

Evaluation of Uterine Contractility by Magnetic Resonance Imaging in Women Undergoing Embolization of Uterine Fibroids

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Abstract

Purpose To assess uterine contractility using ultrafast magnetic resonance imaging (cine MRI) before and after uterine fibroid embolization (UFE).

Materials and Methods This is a prospective study of uterine contractility in 26 patients (age 30–41 years) undergoing UFE for symptomatic uterine fibroids. Cine MRI was performed before and 6 months after UFE. Two

radiologists evaluated uterine contractility and classified it as absent, ordered, or disordered. Patients were then grouped into three distinct patterns of progression: unchanged contractility (group A), modified contractility (B), and loss of contractility (C). These findings were then confronted with factors that might have interfered with uterine contractility pattern (uterine volume, location of dominant fibroid, fibroid/myometrium index, and fibroid necrosis pattern).

Results Of the 26 patients, 8 (30.7%) had no contractility before the procedure, while 18 (69.2%) exhibited some form of contractility (11 [61%] ordered, 7 [39%]

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disordered). All 8 patients who had no contractility at baseline exhibited contractility after UFE (5 ordered, 3 disordered). Of the 11 who had ordered contractility at baseline, 9 remained ordered and 2 lost contractility after UFE. Of the 7 with disordered contractility at baseline, 1 remained disordered, 5 progressed to ordered contractility, and 1 lost contractility. Overall, 10 patients (38%) had no change in contractility after UFE (group A), 13 (50%) had a positive change (group B), and 3 (11%) lost contractility (group C). The potential interference factors assessed had no statistically significant effect in any group.

Conclusion In women of reproductive age with symptomatic fibroids, uterine contractility improved significantly after UFE.

Level of Evidence Level 3—non-randomized controlled cohort/follow-up study.

Keywords Uterine fibroid · Therapeutic embolization · Dynamic MRI · Uterine peristalsis · Infertility · Sperm transport

Introduction

Uterine fibroid embolization (UFE) is a therapeutic alternative to hysterectomy in symptomatic patients. In women who wish to become pregnant, UFE is used only in exceptional situations, when the risk of myomectomy is deemed unacceptable. However, with improvements in operative technique, consolidation of results, the low rate of complications and increasingly frequent reports of pregnancy after embolization [1], UFE can be considered a feasible option in women who wish to reproduce [1].

Although pregnancy is known to be the result of several complex and multifactorial mechanisms related to both partners, the literature has demonstrated a frequent causal correlation between fibroids and infertility [2–19]. One of the main reasons is believed to be interference with endometrial implantation of the embryo and with sperm transport to the fallopian tubes, due to changes in uterine contractility caused by the fibroids [2–19].

Magnetic resonance imaging (MRI) is the gold-standard imaging modality for detailed evaluation of the pelvis, uterus, and fibroids [1, 20–32]. During the first decade of the twenty-first century, extensive research was conducted in an attempt to assess uterine contractility by radiological methods. Ultrafast MRI sequences (cine MRI) have since become the modality of choice for evaluation of uterine contractility [2–19] (Supplementary material—Video 1).

The exact pathophysiological mechanisms involved in uterine contractility, fibroids, and infertility are still unclear [2–19]. Considering that the changes in uterine contractility caused by fibroids may be a contributing factor to infertility [2–19] and that UFE has become increasingly indicated in women of reproductive age [1, 24–26, 30, 33], we designed the present study to ascertain whether uterine contractility is altered after UFE.

Materials and Methods

Study Design

This was a prospective study of patients with symptomatic uterine fibroids and indications for UFE. All were treated at a hospital-affiliated outpatient clinic and then referred to the interventional radiology department, where technical aspects of UFE and MRI were explained. Once patients were confirmed to meet the inclusion, exclusion, and non-inclusion criteria (Table 1) and had signed an informed consent form, they were scheduled to undergo UFE. MRI scans were acquired 30–7 days before and 6 months after UFE, both ideally during the periovulatory phase of the cycle, which was estimated by adding 14 days to the first day of the last menstrual period. None of the volunteers were currently using oral contraceptives or other hormonal agents.

This study was approved by the institutional Research Ethics Committee.

Study Population

Initially, 30 patients were selected for this study. Of these, three patients preferred to undergo hysterectomy and one patient was lost to follow-up and did not undergo control MRI. Therefore, 26 patients were included in our series. Of these 26 patients, 14 presented with bleeding and pelvic pain, 10 had bleeding alone, and 3 had pain alone.

Magnetic Resonance Technique

MRI images were obtained in a 1.5T scanner (MAGNETOM® Espree, Siemens, Erlangen).

The image acquisition parameters consisted of obtaining scout images, followed by an SSFP (true FISP) cine MRI sequence for evaluation of contractility in the sagittal plane of the uterine cavity. This sequence was programmed to acquire a 10-mm-thick slice every 2.5 s for 4 continuous minutes, obtaining approximately 120 images from a single region of interest (Table 2). To avoid interference of any external factors on uterine peristalsis, this sequence was

Table 1 Inclusion, non-inclusion, and exclusion criteria

Inclusion criteria

Women aged 25–45 years with symptomatic fibroids and indications for embolization

Undergoing UFE

MRI performed up to 30 days before UFE and up to 6 months after UFE

Non-inclusion criteria

Patients on hormonal blockade (GnRH analogues)

Changes in hormone profile suggestive of menopause

Exclusively submucosal or subserosal fibroids

Patients undergoing fertility therapies or assisted reproduction techniques (in vitro fertilization, intracytoplasmic sperm injection, intrauterine insemination)

Exclusion criteria

Fibroids with radiological signs predictive of failure, such as calcifications and absence of vascularization

Suspicion of malignancy due to clinical or radiological findings

Refusal of UFE

UFE uterine fibroid embolization

Table 2 Ultrafast MRs sequence (cine MRI) parameters

True FISP sequence	
FOV	300 mm
TR	4.96 ms
TE	2.2 ms
Matrix	320 × 320
Sequence time	4 min
Acquisition time	2 s
Slice thickness	10 mm
Flip angle	80°
NEX	1

obtained without any premedication, including anticholinergic agents.

After cine MRI, two vials of scopolamine butylbromide (Buscopan®) were administered intravenously, and conventional MRI was performed following standard technique for imaging of the female pelvis.

Analysis of Imaging Findings

MR images were assessed in consensus by two radiologists, with 10 and 5 years of experience in pelvic MRI, using a Leonardo digital workstation (Siemens, Erlangen, Germany).

Contractility evaluation images (cine MRI) were viewed repetitively and consecutively at a rate of 17 frames per second.

Uterine contractility was defined as:

Absent when observers were unable to detect any movement of the uterine wall muscles;

Present when observers were able to detect movement of the uterine wall muscles. In the latter case, the observers, by consensus, classified movement into one of two patterns:

Ordered rhythmic/coordinated, wave-like (peristaltic) endometrial/myometrial motion, whether ascending or descending;

Disordered random, sporadic, arrhythmic/uncoordinated uterine motion.

Factors that were considered as possible interferents with uterine contractility were: uterine volume, dominant fibroid location, the fibroid/myometrium index (see below),

Table 3 Variables possibly interfering with uterine contractility as assessed on MRI

Variables of interest	
Uterine contractility	Absent Present (ordered/disordered)
Fibroid location	Intramural Submucosal Subserosal Transmural
Uterine volume	Length × height × width × 0.523 = cm ³
Index	Fibroid-dominant Myometrium-dominant
Fibroid/myometrium	Myometrium-dominant
Necrosis pattern	Absent (0–10%) Partial (10–90%) Total (90–100%)

and the pattern of necrosis of the dominant myometrial nodule (Table 3).

The classification of the dominant location of uterine fibroids (intramural, submucosal, subserosal, transmural) was defined according to the disposition of the nodule in the myometrium, in case of a single lesion. In case of multiple lesions, the dominant localization pattern was considered. Uterine volume was calculated using the formula for volume of a prolate ellipsoid (volume in $\text{cm}^3 = \text{length} \times \text{height} \times \text{width} \times 0.523$).

To determine the degree of myometrial muscle replacement by fibroid tissue and express whether the fibroid component or the myometrial component predominated, we devised a qualitative index for classification of the myomatous uterus. This we termed the fibroid/myometrium index (F/M index). According to this proposal, if the uterus exhibited more muscle than fibroid tissue, it was classified as myometrium-dominant, whereas those in which fibroid tissue was larger than the myometrial constitution were classified as fibroid-dominant. We conceptualized that if a line could be drawn connecting the endometrium to the uterine serosa without crossing any fibroid tissue, the uterus should be classified as myometrium-dominant. When no such line could be drawn without crossing fibroid tissue, the uterus was defined as fibroid-dominant (Fig. 1).

Based on the description by Kroencke et al. [28], the necrosis pattern was evaluated on the MRI(s) performed 6 months after UFE and categorized into various classes or patterns of absence of enhancement (necrosis), either in the dominant fibroid or in the dominant pattern (in case of multiple fibroids). The patterns were defined as follows: total necrosis—when there was more than 90% necrosis (absence of vascular enhancement) in the fibroid(s); partial necrosis—when there was 10–90% necrosis; absence of necrosis—when there was less than 10% necrosis in the fibroid(s).

Uterine Fibroid Embolization (UFE) Technique

Embolization was performed according to standard technique, as widely described elsewhere [1, 24–26, 31–33].

Statistical Analysis

The Chi-square test, Fisher's exact test, and the Williams G test were used for categorical explanatory variables, while the Mann–Whitney U test was used for quantitative explanatory variables. The Wilcoxon test was used for before and after UFE comparisons. The Kruskal–Wallis test was used to for between-group comparisons. In all tests, the level of confidence was set at 5%.

Data were entered into Microsoft Excel® spreadsheets and analyzed in Bioestat®.

Results

Overall, 26 patients with a mean age of 36 years (range 30–41 years; SD, 4 years) were analyzed. Regarding the dominant location of uterine fibroids, 57.7% ($n = 15$) were transmural, 19.2% ($n = 5$) were submucosal, 19.2% ($n = 5$) were intramural, and only 3.8% ($n = 1$) subserosal.

According to the proposed F/M index, 53.8% of the patients ($n = 14$) had a myometrium-dominant pattern and 46.2% ($n = 12$) had a fibroid-dominant pattern.

Six months after UFE, the following necrotic patterns were observed: 88.5% ($n = 23$) with total necrosis, 7.7% ($n = 2$) with absence of necrosis, and 3.8% ($n = 1$) with partial necrosis. Regarding uterine volume, significant reductions ($P < 0.0001$) were observed after UFE, from a mean of $693.1 (\pm 374.1)$ – $406.8 (\pm 297.6) \text{ cm}^3$, for an average reduction of 20.4%.

Regarding uterine contractility, we found that, of the 26 patients, 8 (30.7%) had no contractility before the procedure. Eighteen others (69.2%) exhibited some form of contractility. Of these, 11 (61%) exhibited ordered contractility and 7 (39%) had disordered contractility.

The 8 patients who had no uterine contractility at baseline all exhibited contractility after UFE (5 ordered, 3 disordered). Of the 11 who had ordered contractility at baseline, 9 continued to exhibit such contractility and 2 lost contractility after UFE. Of the 7 with disordered contractility at baseline, 1 remained disordered, 5 progressed to ordered contractility, and 1 lost contractility (Fig. 2).

Of the 18 patients who exhibited contractility before UFE, 3 lost contractility altogether after the procedure (Fig. 2).

Group A (unchanged contractility pattern) consisted of 10 patients (38%) of the studied cohort: 9 with ordered and 1 with disordered contractility. Group B (modified contractility pattern) was composed of 13 patients (50%), of whom 8 initially had no contractility and developed contractility after UFE and 5 initially had disordered contractility which became ordered after the procedure. Group C (loss of contractility), in turn, consisted of 3 patients (11%): after UFE, 2 patients had ordered and 1 had disordered uterine contractility (Table 4, Figs. 2 and 3). Pre- and post-UFE images of one representative patient from each group are available as supplementary material (group A, Supplementary material—Videos 2 and 3; group B, Videos 4 and 5; group C, Videos 6 and 7).

Group A ($n = 10$) had a mean preprocedural uterine volume of 619 cm^3 and a mean volume reduction of 460 cm^3 , a fibroid-dominant pattern in 4 patients (40%),

Fig. 1 **A** T2-weighted turbo spin echo (TSE) sequence, sagittal view, showing dominance of fibroid tissue in relation to endometrial tissue; a line cannot be drawn between the endometrium and the myometrial serosa (fibroid-dominant). **B** T2-weighted TSE sequence, coronal view, showing dominance of fibroid tissue in relation to myometrial tissue (fibroid-dominant). **C** T2-weighted TSE sequence, sagittal view, illustrating dominance of myometrial tissue relative to fibroid tissue; several lines can be drawn between the endometrium and uterine serosa (myometrium-dominant). **D** T2-weighted TSE sequence, sagittal view, illustrating dominance of myometrial tissue relative to fibroid tissue; lines can be drawn between the endometrium and the serosa of the anterior and posterior uterine walls (myometrium-dominant)

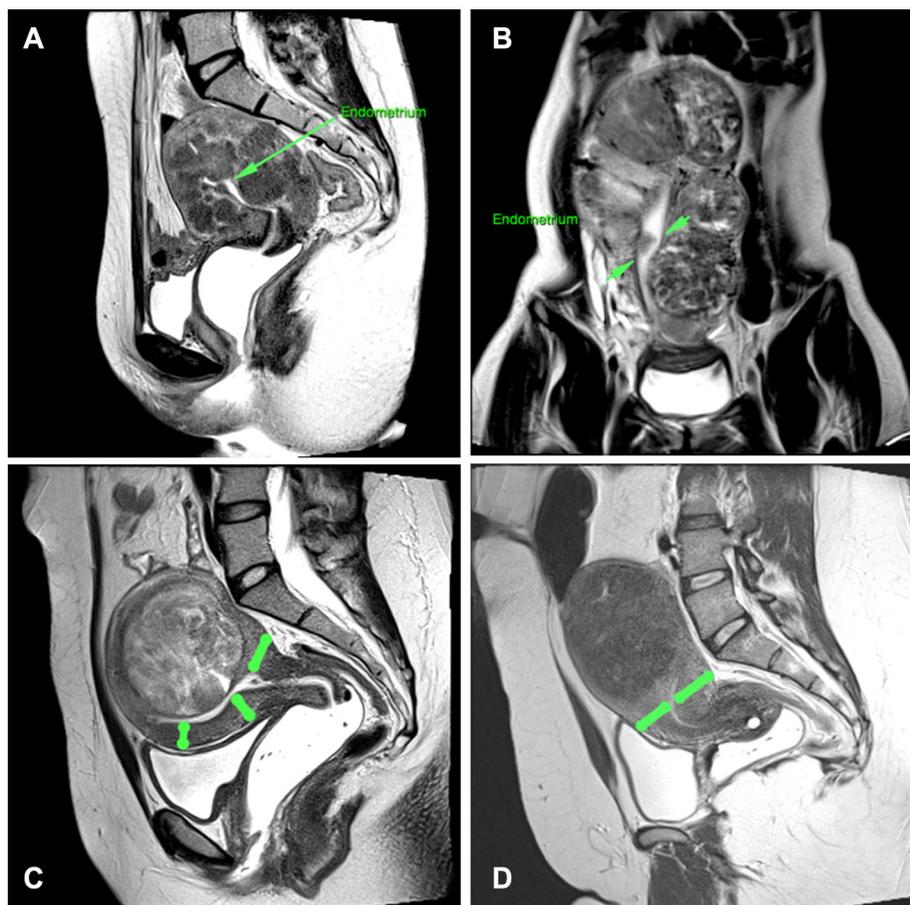
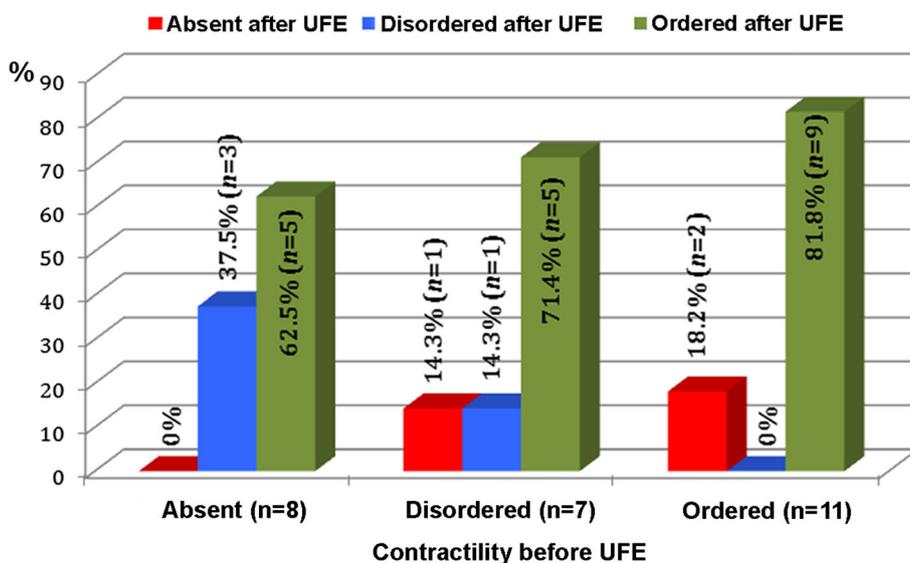


Fig. 2 Analysis of uterine contractility before and 6 months after uterine fibroid embolization (UFE)



and complete necrosis in 8 patients (80%). Four patients (40%) had predominantly transmural nodules. In group B ($n = 13$), the mean preprocedural volume was 819 cm³ and the mean volume reduction was 455 cm³. Seven patients (53.8%) had a fibroid-dominant pattern and 12 (92.3%)

exhibited total necrosis. Ten patients (77.9%) had predominantly transmural nodules. In group C ($n = 3$), the mean preprocedural volume was 397 cm³ and the mean volume reduction was 290 cm³ (37%). The pattern was fibroid-dominant in 1 patient (33.3%) and total necrosis

Table 4 Demographic analysis of groups A, B, and C according to the variables of interest

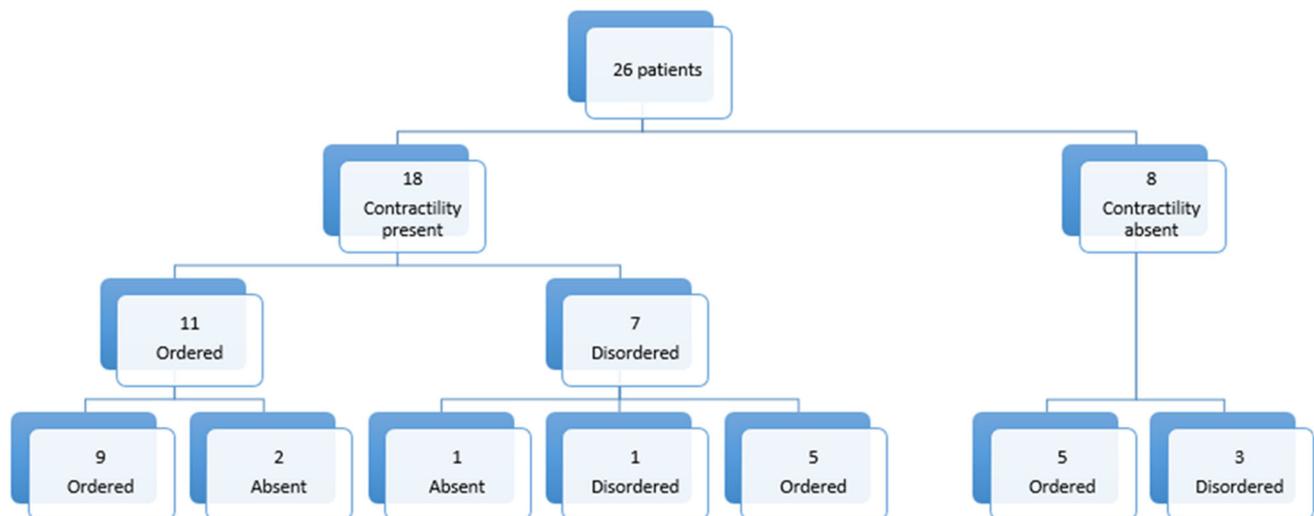
	Group A (38%) Unaltered Peristalsis (n = 10)	Group B (50%) Altered Peristalsis (n = 13)	Group C (12%) Loss of Peristalsis (n = 3)	P value
Mean age (years)	35.5 (29.1–41.0)	35.7 (28.2–40.4)	38.5 (35.2–40.5)	0.7445 ^b
Uterine volume before UFE (cm ³)	619 (220–1080)	818.5 (312–1600)	397 (155–725)	0.1462 ^b
Uterine volume after UFE (cm ³)	384.3 (123.0–751)	455.1 (109–1400)	272.7 (121–397)	0.8650 ^b
P value	0.0025 ^a	0.0007 ^a		
<i>Volume before versus after UFE</i>				
Reduction in volume (%)	38 (4–74)	48 (13–81)	23 (3–45)	0.3465 ^c
Total necrosis	80%	92.3%	100%	0.8336 ^c
Fibroid/myometrium index	40% (4) FD 60% (6) MD	53.8% (7) FD 46.2% (6) MD	33.3% (1) FD 66.7% (2) MD	0.7427 ^c

The small sample size in group C precluded calculation of the P value

^aWilcoxon test

^bKruskal–Wallis test

^cChi-square test

**Fig. 3** Stratification of participants by uterine contractility before and after uterine fibroid embolization (UFE)

was found in all 3 patients (100%). The dominant location of fibroids was balanced (33.3% intramural, 33.3% transmural, 33.3% subserosal) (Table 4, Fig. 3).

Discussion

Due to the combination of postponement of pregnancy by contemporary women and the high prevalence and progressive course of uterine fibroids during the reproductive period, understanding the true impact of fibroids (and their treatment by embolization) on fertility has become increasingly important [2, 3, 7–18, 34–38].

UFE is a well-established technique with consistent, extensively described results in terms of symptom resolution. Although the current literature does not recommend it as first-line therapy for patients who plan to become pregnant, its broadening range of indications in women of reproductive age has generated increased interest in its possible impact on female fertility [26, 33–35].

One hypothesis for the association between fibroids and infertility is abnormal uterine contractility, which would hinder fertilization, endometrial implantation of the embryo, and maintenance of pregnancy [2, 3, 10, 11, 14, 39–42].

With the advent and progression of ultra-rapid MRI techniques, noninvasive assessment of uterine contractility has become possible [2, 3, 7–15, 36–38]. Within this context, we sought to evaluate uterine contractility through cine MRI techniques in patients with indications for UFE.

The abnormality of uterine contractility pattern in women with fibroids is well documented in the literature [3, 9, 13, 16, 18, 19]; however, studies on this topic have largely relied on small, heterogeneous samples, which hinders discrimination of predictive factors. Kido et al. [16] studied patients with a relatively advanced mean age of 45.5 years (range 39–53; SD, 3.7). Orisaka et al. [13] published a series of 19 cases, but all had relatively small fibroids (mean diameter, 3.8 cm). Other limitations in the literature include acquisition of shortened cine MRI sequences, as initially described by Nakai et al. [37, 38], and assessment at different periods of the functional cycle, as in the studies of Orisaka et al. [13] and Nishino et al. [19].

In our sample, we evaluated 26 symptomatic women with a mean age of 36 years (range 30–41 years) who were scheduled to undergo UFE. Cine MRI was performed before UFE and 6 months later, always during the periovulatory phase of the cycle (estimated by adding 14 days to the date of last menstrual period)—according to the literature, the time at which peristaltic movement is most consistently observed [3]. Contractility was classified as absent, present/ordered, or present/disordered. We then further classified patients into three patterns of contractility progression: those in whom it remained unchanged (group A), those in whom the peristalsis pattern changed (group B), and those in whom contractility was lost altogether (group C).

Of the 8 patients (30.7%) with no preprocedural contractility, all developed some contractility after UFE (5 ordered, 3 disordered). Of the 11 patients (61%) who had ordered contractility at baseline, 9 continued to exhibit ordered contractility and 2 lost contractility altogether. Of the 7 (39%) with disordered contractility at baseline, 1 remained disordered, 1 lost contractility, and 5 developed ordered contractility.

Thus, of the 3 patients who lost contractility after UFE, 1 had disordered contractility at baseline and 2 had ordered contractility.

In short, 50% of patients (group B) experienced a change in uterine contractility pattern after UFE; 38% (group A) had the same contractility pattern before and after the procedure; and 11% (group C) had lost contractility 6 months after UFE. Outside of contractility loss in group C, we observed no cases of unfavorable contractility changes (i.e., from ordered to disordered); therefore, group

B was redefined as “favorable change in contractility pattern”.

Considering these three distinct groups, we were unable to identify any predictors of interference with uterine contractility among the variables of interest (uterine volume before and after embolization, dominant location pattern of fibroids, fibroid/myometrium index, or necrosis pattern after UFE).

Kido et al. assessed contractility in 20 patients who underwent UFE. Of these, 6 (30%) who had no contractility at baseline developed contractility after the procedure, as well as a significantly smaller uterine volume (mean 360.52 mL) as compared with the rest of the cohort (mean 609.95 mL) [16]. In our study, a similar percentage of patients with no contractility at baseline developed it after the procedure (8 patients, 30.7%). All of these patients belonged to group B (favorable change in contractility pattern). The total fibroid necrosis rate in this group was 92.3%, and the percent uterine volume reduction was also the highest (48%). The only relevant variable in this group was the prevalence of transmural fibroids (77%).

Replacement of myometrial tissue with fibroid tissue was substantial. (46.2% of patients in our sample were fibroid-dominant.) This prompted us to assess the potential relationship between myomatous replacement and uterine contractility, by determining which patients had a myometrium-dominant or fibroid-dominant pattern, using the F/M index (described by some authors as fibroid density). Despite our efforts, we did not identify this characteristic as having a relevant impact on contractility.

One of the main limitations of this study was the heterogeneity of the patient population in terms of uterine volume, treatment history, obstetric history, and hormone profile. We did not identify any decisive factors that might influence or predict which patients experience improvement in contractility and which might lose contractility after UFE. Studies with larger samples might provide more information in this respect.

In short, the objective of this study was to employ ultra-rapid magnetic resonance imaging to assess the impact of uterine fibroid embolization on uterine contractility. Our results show that, after UFE, uterine contractility remained unchanged in 38% of patients, improved in 50%, and worsened in only 11%.

Conclusion

Uterine contractility showed significant improvement after UFE in women of reproductive age with symptomatic fibroids.

Compliance with Ethical Standards

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

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Consent for Publication For this type of study consent for publication is not required. This study was registered in the National Information System on Research Ethics Involving Human Beings (Sistema Nacional de Informação Sobre Ética em Pesquisa envolvendo Seres Humanos, SISNEP) and approved by the Research Ethics Committee/Plataforma Brasil (CAAE: 22039914.5.0000.5505).

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