

## ORIGINAL ARTICLE

# Multicentre retrospective study to assess diagnostic accuracy of ultrasound for superficial endometriosis—Are we any closer?

Prathima Chowdary<sup>1,2</sup> , Kate Stone<sup>1</sup>, Tony Ma<sup>1</sup>, Emma Readman<sup>1,4</sup>, Kate McIlwaine<sup>1,4</sup>, Marilla Druitt<sup>3</sup>, Lenore Ellett<sup>1,4</sup>, Melissa Cameron<sup>4</sup> and Peter Maher<sup>1,4</sup>

<sup>1</sup>Mercy Hospital for Women, Melbourne, Victoria, Australia

<sup>2</sup>University of Auckland, Auckland, New Zealand

<sup>3</sup>St John of God Geelong, Geelong, Australia

<sup>4</sup>Epworth Hospital, Melbourne, Australia

*Correspondence:* Dr Prathima Chowdary, Mercy Hospital for Women, 163 Studley Rd, Heidelberg, Victoria 3084, Australia. Email: prath1mak@yahoo.co.in

*Conflict of Interest:* The authors report no conflicts of interest in the proof.

Received: 3 April 2018;

Accepted: 16 September 2018

**Background:** To establish whether the ultrasound findings of minimal endometriosis are confirmed at laparoscopy and that a correlation can be established as to the anatomical sites in this mild form of the disease.

**Aims:** Patients with pain and suspicion of endometriosis had an ultrasound scan by a sonologist with expertise in endometriosis as part of their pre-operative workup.

**Measurements and Main results:** The clinical histories of 53 patients who had laparoscopy to investigate pelvic pain were reviewed. Ultrasounds were performed between 2012 and 2015 by a single sonologist with expertise in endometriosis assessments. The ultrasound findings were divided into subgroups as follows – presence of uterosacral ligament thickness, thickened pericolic fat, ovarian mobility and focal tenderness. These were compared with operative findings of those patients with superficial endometriosis. Evidence Level 3 – observational studies with controls and health services research that includes adjustment for likely confounding factors.

**Results:** Seventy-nine percent (42/53) of the patients had laparoscopic findings consistent with their ultrasound findings (95% CI 68–90%,  $P < 0.0001$ ). Of the subgroups that we reviewed, uterosacral thickening ( $P < 0.05$ ) and thickened pericolic fat ( $P < 0.05$ ) were the most associated with superficial endometriosis at the time of laparoscopy.

**Conclusion:** Markers on ultrasound that reliably demonstrated inflammation (thickened uterosacral ligaments and thickened pericolic fat) were shown to be significantly associated with the disease.

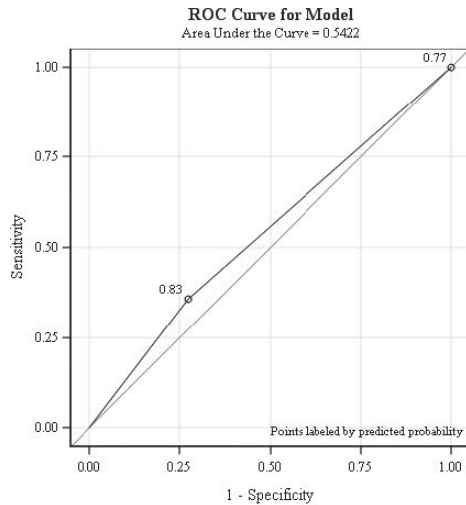
## KEYWORDS

superficial endometriosis, ultrasound scan, endometriosis symptoms

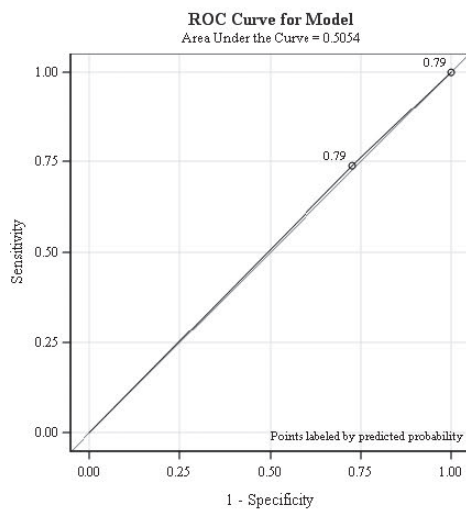
## INTRODUCTION

Endometriosis is a chronic benign condition, the diagnosis made when endometrial glands and stroma are found in locations outside the uterine cavity. Although typically not life-threatening, it is associated with significant morbidity and a negative impact on a woman's quality of life.<sup>1</sup>

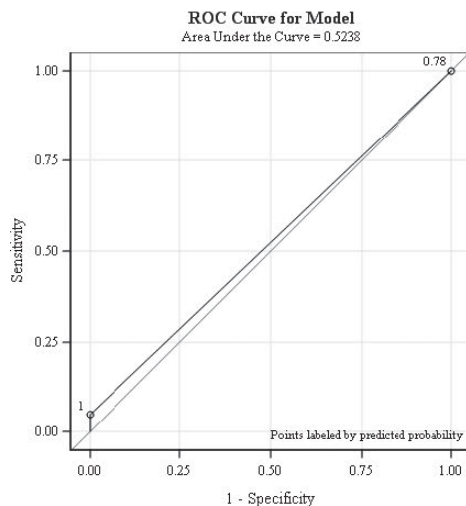
The hunt for a non-invasive test to diagnose mild-moderate endometriosis has been extensive.<sup>2</sup> Considering that the diagnosis of endometriosis is often delayed, the burden of undiagnosed, untreated endometriosis remains poorly understood.<sup>3</sup> Superficial endometriosis presents a challenging surgical problem, particularly when we counsel patients of perceived surgical outcomes. Pre-operative investigations are important in order to provide the



**Ovarian mobility (Model vs. Chance, no difference,  $p = 0.5966$ )**



**Focal tenderness (Model vs. Chance, no difference,  $p = 0.9449$ )**



**Filmy adhesions (Model vs. Chance, no difference,  $p = 0.1522$ )**

patient and surgical team with information regarding the severity of the disease and the likely surgery required, thus improving patient knowledge and facilitating triage of resources and personnel.

**FIGURE 1** Ovarian mobility (Model vs Chance, no difference,  $P = 0.5966$ ). Focal tenderness (Model vs Chance, no difference,  $P = 0.9449$ ). Filmy adhesions (Model vs Chance, no difference,  $P = 0.1522$ ).

One unit (Mercy Hospital for Women) has been managing severe endometriosis patients with a multidisciplinary team over the last six years. The aim of this study was to perform a retrospective univariate analysis to confirm which factors, if any, might be predictive of the presence of superficial endometriosis at the time of surgery. This information will then be used as the basis upon which to develop a scoring system which can be assessed prospectively in a future study.

## MATERIALS AND METHODS

All of the unit's surgical database was reviewed to detect patients who had undergone an ultrasound.

The variables scored in a univariate analysis for predictive capacity were:

- uterosacral thickness
- thickened pericolic fat
- focal tenderness
- ovarian immobility
- filmy adhesions
- symptoms – dysmenorrhoea, dyschezia, dysuria and dyspareunia.

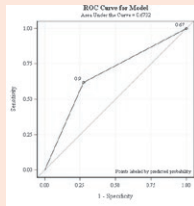
Ethics approval was obtained prior to data collection through low-risk ethics application Mercy Health Human Research Ethics Committee and Epworth Hospital R16/41.

Ultrasounds were performed between 2012 and 2015 by a single gynaecologist/sonologist with expertise in endometriosis assessments. Surgeries at the Mercy Hospital for Women, Epworth hospital, and St John of God Geelong Hospital were performed by surgeons trained in advanced laparoscopy and currently working in a tertiary endometriosis surgical unit. Patients who had deep infiltrative endometriosis, endometriomas and adenomyosis were excluded. Adenomyosis was defined by the ultrasound findings of heterogenous myometrium (venetian blinding), asymmetry of uterine walls and presence of myometrial cysts.<sup>4</sup>

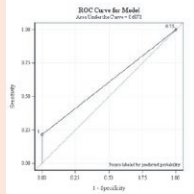
## Statistical analysis

Patient data was entered into an Excel database and imported to SAS version 9.4 (SAS Institute Inc. Cary, NC, USA) for analysis. Each potential ultrasound predictive parameter was analysed

**TABLE 1** Laparoscopic findings matching ultrasound scan findings



**US thickening (Model vs. Chance, significant difference,  $p = 0.0304$ )**



**Thickened pericolic fat**

**(Model vs. Chance, significant difference,  $p = 0.0008$ )**

**Lap match USS (n = 53, 30 patients missing)**

	Number	Proportion	Standard Error	Lower 95% CI	Upper 95% CI	P-value
Yes	42	79.25%	5.57%	68.33%	90.16%	<0.0001

79% of the patients with the lap results were matched to their USS findings (95% CI 68-90%,  $p < 0.0001$ ).

separately as follows: uterosacral ligament thickness, thickened pericolic fat, ovarian mobility and focal tenderness. Other parameters collected were age, body mass index (BMI) and symptoms including dysmenorrhoea, dysuria, dyspareunia, dyschezia and dysmenorrhoea.

Descriptive statistics were used to summarise all variables. Continuous variables were described as mean and standard deviation. Categorical variables were described as frequency and percentage. The proportion of patients with confirmation of superficial endometriosis on laparoscopy was classified as laparoscopic findings consistent with their ultrasound findings and was estimated with 95% confidence intervals. Difference in BMI and age between patients with positive and negative findings was tested using analysis of variance. Standard diagnostic and agreement statistics were calculated to assess the predictive effects of individual soft markers and symptoms on operation findings. Sensitivity, specificity and receiver operating characteristic (ROC) curve were estimated. They are demonstrated as ROC curves (Fig. 1) All statistical tests were two-sided at 5% significance level (Table 1).

The data was assessed for accuracy of single marker predictiveness for superficial endometriosis.

### Imaging protocol

A transvaginal ultrasound was performed in the weeks prior to surgery, as part of routine preoperative care and assessment of pelvic pain. Patients were assessed at any time of the menstrual cycle and the time between initial scanning and surgical date was not analysed in the present study. A Voluson E8, with a 5–9 MHz vaginal probe was used in all cases, and the scans were performed by a single experienced operator.

The operator has gained significant experience in the preoperative ultrasound assessment of cases with known stage four and deep endometriosis working with this tertiary gynaecological unit. Evaluations were made of the uterus, ovaries and the pelvic peritoneum which included the bladder, vesico-uterine pouch, pouch of Douglas, recto-cervical space, rectovaginal septum, and posterior vaginal fornix.



Thickened pericolic fat

**FIGURE 2** Demonstrating thickened pericolic fat.

Bowel preparation in the form of a fleet enema was used prior to ultrasound in a selected group of patients where there was a clinical suspicion of deep rectal endometriosis, or if it was required to allow adequate ultrasound assessment of the rectum, recto-sigmoid and rectovaginal septum. Patients with a finding of deep rectal endometriosis or rectovaginal disease were excluded from the present study due to their diagnosis of deep infiltrative endometriosis.

Bowel preparation in the form of fleet enema was used prior to ultrasound in a selected group of patients where there was a clinical suspicion of deep rectal endometriosis. The decision was made prior to the ultrasound by the referring clinician. Exclusion of deep endometriosis is important in any imaging assessment. If the rectal wall is involved then bowel preparation facilitates a detailed assessment of the rectal disease. Patients with deep endometriosis were excluded from the study. Bowel preparation is not required in the assessment of markers for superficial endometriosis.

Uterosacral ligaments were assessed by obtaining an axial view of the cervix, with angulation of the vaginal probe into the right and left para-cervical areas (Fig. 2) These visceral ligaments were reported to be thickened if they were assessed to be greater than three millimetres. Mobility and tenderness of the uterosacral ligaments were reported in conjunction with this at the time of the scan. Pericolic fat is the fat surrounding the colon. It is commonly involved in inflammatory processes involving the pouch and rectum. This was also reported in a dichotomous scoring system. Thickened pericolic fat appeared to have increased echogenicity/density secondary to inflammatory and fibrotic changes, and was firm to probe pressure. Thickened pericolic fat can be difficult to identify. On computed tomography this is called fat stranding – altered appearance to the lipomatous tissue in rectal wall mesentery rather than rectal wall itself (Figs. 2 and 3).

Normal pericolic fat is pedunculated adipose tissue, with ‘thickened pericolic fat’ equating to ‘fat stranding’ reported in inflammatory bowel conditions.<sup>5</sup>

## RESULTS

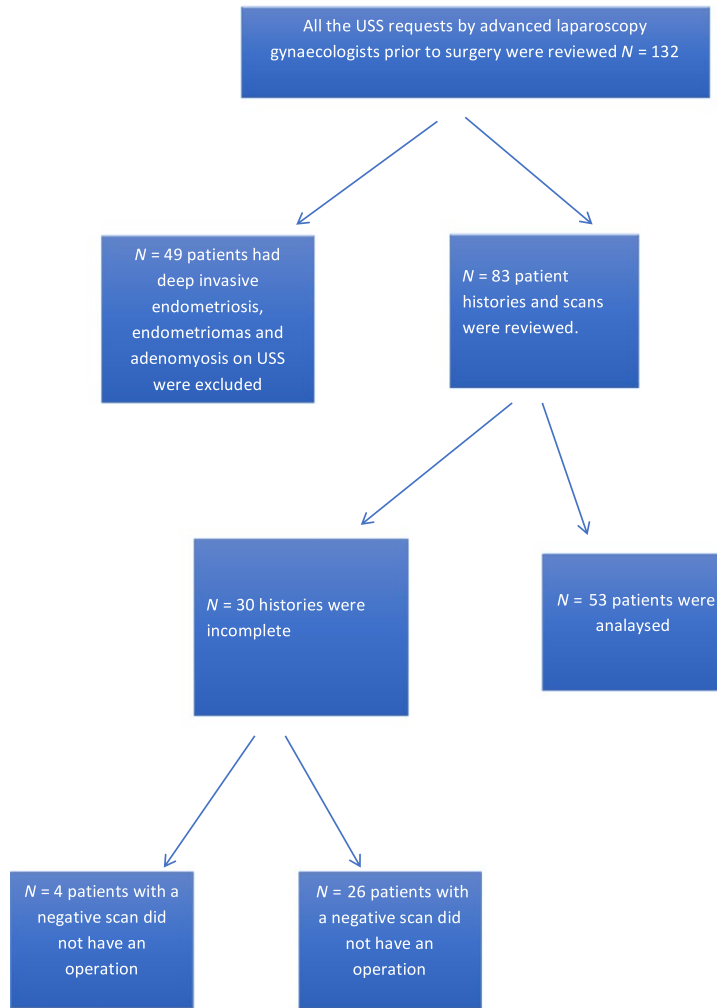
Seventy-nine percent (42/53) of the patients had laparoscopic findings consistent with their ultrasound findings (95% CI 68–90%,  $P < 0.0001$ ; Table 1). Detection of thickened pericolic fat was most associated with mild-moderate endometriosis at the time of laparoscopy. Uterosacral ligament thickening (sensitivity 0.62, specificity 0.73, area under the ROC curve 0.67,  $P < 0.05$ ). ROC curves for the other variables ovarian mobility, focal tenderness and filmy adhesions are demonstrated (Fig. 1).

No association was found between age and operation findings or symptoms. Of the symptoms, dysmenorrhoea had the highest sensitivity (0.98, 95% CI 0.87–0.99) but a very low specificity (0.18, 95% CI 0.02–0.52). The predictive value of a positive test was 0.89 (95% CI: 0.71–0.97) with presence of uterosacral thickening which matched laparoscopic findings.

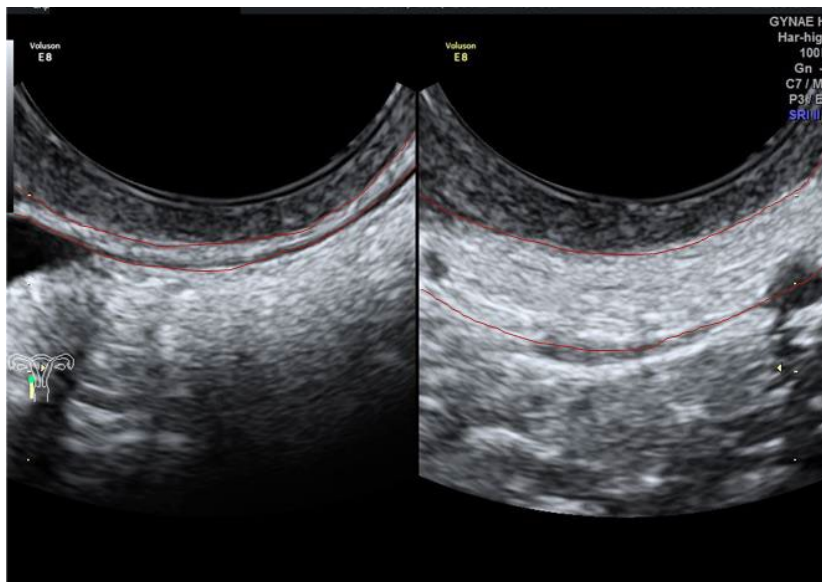
## DISCUSSION

Endometriosis is thought to affect one in ten women with patient healthcare costs estimated at 10 billion dollars in the last decade in Australia, comparable to type 2 diabetes.<sup>6</sup> The development of a non-invasive tool for the diagnosis of superficial endometriosis is of great importance in this cohort of patients who currently have a diagnostic laparoscopy and biopsy as gold standard for diagnosing endometriosis.<sup>7</sup> The importance of early diagnosis has been shown to benefit women in terms of offering management strategies to control symptoms and providing a language in which to express their situation to healthcare providers and the community.<sup>8</sup>

Accurate diagnosis of deep infiltrative endometriosis with ultrasound scan is well recognised.<sup>9,10</sup> However, there is only a small body of work looking at the ultrasound diagnosis of superficial endometriosis.<sup>11</sup>



**FIGURE 3** Participant flow diagram.



**FIGURE 4** Normal versus thickened yterosacral ligament on transvaginal ultrasound.

Although this is a retrospective study with a small sample size, it indicates that superficial endometriosis can be detected with ultrasound scan by an experienced sonologist who has specialised in endometriosis and we would argue that the skill-set required to diagnose these findings could be introduced into the Certificate of Obstetric and Gynaecological Ultrasound training curriculum. Similar to obtaining sound surgical skills in the excision of endometriosis, ultrasound training in the assessment of endometriosis has a learning curve and appropriate exposure and training are required.

An important issue with the current study is the ultrasonologist's assessment of uterosacral ligament thickening. We have been unable to identify in the current medical literature a descriptive measurement in the ultrasound diagnosis of this thickening although there has been some literature on the evidence of fat stranding in patients with acute abdominal pain.<sup>5</sup> The figure of three millimetres and immobility of the ligament were arbitrarily applied by the ultrasonologist based on many years of training and experience in the scanning of endometriosis and crucially the attainment of feedback from surgical colleagues in terms of correlation with surgical findings. Future work should look into reproducibility of this finding; not only is the measurement and mobility critical, but in addition the location of the ultrasound probe and its close proximity to the cervix (Fig. 4). Traditional teaching in the ultrasound assessment of the uterosacral ligaments has not focused on the medial insertion.<sup>12,13</sup> We have demonstrated a statistically significant association between uterosacral ligament thickening (>3 mm) and the operative finding of superficial endometriosis. Some might argue that ligament thickening is in fact diagnosing deep infiltrative disease rather than superficial endometriosis. We would maintain that definition of deep disease is endometriosis invading at a depth of  $\geq 5$  mm and that ligament thickening of >3 mm is not representative of deep disease.<sup>14</sup>

Endometriosis is known for a triad of pain symptoms; however, in our study, as in all other studies, we failed to demonstrate a symptom-based predictive tool.<sup>4,15,16</sup>

## CONCLUSION

This small study demonstrates that a skilled sonologist with specific training may demonstrate superficial endometriosis that correlates to surgical findings with considerable accuracy. There has been an extensive search for non-surgical diagnosis of endometriosis.<sup>17</sup> As the ultrasound assessment of superficial endometriosis advances with appropriate education and training, we believe that this less invasive tool may be able to make a diagnosis of mild endometriosis and potentially decrease the healthcare costs and complications associated with surgery. Appropriate presurgical assessment of the severity of endometriosis will allow improved education of patients, utilisation of theatre time and appropriate allocation of seniority of surgeons.

## ACKNOWLEDGEMENTS

We would like to thank Yannan Jiang for her help with the statistical analysis.

## REFERENCES

1. Simoens S, Dunselman G, Dirksen C *et al*. The burden of endometriosis: cost and quality of life of women with endometriosis and treated in referral centres. *Hum Reprod* 2012; **27**: 1292–1299.
2. Dunselman GAJ, Vermeulen N, Becker C *et al*. ESHRE guideline : management of women with endometriosis. *Hum Reprod* 2014; **29**: 400–412.
3. Soliman AM, Yang H, Du EX *et al*. The direct and indirect costs associated with endometriosis: a systematic literature review. *Hum Reprod* 2016; **31**: 712–722.
4. Nftalin J, Hoo W, Nunes N *et al*. Association between ultrasound features of adenomyosis and severity of menstrual pain. *Ultrasound Obstet Gynecol* 2016; **47**: 779–783.
5. Pereira JM, Sirlin CB, Pinto PS *et al*. Disproportionate fat stranding: a helpful CT finding in patients with acute abdominal pain. *Radiographics* 2004; **24**: 703–715.
6. Eskenazi B, Warner ML. Epidemiology of endometriosis. *Obstet Gynaecol Clin North Am* 1997; **24**(2): 235–258. Review
7. Nisenblat V, Prentice L, Bossuyt PM *et al*. Combination of the non-invasive tests for the diagnosis of endometriosis. *Cochrane Database Syst Rev* 2016; **7**: CD012281.
8. Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. *Fertil Steril* 2006; **86**: 1296–1301.
9. Chamié LP, Pereira RM, Zanatta A, Serafini PC. Transvaginal US after bowel preparation for deeply infiltrating endometriosis: protocol, imaging appearances, and laparoscopic correlation. *Radiographics* 2010; **30**: 1235–1249.
10. Guerriero S, Ajossa S, Orozco R *et al*. Accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in the rectosigmoid: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2016; **47**: 281–189.
11. Menakaya U, Reid S, Lu C *et al*. Performance of ultrasound-based endometriosis staging system (UBESS) for predicting level of complexity of laparoscopic surgery for endometriosis. *Ultrasound Obstet Gynecol* 2016; **48**: 786–795.
12. Guerriero S, Condous G, Valentin T *et al*. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriomas, including terms, definitions and measurements : a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol* 2016; **48**: 318–332.
13. Ramanah R, Berger MB, Parratte BM, DeLancey JO. Anatomy and histology of apical support: a literature review concerning cardinal and uterosacral ligaments. *Int Urogynaecol J* 2012; **23**: 1483–1494.
14. Cornillie FJ, Oosterlynck D, Lauweryns JM, Koninckx PR. Deeply infiltrating pelvic endometriosis: histology and clinical significance. *Fertil Steril* 1990; **53**: 978–983.
15. Wykes CB, Clark TJ, Khan KS. Accuracy of laparoscopy in the diagnosis of endometriosis : a systematic quantitative review. *BJOG* 2004; **111**: 1204–1212.
16. Mathia SD, Kuppermann M, Liberman RF *et al*. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. *Obstet Gynaecol* 1996; **87**: 321–327.
17. Rogers PA, D'Hooghe TM, Fazleabas A *et al*. Priorities for endometriosis research: recommendations from an international consensus workshop. *Reprod Sci* 2009; **16**: 335–346.