Study Question: Can uterine scar healing after laparoscopic intracapsular myomectomy (LIM) be adequately monitored by traditional two-dimensional (2D) ultrasound (US) and Doppler velocimetry?

Summary Answer: The myometrial area of the scar after LIM can be followed by 2D US and Doppler velocimetry.

What is Known Already: Apart from post-surgical adhesions, the main concern linked to laparoscopic myomectomy is the quality of healing of the myometrial incision: it has been suggested that US could be useful for assessing uterine scars after myomectomy. However, no diagnostic method has yet been widely accepted to assess the healing process.

Study Design, Size, Duration: A cohort prospective study (level of evidence II-2), run in University-affiliated hospitals: 149 women with symptomatic uterine fibroids (UFs) underwent LIM, between January 2007 and October 2011. During follow up 13 patients withdrew from the study.

Participants/Materials, Setting, Methods: After LIM, all patients were followed by traditional 2D US scanning and Doppler velocimetry on Days: 0, 1, 7, 30 and 45. Authors evaluated: number, size and location of UFs, scar diameter and Doppler velocimetry and resistance index (RI) of the uterine arteries, at their ascending branch.

Main Results and the Role of Chance: The uterine examination showed a significant (P < 0.05) progressive reduction of uterine scar area from 78% of the previous UF location on the first day, to 19% on 30th day, and 4% on the 45th day. There was no correlation with the size of the fibroid or the relative reduction in the size of the scar, on both Days 1 and 45. There was a significant (P < 0.05) increase in the RI of the ipsilateral uterine arteries from 0.65 on the first post-operative day to 0.83 after 7 days followed by a decrease to 0.71 on the 30th and 0.61 on the 45th post-operative day.

Limitations, Reasons for Caution: This is a cohort investigation on a limited number of patients and it does not surgically compare LIM and ‘classic’ myomectomy in the scar US follow up.

Wider Implications of the Findings: LIM avoided intraoperative bleeding and excessive tissue damage, as post-operative US follow up showed, with just two intra-myometrial hematomas (1.5%). The 2D US and Doppler velocimetry, a non-invasive safe method to check the myometrium after LIM, can detect post-operative hematoma and disechogenic, heterogeneous or ill-defined scar area, all unfavorable signs for myometrial scarring. Moreover, Doppler transvaginal monitoring, evaluating the pulsatility index (PI) and RI of the uterine arteries at their ascending branch, could identify patients with altered PI and RI parameters, possible markers of impaired wound healing.

Study Funding/Competing Interest(s): None.

Key words: myoma pseudocapsule / uterine fibroids / myomectomy / uterine scar / neurovascular bundle
Introduction

The role of uterine fibroids or leiomyomata in female reproductive well being has been the subject of debate for many years. Uterine fibroids (UFs) are benign tumors that vary greatly in number, size, location and symptoms. It has been estimated that the incidence of fibroids ranges from 5.4 to 77% in pre-menopausal women, with a fibroid being the only detected abnormality in 1–2.4% of infertile women (Knox, 2012). UFs generally develop during the reproductive years, often in women desiring pregnancy or affected by infertility (Frischman and Jurema, 2005; Knox, 2012). Minimally invasive myomectomy, by hysteroscopy or laparoscopy, as opposed to hysterectomy, is the preferred surgical procedure for patients who wish to preserve fertility. Myomectomy by laparotomy is a perfectly acceptable and reasonable alternative. The advantages of the laparoscopic approach are well established (Mais et al., 1996; Seracchioli et al., 2000; Dubuisson et al., 2001; Soriano et al., 2003). The authors developed and described a standardized laparoscopic technique to remove UFs, based on the UF pseudocapsule sparing, and it was called laparoscopic intracapsular myomectomy (LIM) (Tinelli et al., 2009, 2010, 2011a,b).

The overall surgical complications and reproductive outcomes of LIMs were recently assessed by a prospective observational study on a series of 235 women who underwent subserous and intramural laparoscopic myomectomy of fibroids of 4–10 cm in diameter. Of all patients, 58.2% had subserosal and 41.8% had intramural UF. At 3 years, only 1.2% had a second laparoscopic myomectomy for recurrent fibroids. Surgical parameters were completely consistent with previous reports, with early post-operative discharge and no late complications. Of the women who underwent myomectomy for infertility, 74% conceived during observation and, at term, 32.9% underwent Caesarean section, 24.8% delivered by vacuum extractor and 42.2% had spontaneous deliveries, with no case of uterine rupture (Tinelli et al., 2012).

Apart from post-surgical adhesions, the main concern linked to LIM is the quality of healing of the myometrial incision; it has been suggested that ultrasound (US) could be useful for assessing uterine healing process. Thus, the authors investigated uterine fibroids (UFs) causing infertility or reproductive dysfunction, large and growing UFs, or menstrual disorders. Regarding menstrual disorders, the authors used similar criteria established by an international consensus that determined normal limits for menstrual parameters in the mid-reproductive years: excessively frequent menses (each <25 days), irregular menses (cycle-to-cycle variation greater than 20 days), excessive duration of flow (prolonged 6–8 days) and high volume of monthly blood loss (Fraser et al., 2007). Pre-surgical vaginal US was performed by an expert clinician to determine the presence of the pseudocapsule as a white ring surrounding the UF, colored by Doppler as a ‘ring of fire’ (Fig. 1A). The number, size and location of UFs were assessed and patients with suspected adenomyosis or adenomyoma were excluded (Reinhold et al., 1995). All 2D-PDU studies were performed either with a Logic 7 Pro US system (GE-Kretz, Zipf, Austria) or IU 22 xMATRIX US System (Philips Healthcare, Eindhoven, The Netherlands) or with a Voluson 730 US System (GE-Kretz, Zipf, Austria), each equipped with a 3.8–5.2 MHz transvaginal transducer. The uterus and the UF were measured in two planes, sagittal and coronal and all the data were recorded. The resistance index (RI) was calculated from the flow velocity waveform of the uterine arteries, at their ascending branch. Magnetic resonance imaging was not used to diagnose fibroids due to expense and time. All UFs were subserous or intramural, single or multiple, and the dominant fibroid measured between 5 and 9 cm in diameter. The study excluded women with UFs that were pedunculated, small (<3 cm in diameter) or submucous. Preoperative evaluation included office hysteroscopy to exclude submucous UFs and other uterine abnormalities. We used the UF classification system of Wamsteker et al. (Table 1) to describe fibroid location (Munro et al., 2011).

Preoperative treatment with GnRH analogs was performed in rare cases, to avoid distortion of the UF pseudocapsule (Tinelli et al., 2010, 2012; Sami Walid and Heaton, 2011). When given, myomectomy was performed almost 6 weeks after the last 3.75 mg GnRH depot injection (Friedman et al., 1991; Verkauf, 1992; Mettler et al., 2012), as GnRH analogs may obscure the surface of the capsule and make UF enucleation difficult (De Falco et al., 2009, Tinelli et al., 2010, 2012)

All patients received prophylactic Cefazolin 2 g i.v. prior to laparoscopy and an intrauterine manipulator was used. Laparoscopic myomectomy was performed under general anesthesia by endotracheal intubation with a standardized four port approach: one port for the laparoscope and three lower quadrant ancillary ports (one suprapubic central 10 mm port, two lateral 5 mm ports). The 10 mm central suprapubic port was often changed to 15–20 mm for the introduction of the morcellator at the end of the procedure. Laparoscopic myomectomy by the intracapsular technique was performed without injection of an ischemic solution, as vasopressin, into the myometrium. Its use could mask the musculature vascularization by collapsing vessels, making difficult the selective and gentle pseudocapsule vessel hemostasis during LIM difficult and favoring subsequent intra-myometrial hematomas.

Authors used the US to monitor the scar size and the muscular healing following LIM, detailed as following for consistency in the study (Tinelli et al., 2010, 2011a, 2012).

The visceral peritoneum was incised in the midline longitudinal plane with monopolar scissors or a crochet needle electrode, quickly proceeding into the myometrium to reach the right plane to detect the fibroid below. Once the pseudocapsule was identified, it was exposed (Fig. 1B) by a Johannes or Manhes clamp or by an irrigator cannula to provide a panoramic laparoscopic view of the pseudocapsule. The pseudocapsule was opened with a longitudinal cut using monopolar scissors or a crochet needle to expose the UF surface. Then the fibroid was secured by a myoma screw or Collins laparoscopic forceps to provide the traction necessary for gentle enucleation. The irrigator cannula was inserted into the space between the UF pseudocapsule and fibroid for assistance.
Hemostasis of the small vessels was selectively achieved using a low energy bipolar clamp or by monopolar crochet, to free the base of the UF and the connective bridges from the pseudocapsule, with minimal trauma, minimal blood loss and pseudocapsule sparing. In cases of deep intramural UFs, chromopertubation was applied via a cervical cannula not only to check tubal patency but also to facilitate the direct recognition of an inadvertently opened uterine cavity. The myometrium was closed in a single (for subserous) or double layer (for intramural) with 1/0 Vicryl (polyglactine; Ethicon, USA), including overlying serosa, with a round CT-1 curved needle, using intra or extracorporeal knots. In subserosal myomectomies (types 5 and 6), the edges of the uterine defect were approximated with introflexing U-inverted stitches (myometrium/serosa-serosa/myometrium direction) at 1 cm increments (a baseball-type suture). Interrupted closure or a traditional unidirectional running suture was chosen by the surgeon. Deep intramural UFs (types 2–5 and 3) were closed in two-layers using introflecting baseball-type sutures. If the uterine cavities were accidentally opened during UF enucleation, 2–3 single or continuous sutures were used to close the edge of the uterine cavity. UFs were morcellated with a reusable Rotocut G1 morcellator (Karl Storz GmbH & Co. KG, Germany) or by a Gynecare Morcellex tissue morcellator (Ethicon, Inc., Somerville, NJ, USA). Patients were re-evaluated by transvaginal US on Days 1, 7, 30 and 45 after surgery. The myometrial scar pattern was compared with the previous myometrial area occupied by the UF. The scar diameter was measured by placing calipers on the outer edge of the echogenic, heterogeneous and ill-defined area to determine the healing pattern of the uterine scar after LIM (Beyth et al., 1992; Pun et al., 1998; Seinera et al., 1999; Darwish et al., 2005). Moreover, authors measured the RI of the uterine arteries at their ascending branch during each US examination. The myometrial area of the scar was calculated as the percentage of the preoperative UF diameter. The parameters were analyzed by an independent statistician using the Student’s t-test for paired samples with \( P < 0.05 \), as for the level of statistical significance.

**Table I** The original uterine fibroids classification system of Wamsteker et al. (1993).

<table>
<thead>
<tr>
<th>Type 0: submucous fibroids</th>
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<tr>
<td>Type 1: &lt;50% intramural</td>
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<tr>
<td>Type 2: fibroids are at least 50% intramural</td>
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<tr>
<td>Type 3: totally intramurals, but about the endometrium</td>
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<tr>
<td>Type 4: are entirely within the myometrium, with no extension to the endometrial surface or to the serosa</td>
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<tr>
<td>Type 5: are subserosals, being at least 50% intramural</td>
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<tr>
<td>Type 6: are subserosals, being &lt;50% intramural</td>
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<tr>
<td>Type 7: are subserosals, being attached to the serosa by a stalk</td>
</tr>
<tr>
<td>Type 8: do not relate to the myometrium at all, and include cervical lesions, those that exist in the round or broad ligaments without direct attachment to the uterus, and other so-called ‘parasitic’ lesions</td>
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Classification of transmural fibroids are categorized by their relationship to both the endometrial and the serosal surfaces. The endometrial relationship is noted first, with the serosal relationship second (e.g. 2–5).
Results

Patients and procedure

One hundred and thirty-six operated patients completed the study and the follow up. The mean age of our population was 37.2 ± 3.6 years (range 33–40 years), mean BMI was 22.9 ± 2.5 and mean parity was 1.3 ± 0.7. The primary preoperative indications included pelvic pain in 24%, menorrhagia or metrorrhagia in 23%, a large growing UF in 13% and infertility in 40%. The size of UFs was 5–6 cm diameter in 35 women (25.7%), 6–7 cm in 37 (27.2%), 7–8 cm in 34 (25%) and 8–9 cm in 30 women (22.1%). UFs were subserosal in 48 women (35.2%) and intramural in 88 (64.8%). Of the 136 women, 82 had a single fibroid (60.2%); 29 subserous (35.3%) and 53 intramural (40.7%). Fifty-four had multiple UFs (39.7%); 19 subserous (35.2%) and 35 intramural (40.8%). Of the 48 subserosal fibroids, 29 were type 5 (60.4%) and 19 were type 6 (39.6%), with no type 7. Of the 88 intramural UF, 21 were transmural types 2–5 (23.8%), 38 were type 3 (43.1%) and 29 were type 4 (33.1%). Single intracapsular myomectomy was performed for intramural fibroids in 7 women with UF types 2–5 (33.3%), 16 with type 3 (42.1%) and 17 with type 4 (58.6%), and for subserous fibroids in 16 patients with type 5 (56.1%) and 11 with type 6 (57.8%). Multiple intracapsular myomectomy was performed for intramural fibroids in 14 women with UF types 2–5 (66.7%), 22 with type 3 (57.9%) and 12 with type 4 (41.4%), and for subserous fibroids in 13 patients with UF type 5 (44.9%) and 8 with type 6 (42.2%). Two women (1.4%) were pretreated with 3.75 mg leuprolide acetate for 3 months before surgery to shrink the UFs. During surgery, a monopolar crochet needle was used to cut the connective bridges of the pseudocapsule from the surrounding myometrium in 59 women (43.4%), and bipolar clamp scissors (30 Watt energy) were used in the remaining 77 (56.6%). The uterine cavity was entered during myomectomy in two women with a single UF (2.4%) and in five with multiple UFs (9.2%). All laparoscopies were successful without conversion to laparotomy.

Post-operative US findings

On the first and 7th post-operative days, the US pattern of uterine scar area was represented by a highly echogenic area having an ill-defined heterogeneous myometrial texture (Fig. 1C); from Day 30 to 45 the image shifted to a normal echogenic myometrial texture (Fig. 1D). There was a progressive reduction of the uterine scar. The scar after LIM was 78% of the previous UF diameter on the first day, and two patients had an anechoic area of 1–2 cm at the myomectomy site (1.5%), possibly indicating the presence of a hematoma.

Discussion

Before interpreting the results of our study, it is essential to consider the physiological events in the myometrial healing process (Hardy, 1989; Garrett, 1990; Best and Hunter, 2000). The wound healing process begins with the inflammatory phase, lasts up to 72 h, and involves a number of inflammatory responses manifested by pain, swelling, redness and increased local temperature. Accumulation of exudates and edema begins the process of tissue repair following injury when a blood clot forms and seals the area. In muscular injuries, there is myofilament reaction and peripheral muscle fiber contraction within the first 2 h. Edema and anoxia results in cell damage and death within the first 24 h, and the release of protein breakdown products from damaged cells leads to further edema, tissue hypoxia and cell death. Phagocytosis then begins to rid the area of cell debris and edema (Huard et al., 2002; Järvinen et al., 2005). The muscular regeneration and repair occurs during the fibro-elastic/collagen-forming phase, which lasts from 48 h up to 6 weeks. During this time structures are rebuilt and regeneration occurs. Fibroblast cells begin to produce Type III collagen at ~4 days, and fiber organization is random and immature. Capillary budding occurs, bringing nutrients to the region, and collagen cross-linking begins. As the process proceeds, the number of fibroblasts decreases as more collagen is laid down. This phase ends with the beginning of wound contracture and shortening of the margins in the injured area (Tidball, 2005; Karalaki et al., 2009). The last phase of healing is the remodeling phase, which lasts from 3 weeks to 12 months. Gradually, cross-linking and shortening of the collagen fibers promote the formation of a tight, strong scar. Final aggregation, orientation and arrangement of collagen fibers occur during this phase. Healing of the injured muscle does not fully restore muscle to its prior state, as fibrous scar tissue slows muscle healing. The two processes of healing and fibrosis compete with each other and impair complete regeneration (Smith et al., 2008; Tidball and Villalta, 2010). Many of these processes are catalyzed by growth factors such as transforming growth factor-beta 1 (TGF-β1), a ubiquitous substance that initiates a cascade of events that activate both myogenesis and fibrosis, and decorin, a proteoglycan that impedes fibrosis by binding to TGF-β1 (Li et al., 2004; Warren et al., 2007). These growth factors are under active investigation to determine their role in muscle healing (Brunelli and Rovere-Querini, 2008).

After this description of myometrial healing, it is important to highlight the lack of evidence of clinically important fluid-filled areas during serial US evaluation of myometrium before and after LIM. This can be explained by selective and gentle coagulation of vessels of the pseudocapsule by low wattage (Tinelli et al., 2012), which avoided excessive bleeding and removed the UF while selectively sparing the pseudocapsule neurovascular bundle (Mettler et al., 2011; Malvasi et al., 2011a) and small peripheral blood vessels. Extensive diathermocoagulation and excessive i.m. bleeding generally worsens the healing process.
and myometrial function in subsequent pregnancy (Mettler et al., 2011; Tinelli et al., 2011b; Frishman and Jurema, 2005).

The US identified few small anechoic areas <5 mm at the site of LIM on the first day. Two patients (1.4%) with multiple intramyometrial UF (types 4 and 5, both 5–6 cm in diameter) had an US scar presenting as an avascular echoic area of 1–2 cm at the myomectomy site, likely due to hematoma. The progressive reduction of uterine scar diameter from 78% the day after surgery to 61% on the 7th post-operative day, to 19% on the 30th and <4% on the 45th post-operative day, corresponds with our understanding of the healing process.

Myomectomy always causes trauma due to the visceral peritoneal incision, opening of the myometrium, removal of the fibroid and closure of the muscle margins by suture. Each major structural and vascular disruption during myomectomy leads to a classical inflammatory reaction and causes irreversible tissue damage and cell necrosis with two plausible options. A regenerative response results in an optimal reconstruction of the damaged tissue and a high quality muscle scar. A fibrotic response results in a poor reconstruction of the myometrium and a fibrotic and inelastic scar. In the first case, the myometrium returns to full function, while in the second case the end result is tissue dysfunction characterized by pain, inflammation and altered internal tissue stress. The injury may result in progressive functional disability and a higher risk of uterine rupture during pregnancy or during labor. The progressive evolution of the uterine scar from a highly echogenic area with an ill-defined heterogeneous myometrial texture to a normal echoic area confirms a normal healing process, whereas a fibrotic scar contains to display hyper or hypoechoic areas and increased mean scar diameter. The second US parameter evaluated, RI, is a measure of the resistance to blood flow and is affected by the micro-vascular bed distal to the site of measurement. A resistance index of 0 corresponds to continuous flow, a RI of one corresponds to diastolic and not systolic flow; and a resistance index greater than one corresponds to reverse diastolic flow. Therefore, the resistance offered by the peripheral circulation is assessed by the RI, and an increase reflects neangiogenesis that occurs in the uterine muscle wall after myomectomy with pseudocapsule vascular surgery (Malvasi et al., 2011b).

Following LIM, a very complex process of angiogenesis occurs, with preliminary 3D mathematical modeling demonstrating an increase vascular tortuosity, disarray, abnormal branching and the presence of ‘cul-de-sac’ vessels. These features are similar to vessels present in malignant tumors caused by angiogenic growth factors. Significantly increased RI of the uterine arteries, especially in the first days after surgery, reflects the complex process of the muscular wall healing, which begins with an inflammatory response, is sustained by intramyometrial angiogenesis, and returns to normal after 30 days, when the healing is complete. More research is needed to determine the role of the UF pseudocapsule neurovascular bundle and growth factors on the formation, growth and pathophysiologic consequences of fibroids, including pain, infertility, reproductive outcomes and healing after LIM (Malvasi et al., 2011b).

Some of the pseudocapsule vessels, moreover, join at the base of the UF creating a little foot that often bleeds during an extra-capsular myomectomy, which creates a hematoma, as occurred and was seen as an avascular echoic area by US in two of our patients. Finally, the persistence of small linear hyperechoic points due to the stitches of polyglactine with a reabsorbable time of 50–60 days supports our theory that excessive points of sutures should be avoided to minimize the problem of foreign body reaction (Malvasi et al., 2009). This theory has a scientific rationale: the UF pseudocapsule is a fibro-neurovascular bundle, created by the uterus during the development and growth of the UF, as stated by a recent study that investigated UF’s pseudocapsule composition using transmission electron microscopy: it proved that their structure is similar to the normal myometrium (Malvasi et al., 2012). When the surgeon gently removes the UF through the pseudocapsule with selective coagulation of its vessel, he/she preserves the muscle surrounding UF and avoids excessive bleeding, returning it to normal healthy uterine tissue. For these reasons, hysterotomy could be closed by simply introducing the muscle edges in one or two layers, since there is little bleeding and muscular damage. The use of multiple sutures in several layers is not recommended by Malvasi et al. (2009) and by Tinelli et al. (2011a), since excessive suture materials produce a foreign body reaction, with submesothelial fibrosis and regenerative mesothelial hyperplasia. All of these inflammatory processes interfere with proper muscle healing and produce a fibrous scar that may compromise reproductive function.

Uterine blood flow can be assessed by Doppler US in the uterine arteries and there is evidence of an association between abnormal uterine artery blood velocities and infertility: a previous study indicated that significantly lower PI (range 1.36–2.17) and RI (range 0.74–0.8) were recorded in the uterine arteries of patients with fibroids than in those with normal uteri. During IVF treatment, uterine blood flow measured by Doppler US is an important factor contributing to uterine receptivity. Patients who become pregnant usually show lower vascular impedance than those who do not. The implantation rate is decreased when uterine artery PI is ≥3.3–3.5 at the time of hCG administration, oocyte retrieval or embryo transfer. Ng and Ho (2002) postulated that the presence of fibroids results in significantly reduced uterine PI and RI, but the blood flow towards the endometrium may be compromised because of drainage of blood towards fibroids.

Evaluating recent relevant literature to better critique our investigations, we noted that Chang et al. (2009) prospectively evaluated vascular perfusion and uterine healing after laparoscopic myomectomy using three-dimensional power Doppler ultrasound (3D-PDU) in 97 women with symptomatic UF’s warranting laparoscopic myomectomy. On the 7th post-operative day, all laparoscopic myomectomy sites appeared as highly echogenic areas with profuse blood flow at the periphery and reduced resistance index and pulsatility index (RI) of the uterine artery. Non-operated areas had significantly more blood flow than healing areas. Two patients had hematomas, which appeared as hypoechoic areas that were almost avascular. By the 3rd post-operative month, the blood flow and uterine volume decreased significantly. However, an 11-cm3 hypo-echoic hematoma with poor tissue perfusion was still seen in one patient with a 720-cm3 UF. The biggest limitation of this study is the lack of clarity of the technique used for myomectomy. A similar technique was used by Seiner et al. (1999), who referenced a 1997 study (Seinera et al., 1997): “...scissors were used to incise the uterus down the pseudocapsule of the UF. The UF was then enucleated with clamp forceps and scissors, by entering into the cleavage plane, between the tumor and uterine. Traction on the UF combined with countertraction on the uterus, facilitated
dissection…’ Unfortunately, this description is general and does not reflect current principles and does not describe the exact method of enucleating the UF. The explanation for their unexpected drop in vascular resistance in the uterine arteries is unclear, as a healing process creates uterine neovascularization. The exact opposite should occur and vascular resistance would be expected to increase.

Conclusion

Intracapsular myomectomy avoids intraoperative bleeding and excessive tissue damage (Mettler et al., 2011; Tinelli et al., 2010, 2011a,b, 2012), and post-operative US follow up showed just two intramyometrial hematomas (1.5%). This supports the technique that emphasizes pseudocapsule sparing and muscle preserving, without important fluid-filled areas after LIM, which can directly affect myometrial healing process, influencing successive reproductive outcomes. No diagnostic method has yet become widely accepted to assess myomectomy site healing. The myometrial area of the scar after LIM can be followed by 2D US and Doppler velocimetry, a non-invasive, safe method to check uterine perfusion, post-operative hematoma and disechogenic, heterogeneous, or an ill-defined scar area, all unfavorable signs for myometrial scarring. Moreover, Doppler transvaginal monitoring, evaluating PI and RI of the uterine arteries at their ascending branch, could identify patients with altered PI and RI parameters, possible markers of impaired wound healing.

Authors’ roles


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Conflict of interest

None declared.

References

Fraser IS, Critchley HO, Munro MG, Broder M. Can we achieve international agreement on terminology and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod 2007;22:635–643.


Ng EH, Ho PC. Doppler ultrasound examination of uterine arteries on the day of oocyte retrieval in patients with uterine fibroids undergoing IVF. Hum Reprod 2002; 17:765–770.


