



The role of cine MR imaging in the assessment of uterine function

Deborah Monteiro Soares¹ · Heron Werner Junior¹ · Leonardo Kayat Bittencourt^{1,2} · Flavia Paiva Proença Lobo Lopes^{1,3} · Marco Aurelio Pinho de Oliveira⁴

Received: 3 April 2019 / Accepted: 19 June 2019 / Published online: 29 June 2019
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Abstract

Purpose To review the literature on uterine contraction and to highlight magnetic resonance imaging using the cine technique as a useful method to evaluate these movements.

Methods The literature research on PubMed database was done up to February 2019 with restriction to English language about articles regarding uterine peristalsis and cine MR.

Results Infertility is a common clinical problem and a source of frustration for those who want to have children. Uterine movements are crucial elements in respect of successful conception, implantation, and the development of a healthy pregnancy. It is known that the direction and frequency of uterine peristalsis are closely related to the different phases of the menstrual cycle, and that changes in its activity may interfere with reproduction. One condition that has been linked with infertility by several studies is dysfunctional uterine contractility. Magnetic resonance imaging, using the cine technique, has been shown to be a useful tool in the evaluation of these movements, allowing the identification of patients with some type of dysfunction and establish strategies to increase pregnancy rates.

Conclusion Cine MR is an excellent imaging method for the evaluation of uterine peristalsis and identification of dysfunctional contractions.

Keywords Uterine peristalsis · Uterine contraction · Infertility · Cine MRI · Sperm transport

Introduction

The female reproductive organs undergo different morphological and functional changes during the menstrual cycle, pregnancy, menopause, and other physiological states [1–11].

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00404-019-05222-9>) contains supplementary material, which is available to authorized users.

✉ Deborah Monteiro Soares
debymonte@hotmail.com

Heron Werner Junior
heronwerner@hotmail.com

Leonardo Kayat Bittencourt
lkayat@gmail.com

Flavia Paiva Proença Lobo Lopes
flaviappl@gmail.com

Marco Aurelio Pinho de Oliveira
endometriose@gmail.com

² Radiology Department, Universidade Federal Fluminense, Av Marques Do Paraná, 303, Centro, Niterói, RJ 24020-071, Brazil

³ Radiology Department, Federal University of Rio de Janeiro (UFRJ), Rua Rodolpho Paulo Rocco, 255, Cidade Universitária, Ilha Do Fundão, Rio de Janeiro, RJ 21941-913, Brazil

⁴ Department of Gynecology, State University of Rio de Janeiro, Avenida Boulevard 28 de Setembro, 77, Vila Isabel, Rio de Janeiro, RJ 20551-030, Brazil

¹ Radiology Department, Clinic of Imaging Diagnosis (CDPI)/DASA, Avenida das Américas, 4666, sala 301B, Centro Médico Barra Shopping, Barra da Tijuca, Rio de Janeiro, RJ 22640-102, Brazil

The uterus exhibits two known patterns of myometrial contraction that have different characteristics and particular functions in the female reproductive system. One is focal and sporadic bulging of the myometrium, which often involves the entire myometrial layer, which may continue for several minutes and are called sustained contractions [12–15]. The other is a subtle and rhythmic, wave-like movement of the subendometrial myometrium, known as peristalsis [16].

The mechanisms and relationships between these two types of myometrial contractions added to the effects of the aging process, medications such as oral contraceptives and a variety of gynecological and obstetric problems are subjects of current studies; however, it is already known that contractions are closely related to important uterine functions, particularly in relation to fertility [17].

Through advances in technology and especially with innovations in magnetic resonance imaging (MRI), it is now possible with the use of the kinematic technique, cine MR, to assess these movements, identify patients with dysfunctional contractility, and to increase the number of pregnancies through treatment of these changes.

Methods of search strategy

A detailed literature research on PubMed database was done up to February 2019 with restriction to English language about articles regarding uterine peristalsis and cine MR. We used a variety of keyword combinations. We combined the terms ‘uterine contractions’, ‘uterine peristalsis’, ‘endometrial waves’, and ‘junctional zone contractions’ with terms including ‘cine MR’, ‘IVF’, ‘in vitro fertilization’, ‘adenomyosis’, ‘endometriosis’, ‘leiomyoma’, ‘transvaginal ultrasound’, ‘intrauterine pressure measurement’, and ‘hysterosalpingo scintigraphy’.

Two authors (DMS and MAPO) selected the studies independently on the basis of the inclusion criteria. In cases of duplication, the study with the most recent data was included.

Uterine function evaluation by magnetic resonance (cine MR)

MRI is a non-invasive imaging modality, free of ionizing radiation, and is especially beneficial for evaluating young women with benign conditions [17].

The uterine anatomy is very well visualized by the method in T2-weighted images. Zonal differentiation is noticeable in the uterine body, especially in women of reproductive age [18–20] (Fig. 1) and is often undifferentiated in prepubertal and postmenopausal women [18, 21].

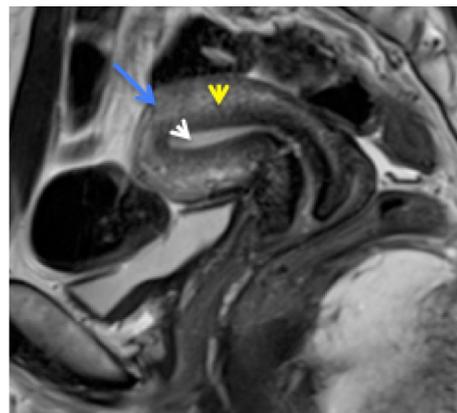


Fig. 1 28-year-old asymptomatic woman during the periovulatory phase. Normal uterus. T2-weighted fast spin echo (FSE) in the sagittal plane. The endometrium shows high signal intensity (white arrowhead); the inner myometrium (junctional zone) shows low signal intensity (yellow arrowhead); and the rest of the myometrium shows relatively high signal intensity (arrow) (personal data)

Recent advances in the techniques of MRI imaging have enabled the evaluation of uterine function by the direct and clear visualization of peristaltic movements [22–24] through the kinematic mode, using the cine technique [12, 22–25], which captures a number of images over a short period of time, thus offering a useful tool to study uterine movements, enabling the characterization of sustained contractions, particularly in peristalsis, and identifying their direction and frequency.

Cine MR is performed with the patients using calm breathing, and a total of 60 serial images of the mid-sagittal plane of the uterus is obtained using the HASTE sequence (echo time: 80 ms; FOV: 300 mm, slice thickness: 5 mm; matrix 512 × 384, FA: 150°), with an image acquired every 2 s (repetition time) for a total period of 2 min. In this technique, the antispasmodic drugs usually used in conventional MR imaging are not administered before imaging, so there is no interference with peristalsis.

Although this technique has lower spatial and contrast resolutions than conventional MR imaging [25], acquisition on 3.0 Tesla devices offers better resolution, specially using a repetition time of 2 s [26], as well as allowing the subsequent observation of images in cine mode at a faster rate, 12 times faster than real time, with the objective of highlighting the slow and subtle movements of uterine peristalsis and providing its proper visualization [27].

Uterine functional anatomy

The myometrium has three separate layers of smooth muscle. The inner layer is called the subvascular layer, the middle layer is the vascular layer, and the outer layer is the

supravascular layer. The vascular stratum is the thickest layer and contains numerous venous plexuses providing lymphatic drainage [28, 29].

The two outer layers and the innermost layer have different embryological origins, indicating that they are two units with functional and structural differences, which has already been demonstrated by some researchers [28]. The inner layer has key functions at the beginning of the reproductive process, being the only layer that contracts when uterine peristalsis occurs [28, 30].

Another aspect that distinguishes internal and external functional units is the expression of estrogen and progesterone receptors, which has already been evaluated by Noe et al., through the immunostaining of all layers of the uterus in different phases of the menstrual cycle. They observed that in the epithelial and stromal parts of the endometrium and in the subvascular layer (inner layer), the receptors are expressed cyclically, different from that occurring in the supravascular layer and in the outer two thirds of the vascular strata, where its expression is stable throughout the cycle [30, 31].

By means of this architecture, the uterus presents an inherent contractility, visible through imaging examinations as two distinct patterns of myometrial contraction, sustained contractions, and uterine peristalsis, which undergoes variations throughout the menstrual cycle [17].

Sustained uterine contractions

These contractions appear in the image as focal masses that distort the zonal appearance of the myometrium [17, 18, 32], being known as pseudolesions, since they may be confused with leiomyomas or adenomyosis in magnetic resonance imaging [18, 32].

This type of contraction assists in the expulsion of the fetus during delivery [28, 30, 31] through contractions, often painful, which also occurs to a lesser degree during menstruation [33].

Uterine peristalsis

Uterine peristalsis represents physiological uterine contractility, and is known to play an important role in the menstrual cycle (aiding in blood release) but its main role is in reproduction, as it helps in the rapid and sustained transport of spermatozoa and directs the embryo to its implantation site. In addition, it helps maintain the early stages of pregnancy, as there is a natural decrease in its frequency after ovulation to facilitate implantation [22–25, 28, 30, 34–37]. Failure of one of these physiological stages may interfere with fertility [35, 37].

The peristaltic movement can be visualized in the cine MR as a subtle wave-like rhythmic contraction of the subendometrial myometrium (subvascular stratum) that undergoes variations throughout the menstrual cycle [17, 28].

The direction and frequency of contractile waves are closely related to the changes in the cycle. They may be retrograde (cervico-fundal) or anterograde (fundal-cervico) and their frequency tends to increase during the follicular phase, mainly during the periovulatory period and decrease during the luteal phase [22, 32–34].

Contractions from the fundus to the cervix (F–C) are observed mainly during the initial/middle follicular phase of menstruation, and decrease as ovulation approaches [28].

In the late follicular phase, the waves from the cervix to the fundus (C–F) are present [28, 34, 38]. It is believed that this type of C–F contraction aids the rapid transport of spermatozoa and is observed mainly in the periovulatory period, in which the frequency of uterine contractions is greater [28, 34].

After ovulation, contractions in the opposite direction appear, defined as simultaneous contractions originating in the cervix and fundus. Their function is to prevent the embryo from being expelled from the cervix, to supply nutrients, and position the embryo before implantation [22, 28].

In the luteal phase, the uterus is in a quiescent state, providing an ideal environment for the implantation of the embryo [19, 29].

According to the literature, the frequency of peristalsis per minute during the menstrual phase is shown in Table 1 [20]. Considering the mean number of contractions in 2 min, a frequency of 4.5, 0.9, and 1.3 is observed in the periovulatory phase, luteal phase, and menstrual phase, respectively [12, 17, 25].

Some conditions have been highlighted as interfering with uterine contraction and triggering dysfunction in peristalsis. Changes in this dynamic were observed in patients taking hormonal contraceptives [18, 39], using intrauterine devices [18, 39], during the menstrual period or lactation [12, 18, 20], in the presence of fibroids [18, 40], as well as in individuals with adenomyosis and endometriosis [12, 18, 41]. The latter two conditions may themselves further contribute to decreased fertility [12, 18, 41]. A decrease in the identification of uterine peristalsis has also been reported during the presence of strong sustained uterine contractions [12, 18].

Table 1 Frequency of peristalsis per minute [22]

Menstrual phase	Middle follicular phase	Late follicular phase	Initial luteal phase	Late luteal phase
0.3–3.0/min	1.5–3.3/min	3.0–6.0/min	2.0–4.0/min	0.8–1.8/min

Cine MR approach

The recognition of peristaltic waves in cine MR [12, 25] is done by visualizing the conduction of the low signal wave within the junctional zone (Fig. 2a, b) or by identifying the movements of depression in the endometrium (Fig. 2c). It is also possible to characterize the direction of the wave, such as cervico-fundal, fundal-cervico or both at the same time, as well as its frequency (Figs. 3, 4 and 5).

The sustained uterine contractions present as transitory low signal intensity focal masses that change the shape and intensity of the signal in the myometrium, starting as

a small focus, which increases, distorts the endometrium and then disappears [18, 25, 39] (Fig. 6).

Dysfunctional uterine contractions and infertility treatments

Changes in the dynamics of uterine contractility may contribute to infertility and especially interfere with the success of treatments [42].

Dysfunctional uterine contractions, such as the C–F direction impaired during the periovulatory period, compromise the transport of spermatozoa, with consequent decreased fertility (Figs. 7 and 8) [43].

Fig. 2 Recognition of peristalsis on cine MR imaging [13, 28]

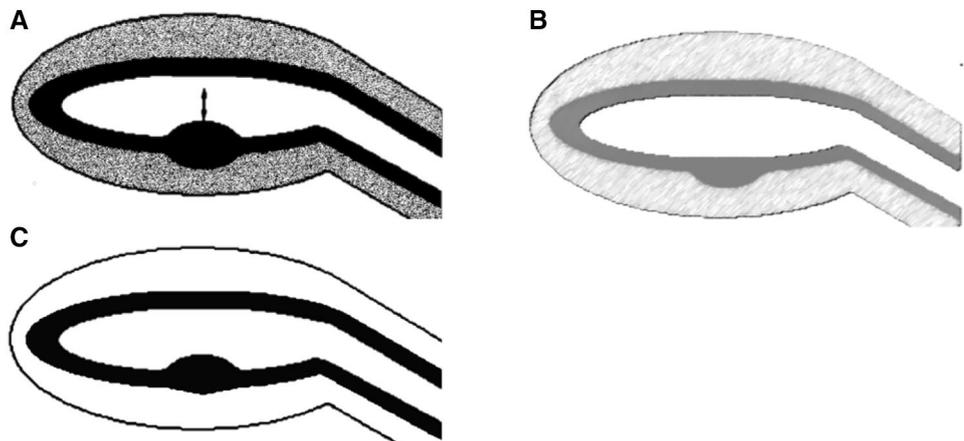


Fig. 3 32-year-old woman with pelvic pain and adenomyosis. Cine MR showing C–F peristalsis, visible as an area of low signal intensity within the junctional zone in the posterior wall of the uterus (yellow arrow), with direction toward the fundus (personal data) (see Electronic supplementary material)

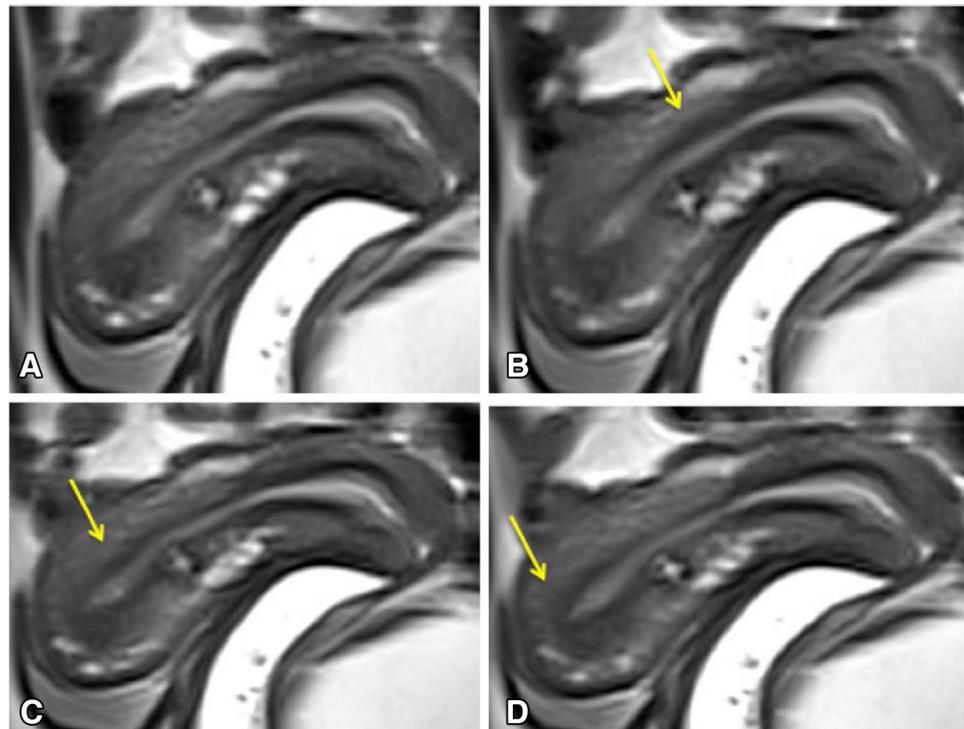


Fig. 4 38-year-old woman with pelvic pain. Cine MR showing F–C peristalsis, visible as an area of low signal intensity within the junctional zone in both anterior and posterior walls of the uterus (green arrow), with direction toward the uterine cervix (personal data) (see Electronic supplementary material)

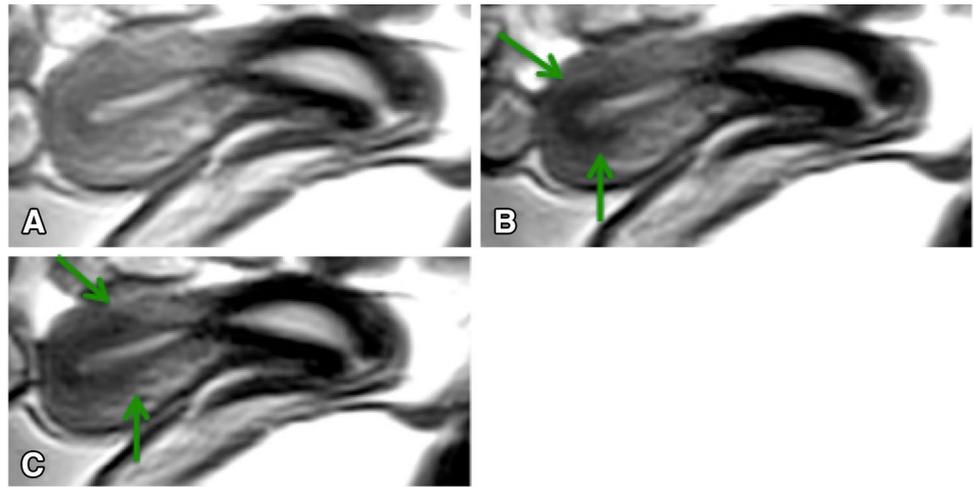


Fig. 5 35-year-old woman with endometriosis. Cine MR during the periovulatory period (a–c) showing C–F peristalsis, visible as conduction of a low intensity signal wave within the junctional zone in the anterior wall of the uterus (red arrow), which produces mild depression of the endometrium with direction toward the uterine fundus (personal data) (see Electronic supplementary material)

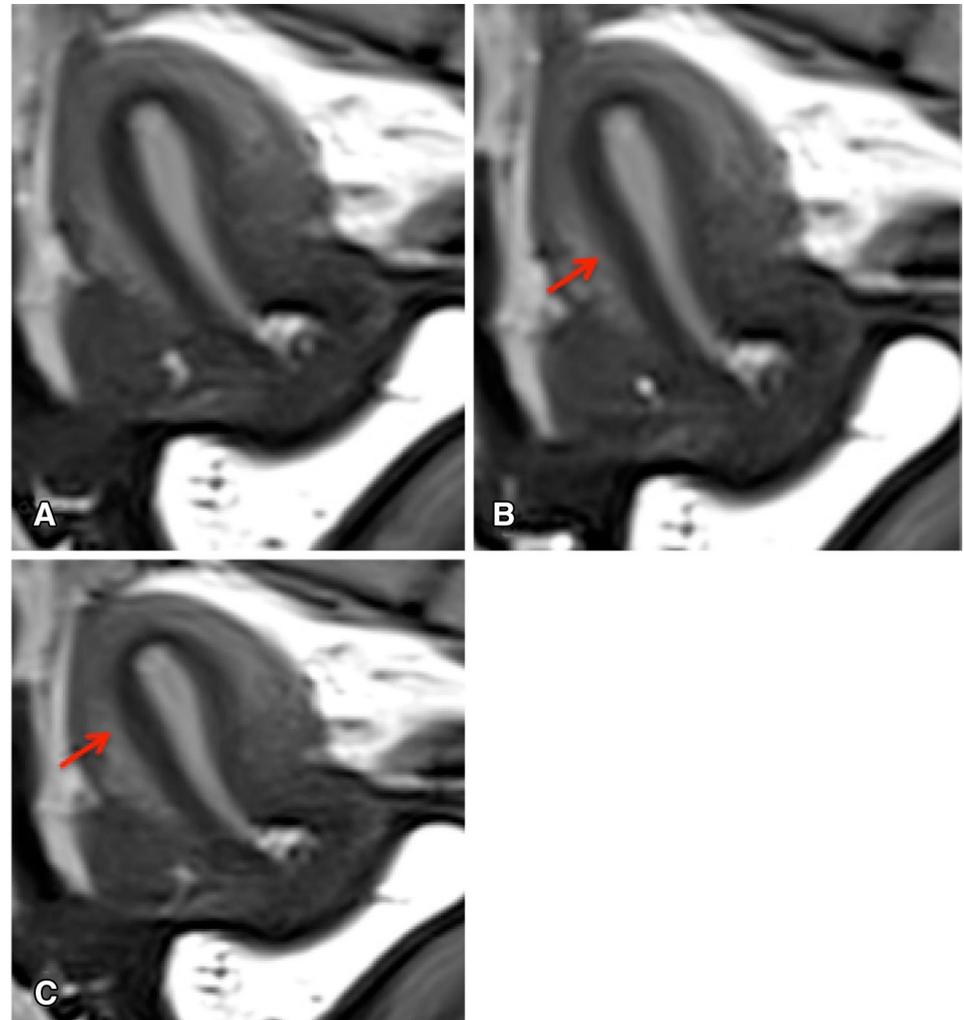


Fig. 6 26-year-old woman with pelvic pain. The uterine pseudolesions (blue arrow) are demonstrated in MR images in the T2 sequence in the sagittal plane as areas of low signal intensity, which distort the endometrial cavity (**a**); however, in a sequential image, we can see that they are not lesions (**b**) (personal data)

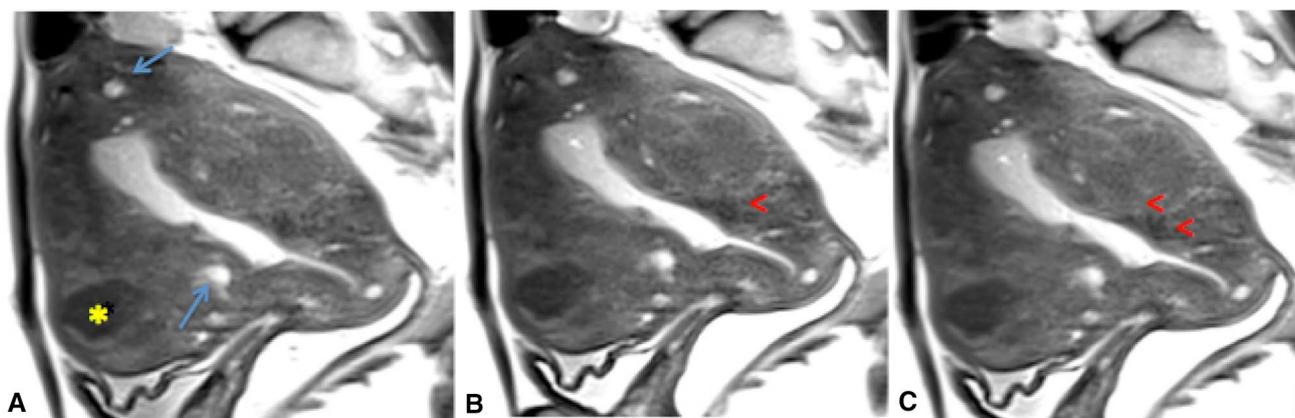
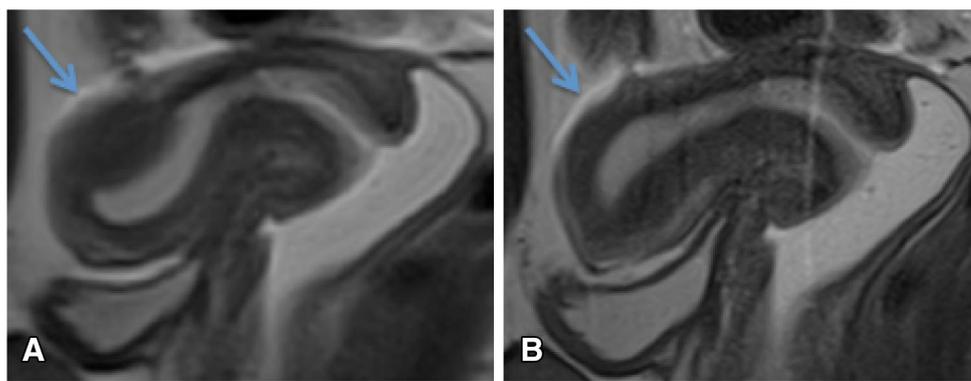


Fig. 7 **a** 41-year-old woman with fibroid (yellow asterisk) and diffuse adenomyosis with intramyometrial tiny cystic component (blue arrow). **b** and **c** Cine MR showing dysfunctional peristalsis, visible as an area of low signal intensity within the junctional zone only in

posterior walls of the uterus (red arrowhead), with direction toward the uterine fundus but which are impaired during the periovulatory period (personal data) (see Electronic supplementary material)



Fig. 8 **a** 32-year-old woman with endometriosis. **b** and **c** Cine MR showing dysfunctional peristalsis during the periovulatory period, visible as an area of low signal intensity within the junctional zone

only in posterior walls of the uterus (red arrow), with direction toward the uterine fundus but which are impaired (personal data) (see Electronic supplementary material)

In physiological cycles, uterine peristalsis rapidly disappears after ovulation, so the uterus is at rest for embryo implantation. This phenomenon is even more important in artificial cycles [43].

Some procedures related to fertilization treatments, such as high levels of steroids in controlled ovarian stimulation [44, 45] and mechanical stimuli in the uterus, during palpation or embryo transfer (ET), have shown interference in

uterus activity, resulting in increased uterine contractions [45, 46]. In addition, increased and prolonged peristaltic activity has also been described after human chorionic gonadotropin administration during in vitro fertilization (IVF) cycles [47], resulting in a 2-day delay in uterine relaxation compared to natural cycles [48, 49].

Fanchin et al. [44] and Zhu et al. [50] investigated uterine peristalsis in IVF. Both found that increased uterine contraction activity, especially in the ET interferes negatively on treatment success. Fanchin et al. [44] furthered the study, extending their data to ongoing pregnancies and implantation rates, and found a significant difference between groups that had high and low frequency of uterine contractions.

This set of findings shows that dysfunctional uterine contraction is more likely to occur in stimulated cycles than in natural cycles, especially at the time of ET.

To increase the rate of pregnancy in infertility treatments, some studies have used therapy with agents that induces uterine quiescence in the luteal phase of artificial cycles (progesterone, prostaglandins, anticholinergic agents, oxytocin receptor antagonists, and prostaglandin synthetase inhibitors) and have shown a statistically significant difference compared to placebo [43].

The oxytocin receptor antagonist (atosiban), is the most tested drug for controlling uterine peristalsis [45]. Two recent meta-analyses that included randomized controlled trials concluded that atosiban treatment is associated with higher rates of implantation, clinical pregnancy, and live births, with no difference in the rates of miscarriage or multiple pregnancies [51, 52].

Conclusion

Uterine peristalsis is a physiological contractility inherent in the normal uterus and is a promising target for increasing success rates in fertility treatment. It is believed to play a crucial role in sperm transport and the maintenance of early pregnancy [12, 23, 53].

It is known that the direction and frequency of the waves are closely related to changes in the menstrual cycle and reproduction [12, 23, 53], and that alterations in the peristaltic activity of the non-pregnant uterus can arise from several conditions, contributing to infertility.

Cine MR has been shown to be an excellent imaging method for assessing uterine function because it does not cause artificial contractions, has excellent tissue contrast, is useful for delineating wave conduction in the subendometrial myometrium [25] and visualizing sustained uterine contractions, as well as identifying other gynecological pathologies that may be related to dysfunction in these movements. Acquisition on 3.0 Tesla device, provides even better spatial resolution images.

The evaluation of physiological and dysfunctional uterine contractility by cine MR may help to support the implementation of new procedures that increase pregnancy success rates in infertile patients.

Author contributions DMS data collection, manuscript writing. HWJ, LKB and FPPLL manuscript editing. MAPO project development, data collection, manuscript editing.

Funding No funding was received for the preparation of this review.

Compliance with ethical standards

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

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

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