Transvaginal ultrasonography versus uterine needle biopsy in the diagnosis of diffuse adenomyosis

Paolo Vercellini1,3, Ilénia Cortesi1, Olga De Giorgi1, Daniela Merlo2, Silvestro G.Carinelli2 and Pier Giorgio Crosignani1

1Clinica Ostetrica e Ginecologica ‘Luigi Mangiagalli’, University of Milano, and 2Servizio di Istituzione ed Anatomia Patologica, Istituti Clinici di Perfezionamento, Milano, Italy

Introduction

Adenomyosis may be associated with dysmenorrhoea and menorrhagia, constitutes a common indication for hysterectomy, and is often encountered on pathological examination of uteri removed at surgery (Azziz, 1989; Vercellini et al., 1993, 1995, 1996; Brosens et al., 1995a; Parazzini et al. 1997).

In the diffuse form of the condition, foci of endometrial glands and stroma are scattered throughout the myometrium. Less frequently, these foci occur in a localized form, the so-called adenomyoma (Zaloudek and Norris, 1994). Until a few years ago, interest in the disease was limited by the impossibility of making a reliable preoperative diagnosis and the absence of alternatives to definitive treatment. Recently, imaging (magnetic resonance imaging, MRI, and pelvic ultrasonography, US) and biopsy (transabdominal or transuterine myometrial biopsy) techniques have been applied to women with suspected adenomyosis in attempts to make diagnoses with the uterus in situ (Fedele et al., 1992a,b; McCausland, 1992; Popp et al., 1993; Wood et al., 1993a,b; Ascher et al., 1994; Brosens and Barker, 1995; Brosens et al., 1995b; de Souza et al., 1995; Reinhold et al., 1995; Vercellini et al., 1996). This may be of clinical relevance now that conservative therapeutic options have been developed (Fedele et al., 1993; Wood et al., 1993c). Moreover, identifying adenomyosis before performing endometrial ablation and differentiating adenomyosis from leiomyomas before offering conservative surgery is important for adequate preoperative counselling and for the choice of the correct type of intervention (Fedele et al., 1992b; McCausland and McCausland, 1996; Goldberg et al., 1997). However, information on the best diagnostic modality and on the utility of combining different tests is limited and sometimes contradictory (Ascher et al., 1994; Arnold et al., 1995; Reinhold et al., 1996). Unfortunately, MRI, considered by some authors the most accurate modality for the preoperative diagnosis of adenomyosis (Ascher et al., 1994), is expensive and not always available; hysteroscopic biopsy does not permit histological assessment of the entire uterine wall thickness and may not be acceptable in women wanting children. Therefore, we set out to compare the accuracy of transvaginal US versus myometrial needle biopsy and to evaluate the reliability of the combination of the two tests in the diagnosis of diffuse adenomyosis in a prospective consecutive series of patients undergoing hysterectomy for benign conditions, considering the histological diagnosis based on removed uteri as the reference standard.

Materials and methods

Consecutive premenopausal patients with a uterus measuring less than a 12 week pregnancy undergoing hysterectomy for menorrhagia and/or worsening dysmenorrhoea in an academic department of obstetrics and gynaecology were included in the study. Women with a grossly distorted uterus due to multiple or large leiomyomata or with known endocavitary or endometrial anomalies, or who received steroidal or gonadotrophin-releasing hormone agonist treatment in the preceding 3 months were excluded from the study. Within the

© European Society for Human Reproduction and Embryology
week prior to hysterectomy, all the women underwent US using Ansaldo AU 440 (Ansaldo, Genoa, Italy) or AU 580 synchronous (Hitachi, Tokyo, Japan) equipment and a transvaginal transducer of 6.5 MHz. The sonographer diagnosed adenomyosis by the presence of indistinctly demarcated heterogeneous myometrial areas with distorted echotexture. Myometrial echotexture was defined as distorted by the presence of abnormally decreased or increased echogenicity and/or round anechoic areas (Figure 1). After removal of the uterus, a single full-thickness myometrial biopsy specimen was taken from along the median line in the upper third of the posterior uterine wall using a 14-gauge Trucut needle (Bio-cut, Sterylab S.p.A., Milan, Italy; Figure 2) (Vercellini et al., 1996). Only one expert sonographer interpreted the US examinations and one surgeon performed the uterine biopsies. The uterus was opened by the pathologist at the left margin and fundus and four blocks of uterine wall were examined. All needle biopsy specimens were labelled and stored and then examined on a single occasion at the end of the study. A diagnosis of adenomyosis was made when the distance between the lower border of the endometrium and the affected myometrial area was more than half of a low-power field (~2.5 mm) (Zaloudek and Norris, 1994). The pathologist was blind with respect to the sonographic diagnosis, and, when examining the needle biopsy specimens, unaware of the original histological uterine findings. In cases of doubtful interpretation at US and histological needle biopsy examination, the findings were considered abnormal.

To assess the accuracy of the ultrasonographic and needle-biopsy diagnoses, the sensitivity, specificity, predictive value of an abnormal (PPV) and normal (NPV) test were calculated, considering as the true diagnoses those made at histological examination of the removed uteri (Altman, 1994; Armitage and Berry, 1994; Jaeschke et al., 1994). To evaluate the reliability of combining transvaginal US with myometrial needle biopsy in the diagnosis of adenomyosis, we also calculated the above variables, considering the combination of the tests positive when either of the two was abnormal (to improve sensitivity) and when both were abnormal (to improve specificity) (Altman, 1994; Armitage and Berry, 1994; Jaeschke et al., 1994). To compare the values of single and combined diagnostic tests in a prevalence-independent manner, we also calculated likelihood ratios for a positive (LR+) and a negative (LR−) test result (Altman, 1994; Armitage and Berry, 1994; Jaeschke et al., 1994). The k statistic was used to evaluate the overall agreement between a test result and the true diagnosis (Landis and Kock, 1977; Fleiss, 1981).

**Results**

A total of 115 patients was recruited for the study of whom 13 were excluded from analysis for various reasons (performance of transabdominal US alone, two cases; presence of multiple small leiomyomata on the posterior uterine wall making accurate US and needle biopsy difficult, five cases; fragmentation of the needle biopsy specimen, six cases). The mean ± SD age of the remaining 102 women was 45 ± 6 years. Eighty-six of them were parous and 16 nulliparous. The pathologist diagnosed adenomyosis in the removed uterus in 29 cases, giving an overall prevalence of the condition of 28%. The sonographer diagnosed adenomyosis in 48 subjects, histologically confirmed in 24 cases; that is, US yielded 24 false positive results. The mean ± SD US uterine volume calculated according to the usual formula for a prolate ellipsoid (length×width×depth×0.5236) was 129 ± 47 ml in the women with and 116 ± 41 ml in those without adenomyosis. The US finding of anechoic lacunae, which were identified

![Figure 1](image-url)
but not measured, was associated with the presence of dilated glands within ectopic endometrium. Transvaginal US did not detect adenomyosis in five instances. Myometrial needle biopsy diagnosed adenomyosis in 16 women, which was demonstrated also at histological examination in 13 cases, the other three being false positives. Needle biopsy did not detect adenomyosis in 16 subjects. The combination of two positive tests recognized 10 of the 29 cases of adenomyosis and gave one false positive result. When only one of the two tests was positive the combination yielded only two false negative results, but 26 of the 53 positive diagnoses were not confirmed. The performance of transvaginal US and myometrial needle biopsy, both singly and combined, as a diagnostic test for diffuse uterine adenomyosis is shown in Table I. US had a low PPV (50%) compared both with needle biopsy and with the two tests combined. The LR+ for the combination of two positive tests was 24.6, which indicated that a subject with adenomyosis was almost 25 times more likely to have a positive test than a healthy subject. Furthermore, the optimal LR− (0.1) was obtained with the combination of the two tests but when only one of them was positive. That is, a woman with adenomyosis was one-tenth more likely to have a negative test than a woman without the disease. Overall, the $k$ index of agreement between single or combined diagnostic tests and actual histological diagnosis was only fair, ranging from 0.40 (combination of US and needle biopsy, both positive) to 0.47 (needle biopsy alone).

### Discussion

Transvaginal US for the diagnosis of adenomyosis has been evaluated by Fedele et al. (1992a) and Brosens et al. (1995b) with partly inconsistent results: specificity was 74% in the former and only 50% in the latter study. This is of practical importance for dealing with a chronic condition like adenomyosis which is not life-threatening. In such a situation it is opportune to rely on a test with high specificity in order to avoid undue invasive procedures and unnecessary surgical interventions (Altmann, 1994; Armitage and Berry, 1994). Reinhold et al. (1995) have reported a specificity as high as 86% for transvaginal US, and, unlike other authors (Ascher et al., 1994), found that the diagnostic accuracy of US and MRI was similar (Reinhold et al., 1996). Also, myometrial needle biopsy has already undergone evaluation as a single test for adenomyosis with variable test performances depending on the number of biopsies taken and the gauge of the Trucut needle used (Popp et al., 1993; Wood et al., 1993b,c; Brosens and Barker, 1995; Vercellini et al., 1996). In fact, adenomyosis is frequently a patchy disease and the predictive value of a normal needle biopsy specimen may be limited (Zaloudek and Norris, 1994; Vercellini et al., 1996). However, the clinical relevance of needle biopsy, whether US or laparoscopically guided, lies in the possibility of an in-vivo diagnosis; in this circumstance, no more than a single specimen should be taken and considerations on test performance when obtaining multiple biopsies are, in our opinion, of more academic than practical interest. In the present study, the biopsies were done in vitro under optimal conditions after hysterectomy; the results of in-vivo biopsies may be less satisfactory because of technical difficulties during the sampling procedure. In all cases we used a 14-gauge Trucut needle, which has a diameter of 2 mm and has been demonstrated to obtain the best specimen for pathological examination (Popp et al., 1993). We performed needle biopsy through the posterior uterine wall because this is the site most frequently involved in diffuse adenomyosis (Zaloudek and Norris, 1994). To our knowledge, this is the first study to compare transvaginal US and needle biopsy in the same series of patients. Three findings at histological examination of needle biopsy specimens were doubtful. In all these instances the positive diagnosis made was false. This was probably due to technical artefacts related to the myometrial
sampling technique and/or the preparation of the slides. Although needle biopsy was more specific than US (95.9 versus 67.1%), the sensitivity of the former was so low (44.8%) that it undermined its overall reliability. This is also true when the two tests, both positive, were combined to increase specificity. In fact, this yielded the lowest rate of false positive results (1.4%) among the various test performances, but at the cost of the worst sensitivity (34.5%). The combination of a positive and a negative test produced figures substantially similar to those of US alone and does not seem to be advantageous; in both these instances, a low PPV was observed (about 50%). This last finding is at odds with previous ones reported by Fedele et al. (1992a) and Brosens et al. (1995b) and may be partly explained by the higher prevalence of disease in those series (respectively 47 and 50%) compared with that in our study population (28%). However, our figure was not unexpected, as it is consistent with the prevalence of adenomyosis observed by us in a large series of patients who underwent hysterectomy for various conditions in our department (Vercellini et al., 1996; Parazzini et al., 1997). The index of agreement with actual histological findings was similar in all diagnostic subgroups and revealed a homogeneously suboptimal performance profile (Landis and Kock, 1977; Fleiss, 1981; Altman, 1994; Armitage and Berry, 1994).

Furthermore, inclusion in the analysis of the cases that were not considered for various reasons would probably have influenced the two test performances unfavourably. In conclusion, in our study transvaginal US and myometrial needle biopsy, whether used singly or in combination, were not highly accurate in the diagnosis of diffuse adenomyosis. According to our experience, myometrial needle biopsy does not seem to add useful information to that obtained at transvaginal US and, in our opinion, should not be implemented in routine practice. Further studies are needed to standardize the correct histological threshold limit for the diagnosis of adenomyosis and to define the potentially more accurate US signs of the disease, as both these variables can greatly influence test performance. Finally, future research should disentangle the contradictory findings on the presumed superiority of MRI compared to US (Ascher et al., 1994; Reinhold et al., 1996) in the preoperative identification of this elusive uterine condition.

References