Accuracy of rectal water contrast transvaginal ultrasound

Abstract

Objectives: To compare the accuracy of rectal water contrast transvaginal ultrasound (RWC-TVS) and double-contrast barium enema (DCBE) in assessing the presence and extent of bowel endometriosis.

Methods: This prospective study included 198 patients of reproductive age with suspicion of bowel endometriosis. RWC-TVS and DCBE were performed before operative laparoscopy by two groups of physicians specialized in endometriosis, each blinded to the results of the other groups. Findings of RWC-TVS and DCBE were compared with histological results. The severity of pain experienced during RWC-TVS and DCBE was measured by a 10 cm visual analog scale.

Results: In total, 110 of the 198 women had bowel endometriosis nodules confirmed at laparoscopy and histopathology patients. For the diagnosis of bowel endometriosis DCBE and RWC-TVS had a sensitivity of 96. 4% and 88. 2%, specificity of 100% and 97. 3%, positive predictive value of 100% and 98. 0%, negative predictive value of 98. 0% and 88. 0% and accuracy of 98. 0% and 92. 4% respectively. DCBE was associated with more intense pain than was RWC-TVS.

Conclusions: RWC-TVS and DCBE have similar accuracy in the diagnosis of bowel endometriosis, but patients tolerate RWC-TVS better than they do DCBE.

Keywords: double-contrast barium enema; rectal water contrast transvaginal ultrasound; bowel endometriosis; diagnosis

Introduction

Bowel endometriosis affects between 4-37% of patients with endometriosis [1] . Intestinal endometriosis lesions may have variable size [2] . Small endometriosis nodules located on the serosal surface of the bowel rarely cause symptoms and, therefore, do not require treatment [2] . Larger endometriosis nodules infiltrate the bowel wall and may cause various gastrointestinal complaints such as dyschezia, diarrhea, constipation, abdominal bloating and intestinal cramping [1, 3] . These symptoms may mimic irritable bowel syndrome. Symptoms caused by bowel endometriosis are nonspecific, often resulting in misdiagnosis or delay in diagnosis [4] . Physical examination may suggest the presence of rectovaginal endometriosis; however, it has poor accuracy in diagnosing rectosigmoid nodules [5, 6] .

Until recently, the ultrasonic diagnosis of endometriosis was limited to patients with ovarian endometriomas and other imaging techniques were used for the assessment of bowel endometriosis including rectal endoscopic ultrasound, transvaginal ultrasound (TVS), double-contrast barium enema (DCBE), magnetic resonance imaging (MRI), multidetector computerized tomography enema (MDCT-e) and virtual colonoscopy [7-10] . TVS is a reliable non-invasive method to assess the presence and the extent of bowel endometriosis [11] . Injecting saline through a catheter into the rectum during TVS (rectal-water contrast TVS, RWC-TVS) may facilitate the identification of rectosigmoid nodules, the assessment of the depth of infiltration of endometriosis in the intestinal wall and estimation of the degree of stenosis

of the bowel lumen. However, no previous study compared the accuracy of DCBE and RWC-TVS in the diagnosis of rectosigmoid endometriosis [4, 12, 13] .

A preoperative diagnosis of the presence and extent of bowel endometriosis is necessary to determine whether surgery is required and to plan the surgical procedure with the colorectal surgeon [14] . Knowing before surgery the size and number of intestinal endometriosis nodules, the depth of infiltration of the nodules in the intestinal wall and the degree of stenosis of the bowel lumen allows determining whether surgery is required and may allow the surgeons to choose between nodulectomy and bowel segmental resection [15, 16] .

In addition, determining before surgery the extent of bowel endometriosis allows the surgeon to inform the patient about the potential benefits and complications of the surgical procedure that will be performed. In fact, postoperative complications and evolution of digestive symptoms after surgery may differ between patients undergoing nodulectomy and those undergoing segmental resection, with a higher incidence of bladder-voiding dysfunction and postoperative constipation in patients undergoing the latter procedure. In this study, we compared the accuracy of DCBE and RWC-TVS in assessing the presence and extent of bowel endometriosis.

Methods

Study population

This prospective study was performed between May 2012 and Aug 2016. Participants were recruited among patients of reproductive age scheduled for laparoscopy with strong suspicion of intestinal endometriosis based on

symptoms and clinical examination. During this period, the imaging workup required that both DCBE and RWC-TVS were performed in patients with suspicion of bowel endometriosis. Institutional review board approval was obtained before initiating the study. Patients participating in the study signed a written consent form. Inclusion criteria for the study were: reproductive age and suspicion of deep pelvic endometriosis; presence of gastrointestinal symptoms that might be caused by bowel endometriosis; and desire to undergo complete surgical excision of the endometriosis. Patients were excluded from the study if they had previous bilateral ovariectomy; previous barium radiological examination or radiological diagnosis of bowel endometriosis; previous colorectal surgery; previous episodes suggestive of intolerance to iodinated contrast medium; renal or hepatic failure; refusal to undergo DCBE and psychiatric disorders.

Symptoms were systematically investigated during the study period and they were recorded in a database. The presence of dysmenorrheal, deep dyspareunia, non-menstrual pelvic pain and dyschezia was investigated and the intensity of their symptoms was assessed in all patients on a 10 cm visual analog scale (VAS), on which the left extremity represented absence of pain and the right extremity indicated maximum intensity of pain. The presence of the following gastrointestinal symptoms was assessed: diarrhea-predominant irritable bowel syndrome; constipation-predominant irritable bowel syndrome; passage of mucus in the stools; rectal bleeding; intestinal cramping; and abdominal bloating. A symptom analogue scale questionnaire was used to estimate the severity of each gastrointestinal symptom.

DCBE and RWC-TVS results were compared with surgical and pathologic findings. The radiologists performing DCBE and the gynecologists performing TVS were each blinded to the others' results. They were blinded to the clinical data and knew only that the presence of intestinal endometriosis was suspected. All patients underwent laparoscopy within 1 month from the completion of the diagnostic investigations. Intestinal endometriosis was defined as the disease infiltrating at least the muscularis propria. Endometriosis foci located on the bowel serosa were considered peritoneal and not bowel endometriosis. The present study determined the accuracy of DCBE and RWC-TVS in assessing the presence of bowel endometriosis, estimating the size and the number of bowel endometriosis nodules and determining the presence of peritoneal endometriosis infiltrating only the intestinal serosa.

Rectal water contrast transvaginal ultrasound technique

Two physicians performed all the examinations according to a standardized procedure.

RWC-TVS was performed by using a Voluson E6 machine connected to a transvaginal transducer. After the transducer had been introduced into the vagina, an assistant inserted a 6-mm flexible catheter through the anus into the rectal lumen up to a 15 cm distance from the anus. A gel infused with lidocaine was used to facilitate passage of the catheter. A 50 mL syringe was connected to the catheter and warm sterile saline solution was injected inside the rectum and the sigmoid under ultrasonic control. The amount of saline solution needed to show the rectosigmoid ranged between 100 and 350 mL, depending on the distensibility of the intestinal wall. One hundred

milliliters of saline solution were continuously and slowly infused at the beginning of the procedure; the rest of the solution was infused when requested by the ultrasound. During ultrasound, when saline solution was not being infused, backflow through the catheter was prevented by placing a Klemmer forceps on the catheter. There was no significant leakage of saline solution into the space between the catheter and the anus. Images were obtained before, during and after saline injection.

Bowel endometriosis appears ultrasonographically as a nodular, solid, hypoechoic lesion, adjacent to and/or penetrating the intestinal wall. Hyperechoic foci may sometimes be present within the lesion. Intestinal distension allows defining the limits of the intestinal nodules and in particular the various layers of the rectal wall in order to estimate the depth of infiltration. The intestinal serosa is hyperechoic; the two layers of the muscularis propria appear as hypoechoic strips separated by a fine hyperechoic line; the submucosa is hyperechoic; the muscularis mucosa is hypoechoic and the interface between the lumen and the mucosal layer is hyperechoic. Rectal endometriosis infiltration is demonstrated by the fact that the hypoechoic nodule penetrates the intestinal wall and, in general, it thickens the muscularis mucosa. Two different ultrasonic signs are commonly used to describe this condition.

Double-contrast barium enema

All DCBE procedures were carried out using a motorized tilting table for fluoroscopic and radiological examination. In preparation, patients maintained a low-residue diet for 1 day prior to the examination in order to keep the enteric content fluid. The examination was performed after

intramuscular administration of 20 mg (1 ampoule) Scopolamine in order to induce colonic hypotonia. The presence of bowel endometriosis was diagnosed on DCBE when the bowel lumen was narrowed at any level from the sigmoid to the anus in association with crenulation of the mucosa and/or speculation of contour.

Tolerability of the examinations

Immediately after each examination patients were asked to rate the discomfort encountered during DCBE and RWC-TVS by means of a 10 cm visual analogue scale (VAS), mild pain was defined as a VAS score of <2, moderate pain as a VAS score ≥2 and≤5 and severe pain as a VAS score > 5.

Surgery and histological evaluation

The surgeons examined the reports and the images of DCBE and RWC-TVS prior to laparoscopy. Although the diagnosis of recto-sigmoid endometriosis and its treatment were based on laparoscopic findings. All surgical procedures were performed laparoscope by a team of gynecological and colorectal surgeons with extensive experience in the treatment of pelvic and bowel endometriosis. In all cases, after adequate adhesiolysis, the sigmoid colon and rectum were systematically examined to verify the presence of endometriosis lesions. Bowel endometriosis lesions were removed by intestinal resection in cases of a single lesion > 3 cm in diameter, a single lesion infiltrating at least 50% of the circumference of the intestinal wall or three or more lesions infiltrating the muscular layer. In all other cases of bowel endometriosis partial- or full-thickness disk resection was performed. Intestinal lesions infiltrating only the serosal layer of the bowel wall were

excised by shaving. All visible lesions suspected to be endometriosis were excised and sent for histological examination in agreement with our clinical protocol.

The surgical specimens were evaluated by histological; the depth of infiltration of the endometriosis nodules in the bowel wall was assessed. In cases of nodulectomy the specimens were macroscopically oriented along the intestinal wall (from the serosa towards the mucosa) and cut into macro sections of 2 mm thickness. From each macrosection tissue blocks of 1. 5 cm length were obtained in variable numbers according to the size of the lesion, and from each tissue block a 5 µm section was obtained for microscopically evaluation. In cases of bowel resection the specimen was opened longitudinally through its entire length and 2mm longitudinal bands of bowel wall, reaching the two resection margins and passing through all macroscopically visible lesions, were cut. These bands were sampled in tissue blocks and 5 µm sections were obtained for microscopic evaluation.

Statistical analysis

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for both DCBE and RWC-TVS. The diagnostic value of each test was also assessed using positive likelihood ratio (LR+) and negative likelihood ratio (LR-). Efficacy parameters were calculated with 95% confidence intervals (CIs). McNemar’s test with the Yates continuity correction was used to compare the accuracy of DCBE and RWC-TVS in the diagnosis of intestinal endometriosis. McNemar’s test was used to compare the number of patients in which the number of rectosigmoid nodules was correctly identified by DCBE and RWC-TVS. The

accuracy of the measurement of nodule size by imaging techniques was estimated by subtracting the size of the nodule as measured by the techniques from the size of the nodules measured at histology. The nonparametric Mann-Whitney test was used to compare the intensity of pain experienced by patients during DCBE and RWC-TVS, the chi-square test was used to compare the type of pain (mild, moderate or severe) and Spearman's rank correlation coefficient was used to determine whether there was a correlation between the intensity of pain experienced by patients during the two techniques. Data were analyzed using the SPSS software. $p < 0.05$ was considered statistically significant.

Results

Study population

A total of 198 patients were enrolled in the study and all underwent surgery were included in this study (Figure 1). The main demographic characteristics of the study are demonstrated inTable 1. The intensity of pain and gastrointestinal symptoms are presented inTable 2.

Surgery and histology demonstrated that 110 patients (55. 6%) had bowel endometriosis nodules. The endometriosis lesions infiltrating the intestinal serosa in 28 patients. The remaining 82 patients had only pelvic endometriosis with no evidence of intestinal lesions. The largest intestinal endometriosis nodule was found locate on the sigmoid colon in 53 patients, on the rectum in 30 patients, at the rectosigmoid junction in 20 patients, on the ileum in 5 patients and on the caecum in 2 patients. The endometriosis lesions infiltrating only the intestinal serosa were located on the sigmoid colon in 15 cases, on the rectum in 5cases and at the rectosigmoid junction

in 3 cases. The mean (±SD) length of the resected bowel segment was 12. 2 ± 3. 6 cm. The diagnosis of endometriosis was confirmed in all the excised nodules by histological exam. Furthermore, it demonstrated that the deepest endometriosis nodule infiltrated the muscularis propria in 62 patients (56. 4 %), the submucosa in 31 patients (28. 2%) and the mucosa in 17 patients (15. 5%).

Accuracy of RWC-TVS and DCBE in the diagnosis of bowel endometriosis

The accuracy, sensitivity, specificity, PPV, NPV, LR+ and LR- of DCBE and RWC-TVS in the diagnosis of bowel endometriosis are described inTable 3. DCBE identified 106 of 110 patients with bowel endometriosis (96. 4%). In 4 patients endometriosis nodules infiltrating the muscularis propria of the rectum were not identified, which were excised by partial-thickness nodulectomy. RWC-TVS identified 97 of 110 patients with intestinal endometriosis (88. 2%). RWC-TVS did not identify 4 ileal lesions, 2 cecal lesions, 4 sigmoid nodules and 3 rectal nodules infiltrating the muscularis propria. Furthermore, we identified 4 of these patients had large bilateral endometriosis ovarian cysts, which may have hampered the identification of intestinal nodules. There was 2 false positive on RWC-TVS-a rectovaginal endometriosis nodule that was judged to infiltrate the muscularis of the rectum.

Surgery confirmed the presence of the rectovaginal nodule but did not reveal infiltration of the rectal muscularis. The sensitivity, specificity, PPV, NPV, LR+, LR- and accuracy of the two techniques in the diagnosis of intestinal endometriosis were shown inTable 3. McNemar’s test showed that there was no significant difference in the accuracy of the two techniques in the

diagnosis of bowel endometriosis (P= 0. 109). Histology examination demonstrated that endometriosis infiltrated the submucosa or mucosa of the rectosigmoid colon in 53 patients. DCBE correctly identified the depth of infiltration in 27 of these patients (50. 9%), while RWC-TVS correctly identified the depth of infiltration in 20 of them (37. 7%) (P= 0. 126). All the other nodules that were seen to infiltrate the submucosa or mucosa at histology were judged to reach only the muscularis at DCBE and RWC-TVS. Both techniques had no cases of false-positive diagnosis of submucosal or mucosal infiltration. Both DCBE and RWC-TVS underestimated the size of the endometriosis nodules; however, the underestimation was greater for RWC-TVS than for DCBE (Table 4). In addition, in both imaging techniques the underestimation was greater for nodules with diameter≥30 mm.

Tolerability of DCBE and RWC-TVS

DCBE was safely performed in all the patients. During both the examinations all patients tolerated intestinal distension and in no patient was it necessary to interrupt the procedure. However, the intensity of pain experienced during DCBE was significantly higher than the intensity of pain experienced during RWC-TVS (Table 5). A positive correlation was observed between the intensity of pain experienced by the patients during the two examinations (Spearman correlation coefficient= 0. 575; $p < 0.001$).

Discussion

To the best of our knowledge, this is the first study demonstrated that DCBE and RWC-TVS have similar accuracy in the diagnosis of bowel endometriosis. Both RWC-TVS and DCBE underestimated the size of bowel endometriosis nodules, but under estimation was greater for RWC-TVS than for DCBE,

particularly when the nodules had largest diameter ≥ 30 mm (Table 4). The choice of the ultrasonic technique is often based on the experience of the ultrasonographers rather than on evidence of superiority of one technique compared to the others. In fact, TVS must be performed by highly skilled, it has been recently estimated that the learning curve for an accurate diagnosis of deep pelvic endometriosis by TVS requires performing about 40 cases [17] . Therefore, it may be difficult to achieve such experience for ultrasonographers working in small hospital. The main advantage of DCBE could be that, with a retrograde distension of the entire colon, this technique may provide a complete overview of the whole colon [18] . In the current study, the distension was targeted to the rectosigmoid because the aim of the study was the comparison with RWC-TVS and endometriosis lesions of the right colon are beyond the field of view of a transvaginal approach. Furthermore, we did not compare the accuracy of RWC-TVS with TVS alone, which was the objective of a previous study. RWC-TVS was chosen for the comparison with DCBE because of the personal experience of the authors and of the common criterion of bowel distension with fluid. The usefulness of this technique was subsequently confirmed by the same authors in larger series. Furthermore, other authors confirmed that intestinal distension and opacification using ultrasound gel helps to visualize rectosigmoid endometriosis nodules [19, 20] .

Previous studies have suggested that TVS could reliably diagnose rectosigmoid endometriosis. The sensitivity of TVS for detecting rectosigmoid endometriosis is between 91 and 98%, the specificity between 97 and 100%,

the PPV between 97 and 100% and the NPV between 87 and 98% [21-24] . Recently, RWC-TVS has been developed to facilitate identification of intestinal lesions in patients with rectovaginal endometriosis and to determine the depth of infiltration of endometriosis in the intestinal wall [25] . TVS has been extensively used in patients with bowel endometriosis; while only little data is available on the use of DCBE in these patients. This study demonstrated that DCBE and RWC-TVS have similar accuracy in the diagnosis of bowel endometriosis. Both techniques precisely estimated the length of the rectosigmoid nodules, but DCBE was more precise than RWC-TVS in assessing the distance between the endometriosis nodule and the anal verge [9] . Obviously, the extensive experience of the radiologist and the gynecologist in DCBE and RWCTVS, respectively, may have influenced the accuracy of these techniques in diagnosing bowel endometriosis [24, 26] . The findings may be explained by the fact that when performing imaging techniques, particularly RWC-TVS, it might be difficult to choose the plane in which the irregular endometriosis nodule has the largest diameter. However, the difference between the estimated size of the nodule and the largest diameter as measured on histopathology was quite small and, in most cases, it seems unlikely that this difference would affect the choice of nodulectomy or bowel resection as treatment [27] . Importantly, patients tolerated RWC-TVS better than they did DCBE. These findings are in line with those of previous studies demonstrating the accuracy of TVS in the diagnosis of bowel endometriosis and comparing TVS with other techniques such as MRI and rectal endoscopic ultrasound [11, 28-30] .

The potential benefits of introducing aqueous contrast medium into the rectum during TVS have been questioned. TVS is an operator-dependent procedure and it is possible that the differences observed in the accuracy of this technique are determined by the experience of the ultrasonographer carrying out the procedure [31] . However, adding intestinal aqueous contrast to TVS may facilitate the identification of rectosigmoid lesions. Other techniques have been proposed for improving the accuracy of TVS in the detection of deep endometriosis, such as sonovaginography or the use of large quantities of ultrasound transmission gel (12 mL) in the probe cover [32] . Up to now, no study has established whether any one of these ultrasonic techniques is superior to the others in the diagnosis of deep endometriosis.

TVS should be considered the first-line investigation in patients with deep endometriosis, and allows the diagnosis of intestinal lesions [24] . Other investigations such as RWC-TVS, MDCT-e, MRI, rectal endoscopic ultrasound and DCBE may be used to determine the characteristics of intestinal endometriosis, such as the size and number of nodules, the depth of infiltration of the nodules in the intestinal wall and the degree of stenosis of the bowel lumen [33-35] . RWC-TVS has several advantages over the other techniques. It is less expensive than MDCT-e and MRI and the equipment required to perform the procedure is commonly available to gynecologists, who are usually involved in the management of patients with endometriosis. A recent study has shown that RWC-TVS allows estimation of the degree of stenosis of the intestinal lumen caused by endometriosis [36] . Unfortunately, this parameter was not examined in the current study- the major limitation

of our investigation. Theoretically, RWC-TVS may also allow determination of the extent of the disease along the longitudinal intestinal axis. Obviously, RWC-TVS cannot determine the presence of intestinal nodules located proximally to the sigmoid because these lesions are beyond the field of TVS.

This study had several limitations. First, the experience of the ultrasonographer in RWC-TVS may influence the accuracy of these techniques in diagnosing bowel endometriosis. Second, the surgeons were aware of the findings of DCBE and RWC-TVS. Although in an ideal prospective study the surgeons should be blinded to the findings of the preoperative investigations, this theoretical study design appears unethical in clinical practice because diagnostic imaging may facilitate the identification of intestinal endometriosis nodules during surgery. Furthermore, the knowledge of the findings of the preoperative investigations may only help the surgeons in identifying endometriosis nodules that were actually present. Third, RWC-TVS and DCBE did not estimate the percentage of the circumference of the intestinal wall infiltrated by endometriosis, a criterion used to choose between nodulectomy and bowel resection. Therefore, patients scheduled for nodulectomy on the basis of DCBE and RWC-TVS findings should be informed that bowel resection might be required for the complete excision of intestinal endometriosis. Future studies should examine whether DCBE and RWC-TVS can reliably estimate what percentage of intestinal circumference is infiltrated by endometriosis. DCBE may still have a role in the diagnostic workup of patients with suspected bowel endometriosis. When TVS or RWC-TVS demonstrates large intestinal nodules infiltrating the bowel muscularis,

bowel resection can probably be performed without further investigation unless the surgeon wants to exclude intestinal lesions located proximally to the sigmoid. In contrast, when ultrasound demonstrates a single bowel nodule that may be excised by nodulectomy, DCBE should be used to exclude the presence of other intestinal nodules and, thus, to adequately plan the surgical procedure with the colorectal surgeon and the patient.

Conclusions

This study showed that RWC-TVS is a reliable technique for determining the presence and extent of bowel endometriosis and that it has an accuracy similar to that of DCBE. However, RWC-TVS may sometimes underestimate the presence of multiple bowel nodules and can be performed easily in an ambulatory setting and it is better tolerated by patients. It may be hypothesized to combine TVS and DCBE to achieve a complete preoperative assessment of the bowel in order to offer to the patients an adequate counseling and the most appropriate one-step surgical treatment.