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REVIEW

Use of pre-operative imaging for symptomatic uterine myomas during pregnancy: a case report and a systematic literature review

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Abstract

Purpose Uterine fibroids (UFs) occur in 10% of pregnancies and may lead to severe maternal–fetal complications, mainly depending on UFs characteristics and the distance to the uterine cavity (UC). When symptomatic, UFs are managed medically. Nevertheless, in about 2% of cases, surgery becomes necessary. Entry into the UC should be avoided during myomectomy. Consequentially, pre-operative assessment of this risk could be beneficial. Ultrasonography (US) represents the gold standard for UFs assessment; however, scarce evidence has been produced to assess the role of magnetic resonance imaging (MRI). The aim of the present study was to summarize current evidence about the pre-operative use of imaging techniques for UFs during pregnancy.

Methods A systematic research of the literature was conducted in Scopus, PubMed/MEDLINE, ScienceDirect and the Cochrane Library, including case reports and case series. A case report was also discussed. We collected data regarding patients, imaging assessment, UFs characteristics, surgical information, timing and modality of delivery.

Results According to our search strategy, 66 articles were selected and 210 patients were included. US assessment was reported in 36 (17%) cases. MRI was reported in 10 (4.7%) cases. Only in one case, MRI was used to measure the distance between UFs and UC.

Conclusion US allows an adequate pre-operative evaluation of anterior, submucosal or pedunculated symptomatic UFs in pregnancy. However, compared to US, MRI may provide a more accurate evaluation of multiple, large, intramural or posterior UFs and could measure the distance between UFs and UC more accurately.

Keywords Laparoscopy myomectomy · Laparotomy myomectomy · Leiomyoma · Magnetic resonance imaging · Pregnancy

Introduction

Uterine fibroids (UFs) are the most common benign solid tumor of the female genital tract [1]. UFs occur during pregnancy in between 2.3 and 10.7% [2, 3] of women and are mainly asymptomatic. When symptoms occur (in about 10% of cases [4]), the most common are: low abdominal pain, pelvic pressure, and/or vaginal bleeding (mainly correlating with UFs position and size, especially if > 5 cm) [5]. Symptomatic UFs during pregnancy are more common in the case of large tumors, and typically occur in the late first/early second trimester due to the increase of sex-hormone levels [6–10]. UFs can negatively influence pregnancy outcomes and the risk of maternal–fetal complications mainly depends on UF number, size, position and proximity to the uterine cavity (UC) [11]. Specifically, it has been estimated that women suffering from UFs during pregnancy have a higher risk of pre-term labor [12], premature rupture of membrane (PROM) [11], placenta previa, abruption placenta [13], dysfunctional labor, breech presentation [14], cesarean section and neonatal morbidity and mortality [12–14]. In

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the case of symptomatic UFs, medical management (with analgesics) is actually the first-line approach. Nevertheless, in specific situations (i.e., severe abdominal pain unresponsive to analgesics or in case of bulky myomas of the lower uterine segment), surgery becomes necessary to avoid severe maternal–fetal complications [15, 16]. The critical issues of performing myomectomy during pregnancy are related to the risk of opening the uterine cavity (UC) (thus running the risk of damage to the amniotic sac), damaging placental insertion or causing massive bleeding secondary to the increased uterine blood flow. It is widely assumed that myomectomy should be avoided when entering the UC cannot be excluded, or when a safe distance between the UFs and the endometrial cavity cannot be assured [11, 16]. An accurate pre-operative assessment of UFs (including position, number, size and distance from uterine cavity and placenta) can hypothetically improve the accuracy of surgical excision and reduce the risk of intra-operative complications. In addition, a detailed evaluation of UFs may be also helpful in counseling couples about the risk associated with myomectomy for both fetus and mother [15–19]. In fact, when surgery is not deferrable, as occurs in other stressful obstetric and gynecological conditions [20–25], psychological support and "ad hoc" counseling should be always offered [26–28]. Ultrasonography (US) is the first-line imaging technique in the evaluation of UFs during pregnancy and it has proven to be useful and adequate in determining crucial features such as number, localization, vascularization, shape and the relationship between UFs and UC [5, 29]. However, poor evidence is available regarding the use of magnetic resonance imaging (MRI) in the pre-operative evaluation of UFs during pregnancy [30, 31]. The aim of the present study was to summarize the available evidence concerning the use of US and MRI in the pre-operative evaluation of UFs during pregnancy, starting from the description of a peculiar case in which pre-operative MRI resulted in a successful, uncomplicated myomectomy at our institution.

Materials and methods

Study design

This was a case report with systematic review of the literature on the use of pre-operative imaging techniques for symptomatic UFs during pregnancy. The review was written following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [32]. The review protocol was registered in PROSPERO prior to carrying out the literature search (registration number: CRD42018087118). No Institutional Review Board (IRB) approval was required for this study.

Inclusion criteria

Population Pregnant women with symptomatic UFs (submucosal, intramural, subserosal) who underwent myomectomy (with laparoscopic/laparotomy approach). Leiomyosarcoma or leiomyomatous neoplasia of uncertain malignant potential were excluded.

Intervention preoperative assessment of UFs by imaging tools (US and MRI) or no intervention.

Comparators No comparators.

Outcomes To evaluate the role of imaging tools (US and MRI) in the preoperative evaluation of symptomatic UFs during pregnancy.

Study design Observational studies (retrospective chart review, case series and case reports) were included.

Language A language restriction including Italian, English, Spanish and French was adopted. For Spanish and French articles, the support of a qualified native speaker was used.

Search strategy

A systematic search of literature was conducted in Scopus, PubMed/MEDLINE, ScienceDirect and the Cochrane Library from their inception to December 2017. A specific combination of key words and data base index terminology alone or in combination was used: uterine fibroids OR myoma OR leiomyoma AND myomectomy OR laparoscopy OR laparotomy OR excision OR surgery OR removal AND pregnancy OR gestation.

Study selection and data extraction

Two authors (FS and SD) independently checked the titles and abstracts of the studies obtained by the search. They obtained the text of eligible studies and assessed studies for inclusion. Two other authors (LC and GV) performed a manual search of reference lists in order not to miss relevant or recent publications. Any disagreement between them on the eligibility of studies was resolved through discussion with a third author (MF). Two authors (GV and FS) extracted data regarding study features (US and MRI findings, leiomyomas characteristics, surgical information, complication, mode and timing of delivery) and population characteristics (age, parity, gestational age, symptoms). Two additional authors (MF and PM) checked the data extraction. This study was in accordance with the Helsinki Declaration, conforms to the Consensus-based Clinical Case Reporting Guideline Development (http://

www.equator-network.org/) the Committee on Publication Ethics (COPE) guidelines (http://publicationethics.org/).

Objective of the systematic review

The objective of the present systematic review was to summarize the use of imaging tools, US and MRI, in the evaluation of UF features (UFs number, size, location and distance from the uterine cavity) prior to myomectomy during pregnancy.

Data synthesis

We used a standardized, pre-specified format for data extraction. We extracted descriptive characteristics of the studies including: year of publication, number of cases, patient features (age, parity, gestational age at time of surgery), US and MRI findings, characteristics of UFs (size, number and position), surgical approach and complications, timing and modality of delivery. These data are shown separately for laparoscopic myomectomy (Table 1) and for laparotomic myomectomy (Table 2). Since there was a great heterogeneity between studies, a quantitative data synthesis was not performed.

Results

The search strategy, based on pre-defined key search items, provided a total of 1623 articles, after removing duplicates. After title screening, 97 were initially eligible. Of these, 33 studies were subsequently excluded after the examination of the abstract and full text: 23 ones due to language (written in languages excluded from the present review) and 10 because only the abstract was retrieved. Finally, 64 articles [15–17, 19, 26, 31, 33–89] were included in the present study (Fig. 1).

Patients' characteristics and symptoms

Our review included a total of 210 women. All patient characteristics are reported in Tables 1 and 2. The average age was 32.6 years old; the average gestational age (GA) at the time of surgery was 16 gestational weeks. Parity was reported only in 33 studies, resulting in 15 nulliparous [19, 33, 35, 37, 39, 44, 66, 71, 74, 78, 80, 83, 85, 86, 90] and 18 multiparous [26, 31, 34, 38, 41, 52, 53, 65, 67, 69, 70, 75, 76, 79, 81, 82, 88, 89] women. Pelvic pain was the most common indication for surgery (in both laparotomy [LPT] and laparoscopy [LPS] groups, reported in 36 (17.1%) cases [16, 17, 19, 26, 31, 34–38, 41, 44, 51–53, 60, 62, 66–69, 71–76, 78–84, 88, 90, 91]. Other symptoms included: fever (1 case, 0.5%) [34]; dyspnea due to diaphragm compression (2 cases, 1%) [81, 89]; edema of lower extremities (3 cases, 1.4%) [69, 73, 89]; urinary symptoms [26, 80]; severe gastrointestinal symptoms (7 cases, 3.3%) [26, 31, 44, 65, 69, 74, 80]; threat of miscarriage (2 cases, 1%) [68, 83]; vaginal bleeding (3 cases 1.4%) [67, 68, 85]. The presence of UFs was reported as asymptomatic in 2 cases (1%) [70, 86]. Data concerning symptomology were not reported in the remaining 21 studies [15, 33, 42, 43, 46–50, 54–59, 61, 63, 64, 72, 77]. Among these, fetal postural deformity and oligohydramnios (detected by US) were the indications for surgery in a single case (0.4%) [92].

Type of uterine fibroids

Pedunculated UFs were reported in 24/210 (11%) cases [31, 33, 35–39, 41, 42, 44, 60, 63, 65, 70, 73–75, 77, 81, 85, 86, 88, 90, 91]. Subserosal UFs or intramural UFs were reported in 16/210 (7.6%) cases [17, 19, 26, 34, 62, 66, 67, 69, 76, 78–80, 82–84, 89]. A sub-mucous, pedunculated UF, arising from the cervix, was reported in 1 case [85]. In the other cases, the UF type was not reported.

Surgical approach

LPS myomectomy was performed in 14 of 210 cases (6.6%) [33–44]. The most common documented UF type was pedunculated myoma, 13/14 cases (92.8%). Subserosal UFs were reported in only one case of 14 (7.2%) [34]. The maximum diameter of UFs ranged from 4 cm to 24 cm with an average of 9 cm. The abdominal extraction of removed UFs was performed via endobag extraction in 5/14 (35%) cases [33, 36, 37, 44, 90], through free morcellation into the abdominal cavity in 4/14 (28%) cases [34, 38, 41, 91] and through a small Pfannenstiel incision only in 1/14 (7.2%) case [35]. No intra- or post-operative complications were reported, except in 1/14 (7.2%) case where a 10 cm abdominal abscess originated from the scar of the resected pedunculated myoma site [41].

LPT myomectomy occurred in 183/210 (87%) cases [15–17, 19, 26, 31, 45–89]. Subserosal and intramural were the most common documented type of UFs. The maximum diameter of UFs ranged from 3.5 cm to 30 cm with an average of 15.8 cm. Information concerning the abdominal incision was reported in only 12/183 (6.5%) papers. Longitudinal incision was described in 7 case reports [19, 26, 31, 52, 75, 81, 88]. Pfannenstiel incision was reported in 4 case reports [70, 74, 82, 93]. The intra- or post-operative reported complications were: 2/183 hemo-transfusions (1%) [19, 31], 1/183 hysterectomy (0.5%) [53], 1/183 left salpingo-oophorectomy (0.5%) [76] and 1/183 hemoperitoneum (0.5%) [31]. In one case (1/183; 0.5%), a partial myomectomy was performed via vaginal route, in which the extrinsic part of a semi-pedunculated myoma arising from the posterior wall

Table 1 Laparotomy myomectomy during pregnancy: relevant literature background

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Basso et al. 2017 [88]	1	36, multiparous	17	PP	3 subserous uterine myomas on anterior wall Max: 132 mm	Nr	Necrotic subserous pedunculated myomas, torsion of pedicle	LI	No	Cervical effacement at 21 wks; VD at 38 wks
Jhalta et al. 2016 [86]	1	34 nulliparous	13	Asymptomatic	Abdomino-pelvic mass of 160 × 100 mm with minimum vascularity	Nr	Subserosal pedunculated myoma arising from right fundal region of 160 × 120 × 100 mm	Nr	NIC	Spontaneous VD at 39 wks
Pelissier-Komorek et al. 2012 [81]	1	34 multiparous	10	PP; dyspnea for right diaphragm compression	Presence of large myoma	Subserosal fundal pedunculated myoma of 220 mm; a posterior Myoma of 4 cm and an anterior Myoma of 40 mm	Pedunculated myoma with necrosis weighing 2040 g	LI	NIC	Spontaneous VD at 35 wks
Domenici et al. 2014 [84]	1	35 multiparous	16	PP	Subserous myoma of 200 mm	MRI confirmed	Nr	Nr	NIC	CS at 38 wks
Lozza et al. 2011 [80]	1	28 nulliparous	15	PP, US, GIS	3 bulky uterine myomas: the largest intramural posterior, 120 × 100 mm vacuolated inside; the second anterior, submucosal, 100 × 90 mm; the smallest anterior intramural 50 × 26 mm in size	Nr	Anterior isthmic myoma of 140 mm × 80 mm × 60 mm; posterior 18 mm × 11 mm × 6 mm	Nr	NIC	CS at 35 + 5 wks for PROM

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Bhatla et al. 2009 [19]	1	30 nulliparous	19	PP	Fundal, subserous uterine leiomyoma 250 × 200 × 200 mm	Nr	Single large myoma 300 × 280 × 260 mm, weighing 3900 g	LI	2 units of blood transfusion	Normal VD at 38 wks for PROM
Isabu et al. 2010 [78]	1	28 nulliparous	14	PP	Large fundal multi- lobulated Myoma	Nr	Large leiomyoma with degenerative areas	Nr	NIC	Elective CS at 37 wks for type III placenta praevia
Adeyemi et al. 2007 [71]	1	27 nulliparous	13	PP	Huge mass with cystic component, extending from the pelvis to the whole abdomen	Nr	Nr	Nr	NIC	Spontaneous VD at 39 wks
Makar et al. 1989 [60]	1	Nr	14	PP	Pedunculated myoma	Nr	Posterior degenerating myoma of 120 mm with short thick pedicle (40 mm diameter)	Nr	NIC	Spontaneous VD
Wittich et al. 2000 [66]	1	31 nulliparous	12	PP	Large fundal heterogeneous mass	MRI confirmed	Large leiomyoma with degenerative changes	Nr	Nr	Elective CS at 37 wks
Usifo et al. 2007 [74]	1	31 nulliparous	13	PP, GIS	168 × 157 × 142 mm mass with mixed echogenicity in the pouch of Douglas	Nr	Pedunculated sub-serous fibroid with red degeneration areas	TI	NIC	Elective CS at 38 wks
Michalas et al. 1995 [62]	1	Nr	15	PP	Nr	Nr	Large myoma of 230 mm	Nr	Nr	39 wks
Danzer et al. 2001 [67]	1	44 multiparous	12	PP, VB	Large posterior subserous uterine myoma	Nr	Large myoma of 10 cm	Nr	Nr	CS at 37 wks
De Carolis et al. 2001 [68]	18	21–34	6–24	PP, VB, 1 threat of miscarriage	Nr	Nr	1–6 myomas	Nr	Nr	14 CS 2 VD 1 abortion

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Joo et al. 2001 [92]	1	32	25	Fetal postural deformity and oligohydramnios	Nr	Nr	Nr	Nr	Nr	CS at 40 wks
Celik et al. 2002 [17]	5	31.4	13–22	PP	Nr		10 of the myomas (71.4%) were subserous and 4 (28.6%) intramural Mean size 14.0 cm	Nr	Nr	CS
Umezurike et al. 2005 [69]	1	30 multiparous	30	PP, GIS Edema of low extremities	Multi-loculated cystic tumor of 300 mm with a capsule located on the right posterior superior wall of the uterus Free fluid in abdominal cavity	Nr	Subserus myoma of 320 mm with areas of hyaline generation	Nr	Nr	Spontaneous VD at 38 wks
Suwandinata et al. 2008 [76]	1	28 multiparous	15	PP	Intramural myomas of 150 mm	Nr	14 × 12 × 11 cm intramural myoma weighted 649 g with focal degeneration of 80 × 65 × 60 mm	Necrotized left ovary due to torsion	Left annessiectomy	CS at 37 wks
Leach et al. 2011 [26]	1	30 multiparous	11	PP, GIS, US	Right-sided posterior myoma of 115 × 110 mm displacing uterus to the left. 2 cm distance between myoma and uterine cavity	Compression of colon, bladder and proximal urethra	Major myoma: subserosal 130 × 90 × 60 mm myoma with areas of cystic degeneration Other myoma: 70 × 50 × 250 mm located in the internal cervical orifice	LI	Nr	CS at 40 wks

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Doerga-Bachasing et al. 2012 [31]	1	33 multiparous	10	PP, GIS	Subserous pedunculated Myoma of 175 × 130 mm located on the posterior wall of the uterus	Pre-operative MRI: distance between the gestational sac and the peduncle of the myoma was 13 mm Post operative MRI: myometral thickness of 5 mm	Nr	LI	Hemoperitoneum and 4 packed cells and 2 units of fresh frozen plasma needed	CS at 40 wks
Shafiee et al. 2012 [82]	1	38 multiparous	15	PP	Anterior myoma 100 mm	Nr	Intramural fibroid	TI	Nr	CS at 38 wks
Finn et al. 1950 [53]	14	Nr	Nr	Nr	Nr	Nr	Nr	Nr	Nr	6 abortion 8 VD at term
Kasum et al. 2010 [79]	1	37 multiparous	15	PP	Subserous leiomyoma of 8.5 × 6.5 of 85 × 65 mm with areas of necrotic generation	Nr	Emoperitoneum	Nr	Nr	Spontaneous VD at 38 wks
Okonkwo et al. 2007 [73]	1	40	19	Edema of low extremities	Huge complex mass extending from the uterine fundus and extending into the pelvis. Bilateral hydronephrosis	Nr	Pedunculated Myoma with hyaline and cystic degeneration	Nr	Nr	Elective CS at 38 wks
Dracea et al. 2006 [70]	1	39 multiparous	14	Asymptomatic	Pedunculated myoma of fundus of 240 mm, others myomas	Nr	Nr	TI, 'total removal of myomas except for hemi-resected intramural myomas	Nr	Spontaneous VD at 37 wks
Lolis et al. 2003 [16]	13	Nr	15–19	PP	Nr	Nr	Nr	Nr	Nr	12 CS and 1 foetal demise at 15 wks

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Donnez et al. 2002 [89]	1	29, multiparous	Nr	Dyspnea and edema of lower extremities	Intramural myoma of 220 mm	Compression between the pubic bone and the promontory with compression of iliac veins and vena cava	Benign myoma with no signs of atypia. 2.250 kg	Nr	Nr	Elective CS at 35 wks
Stewart et al. 1906 [47]	1	20	Nr	Nr	Nr	Nr	Myoma of 240 mm	Nr	Nr	VD at 40 wks
Williamson et al. 1908 [49]	1	22	Nr	Nr	Nr	Nr	Myoma of 320 mm	Nr	Nr	VD at 23 wks and foetal death
Majid et al. 1997 [65]	1	35, multiparous	17	GIS	Large lower abdominal mass suggesting a degenerated myoma	Nr	7 Myomas (4 of them were pedunculated) the largest 240 × 200 × 170 mm arising from the right cornual region	Nr	Nr	Foetal demise 19 wks
Lockyer et al. 1914 [52]	1	41, multiparous	15	PP	Nr	Nr	2 myomas	LI	Nr	VD
Von Hoffmann et al. 1911 [51]	3	Nr	14–22	PP	Nr	Nr	Nr	Nr	Nr	2 VD at 40 wks; 1 foetal demise at 25 wks
Andrews et al. 1910 [50]	1	Nr	9	Nr	Nr	Nr	Nr	Nr	Nr	VD at 40 wks
Swayne et al. 1908 [48]	2	Nr	16–20	Nr	Nr	Nr	Nr	Nr	Nr	VD at 40 wks
Evans et al. 1899 [45]	1	Nr	20	Nr	Nr	Nr	Myoma of 70 mm.	Nr	Nr	Nr
Doran et al. 1906 [46]	1	Nr	21	Nr	Nr	Nr	Myoma of 100 mm	Nr	Nr	VD at 24 wks
Exacoustòs et al. 1993 [61]	13	Nr	26	Nr	Nr	Nr	Nr	Nr	NIC	8 delivered at term and 5 delivered preterm after the 32nd week of gestation

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Burton et al. 1989 [59]	8	Nr	15	Nr	Nr	Nr	Myomas ranging between 50 and 180 mm	Nr	Nr	7 VD at 40 wks; 1 foetal demise at 15 wks after surgery
Rella et al. 1980 [58]	1	Nr	12	Nr	Nr	Nr	Nr	Nr	Nr	VD at 27 wks, neonatal death
Mollica et al. 1996 [15]	18	Nr	10–19	Nr	Nr	Nr	Nr	Nr	Nr	17 CS; 1 VD
Febo et al. 1997 [64]	3	Nr	12–19	Nr	Nr	Nr	Nr	Nr	Nr	2 CS at 37 and 38 wks; 1 abortion
Bonito et al. 2007 [72]	5	Nr	9–15	Nr	Nr	Nr	Myomas ranging between 35 and 145 mm	Nr	Nr	2 CS, 3VD at 38 wks
Vázquez et al. 2009 [77]	1	Nr	12	Nr	Mimicking image of ovarian tumor	Nr	Torsion of a pedunculated myoma of 62 mm	Nr	Nr	VD at 40 wks
Horno et al. 1962 [55]	1	Nr	16	Nr	Nr	Nr	Nr	Nr	Nr	VD at 40 wks
Alanis et al. 2008 [75]	1	22, multiparous	12	PP	Nr	Giant pedunculated myoma of 30 × 27 × 19 cm	Pedunculated leiomyoma of 300 × 270 × 190 mm arising from the right fundus with multiple areas of cystic degeneration	LI	NIC	VD at 38 wks
Ardizzone et al. 1955 [54]	27	Nr	8–24	Nr	Nr	Nr	Nr	Nr	Nr	6 Foetal demises; 2 early miscarriage
Cozzi et al. 1967 [57]	16	Nr	8–20	Nr	Nr	Nr	Nr	Nr	Nr	VD between 36 and 40 wks
Rochet et al. 1964 [56]	14	Nr	Nr	Nr	Nr	Nr	Nr	Nr	Nr	Nr
Sciannameo et al. 1996 [63]	1	31	20	Nr	Nr	Torsion of pedunculated uterine leiomyoma	Nr	Nr	Nr	Nr

Table 1 (continued)

References, year	Number of cases	Age and parity	Gestational age	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Kobayashi et al. 2013 [83]	1	38, nulliparus	21	PP, threatened miscarriage	Large heterogeneous fundal uterine mass measuring 80 × 74 × 60 mm	Areas of degeneration among uterine leiomyoma	Subserous uterine myoma with purulent exudating into the peritoneal cavity	TI	Nr	CS at 37 wks
Obara et al. 2014 [85]	1	31, nulliparus	13	VB	Presence of a cervical myoma	Sub-mucous myoma measuring 62 43 mm, arising from the posterior wall of the uterine cervix	Semi-pedunculated myoma 62 × 34 mm	Partial vaginal myomectomy (The residual 3 to 4 cm cavity at the posterior wall of the cervix was sutured)	Nr	Induced labour for oligohydramnios and VD at 40 wks

PP pelvic pain, *MRI* magnetic resonance imaging, *US* urinary symptoms, *GIS* gastro-intestinal symptoms, *VB* vaginal bleeding, *LI* longitudinal incision, *TI* transversal incision, *NIC* no intraoperative complication, *VD* vaginal delivery, *CS* cesarean section, *Nr* not reported, *PROM* premature rupture of membrane, *wks* weeks

of the cervix and extending through the cervical canal into the vagina was removed [85].

Pre operative imaging evaluation

Taking into account that US was broadly introduced into clinical practice in the late 1980s [94, 95], US was reported as the primary diagnostic instrument in almost all modern documented cases (36 cases) [19, 26, 31, 33–39, 41, 44, 65, 66, 69–71, 73, 74, 76–86, 88–90, 96, 97] in evaluating general fetal condition and estimating number, size and position of UFs. Other features of UFs such as necrotic or degenerative aspects were also reported [44, 65, 79]. Preoperative MRI was carried out only in 10 (4.7%) cases [26, 31, 33, 66, 75, 81, 83–85, 89] and it was performed postoperatively only in 1 case [31]. In two studies, [66, 84] MRI was reported to be useless after US valuation. Three authors [33, 81, 83] asserted that MRI enriched the final report by giving additional details concerning some features of UFs. Two authors reported that MRI detected the presence of ab-extrinseco extra-uterine structures compression such as colon, bladder and proximal urethra [26] or the iliac and caval veins [89]. In one case [85], due to the peculiar rise of the UF from the uterine cervix (with an extension from the cervical canal into the vagina), the authors decided to perform a MRI to identify the base of the cervical myoma better. In one case, MRI was the only diagnostic tool used to evaluate UF presence [75].

Evaluation of the distance between UFs and1 UC

Among cases in which the pre-operative evaluation of UFs was assessed by MRI, in one single case [31], MRI was used to assess the exact distance between the gestational sac and the pedicle of the UF (13 mm). Furthermore, the same author used MRI post-operatively, to evaluate the myometrial thickness at the site of the dissected peduncle.

Case report

Informed consent was obtained before data collection. A statement of consent to the use of anonymous data for research and publication purposes was also obtained. A 29-year-old woman, in the 18th week of gestation (gravid 1, para 0) was referred to our Department of Obstetrics and Gynaecology due to abdominal and pelvic pain and constipation. During the clinical examination, the uterus was found to be large for GA and the abdomen was painful. On pelvic examination, we observed a large uterus with an irregular shape exceeding the pelvis and filling the whole abdomen. Subsequently, we performed a trans-abdominal ultrasonography (TA-US) that confirmed the presence of a fetus with

Table 2 Laparoscopy myomectomy during pregnancy: relevant literature background

References, year	Number of cases	Age and parity	Gestational age of treatment (weeks)	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Son et al. 2011 [33]	1	31, nulliparous	18	Nr	Septate cystic tumor (90 × 60 × 60 mm) with a thick capsule on the right posterior wall of the uterus	Subserosal uterine myoma with secondary degeneration	Pedunculated, infarcted, subserosal myoma weighing 108 g	EE	NIC	Spontaneous VD at 39 wks
Melgrati et al. 2005 [34]	1	29, multiparous	24	PP, fever	Subserosal myoma measuring 70 × 70 mm on the uterine fundus	Nr	Myoma with large base on the uterine fundus without torsion	FM	NIC	Spontaneous VD at 39 wks
Currie et al. 2013 [35]	1	29, nulliparous	11	PP	Large anterior myoma of 80 mm	Nr	A large twisted pedunculated subserosal myoma of anterior surface adherent to the sigmoid and small bowel	Small Pfannenstiel incision	NIC	Nr
Kosmidis et al. 2015 [36]	1	31, multiparous	10	PP	Leiomyoma in the fundus of the uterus of 77 mm	Nr	Twisted pedunculated leiomyoma	EE	NIC	Nr
Fanfani et al. 2010 [37]	1	39, nulliparous	25	PP	Subserous myoma in the lateral fundus side of the uterus of 90 × 50 × 74 mm	Nr	Pedunculated leiomyoma of 95 g	EE	NIC	Spontaneous VD at 40 wks
Ardovino et al. 2011 [38]	1	31, multiparous	14	PP	Subserous pedunculated fundic myoma of 48×52×63 mm, with an implantation base of 22×18 mm	Nr	Fundic myoma of 48×52×63 mm weighing 127 g	Partial removal of external portion with Plasmas patula and FM	NIC	Spontaneous VD at 40 wks
Saccardi et al. 2014 [39]	1	35, nulliparous	15	PP	Pedunculated myoma of 240 mm with an implantation base of 50 mm	Nr	Anterior pedunculated myoma of 240 mm weighing 1363 g	FM	NIC	CS for fetal distress at 41 wks

Table 2 (continued)

References, year	Number of cases	Age and parity	Gestational age of treatment (weeks)	Symptoms	Ultrasonography findings	MRI findings	Leiomyoma(s) characteristics	Surgical information	Complication	Mode and timing of delivery
Maccio et al. 2012 [44, 90]	3	33, nulliparous	19	PP, GIS, VB	5 myomas, 2 of which were pedunculated and 3 of which were intramural and/or subserosal	Nr	Pedunculated myomas: the largest was 150 × 60 mm	EE	NIC	CS secondary to malpresentation at 39 wks
		24, nulliparous	20	PP	Pedunculated myoma of 100 mm. × 100 mm	Nr	Myoma with edema in many areas weighing 170 g	EE	NIC	Spontaneous VD at 40 wks
		34, nulliparous	20	PP, Fever	Pedunculated myoma of 40 × 10 mm with signs of degeneration	Nr	Myoma with edema and necrosis weighing 240 g	Nr	Nr	Spontaneous VD at 39 wks
Algara et al. 2015 [40]	1	36, Nr	18	PP	Nr	Nr	Torsion of a pedunculated subserosal myoma	Nr	Nr	Emergency cerclage; ammonites and early fetal demise due to vehicle accident
Sentilhes et al. 2003 [41]	1	35, multiparous	17	PP	Uterine mass in the left lateral wall of the uterus of 50 mm	Nr	Degenerated pedunculated uterine leiomyoma without torsion of the pedicle	FM	Abdominal abscess of 100 mm situated on the scar of pedicle	Elective CS at 37 wks
Pelosi et al. 1995 [42]	1	Nr	Nr	Nr	Nr	Nr	Pedunculated myoma weighing 1500 g	Nr	Nr	Nr
Lucas et al. 1994 [43]	1	Nr	Nr	Nr	Nr	Nr	Nr	Nr	Nr	Nr

PP pelvic pain, *MRI* magnetic resonance imaging, *GIS* gastro-intestinal symptoms, *VB* vaginal bleeding, *EE* endobag extraction, *FM* free morcellation into abdominal cavity, *NIC* no intraoperative complication, *VD* vaginal delivery, *CS* cesarean section, *Nr*: not reported, *wks* weeks

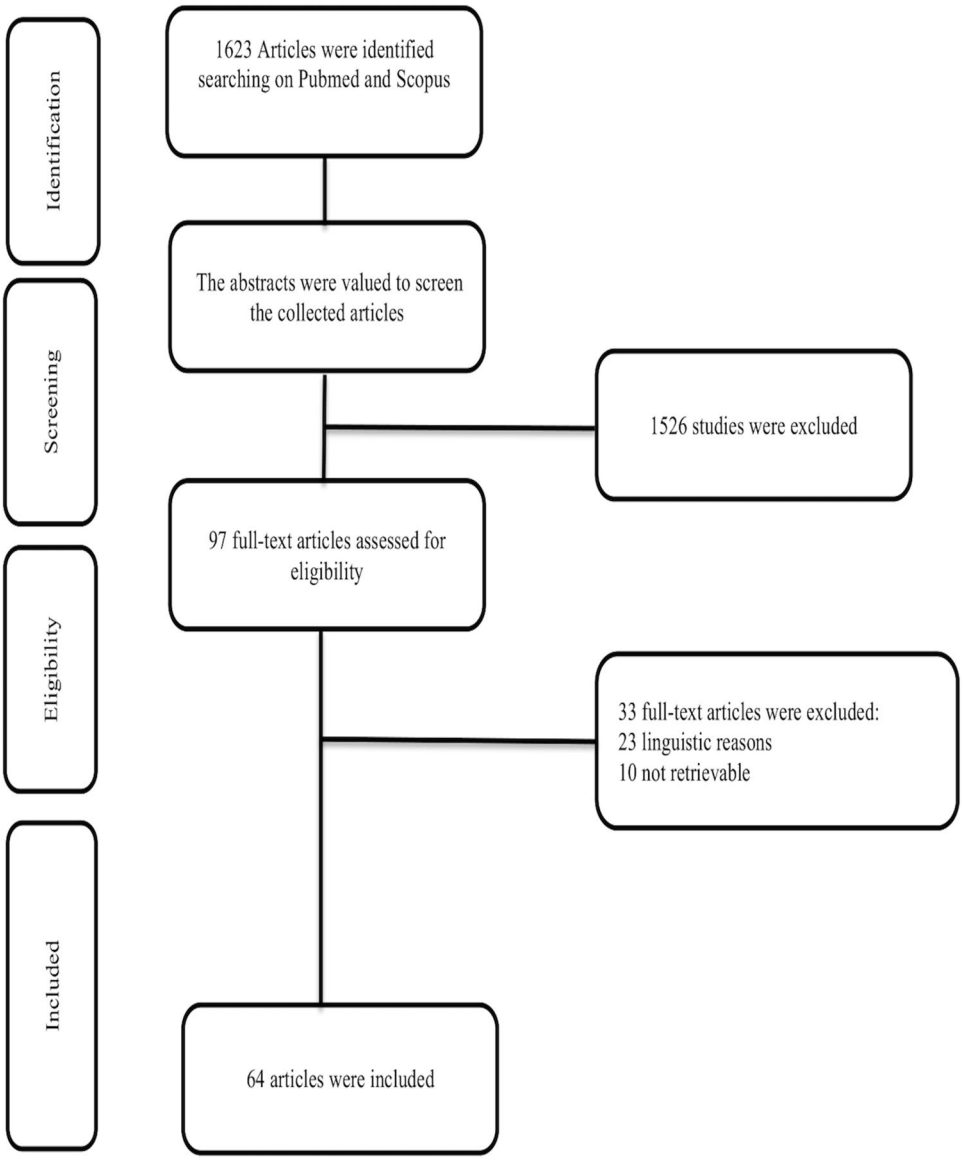

Fig. 1 Searching strategy. Adapted from Moher, Liberati, Tetzla, Altman, and e PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: e PRISMA statement

normal vital sign, normally developed with a corresponding GA and with a regular heartbeat but located in the upper left quadrant of the abdomen. During a trans-vaginal ultrasonography (TV-US), no gestational chamber was detected in the sonography field. Conversely, there was evidence of a huge mass with inhomogeneous, iso-hypoechogenic areas, suggesting the presence of a broad UF with some areas of colliquation. However, no exhaustive information regarding the relationship between UF and UC was obtained. TA-US also detected the presence of three UFs embedded in the anterior uterine wall. After the administration of analgesic therapy (paracetamol and tramadol) for 24 consecutive hours, there was no substantial relief of symptoms, therefore, leading to the choice of myomectomy.

A pre-operative MRI was performed to estimate the precise position of UF and its relationship distance from UC. At the MRI, the UC appeared to be displaced upward and laterally, deviated into the upper left quadrant of the abdomen (Fig. 2). The large subserosal UF measured $175 \times 123 \times 103$ mm, with heterogeneous hyper-intense T2-weighted areas, rising from the isthmic area (Fig. 3).

Three additional UFs were identified in the anterior uterine wall. One was located very close to the UC and placenta implant area, partially deforming it. A posterior intramural UF (about 40 mm in mean diameter) near the posterior wall of the gestational sac was also detected (previously missed by TA-US, Fig. 4). In addition, right hydronephrosis was observed. MRI not only estimated the exact position of the UFs, but also permitted an exact calculation of the distance between UFs and the UC. This information was essential for the surgeon in deciding to safely remove only the larger UF, given that such

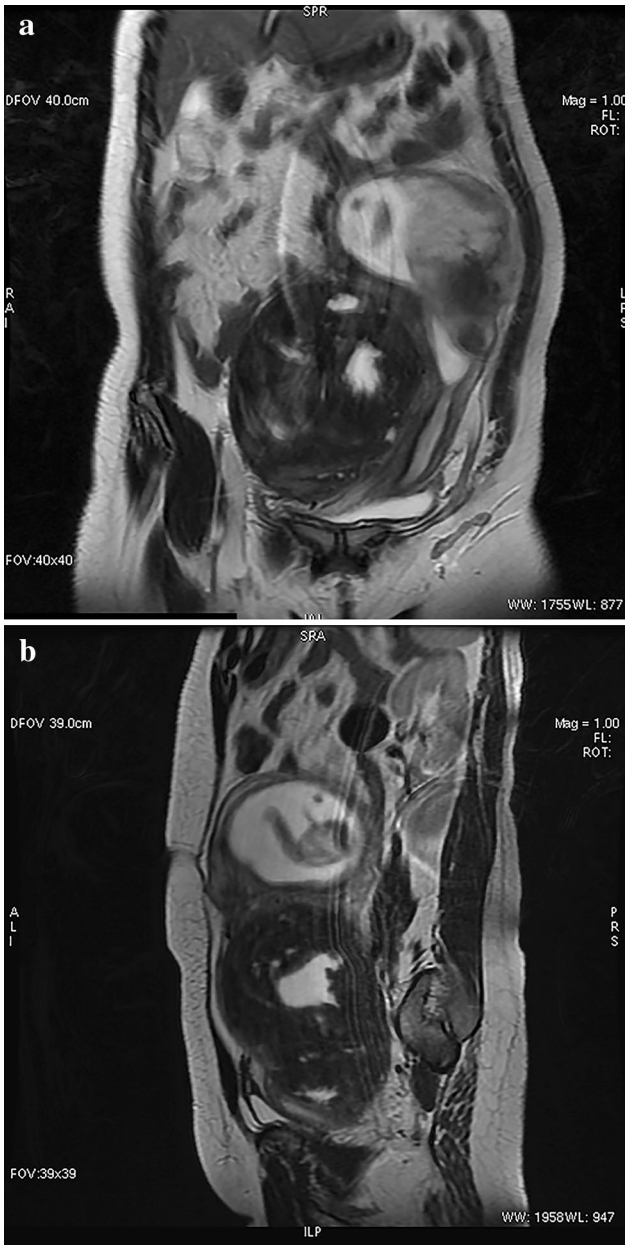

Fig. 2 Subserous myoma, with heterogeneous hyper-intense T2-weighted signal areas, arises from the isthmic region and displaces the uterine cavity and fetus upward and laterally into the upper left quadrant of the abdomen. **a** Coronal; **b** oblique sagittal

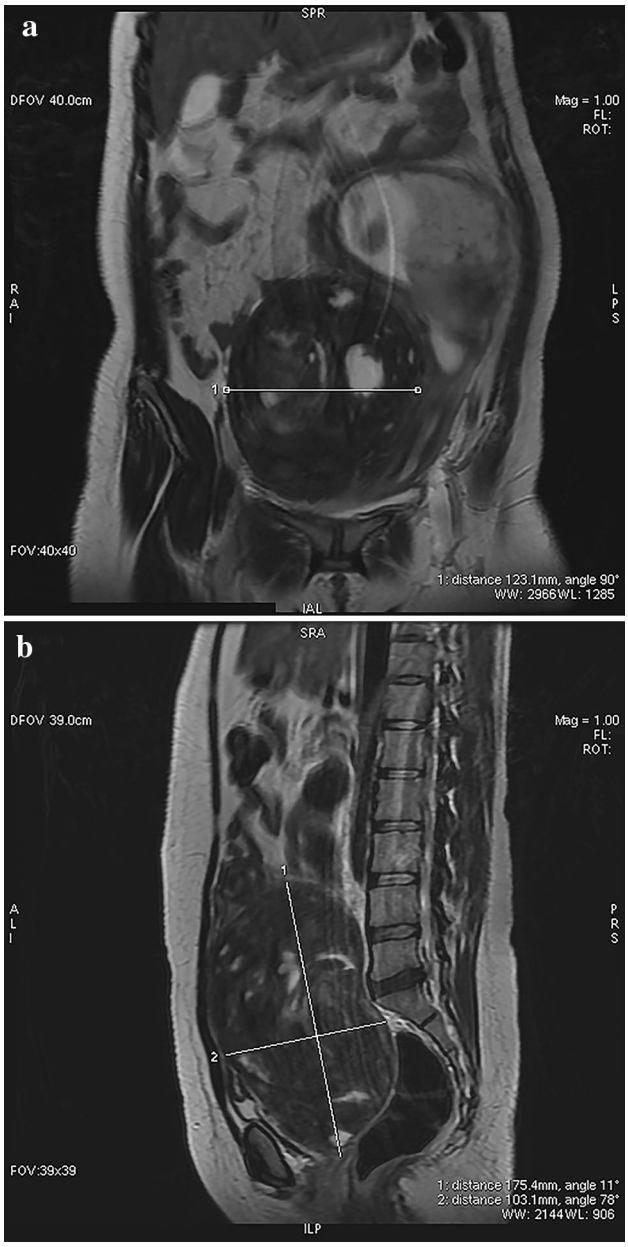

Fig. 3 Subserous myoma in T2-weighted signal areas, estimated size 175 × 123 × 103 mm that arises from the isthmic area and occupies the entire pelvic area and lower part of the abdomen. **a** Coronal; **b** oblique sagittal

a distance ranged between 9.8 mm and 11.7 mm, while the remaining UFs showed a non-permissive distance for surgery (less than 5 mm to the UC) (Figs. 4, 5). The patient was informed of the risk to her clinical status, of the surgical and post-surgical risks connected with uterine surgery, of the unfavorable outcome without any surgical intervention, and subsequently underwent an LPT myomectomy. A longitudinal pubic-supraumbilical LPT was performed (due to the volume and position of UFs). The largest UF, according to pre-operative MRI findings, was successfully removed without entering the UC; conversely, the removal of the anterior and posterior UFs (lying within a non-permissible distance from the UC) was avoided. Fetal well-being was evaluated post-surgery through a sonographic assessment. There were no major or minor complications in the post-operative period. The patient received antibiotic and analgesic therapy and was discharged after 6 days from surgery. Histological

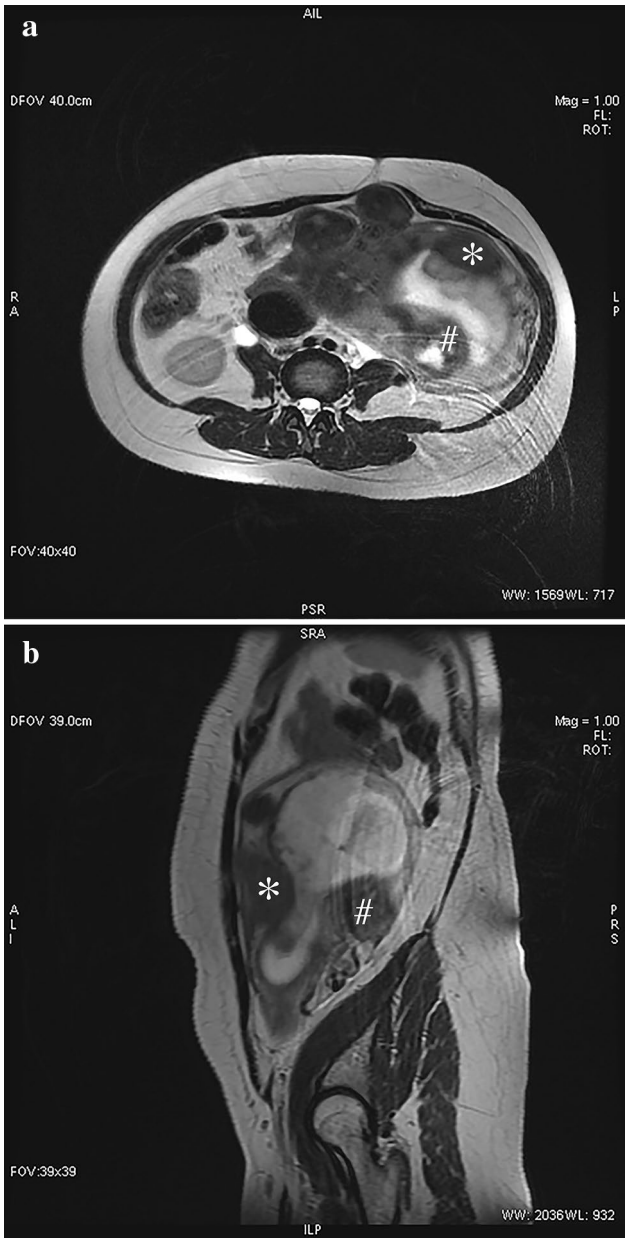

Fig. 4 Three myomas of the anterior uterine wall. One of them is very close with the uterine cavity and placenta implant area (*). A posterior intramural myoma (#), with hyper-intense T2 weighted signal areas, in close relation with posterior wall of gestational sac. **a** Axial; **b** oblique sagittal

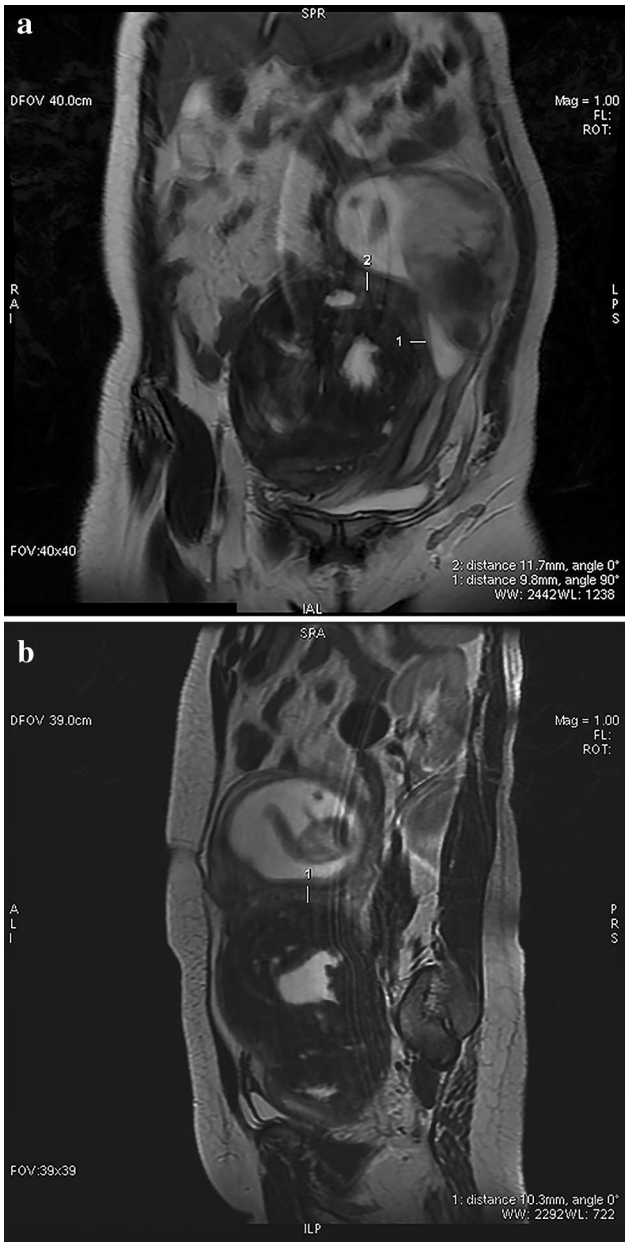

Fig. 5 Distance between myoma and uterine cavity: the larger myoma has a distance to uterine cavity ranging between 9.8 and 11.7 mm. **a** Coronal; **b** oblique sagittal

examination confirmed the diagnosis of a UF with areas of ischemic necrosis, a maximum diameter of 175 mm and a weight of 1350 g. Pregnancy continued normally with periodical (3 weeks) evaluations of fetal well-being until 38 weeks of gestation when a cesarean section was performed. The patient delivered a healthy female baby weighing 2180 g.

Discussion

Main findings

Starting from the description of a peculiar case in which MRI played a key role in the decision regarding a symptomatic UF in a pregnant woman, in the present paper, we summarized the available evidence on the pre-operative use of imaging techniques (MRI and US) for UFs during pregnancy. A total number of 64 articles and 210 women were

evaluated. The most reported pre-operative diagnostic imaging tool was US reported in 38 cases. Conversely MRI was reported in only 8 cases. Importantly, among the reports and series included, only 9 cases of fetal demise were reported [16, 40, 49, 51, 54, 58, 59, 64, 65]. In 7 cases, fetal demise occurred as a direct consequence of the myomectomy, ranging from 5 days to 14 days following the surgical procedures [16, 49, 51, 54, 59, 64, 65]. In 1 case, fetal demise occurred late [58]; whereas in another, [40] it occurred as an independent event. Accordingly, it might be apparently deduced that US can provide an accurate pre-operative evaluation of UF features in the majority of situations. However, some considerations need to be taken into account in this regard: Firstly, negative results from interventions are less likely to be reported (publication bias due to "positive results"), potentially reducing the amount of available reports concerning fetal complications related to myomectomy. Secondly, there are many reasonable advantages from the additional use of MRI, especially in specific situations (such as huge intramural UFs of the posterior uterine wall). US is the diagnostic gold standard for fetal diseases [98–102], but it is also the first-line technique (both TV-US an TA-US) in the assessment of several maternal conditions, including abdominal masses and UFs [103]. Nevertheless, US is not faultless and its accuracy is mainly dependent on the sonographer's skill [104, 105]. Specifically, in the evaluation of UFs, US was associated with a high positive predictive value (97%), but poor sensitivity (40–47%), mainly depending on the volume of UFs. Furthermore, US may be lacking when it comes to accurately localizing UFs, especially when intramural. TV-US shows a good sensitivity when UFs are few and small. However, when the uterus is enlarged, especially when the volume is > 375 mL or in cases of multiple UFs (> 4), the capability of both TA-US and TV-US in "myoma mapping" was shown to be lower in comparison to MRI [106, 107]. Furthermore, some patient features, such as obesity or intestinal meteorism, may further limit the accuracy of TA-US examination. Last but not least, warped uterine anatomy during pregnancy could not allow a thorough evaluation of the posterior uterine wall [108]. Conversely, poor evidence is available regarding the potential role of MRI in the pre-operative evaluation of UFs during pregnancy [30, 31]. MRI is a secondary imaging technique that is mainly used for evaluation of adnexal masses and endometrial/pelvic lesions [109]. It can recognize all the characteristics of non-degenerated, degenerated and complicated UFs (edema, hemorrhages, red degeneration) [29, 110] with high degree of accuracy. With regard to obstetric use, the American College of Radiology (ACR) asserts that MRI displays no evidence of any harmful effects on the fetus [30]. However, its use, especially with gadolinium-based contrast agents, should be reserved only when a potential significant benefit to the patient or fetus is predictable [111, 112]. MRI has a slightly lower PPV (91%) but a significantly higher sensitivity (80%) and a minimal measurement discrepancy to histology report when compared to US [105]. MRI also showed a higher sensitivity in identifying UFs correctly than TV-US with regard to uterine wall embedment and position. Particularly, the proportion of UFs that were misclassified in embedment was significantly higher by TV-US [106, 113]. Consequentially, MRI is considered as the best diagnostic approach when an ultrasonography result is inconclusive, especially when the degenerating UFs are hidden in the pelvis or are embedded posteriorly, unattainable by US [114, 115] or when US cannot differentiate a complicated adnexal masses from a twisted UF [109, 116].

Implications

Despite the high accuracy of MRI in evaluating UFs, such a technique is not widely used in the pre-operative assessment of symptomatic UFs during pregnancy, mainly due to lower costs and easy access of US. Its use is restricted to specific obstetric situations, such as in the evaluation of endometriosis and prior to uterine artery embolization [117–119]. Nevertheless, we want to stress the concept that MRI can clearly demonstrate the relationship between UFs, UC and placenta before surgery. Specifically, it can provide some key information about the feasibility and the risk of performing the excision of UFs during pregnancy, guiding physicians in clinical management and in patient counseling. It is interesting to note that scanty shreds of evidences can be gathered from the literature regarding the distance between UC and UFs as measured by MRI, notwithstanding the recommendation of not opening the UC unless a safe removal distance is guaranteed [11]. Only one author [31] documented the use of MRI for this purpose. Doerga et al. performed both US and MRI to evaluate the general characteristics of the myoma, using the MRI to estimate exactly the distance between the gestational sac and the peduncle of the myoma (13 mm) [31]. After all, the trigger to set up a systematic review pointing out the diagnostic tools utility in the evaluation of UFs in pregnancy arose from the analysis of our case, where the pre-operative MRI valuation was decisive helping the surgeon to remove only the largest UF, leaving the smallest anterior and posterior UFs. Conversely, evaluating the other cases where MRI was performed, no authors mentioned this measurement [26, 33, 66, 75, 81, 83–85, 89]. Furthermore, regardless of the risk of opening the UC, MRI becomes necessary when a rapid growth of UFs could be indicative of a malignant neoplasm [120]. It could be affirmed that the utility of MRI is strictly correlated with UF characteristics, particularly its localization. In the case of pedunculated UFs, US evaluation can gather all suitable information and, generally, no further pre-operative evaluation should be requested. Concerning this type of UFs, they

represent the best laparoscopically approachable leiomyoma in pregnancy. In fact, the most decisive factor that influences the type of access (LPS or LPT) is localization (pedunculated vs. embedded myomas) [44, 121]. This depends mainly on the possibility of performing a safe cut without affecting the uterine body and without performing any particular suture, avoiding any risk of wound break during pregnancy or delivery [33, 122]. It is interesting to note that only two non-pedunculated laparoscopy myomectomy cases were reported in literature. Melgrati et al. [34] described a LPS myomectomy of a subserous pedunculated myoma using a gasless approach and, consequentially, using conventional laparotomy instruments. Ardovino et al. described the removal of a subserous pedunculated myoma by laparoscopy through a partial enucleation, leaving a minimal intrauterine residual tissue and without performing any needle sutures [38]. Concerning submucosal UFs, which usually cause infertility or a high rate of vaginal discharge, they were previously treated during a preliminary fertility-planning program [123–130] and they will not be considered in our discussion, although the removal of a submucosal UF has been reported in literature. Obara et al. [85] performed a partial vaginal myomectomy for a sub-mucous, pedunculated UF that arises from the posterior wall of the cervix. Finally, in pregnancy, when UFs are embedded (intramural), laparotomy is likely to be more suitable to achieve safety sutures such as baseball suture, with interrupted sutures at the bottom and with continuous sutures at the uterine incision or unidirectional knotless barbed suture [131]. In these cases, especially for intramural myomas where US lacks localization accuracy, the pre-operative use of MRI should be considered. Some doubts concerning the use of MRI in complicated UF evaluation during pregnancy have been raised. A probable delay in the management of an acute condition such as a sudden torsion of a uterine UF has been proposed [35]. However, even in the case of a sudden torsion of a pedunculated UF, it would be reasonable to perform a successful pre-operative evaluation because they do not immediately affect either mother or fetal life [15, 19, 40]. Moreover, the presence of a pedunculated UF (with or without torsion) removes all risks of affecting the UC during a hypothetical surgical intervention. In this case, the use of MRI could be discussed. Kosmidis et al. [36] rightly pointed out the difficulty of receiving MRI in every hospital. However, when a US evaluation result is inconclusive, transferal of the patient to a reference hospital could be necessary.

Limits

The main limitations of our review are related to the design of original studies (all case report or series) and to the lack of detailed descriptions of imaging findings provided by authors. Nevertheless, due to the rarity of the condition, prospective studies evaluating the use of MRI prior to myomectomy during pregnancy are unlikely to be implemented. Moreover, many non-reported/non-retrieved data derived from the absence of the diagnostic technology used (US and/or MRI) in the clinical practice at the time when the case report/case series were written. Another important issue is the scanty evidences in the literature of the MRI preoperative evaluation to asses UFs features, in particular its application concerning the distance to the UC. However, the stated purpose of systematic reviews is to help healthcare providers by providing a reliable synthesis of the available evidence on a given topic, even if data are few. Starting from this premise, we hope that our review may figure as an eye-opener for clinicians and scientists on this topic, by stressing the need for future research on the impact of diagnostic tools (ultrasound/MRI) on the management of UFs during pregnancy. This review pointed out the use of imaging tools, US and MRI, in the evaluation of UF features in pregnancy discussing marginally the surgical management. Consequentially, a dedicated review, concerning the surgical management of myoma during pregnancy, focusing on the indication, fibroma characteristics, and obstetrical outcome could be complementary. The main strong point of the present study lies in its originality, as no prior review investigating such a topic has been published to date.

Conclusion

In pregnant women suffering from symptomatic UFs, the pre-operative use of MRI might be considered. Compared to US, MRI may provide a more objective evaluation of UFs, especially if large (with a uterus with a total volume > 375 ml), intramural or posterior. Additionally, MRI could measure the distance between UFs and UC with better precision, potentially informing clinicians about the feasibility of surgical removal of the tumor and regarding the risks of opening the uterine cavity during surgery.

Conversely, US may allow an adequate pre-operative evaluation of anterior, submucosal or pedunculated UFs in the majority of cases. Therefore, in such cases, MRI may not be required.

Further studies are needed to elucidate further the advantages associated with the pre-operative use of MRI for UFs during pregnancy. Further studies will also clarify its real impact on success during surgery and on fetal health after surgery.

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formal analysis; methodology; investigation. MF: Project administration; Conceptualization; investigation; supervision; validation.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent for research and publication purposes was obtained from the patient mentioned in the study before collecting data.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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