Should a detailed ultrasound examination of the complete urinary tract be routinely performed in women with suspected pelvic endometriosis?

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STUDY QUESTION: Is there any benefit to including the routine examination by ultrasound of the bladder, ureters and kidneys of women with endometriosis?

SUMMARY ANSWER: The benefit of examination of the complete urinary tract of women with suspected endometriosis is that ureteric endometriosis, with or without hydronephrosis, can be detected which facilitates early intervention to prevent nephropathy.

WHAT IS ALREADY KNOWN: Women with endometriosis can get ureteric obstruction but there is no clear consensus on the correct diagnostic technique. Ultrasound is accurate at detecting women with bladder endometriosis but ureteric involvement has not been assessed previously.

STUDY DESIGN, SIZE, DURATION: This was a prospective observational study, conducted at a teaching hospital over a period of 14 months. A total of 848 women presenting with chronic pelvic pain were included into the study.

PARTICIPANTS/MATERIALS, SETTING, METHODS: All women with chronic pelvic pain underwent a detailed transvaginal and transabdominal pelvic ultrasound examination to investigate possible causes of their symptoms. This included a systematic assessment of the urinary bladder, pelvic sections of the ureters and kidneys. The ultrasound findings were compared with findings at surgery and the results of targeted urological imaging and interventions.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 848 women presenting with chronic pelvic pain were included into the study. 28/848 women (3.3% 95% CI 2.1—4.5) had evidence of urinary tract abnormalities on initial ultrasound scan. Among these 17/848 (2.0% 95% CI 1.06—2.94) had evidence of urinary tract endometriosis, whilst 11/848 (1.3% 95% CI 0.54—2.06) women had other urinary tract abnormalities. Among women with urinary tract endometriosis 11/17 (65%) had evidence of ureteric involvement, 3/17 (18%) had both ureteric and bladder disease and 3/17 (18%) had bladder disease only. 12/17 (59%) women with urinary tract endometriosis also had evidence of hydronephrosis. The diagnosis of ureteral endometriosis had a sensitivity of 12/13 (92%) (95% CI 63.9—99.8), specificity 151/151 100% (95% CI 97.6—100), PPV 100% (95% CI 73.5—100), NPV 99.3% (95% CI 96.3—99.9) LR — 0.08 (95% CI 0.01—0.39).

LIMITATIONS, REASONS FOR CAUTION: The routine examination of the complete urinary tract including the distal ureters is a novel technique that should be evaluated in different populations.

WIDER IMPLICATIONS OF THE FINDINGS: Ultrasound is an accurate test to diagnose urinary tract involvement in women with suspected pelvic endometriosis and examination of the complete urinary tract should become an integral part of ultrasound assessment of women with suspected endometriosis.

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Key words: endometriosis / diagnosis / ultrasound / urinary tract / ureter / urinary bladder / hydronephrosis
Introduction

Endometriosis is defined as the presence of endometrial glands and stroma at anatomically ectopic locations. The prevalence of endometriosis in the general population is unknown but can be inferred to be 6–30% from rates at laparoscopic sterilization (Mahmood and Templeton, 1991; Melis et al., 1994). The prevalence rises to 30–45% in women with pain and infertility (Dunsleman et al., 2014). The most common sites of endometriosis are the ovaries, uterosacral ligaments and rectovaginal septum (Duffy et al., 2014).

The prevalence of urinary tract endometriosis varies in the literature from 0.3 to 12% (Abrao et al., 2009; Chapron et al., 2010; Maccagnano et al., 2013). These differences can be explained by variations in the study populations and the selection criteria. The bladder was reported to be affected by endometriosis twice as often as the ureters (Abrao et al., 2009).

Until recently magnetic resonance (MR) was the only imaging method which enabled a complete examination of the urinary tract for the presence of endometriosis; however this method is complex, time consuming, costly and therefore is not suitable to be used routinely in the initial assessment of women presenting with pelvic pain.

Previous studies have shown that ultrasound mapping of pelvic endometriosis is accurate (Goncalves et al., 2009; Holland et al., 2010, 2013a; Hudelist et al., 2011) and reproducible (Holland et al., 2013b). We have also demonstrated that transvaginal ultrasound scan enables visualization of pelvic sections of the ureters and assessment of their peristalsis in the vast majority of women (Pateman et al., 2009).

The aim of this study was to assess the value of integrating systematic examination of the urinary tract into routine ultrasound assessment of women with suspected pelvic endometriosis and to assess the prevalence of urinary abnormalities in this population of women.

Materials and Methods

This was a prospective observational study, conducted at the Endometriosis Centre at University College London Hospital from January 2013 until March 2014. All women referred to the Centre had presented with chronic pelvic pain.

Demographic data were obtained, as were indications for ultrasound scan, past medical, gynaecological, obstetric and surgical history. In addition endometriosis-related symptoms such as dysmenorrhoea, chronic pelvic pain, dyspareunia, dyschezia, dysuria and subfertility were recorded on a dedicated clinical database (Viewpoint, GE Healthcare, Fairfield, Connecticut, USA).

A transvaginal scan was performed first (Voluson E8, GE Medical Systems, Milwaukee, WI, USA). We used a previously described systematic standardized approach to the assessment of the gynaecological organs in women with suspected endometriosis (Holland et al., 2010). All women were asked to empty their bladders prior to the transvaginal assessment, so that the bladder was only partially filled when the examination took place. The probe was then positioned in the anterior vaginal fornix in using the technique first described by Fedele (Fedele et al., 1997). The presence of a hypoechoic or isoechocic nodule on the bladder wall or a nodule with a heterogeneous echotexture containing numerous anechoic (‘bubble-like’) areas within the bladder wall was considered indicative of bladder endometriosis (Fedele et al., 1997; Savelli et al., 2009). We also routinely examined pelvic sections of the ureters using a technique, which has been described previously (Pateman et al., 2013). The ureters were examined at rest (Figs 1 and 2) and whilst peristalsing to identify any evidence of ureteric dilatation, abnormal bending or differences in peristalsis frequency between the ureters. In women with evidence of partial (Fig. 3) and complete (Fig. 4) ureteric obstruction the distance from the stricture to the ureteric orifice was measured (Fig. 5). We also recorded the presence of any other ureteric abnormalities such as ureterocele (Fig. 6) and ureteric stones.

The examination was completed by performing an abdominal ultrasound scan to assess the kidneys using a 3.5–5 MHz probe. For examination of the left kidney, the patient lay in the right lateral decubitus position with the probe placed in the lower intercostal space on the posterior axillary line. For examination of the right kidney, the patient lay supine and the probe was placed in the right lower intercostal space in the midaxillary line. The entire kidneys were scanned through obtaining longitudinal (long axis) and transverse (short axis) views.

Hydronephrosis was diagnosed and graded using a generally accepted ultrasound criteria (Block, 2011). Any dilated ureter was followed abdominally to the level of obstruction if not already seen vaginally. Renal cysts were classified using the Bosniak classification (Bosniak, 2012).

All women with ultrasound evidence of urinary tract abnormalities, except Bosniak category 1 renal cysts, were referred for urological review. Those with evidence of ureteric obstruction and/or hydronephrosis had a blood sample taken to measure renal function and were referred to consultant urologists, for further assessment, which routinely included computerized tomography of the kidneys, ureters and bladder (CT KUB) and radioisotope renography (mercapto acetyl triglycine: MAG3) scans to assess renal function.
All women were then reviewed by our multidisciplinary endometriosis team to agree on the optimal management plan. Surgery for endometriosis was performed by a team of dedicated expert surgeons who are part of our Endometriosis Centre. This included gynaecologists, urologists and colorectal surgeons. They used a standardized approach to surgical treatment and documentation of laparoscopic findings (Pandis et al., 2010).

In all women with severe endometriosis, a full dissection of the ureters was performed and they were checked for signs of endometriosis involvement. The presence of bladder nodules was also reported. All lesions, which were removed at surgery, were sent for histological examination.

Statistics

All statistical analysis was performed using Stata, version 12.1 (StataCorp LP, Texas, USA).

Graphical representation was used to assess for normality. Age was normally distributed and was expressed as mean and standard deviation (SD). Gravidity and parity were non-normally distributed and are expressed as median and inter-quartile range (IQR). Proportions were expressed as percentage (95% CI). Fisher’s exact test was used to compare proportions. The diagnostic accuracy of the test was assessed using sensitivity, specificity, positive (PPV), negative (NPV) predictive value and positive and negative likelihood ratio (LR+ and LR−, respectively).

Ethics

Ethical approval was sought from the local research ethics committee, who deemed that as assessment of the urinary tract is part of routine assessment in women with endometriosis, full ethical review was not required.

Results

Eight hundred and forty-eight women presenting with history of chronic pelvic pain attended our Endometriosis Centre over the period of 14 months. All women were premenopausal and their mean age was 36.1 years (SD 7.8).

There were 520/848 (61.3%) who had not been pregnant before, whilst 180 (21.2%) women had one and 148 (17.5%) had two or more previous pregnancies. Out of 328 women who were previously pregnant 112 (34.1%) had one and 110 (33.5%) had two or more previous deliveries.

Among the 848 women 518 (61.1%) underwent one or more laparoscopic or open surgical procedures prior to the referral. A total of 308 (36.6%) women had previous surgery for endometriosis, whilst the remaining 210 (24.8%) women had various other gynaecological and
Urinary tract ultrasound in endometriosis

Our study has shown that ultrasound is an effective test for the diagnosis of endometriosis involving the urinary tract. The findings are highly specific and all women with ultrasound evidence of urinary tract endometriosis had the diagnosis confirmed at surgery or on additional imaging. There was only one case of endometriosis causing partial obstruction of the ureter without hydronephrosis which was not detected on ultrasound. These findings are in agreement with the results of previous studies which also showed that ultrasound is an accurate test for the diagnosis of deep infiltrating pelvic endometriosis (Holland et al., 2010; Hudelist et al., 2011; Exacoustos et al., 2014). However, our study is the first to examine the accuracy of ultrasound diagnosis of ureteric endometriosis.

Our findings compare favourably with results of a previous study which assessed the accuracy of diagnosis of ureteric endometriosis with MRI (Chamié et al., 2009) and found a sensitivity of 50% and a specificity of 100%. Our results have shown a similarly high specificity with ultrasound but the sensitivity was much better. This could be explained by our scanning protocol, which requires that the pelvic segments of both ureters are routinely visualized in every woman.

In order to achieve a high level of accuracy pelvic ultrasound scans for the diagnosis of endometriosis should be performed by experienced operators and they should include both the assessment of morphological appearances of pelvic organs and their mobility. Bowel involvement is common in endometriosis and the assessment of the anterior wall of the recto-sigmoid colon has already been incorporated into the examination of women with suspected endometriosis. The ultrasound examination of the bladder, ureters and kidneys usually requires up to five additional minutes to complete which should be taken into account when scheduling ultrasound scans in endometriosis/pelvic pain clinics.

Pre-operative detection of urinary tract endometriosis is important as these women often require more complex surgery with the involvement of urological surgeons with specialist expertise in this area. Ureteric lesions were left sided in 8/14 (57.1% 95% CI 31.1 – 83.0%) cases and right sided in 6/14 (42.8% 95% CI 16.9 – 68.7%) cases. There were two cases of women referred to our unit, who had already had ureteric stents inserted due to hydronephrosis but these were excluded from the analysis of diagnostic accuracy as ureteric endometriosis was the reason for referral. Among the remaining women with ureteric endometriosis 10/12 (58.8% 95% CI 35.4 – 82.2) had evidence of hydronephrosis of the ipsilateral kidney. The other 2/12 (16.7% 95% CI 0 – 37.8%) women had distal ureteric dilation without hydronephrosis, suggesting incomplete obstruction of the ureter (Fig. 3).

One hundred and sixty-six women underwent surgery and/or further imaging (CT or MRI). In all women the ultrasound diagnosis of bladder and ureteric endometriosis was confirmed. There was one false negative case found at surgery, where the ureter was compressed by an extrinsic endometriotic implant above the level of the bifurcation of the common iliac vessels. Two women with ureteric stents in situ were excluded leaving 164 women in the final analysis. Using surgery and/or additional imaging of urinary tract as a reference standard the pre-operative ultrasound examination for the diagnosis of ureteral endometriosis had a sensitivity of 12/13 92.3% (95% CI 63.9 – 99.8), specificity 151/151 100% (95% CI 96.3 – 99.9) LR – 0.08 (95% CI 0.01 – 0.39).

### Table I Indications for past surgery.

<table>
<thead>
<tr>
<th>Previous operations</th>
<th>1 operation N(%) [95% CI]</th>
<th>2 or more operations N(%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery for endometriosis</td>
<td>176 (21%) [18%, 24%]</td>
<td>132 (16%) [13%, 18%]</td>
</tr>
<tr>
<td>Other gynaecological*</td>
<td>185 (22%) [19%, 25%]</td>
<td>79 (9%) [7%, 11%]</td>
</tr>
<tr>
<td>Non-gynaecological</td>
<td>84 (10%) [8%, 12%]</td>
<td>2 (0.2%) [0.0%, 0.8%]</td>
</tr>
</tbody>
</table>

*Including Caesarean section.

### Table II Urinary tract abnormalities identified on ultrasound scan (N = 28).

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal cyst</td>
<td>5</td>
</tr>
<tr>
<td>Ureteric stone</td>
<td>3</td>
</tr>
<tr>
<td>Pelvic kidney</td>
<td>1</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>1</td>
</tr>
<tr>
<td>Uretercele</td>
<td>1</td>
</tr>
<tr>
<td>Urethral diverticulum</td>
<td>1</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>10</td>
</tr>
<tr>
<td>Hydrourerter</td>
<td>12</td>
</tr>
<tr>
<td>Bladder endometriotic nodule</td>
<td>6</td>
</tr>
</tbody>
</table>
obstruction with hydronephrosis is usually clinically silent and timely diagnosis may help to preserve renal function by prioritizing women with ureteric endometriosis for urgent treatment. The main advantage of visualizing the ureters on ultrasound examination is detection of partial ureteric obstruction before hydronephrosis develops. In these women early treatment with ureteric stenting and/or laparoscopic ureterolysis helps to prevent any loss of renal function. Another advantage of assessing the ureteric stricture on ultrasound is that it enables a measurement of the distance between the lesion and ureteric orifice. This tells the surgeons where to look for the ureteric lesions, which may not be easily detectable at laparoscopy due to concomitant pelvic adhesions.

The prevalence of endometriosis in our study population was very high which reflects the nature of work in a tertiary referral centre. In the subgroup of women with evidence of endometriosis on ultrasound scan 5.1% had urinary tract endometriosis. The ureters were the affected in 4.1% of cases which is very similar to the rate of 4.4% reported by Donnez et al. (2002). The left ureter was more commonly affected which was also noted in previous studies (Vercellini et al., 2000; Donnez et al., 2002). The prevalence of ureteric endometriosis in our population was significantly higher than for bladder endometriosis, which is discordant with the results of previous studies (Abrao et al., 2009). This could be explained by patient selection as our Centre often receives referrals of women with particularly severe disease from other tertiary centres. Abrao et al. reported that bladder endometriosis tends to be isolated and presents with cyclic dysuria, whilst ureteric endometriosis is almost always associated with retrocervical deep infiltrating lesions and the symptoms are no different from the classic symptoms of rectovaginal endometriosis (Abrao et al., 2009). They postulated that endometriosis in these two locations represents different forms of disease, which are rarely found in same women. Our study has shown; however, that half of women with bladder endometriosis also had evidence of ureteric involvement. Although our data set is not very large, our findings suggest a strong association between bladder and ureteric disease indicating that they both may simply be manifestations of extensive deep infiltrating disease affecting most pelvic organs.

Our study has also shown that the examination of the urinary tract can reveal other causes of pelvic pain such as ureteric stones. We also detected five simple renal cysts (Bosniak Type I) which are not clinically significant and they do not require further follow-up or treatment. Other pathologies, which are unlikely to cause significant harm such as megaureter or ureterocele could also be picked up and it is important that suitable clinical protocols are put in place to ensure appropriate referral without causing unnecessary anxiety to women. It is also important to establish a close collaboration between gynaecologist, radiologist and urologist in cases, which are of uncertain clinical significance.

In summary, we have shown that it is feasible to incorporate assessment of the urinary tract in ultrasound examination of women with suspected pelvic endometriosis. We have also shown that ultrasound is an accurate method to detect ureteric endometriosis with or without hydronephrosis. Routine assessment of ureters and kidneys helps to identify women in whom prompt ureteric stenting or surgery should be employed to prevent or reduce injury to the kidneys. In view of this we believe that a detailed assessment of the urinary tract should be performed in all women presenting with pelvic pain and clinical suspicion of pelvic endometriosis.

Authors’ roles
K.P. produced the research protocol, performed the ultrasound examinations, collected data, analysed the data and drafted the manuscript; T.K.H. advised on the research protocol, performed statistical analysis and drafted and redrafted manuscripts and selected figures; J.K. assisted in drafting the manuscript and helped select figures; G.D. assisted in data collection and in drafting the manuscript; A.C. assisted in data collection and in drafting the manuscript; E.S. assisted in data collection and in drafting the manuscript; D.J. conceived of the study, supervised the drafting and redrafting of the manuscript and advised on statistical analysis.

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Conflict of interest
None declared.

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Holland TK, Hoo W, Mavrelis D, Saridogan E, Cutner A, Jurkovic D. Reproducibility of assessment of severity of pelvic endometriosis...


