The surgeon was only notified of the presence of hard markers, e.g. endometrioma or hydrosalpinx, but blind to the ultrasound findings based on the presence or absence of soft markers. The surgeon was required to comment specifically in the notes on the following: the presence or absence of all pathology, but specifically endometriosis or pelvic adhesions, and their exact location. Ovarian mobility was assessed using a blunt probe or grasping forceps, via a 5-mm secondary port. The ovary was described as mobile if it was possible to rotate the ovary as to expose the ovarian fossa. The ovary

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was described as fixed if it was not possible to rotate it to expose the ovarian fossa, as a result, for example, of pelvic adhesions or endometriosis. The degree of severity of the adhesions and endometriosis was determined using the revised American Fertility Society (r-AFS) classification system.[10] Detailed and complete operation records were available for all cases. The operation findings were entered on to a database. The operation findings were correlated with the ultrasound findings. The likelihood ratios were calculated for TVS using the laparoscopy findings as the end point. Associated 95% confidence intervals were calculated for each of the estimates of sensitivity and specificity. Data were analysed using the chi-square test and the nonparametric Wilcoxon rank sum test. For all analysis, a two-tailed *P* value of less than 0.05 was considered to indicate a statistically significant difference.

Results

The mean age of the patients was 31 years (range 18–50 years), and the mean duration of pain was 46 months (range 6–180 months). All women had a negative infection screen prior to laparoscopy. At laparoscopy, 70 (58%) women had pelvic pathology and 50 (42%) had a normal pelvis. Of 70 women with pelvic pain, 51 had endometriosis alone, 7 endometriosis and pelvic adhesions, 6 pelvic adhesions alone, 1 hydrosalpinx with endometriosis and 5 a hydrosalpinx and pelvic adhesions. Of the 59 women with endometriosis, 39 had grade I–II, while 20 had grade III–IV disease based on the r-AFS classification. Of the 18 women with pelvic adhesions, 12 had grade II adhesions and 6 had grade I adhesions.

The TVS results were classified as abnormal based on the presence of hard and soft markers. The performance of the scan markers versus laparoscopy is shown in Table 1. Normal ultrasound findings based on the absence of hard markers were found in 96 women, and 24 women had an abnormal scan based on the presence of hard markers. Of the 24 women with hard markers, 17 had a cyst with characteristic low-level echoes consistent with an endometrioma, 6 had a dilated cystic structure in the adnexa distinct from the ovary consistent with a hydrosalpinx and 1 had an endometrioma and hydrosalpinx. All 18 endometriomas were confirmed at laparoscopy and by histological analysis. Five of the six (83%) hydrosalpinges detected on TVS were confirmed at laparoscopy; in the sixth case, the tubes were normal.

Of the 96 women with a normal ultrasound scan based on the absence of hard markers, 51 (53%) had an abnormal scan based on the presence of soft markers. The remaining 45 women had no soft markers suggestive of pelvic pathology. On TVS, no patient had loculated fluid, so this variable was excluded from the analysis. At laparoscopy, 46 women (48%) had pelvic pathology (41 endometriosis [29 grade I–II and 12 grade III–IV] and 5 pelvic adhesions [grade II]), while 50 (52%) had a normal pelvis. The women with an abnormal scan diagnosis had significantly more tenderness in the left ovary/adnexa, right ovary/adnexa, uterus and pouch of Douglas than those with a normal scan diagnosis ($P < 0.001$) (Table 2). Also, women with an abnormal scan diagnosis had fixed ovaries. At laparoscopy, 37 women in the soft marker subgroup had a true positive scan result. The diagnoses were 30 cases of endometriosis, 6 cases of adhesions and a case of endometriosis and adhesions. Nine women had a false-negative diagnosis by TVS. At laparoscopy, 8 of 9 women had grade I–II endometriosis and the remaining case was stage III disease. In this study, the strength of the agreement between TVS-based hard and soft markers and laparoscopy for the diagnosis of pelvic pathology (0.63 kappa) and assessing ovarian mobility (0.80 kappa) were substantial and almost perfect, respectively.

Discussion

This prospective study has highlighted an approach to the use of TVS in the evaluation of women with CPP that uses all the information made available by the scan.

In our series, the pre-test probability of detecting pathology at the time of laparoscopy was 58%. This finding is in keeping with the published literature.[7] Forty-nine percent of women

Table 1. The performance of scan markers vs laparoscopy (n = 120)

TVS	Laparoscopy		Likelihood ratios (95% CI)	Post-test probability (%) for the study population*
	Abnormal	Normal		
Hard marker	24	0	Infinity	100
Soft marker	37	14	1.9 (1.2–3.1)	73
Normal	9	36	0.18 (0.09–0.34)	20
Total	70	50		

*The pre-test probability of pelvic pathology in our study population was 58% (70/120).

Table 2. The performance of site-specific tenderness and ovarian mobility in all women based on scan diagnosis

Soft markers	Scan diagnosis		*P* value
	Normal (*n* = 43)	Abnormal (*n* = 77)	
Tender uterus (1–10) (mean ± SD)	0.1 ± 0.7	3.8 ± 3.3	<0.001
Tender left ovary/adnexa (1–10) (mean ± SD)	0.23 ± 0.9	4.5 ± 3.2	<0.001
Tender right ovary/adnexa (1–10) (mean ± SD)	0.1 ± 0.7	4.0 ± 3.2	<0.001
Tender pouch of Douglas (1–10) (mean ± SD)	0 ± 0	4.2 ± 3.4	<0.001
Fixed ovaries (%)	0	34	<0.001

had endometriosis, although some studies have shown the prevalence to be as high as 71–80%.[11,12] Two-thirds of the women in our series had grade I–II disease.

The efficacy of ultrasonography for the assessment of women with CPP has not been widely evaluated. Ozaksit *et al.*[13] reported on the use of clinical examination, TVS and laparoscopy in 45 women with CPP. The positive predictive value of an abnormal scan was 94%, and the negative predictive value of a normal scan was 60%. This study did not define a normal and abnormal scan and included only adolescent women. In another study, Harris *et al.*[14] evaluated the clinical outcome of women with all types of pelvic pain and normal TVS findings. Overall, the pain improved in 77% (66/86) of women; however, the pain improved in only half of the 14 women with CPP. A normal TVS was not defined, and the study commented on the negative predictive value of a normal scan only, and it is not possible to comment on sensitivity or specificity.

In our study, on the basis of hard markers alone, TVS had a likelihood ratio of infinity (specificity was 100%). Not surprisingly, the use of hard markers alone resulted in a high false-negative rate. This is because adhesions and peritoneal endometriosis are generally not detected. In contrast, all 18 endometriomas diagnosed by TVS were confirmed by laparoscopy and histology, which is consistent with previously published data.[15,16] Five of the six hydrosalpinges diagnosed by ultrasound were confirmed at laparoscopy, which again is in agreement with previous studies.[17]

In a bid to harness, the additional information available to us when we perform a TVS is that we have developed the concept of TVS-based soft markers. In this series, 80% (96/120) of the women would have conventionally had their scans classified as normal due to the absence of hard markers. However, 53% (51/96) of those women had an abnormal scan on the basis of soft marker analysis. Seventy-three percent of (37/51) of these women with soft markers had pelvic pathology at laparoscopy. This pathology consisted of pelvic adhesions and peritoneal endometriotic deposits, which challenges the assertion that pelvic sonography has no role in the detection of these conditions.[18] Those patients with an abnormal scan were more likely to have site-specific tenderness and fixed ovaries ($P < 0.001$). There was a substantial correlation between the scan diagnosis and the laparoscopic findings (0.63 kappa). Similarly, there was near-perfect correlation between ovarian mobility on TVS and at laparoscopy (0.81 kappa) as an indirect marker of pelvic pathology. In this series, no patient had loculated fluid on TVS. However, when present, pelvic adhesions may be identified as fine hyperechoic strands that are frequently seen to sway when pressure is applied with the vaginal probe.[9] Guerriero *et al.*[19] evaluated TVS for the diagnosis of pelvic adhesions. They evaluated clinical factors alongside an ultrasound-based assessment of ovarian mobility, using the distance from the ovary to the probe and blurring of the margins of the ovary in women with a variety of clinical symptoms. In their study, ovarian mobility was the most accurate marker of pelvic adhesions but only had a moderate kappa score of 0.50. Our study differs from that of Guerriero *et al.* in that we have used pressure with the probe to assess ovarian mobility. In our experience, this alone is an accurate measure of ovarian mobility and is not affected by the habitus of the patient. As the majority of women with CPP have endometriosis as the most common laparoscopic diagnosis, blurring of the margins of the ovary is not an important marker in our population.

In our series, those patients with a false-negative scan result were found to have endometriosis at laparoscopy, and the majority were of a low grade, which would be amenable to medical therapy. The assessment of ovarian mobility and site-specific tenderness is subjective and requires expertise in the use of transvaginal ultrasound in assessing pelvic pain, and in this series, consecutive patients who met the criteria for CPP were included in the study. Laparoscopy is the established gold standard for assessing women with CPP. Our results suggest that TVS can be used to triage patients with CPP into low- and high-risk groups in terms of finding common pelvic pathology such as endometriosis or pelvic adhesions during laparoscopy.

Laparoscopy is not without complications[20,21] and must not be viewed as a panacea for CPP. Realistically, the primary role of laparoscopy in women with CPP is to diagnose endo-

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metriosis or adhesive disease. The need for laparoscopy for the diagnosis or treatment of CPP secondary to endometriosis has been debated.[7] This is emphasised by the fact that during laparoscopy, it may be difficult to diagnose minimal disease or lesions, which are atypical in appearance.[22] Our data suggest that TVS-based soft markers can facilitate appropriate patient selection for further investigation including surgery.

Nine women had a false-negative diagnosis using soft markers; the majority of these cases were grade I–II disease. The fact that these cases were not detected may represent the poor correlation between symptoms and signs with women with endometriosis. In our practice, we reassure those patients with no soft markers as the majority will have a normal pelvis at laparoscopy, and offer then expectant management, and a review in 6 months. In women with soft markers, one option would be a trial of medical therapy. Gonadotrophin-releasing hormone analogues have been shown to suppress pelvic pain in women with endometriosis compared with placebo.[23] The oral contraceptive pill (OCP) has also been shown to have a high degree of success in relieving pain as initial management of primary dysmenorrhoea.[24,25] In women with positive soft markers, the differentiation between endometriosis and pelvic adhesions can be difficult, and the use of serum markers such as CA125 has been suggested; however, this may not be helpful as CA125 is elevated in both conditions.[26,27] In our clinical practice, we suggest the OCP to the majority of our patients as first-line therapy, and in 2002 CPP/endometriosis working group have recommended that in the absence of an endometrioma, a trial of medical therapy is justified in women with CPP suspected of having endometriosis prior to laparoscopy.[28] The working group did not assess the role of TVS in CPP, and although we welcome their recommendations, we believe that TVS-based triage may improve patient selection for further management, avoiding surgical intervention in women without soft markers. Using TVS-based soft markers to assess women with CPP, it may be possible to significantly reduce the number of laparoscopies carried out on women with CPP. This would be advantageous both to patients and to hospitals in that they could reallocate resources elsewhere.

Conclusion

Our data suggest that the inclusion of site-specific tenderness and ovarian mobility as indirect ultrasound-based markers of pelvic pathology improves our ability to predict or exclude the presence of pelvic pathology in women with CPP. In this series, the pre-test probability of pelvic disease in our population was 58%, and this probability of disease was raised to 100% with the presence of hard markers and to 73% with the presence of soft markers. The pre-test probability of 58% fell to 20% when ultrasound findings were found to be normal. The use of both TVS-based hard and soft markers may lead to a significant reduction in the number of diagnostic laparoscopies performed in women with CPP. We recognise that these data relate to a relatively small number of patients derived from one unit. Prospective studies are needed to assess the reproducibility of the use of TVS-based soft markers in different centres on different patient populations.

Contributors

E.O. planned the study, performed the scans, obtained the background information and data, and wrote the paper. G.C. and A.K. obtained the data and commented on drafts. D.T. supervised the statistical analysis and commented on drafts. L.A. and S.V.H. carried out the statistical analysis and commented on drafts, and T.B. suggested the idea for the paper and commented on drafts and supervised the project overall. E.O. is guarantor. The statistical analysis was carried out under the framework of the Belgian Programme on Interuniversity Poles of Attraction, initiated by the Belgian State Prime Minister's Office for Science, Technology, and Culture (IUAP Phase V-22). The Concerted Action Project MEFISTO-666 (Mathematical Engineering for Information and Communications Technology) of the Flemish Community, and the IDO/99/03 project entitled 'Predictive computer models for medical classification problems using patient data and medical expert knowledge' (K.U. Leuven).

Conflict of interest

None declared. ■

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