

The influence of uterine abnormalities on uterine peristalsis in the non-pregnant uterus

Citation for published version (APA):

de Boer, A., Rees, C., Mischi, M., van Vliet, H. A. A. M., Huirne, J. A. F., & Schoot, B. C. (2023). The influence of uterine abnormalities on uterine peristalsis in the non-pregnant uterus: A systematic review. *Journal of Endometriosis and Uterine Disorders*, 3, Article 100038. <https://doi.org/10.1016/j.jeud.2023.100038>

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DOI:
[10.1016/j.jeud.2023.100038](https://doi.org/10.1016/j.jeud.2023.100038)

Document status and date:
Published: 01/09/2023

Document Version:
Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
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Review

The influence of uterine abnormalities on uterine peristalsis in the non-pregnant uterus: A systematic review

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ARTICLE INFO

Keywords:

Uterine peristalsis
 Uterine abnormalities
 Leiomyoma
 Adenomyosis
 Congenital uterine anomalies

ABSTRACT

Uterine peristalsis is the rhythmic wave-like motion of the subendometrial layer of the uterus. These contractions change throughout the menstrual cycle in terms of direction, frequency and amplitude, and can be analysed with various methods. Not much is known about uterine peristalsis in patients with uterine abnormalities. To that end, we decided to systematically review the available studies for evidence on the influence of uterine abnormalities, including leiomyomas, endometriosis, adenomyosis and congenital uterine anomalies, on uterine peristalsis. After a systematic search of relevant databases, sixteen eligible studies were included in this review; eight case-control studies and eight controlled prospective cohort studies. The sample sizes ranged from twelve to 205 participants. Various methods of analysing uterine contractions were used, including transvaginal ultrasound, hysterosalpingo-radiationuclide scintigraphy, cine MRI and intrauterine pressure measurement. Studies varied in their design, uterine contraction measurement method and patient groups. Generally however, uterine abnormalities do seem to have an influence on uterine peristalsis. Compared to healthy controls, the specific phase of the menstrual cycle (namely the periovulatory and luteal phases) seems to play a major role in the observed effect on uterine contractions. The included studies were difficult to compare directly due to heterogeneity however, and sample sizes were relatively small. Despite these limitations, it can be concluded that uterine abnormalities likely have a menstrual phase-dependent effect on uterine peristalsis and contraction features. These aberrant contractions potentially play a role in the relationship between (benign) uterine abnormalities and infertility, along with other associated symptoms (i.e., dysmenorrhea, abnormal uterine bleeding). It is not yet possible to make a definite conclusion on the nature of this effect however. Further research is needed on objective measurement tools, treatment and clinical consequences of abnormal uterine peristalsis in patients with uterine abnormalities.

1. Introduction

Contractions of the uterus during labour have been extensively studied and are basic knowledge amongst the population. On the contrary, knowledge of these wave-like motions (peristaltic contraction and relaxation of the subendometrial layer) outside pregnancy is relatively unknown and research into its characteristics has been hampered by the subjectivity of the available measurement tools [1]. Today, no comprehensive and fully objective measurement tool is widely used.

Multiple methods have been used to visualise and analyse uterine contractions and its different characteristics [1]. Intra-uterine pressure (IUP) measurement using a catheter is a precise method which is able to measure contraction frequency, direction and amplitude; however, the introduction of the catheter itself may influence the natural behaviour of the uterus. Measuring contraction direction is also not feasible when

using one single (lumen) catheter [2]. Transvaginal ultrasound (TVUS) is another method that can visualise uterine contractions [3]. TVUS investigation, and the subsequent analysis of the imaging loops, can however be subjective due to a dependence on the observer's sonographic skills and ability to interpret the TVUS recordings. Furthermore, although several peristalsis parameters (e.g., frequency and direction) can be assessed on TVUS, it is not possible to quantify the amplitude of the waves. Another way to visualise uterine contractions is hysterosalpingo-radiationuclide scintigraphy (HSSG). It is excellent for demonstrating the contraction direction, however contraction amplitude and frequency cannot be assessed by HSSG. Recent studies have also used MRI to visualise and assess contractions [1]. The so-called cine MRI is used to visualise peristalsis of the uterus in real-time [4]. Similar to TVUS and HSSG, and despite its cost and sophistication, the evaluation of contraction amplitude is not possible by MRI [1].

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Table 1

Overview of study characteristics and main findings on leiomyomas, adenomyosis and endometriosis, congenital uterine anomalies and chronic endometritis.

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
Bulletti et al. (1997)	Case-control study	Endometriosis	16 patients, 12 controls	Patients: laparoscopically diagnosed endometriosis Controls: normal menstruating, parous, no spontaneous abortion or symptoms of endometriosis	Age 30.55 years \pm 4.82	Age 35.50 years \pm 7.72	Intrauterine pressure measurement with two probes, one near the fundus and one near the cervix. For 20 minutes	Frequency, amplitude and basal pressure tone	–	–	Abnormal contractility	Fundus (patient vs. control): frequency 28.40 \pm 8.96 vs. 11.90 \pm 7.05 os/10 min, amplitude 11.63 \pm 8.48 vs. 6.41 \pm 4.29 mmHg, basal pressure tone 65.33 \pm 23.76 vs. 25.28 \pm 19.94 mmHg
Bulletti et al. (2002)	Controlled prospective case-control study	Endometriosis	22 patients, 22 controls	Both patients and controls: normal menstruation with unexplained fertility, nulliparous, no pelvic inflammatory disease, no severe adhesions and no adenomyosis Patients: stage 2 or 3 endometriosis Controls: no evidence of endometriosis	Age 27.9 years \pm 5.5, 91% dysmenorrhea	Age 28.1 years \pm 6.2, 27% dysmenorrhea	Intrauterine pressure measurement with two probes, starting one near the fundus and one near the cervix. For 20 minutes while pulling out	Frequency, amplitude and basal pressure tone	Cycle day 2–4	Laparoscopic treatment	Uterine contractions, retrograde bleeding	Patient vs. control: frequency 22.73 \pm 5.66 vs. 11.09 \pm 3.26 os/10 min, amplitude 20.82 \pm 3.94 vs. 6.77 \pm 2.83 mmHg, baseline uterine pressure 50.14 \pm 16.30 vs. 24.68 \pm 6.14 mmHg
Fornazari et al. (2019)	Controlled prospective study	Leiomyomas	26 patients	Symptomatic fibroids and indication for embolisation with UFE, no hormonal blockade, premenopausal, not exclusively submucosal or subserosal fibroids, no current fertility therapies	Age 30–41 years (mean 36) 15 transmural, 5 submucosal, 5 intramural, 1 subserosal	–	Cine MRI, 4 min.	Presence, contraction pattern, fibroid location, uterine volume	Perioviulatory phase	UFE	Uterine peristalsis	Cervix (patient vs. control): frequency 25.90 \pm 10.21 vs. 17.90 \pm 8.46 os/10 min, amplitude 9.18 \pm 7.36 vs. 6.95 \pm 4.07 mmHg, basal pressure tone 58.02 \pm 23.13 vs. 42.41 \pm 14.18 mmHg
Kido et al. (2007)	Case-control study	Endometriosis	26 patients, 12 controls	Patients: premenopausal, diagnosed with endometrial cysts, no hormonal/surgical treatment, no	Age 24–51 years (mean 35.1), 10 perioviulatory, 13 luteal, 3 menstrual phases 8 gravidities, 7	Age 23–32 years (mean 25.9)	Cine MRI, 2 min.	Presence, frequency, direction, sustained contractions	Perioviulatory, luteal and menstrual phase	–	Uterine peristalsis	Patient vs. control perioviulatory phase: presence 30% vs. 92%, < CF waves in patients, frequency 2.5 \pm 1.0

Table 1 (continued)

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
Kido et al. (2011)	Controlled prospective study	Leiomyomas	20 patients	adenomyosis, no leiomyomas Controls: no visible gynaecological anomalies, nulliparous, no gynaecological treatment, no fertility treatment, no hormonal treatment Symptomatic uterine leiomyomas, premenopausal, no hormone therapy, endometrium well visible, undergoing UAE	parous 4 rights, 9 left, 13 bilateral cysts of the ovaries Mean size cysts 4.2 ± 2.2 cm Age 39–53 years (mean 45.5 ± 3.7)	–	Cine MRI, 3 min.	Presence, direction, frequency, uterine volume, index leiomyoma volume and location, number of leiomyomas	Periovulatory phase	UAE	Uterine peristalsis	vs. 4.4 ± 1.6 per 2 min. Patient vs. control luteal phase: presence 23% vs. 25% Patient vs. control menstrual phase: presence 100% vs. 42% After UAE: frequency increased ($P > 0.05$) Direction remained mainly CF Presence increased: 6 cases (3 intramural, 2 submucosal, 1 subserosal) with new UP
Kido et al. (2014)	Case-control study	Leiomyomas	20 patients, 20 controls	Patients: premenopausal, no hormone therapy, UP well assessed Controls: no pelvic abnormalities, no hormone therapy	Age 39–53 years (mean 45.5 ± 3.7)	Age 19–46 years (mean 33.3)	Cine MRI, 3 min.	Presence, direction, frequency, index leiomyoma volume and location, number of leiomyomas	Periovulatory phase	–	Uterine peristalsis	Presence and frequency lower in patients directions in both mainly CF Larger uterine volume and index fibroid (located intramurally) when UP No UP then fibroid submucosal, intracavitary or subserosal
Kissler et al. (2007)	Controlled prospective case-control study	Endometriosis and adenomyosis	80 patients, 24 controls	Patients: diagnosed with endometriosis Controls: good health	Most rAFS-stages 1 and 2. Fifty with peritoneal endometriosis of which 42 with additional adenomyosis of which 28 with focal spread of ≥ 1 adenomyotic lesions and 12 with diffuse adenomyosis	Not noted	HSSG, scans made up to 30 min. after application of marked micro-albumin aggregates	Direction	Late follicular phase	–	Direction of utero-tubal transport	Patients (endometriosis) vs. controls: 38.5% vs. 67% intact utero-tubal transport capacity, 61.5% vs. 33% pathologic transport Endometriosis, no adenomyosis vs. focal spread vs. diffuse adenomyosis: 62.5% vs. 46%

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Table 1 (continued)

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
Leyendecker et al. (1996)	Case-control study	Endometriosis	111 patients, 94 controls	Patients: history of infertility, diagnosed endometriosis, tubal patency Controls: regular cycles, history of fertility, tubal patency, no endometriosis	Age 21–38 years (mean 29), 1–7 years of infertility (mean 4), 82 minimal – mild, 29 moderate – severe endometriosis Most regular cycle, some prolonged proliferative and short luteal phase	Age 22–46 (mean 30)	TVUS, 5 min. and HSSG	Presence, frequency, direction	VSUP: menstrual and early, mid and late follicular, mid-luteal phase HSSG: early, mid and late follicular phase	–	Uterine peristalsis	vs. 21.5% intact transport, 37.5% vs. 54% vs. 78.5% pathologic transport Patient vs. control: doubling of frequencies during early, mid and late follicular and mid-luteal phase. Also increase in frequency during menses Both decrease in FC contractions throughout cycle Late follicular: patients show irregular contractions
Nishino et al. (2005)	Controlled prospective study	Leiomyomas	26 patients	Leiomyomas detected on TVUS; whole uterine cavity visible, able to visualise UP	Age 19–51 years (mean 41) 16 submucosal, 13 intramural/subserosal leiomyomas, 3 both (included in submucosal) Leiomyoma size 1.5–10 × 1.5–8 cm Submucosal: 1 menses, 3 follicular, 1 periovulatory, 10 luteal, 1 phase unclear Intramural: 2 menses, 2 follicular, 2 periovulatory, 4 luteal phase	–	Cine MRI, 2 min.	Presence, direction, frequency, conduction, focal loss of waves and focal movements (direction and frequency)	Menstrual, follicular, periovulatory and luteal phase	–	Uterine peristalsis	Submucosal: UP present: 12/16, direction: 4/5 CF midcycle, 1/1 FC menstrual phase, frequency: 1–3 × /2 min. luteal phase, 2–5 × /2 min. remaining cycle, conduction of UP: 4/12 obscured, non-propagating movement adjacent to leiomyoma 9/16 with frequency of 5–14 × /2 min. 4 showed loss of UP Intramural/subserosal: UP present: 10/10, direction: 2/3 CF midcycle, 2/2 FC menstrual phase, frequency 1–4 × /2 min luteal phase, 2–5 × /2 min. remaining cycle. Conduction of UP good

Table 1 (continued)

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
Oliva et al. (1992)	Controlled prospective study	Bicornuate uterus	12 patients	Bicornuate uterus	7 symmetrical cavities, 5 asymmetrical cavities	–	Intrauterine pressure measurement with 2 balloon-closed catheters, 1 in each horn	Frequency, amplitude, basal pressure tone	Ovulation and premenstrual phase	Oxytocin and methyl ergobasine	Uterine motility	Before drugs: symmetrical cavities: ovulation: UP similar in horns, pressure: 5–12 mmHg, frequency: 3–5×/min. Premenstrual: UP similar in horns, pressure: 20–30 mmHg, frequency: 1/min. Asymmetrical cavities: ovulation: UP dissimilar in horns Premenstrual: UP in larger horn typical, smaller horn different UP present in all women Direction: almost similar in both groups in follicular, periovulatory, early luteal and late luteal phase Patient vs. control: menstrual phase: FC + isthmic + opposing vs. FC, midluteal phase: isthmic + CF + FC + opposing vs. isthmic
Orisaka et al. (2007)	Case-control study (pilot)	Leiomyomas	19 patients, 3 controls	Patients: premenopausal, normal menstrual cycles, diagnosed with leiomyomas Controls: healthy women	Age 24–42 years (mean 34.8) 15 intramural, 2 subserosal and 2 submucosal leiomyomas	Age 28–36 (mean 32), mean length cycle: 30.3 days	Cine MRI, 3–4 min.	Presence, direction, frequency	Menstruation, follicular, periovulatory and early, mid- and late luteal phase	–	Uterine peristalsis	Direction: almost similar in both groups in follicular, periovulatory, early luteal and late luteal phase Patient vs. control: menstrual phase: FC + isthmic + opposing vs. FC, midluteal phase: isthmic + CF + FC + opposing vs. isthmic
Pinto et al. (2015)	Case-control study	Chronic endometritis	45 patients, 45 controls	Both patients and controls: no use of drugs (2 months), no smoking, no alcoholics, no uterine and adnexal pathology, no previous pelvic surgery Patients:	Age 30.4 years ± 4.5. Indication for hysteroscopy: infertility 42.3%, recurrent miscarriages 35.5%, abnormal uterine bleeding 22.2%	Age 30.2 years ± 3.5. Indication for hysteroscopy: infertility 56.3%, recurrent miscarriages 15.5%, abnormal uterine bleeding 28.2%	TVUS, 3 min.	Presence, direction, frequency	Periovulatory and midluteal phase	–	Direction and frequency of endometrial waves	Patient vs. control: periovulatory phase: CF 26.7% vs. 88%, FC 24% vs. 0%, opposing 22.7% vs. 12%, not propagated 13.3% vs. 0%, absent 13.3% vs. 0%. Frequency of

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Table 1 (continued)

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
				diagnosis of chronic endometritis Controls: no evidence of chronic endometritis								UP higher in control group
Qu et al. (2019)	Controlled prospective study	Leiomyomas	30 patients	> 18 years, premenopausal, planning to undergo USgHIFU treatment, diagnosed with non-malignant symptomatic leiomyomas, agreed to MRI, safe execution of MRI possible, myoma clearly visible with TVUS, no prior treatment of leiomyomas, no other pelvic/systemic diseases and no scarring, no hormone therapy or IUD	Age 24–47 years (mean 37)	–	Cine MRI, 2 min.	Presence, direction, frequency, uterine volume, index leiomyoma volume and location, number of leiomyomas	Perioovulatory phase	USgHIFU	Uterine peristalsis	After USgHIFU: frequency: increased Direction: remained CF Presence: in 22–23 compared to 10–11 before intervention. Leiomyomas smaller and mainly intramural or submucosal and/or larger reduction rate of index leiomyoma when UP arose No differences in uterine volume and reduction rate, location of largest fibroid, number of fibroids Submucosal fibroids showed no UP
Szamatowicz et al. (2007)	Controlled prospective study	Leiomyomas	12 patients	Regularly menstruating women undergoing myomectomy	Age 29–43 years Indication for myomectomy: 7 infertility, 5 dysmenorrhea/menorrhagia	–	Intrauterine pressure measurement with one catheter in the tip of the fundus, 2–4 hours	Presence, amplitude, deformation index	Perioovulatory phase (day 10–15)	Myomectomy, oxytocin and vasopressin	Spontaneous uterine contractions	After myomectomy: presence: increased Amplitude: increased Deformation index: increased
Yoshino et al. (2010)	Controlled prospective study	Leiomyomas (partially endometriosis)	51 patients	Solely intramural leiomyomas, no other infertility factors (except endometriosis), MRI during implantation window	Age 29–41 years, normal menstrual cycles with normal hormones (FSH, LH, prolactin, oestradiol and progesterone), tubal patency, normal BBT cycle	–	Cine MRI, 3 min.	Presence, frequency, presence of endometriosis, location and number of leiomyomas	Implantation/luteal phase (day 5–9)	Infertility treatment	Junctional zone movement	57% low frequency (0–1×/3 min.) and 43% high frequency (3–6×/3 min.) UP Endometriosis morbidity same in both groups
Yoshino et al. (2012)	Controlled prospective study	Leiomyomas	15 patients	Infertility ≥ 24 months with intramural	Age 29–41 years, normal menstrual	–	Cine MRI, 3 min.	Presence, frequency	Luteal phase day 5–9	Myomectomy	Junctional zone movement	Frequency normalized in 14/15 patients from

Table 1 (continued)

Author (year)	Study design	Topic	Sample size	Inclusion/exclusion criteria	Relevant patient demographics	Relevant control demographics	Method of measuring peristalsis	Assessed parameters	Moment of measurement	Intervention	Outcome measure	Results
				leiomyoma, ≥ 12 months when severe symptoms present, no other infertility factors, MRI before and after myomectomy at luteal day 5–9, high frequency ($\geq 2 \times / 3$ min.) UP before surgery	cycles with normal hormones (FSH, LH, prolactin, oestradiol and progesterone), tubal patency, normal BBT cycle							$\geq 2 \times / 3$ min. to $0-1 \times / 3$ min. 1 patient from $5 \times / 3$ min. to $3 \times / 3$ min.

UFE: uterine fibroid embolisation; UAE: uterine artery embolisation; CF: direction of uterine contractions cervix-to-fundus; UP: uterine peristalsis; rAFS-stage: revised American Fertility Society-stage; HSSG: hysterosalpingoscintigraphy; TVUS: transvaginal ultrasound; VSUP: video sonography of uterine peristalsis; FC: direction of uterine contractions fundus-to-cervix; USgHIFU: ultrasound-guided high-intensity focused ultrasound; IUD: intra-uterine device; BBT: basal body temperature.

In a healthy uterus, rhythmic contractions change in intensity as well as direction during the menstrual cycle to support sperm propagation and embryo implantation in response to hormonal variations [5]. Other characteristics of uterine contractions – frequency and amplitude – are altered throughout the menstrual cycle as well [6]. During menstruation for instance, uterine contractions are directed with high amplitude and low frequency from the uterine fundus to the cervix, whereas the periovulatory phase is characterised by contractions directed towards the fundus at a high frequency. Uterine peristalsis is relatively quiescent during the luteal and early-to-mid follicular phases [7]. If uterine contractile patterns differ significantly from the norm, dysperistalsis occurs, leading to uncoordinated and ineffective uterine contractions.

Relative consensus exists as to how uterine behaviour changes throughout the menstrual cycle; however, little is known about uterine activity in abnormal uteri, and if altered contractions are the intermediate for lower fertility outcomes and/or other symptomatology. It is well known that uterine abnormalities are associated with subfertility [8–11]. We hypothesise that these uterine abnormalities such as uterine fibroids, adenomyosis and congenital uterine anomalies may disrupt uterine peristalsis thereby contributing to the associated symptoms of these disorders. In this systematic review, we investigated the available literature to assess if uterine peristalsis is adversely affected in women with such uterine abnormalities. The primary objective of this review is to assess the influence of uterine abnormalities on uterine peristalsis, including leiomyomas, adenomyosis and congenital uterine anomalies.

2. Materials and methods

2.1. Review protocol

The review protocol is available on PROSPERO under the ID CRD42021244280.

2.2. Study eligibility criteria

The researched population in this review were women with uterine abnormalities such as leiomyomas, adenomyosis, endometriosis and congenital uterine anomalies. Studies were only included if in vivo uteri were studied. Studies were included if uterine peristalsis was investigated in premenopausal women aged over 18 with regular menstrual cycles without hormonal therapy. The patients should not have received any surgical uterine treatment at baseline. Intervention studies, studying the effect of treatment of uterine abnormalities on uterine peristalsis were included if measurement of uterine peristalsis was also done prior to treatment. Cohort studies and case-control studies were deemed eligible for inclusion. Data reported in secondary analysis (reviews), case reports, letters to editors, conference abstracts, and protocols for ongoing studies were excluded. Due to the expected scarcity of relevant studies, studies were not excluded based on the method employed for the uterine contraction measurement. Articles were only included if published in English.

2.3. Data sources

Multiple databases were accessed on April 28th, 2022, in the search for relevant literature, namely: PubMed, the Cochrane Library and Embase. The search was repeated on June 17th, 2023, with no new relevant studies found.

Table 2
Definitions of the overall risk of bias quality scores.

Percentage (%)	Overall quality score	Colour code
> 90	Excellent	□
66.7–90	Good	●
50–66.7	Fair	●
< 50	Poor	●

2.4. Search strategy

Several keywords were selected and included the terms “Uterine Contraction”, “Peristalsis”, “Uterus”, “Uterus/abnormalities”, “Leiomyoma”, and “Adenomyosis”. Not only MeSH terms, but also free text terms [tiab] were used including “junctional zone contraction”, “endometrial wave”, “subendometrial contraction” and “congenital uterine anomaly”. Snowballing was also used to find further relevant articles. The full literature search including all used keywords can be found in Appendix A.

2.5. Study screening and selection

The articles found during the initial literature search were assessed for relevance by one researcher (AB). The articles were first screened based on titles and abstracts, whereafter the remaining studies were evaluated based on the full text to assess final eligibility. The application Rayyan QCRI [12] was used to remove duplicates and support during study screening and selection. If more than one paper used same data, the publication with the largest included numbers was selected. Experts in the field (CR, BS) supported the study screening and selection process to confirm the literature search was sufficient to identify key publications on this topic, and to make sure that all relevant articles were included.

2.6. Data collection

Data was extracted by one researcher (AB) from the included articles using a pre-defined data-extraction table, Table 1.

2.7. Data items

Outcomes of interest included the contraction presence, frequency, amplitude and direction. Secondary outcomes of interest were the

influence of treatment of uterine abnormalities on uterine peristalsis. Other variables collected were relevant demographic patient characteristics (e.g., age, menstrual phases) and the specific method employed for measuring uterine peristalsis.

2.8. Risk of bias assessment

Due to anticipated heterogeneity of the studies, no one dedicated methodological quality assessment tool is available. For this reason, the Downs and Black checklist for measuring study quality was adjusted to suit the design of each included article [13]. Question 27 of the original Downs and Black checklist was adjusted for all studies. A study was awarded a maximum of one point when a power calculation was done. If a question was not applicable to a study, it did not contribute to the final risk of bias evaluation. If due to missing information in a synthesis resulting from reporting bias a question from the Downs and Black checklist could not be answered, a question was awarded with zero points and put as unable to determine (UTD). Based on the risk of bias assessment, an overall quality score was awarded to the studies based on the percentage of points achieved, Table 2.

2.9. Synthesis methods

A narrative approach was used to discuss the data extracted from the included studies. A meta-analysis was not carried out due to the expected heterogeneity of included studies.

3. Results

3.1. Study selection

The literature search provides us with 445 unique records. Four hundred and nineteen studies were excluded based on title and abstract.

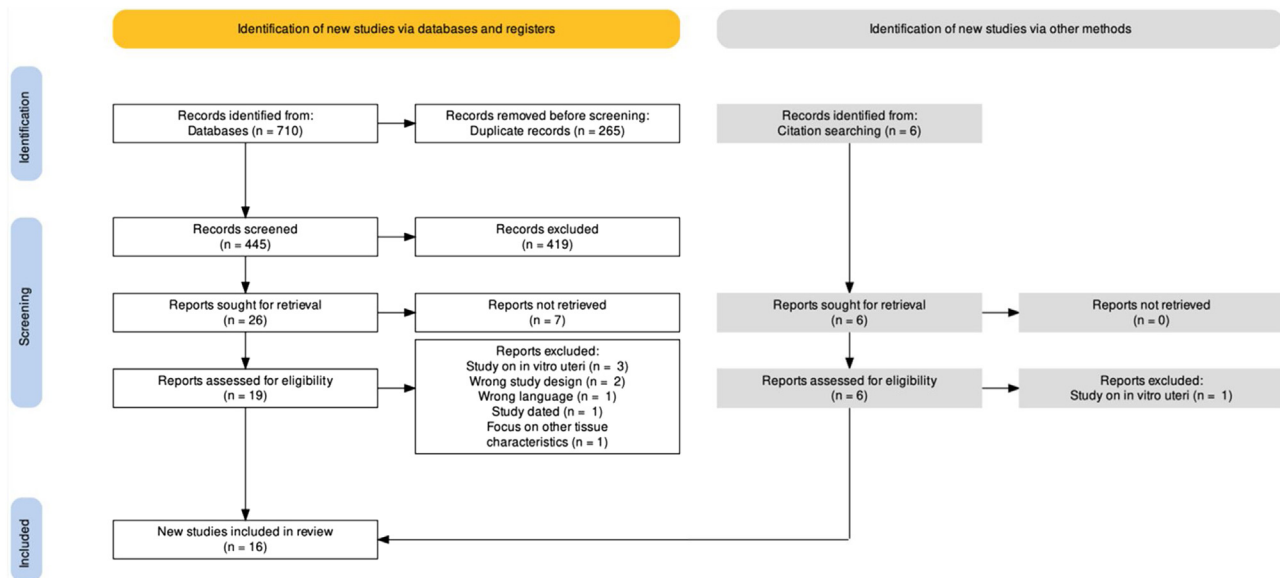


Fig. 1. PRISMA flowchart for the selection of papers included in this systematic review.

Table 3 Summary of uterine contractility measurement tools used in included studies.

	Measurement method	Contraction features assessed	Studies used
Cine MRI	Subjective visualisation of contractions in the junctional zone of the uterus on 2D MRI	Frequency, direction	[14–21]
IUP catheter	Intra-uterine catheter with sensors at different points	Frequency, amplitude, direction	[22–25]
HSSG	Visualisation of displacement of vaginally administered radio-isotope over time using scintigraphy imaging	Direction	[26]
TVUS	Subjective visualisation of contractions in the junctional zone of the uterus on 2D ultrasound	Frequency, direction	[26–28]

Reasons for exclusion include, but are not limited to inappropriate study design, animal-based studies or publication in a language other than English. A total of sixteen studies were eventually included in this systematic review. A schematic overview of the study screening and selection process can be seen in Fig. 1.

3.2. Study characteristics

Full details of the characteristics of the included studies are shown in Table 1. Of the sixteen included studies, nine studies assessed uterine peristalsis using cine MRI, two using TVUS, one using HSSG and four using intrauterine pressure measurement. Table 3 shows an overview and definition of the measurement tools employed in the included studies. Eight studies assessed uterine peristalsis in patients with leiomyomas (women), five studies assessed uterine peristalsis in patients with endometriosis and/or adenomyosis and one study assessed uterine peristalsis in patients with congenital uterine anomalies, namely patients with a bicornuate uterus. One included study assessed uterine peristalsis in patients with leiomyomas and endometriosis. An additional paper on the influence of chronic endometritis on uterine peristalsis was identified and included, as chronic endometritis is classified as a uterine abnormality. No studies were identified that focused solely on the influence of adenomyosis on uterine peristalsis. As described above, adenomyosis and endometriosis are associated and usually occur simultaneously to varying degrees however. Therefore, studies focusing on the influence of endometriosis on uterine peristalsis are included as well.

3.3. Risk of bias in studies

Table 4 shows the risk of bias per included study. Five studies were of good quality, seven studies of fair quality and four of the included studies of poor quality. No studies were of excellent quality. The extensive, non-simplified, quality assessment is included in Appendix B. The completed Downs and Black checklists for all studies with justification for the awarded points are included in Appendix C.

3.4. Results of individual studies

An overview of the study characteristics and a summary of the extracted data are included in Table 1.

A summary of study findings per uterine contraction feature and uterine abnormality is shown in Table 3. Table 5 shows a summary of contraction feature differences versus controls per uterine abnormality and menstrual cycle phase.

3.4.1. Leiomyomas and uterine peristalsis

Five out of six included studies investigating uterine contractility in leiomyoma patients used cine MRI, with one study investigating uterine contractility using an IUP catheter.

3.4.1.1. Presence of uterine contractions. In a case-control study by Orisaka et al. (2007), in all patients with leiomyomas ($n = 19$) and healthy controls ($n = 3$) uterine contractions were observed [14]. Their conclusion that leiomyomas have no influence on the presence of uterine contractions was not confirmed by studies by Yoshino and Kido [15,16]. Yoshino observed in a prospective study an increased presence of uterine contractions in patients with leiomyomas ($n = 15$) during the midluteal phase [15]. In the study by Kido et al., fewer patients with leiomyomas ($n = 20$) showed uterine contractions compared to healthy controls ($n = 20$) during the periovulatory phase [16]. Nishino et al. (2005) reported that presence of uterine contractions may be correlated to the subtype of leiomyomas: patients with intramural leiomyomas ($n = 26$) universally presented uterine peristalsis, whereas this was not seen in patients with submucosal leiomyomas [17]. Four controlled-prospective studies observed an increase in presence of uterine contractions during the periovulatory phase after the treatment of leiomyomas by uterine

Table 4 Simplified risk of bias assessment of the included studies.

	Bulletti et al. (1997)	Bulletti et al. (2002)	Fornazari et al. (2019)	Kido et al. (2007)	Kido et al. (2011)	Kido et al. (2014)	Kissler et al. (2007)	Leyendecker et al. (1996)	Nishino et al. (2005)	Oliva et al. (1992)	Orisaka et al. (2007)	Pinto et al. (2015)	Qu et al. (2019)	Szamatowicz et al. (1997)	Yoshino et al. (2010)	Yoshino et al. (2012)
Reporting	5/8	6/11	9/11	7/8	7/11	5/8	2/9	6/8	5/7	2/10	5/7	4/8	9/11	7/11	7/9	10/11
External validity	0/2	2/3	1/3	0/2	1/3	0/2	0/2	0/2	2/2	0/2	0/2	0/2	0/3	1/3	2/3	1/3
Internal validity – bias	3/3	4/4	5/5	3/3	4/5	3/3	2/3	3/3	2/2	4/4	2/2	3/3	4/5	4/5	4/5	3/5
Internal validity – confounding (selection bias)	1/3	1/4	2/2	0/3	1/2	0/3	0/4	0/3	2/3	0/4	0/3	2/3	2/2	0/2	2/4	1/2
Power	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
Score	9/17	13/23	17/22	10/17	13/22	8/17	4/19	9/17	11/15	6/21	7/15	9/17	15/22	12/22	15/22	15/22
Overall quality assessment	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Table 5 Summary of study findings per contraction feature and type of uterine abnormality versus healthy controls.

Cycle phase ^a	Leiomyomas (n = 7 studies)			Adenomyosis/endometriosis (n = 6 studies)			Congenital uterine anomalies (n = 1 study)			Endometriosis (n = 1 study)		
	Menstrual	Perioviatory	Luteal	Menstrual	Perioviatory	Luteal	In symmetric uteri: no difference seen [25]	Menstrual	Perioviatory	Luteal		
Contraction frequency	No data	Decreased frequency ^b [16]	Increased frequency [15]	Increased frequency [21,23,24,27]	Increased frequency [27]	Increased frequency [21,23,24,27]	No data	No data	Decreased frequency [28]	No difference		
Contraction amplitude	No data	No data	No data	Increased amplitude [23,24]	No data	No data	No data	No data	No data	No data		
Contraction direction	F2C [16]	C2F [15,16]	No data	No data	Fewer C2F contractions [21,27]	No data	No data	No data	Fewer C2F contractions [28]	No data		
Effect of treatment	No data	Increased frequency [20]	Decreased frequency [16,20,29]	No data	Dysperistalsis seen across all phases [26]	No data	No data	No data	No data	No data		
Other findings	Fewer contractions with submucosal vs. intramural leiomyomas [17]	No influence of myoma localization	Increased frequency of contractions in immediate vicinity of myoma [17]				Dysperistalsis in uteri with asymmetric horns [25]			Dysperistalsis [28]		

F2C: fundus-to-cervix; C2F: cervix-to-fundus.

^a If reported.

^b Reported findings are the conclusion of relevant studies in comparison to healthy controls.

artery embolisation (UAE), ultrasound-guided high-intensity focused ultrasound treatment (USgHIFU), uterine fibroid embolisation (UFE) and myomectomy compared to before treatment [18,19,22,29].

3.4.1.2. Contraction frequency. The case-control study by Orisaka et al. observed almost identical peristaltic patterns regarding contraction frequency in patients with leiomyomas (n = 19) versus healthy controls (n = 3) during all phases of the menstrual cycle [14]. Two studies, on the other hand, observed altered peristaltic patterns in patients with leiomyomas and suggested the influence of leiomyomas on contraction frequency seemed menstrual-phase dependent [15,16]. A decreased contraction frequency in patients with leiomyomas (n = 20) was reported during the perioviatory phase [16], whereas an increased frequency was noticed in some patients with leiomyomas (n = 20) during the mid-luteal phase compared to controls (n = 20) [15]. Leiomyoma localization seemed to have no effect on the contraction frequency [17]. In three controlled prospective studies, initially altered uterine peristalsis normalised after treatment of uterine leiomyomas, including myomectomy, UAE and USgHIFU [18,20,29]. After treatment, a relatively decreased contraction frequency was noted during the mid-luteal phase [20], whereas an increase in frequency was observed during the perioviatory phase [18,29].

3.4.1.3. Contraction amplitude. The contraction amplitude in patients with leiomyomas has not been compared yet with the contraction amplitude in healthy controls. A study by Szamatowicz et al. reported a higher contraction amplitude after myomectomy however [22].

3.4.1.4. Contraction direction. In five studies, the contraction direction during the perioviatory phase was observed form cervix-to-fundus in both patients with leiomyomas and healthy controls [14,16–18,29]. One of these case-control studies also concluded that contraction direction in the follicular and late luteal phase was almost identical in patients (n = 20) and healthy women (n = 20) [16]. Differences in contraction direction between patients with leiomyomas (n = 19) and healthy women (n = 3) were noted during menstruation and the mid-luteal phase [14]. Nishino et al. (2005) showed a fundocervical contraction direction during menses in all patients with leiomyomas (n = 26). The location of the leiomyomas seemed to be of no statistically significant influence [17]. After treatment of uterine leiomyomas by either UAE or USgHIFU, the cervicofundal movement during the perioviatory phase remained unchanged [18,29].

3.4.1.5. Additional peristaltic observations. A case-control study reported that 33% of the patients (n = 9/16) with submucosal leiomyomas had disturbed uterine peristalsis. Specifically, higher frequency focal myometrial movements in the immediate vicinity of the leiomyoma were observed [17]. After treatment of uterine leiomyomas with UFE, uterine contractions were noted to become more coordinated [19].

3.4.2. Adenomyosis/endometriosis and uterine peristalsis

Five studies investigated uterine peristalsis in adenomyosis/endometriosis patients, with two studies using IUP catheter measurement, one TVUS and HSSG, one only HSSG, and one cine MRI.

3.4.2.1. Presence of uterine contractions. Uterine peristalsis was noted in both patients with endometriosis and healthy controls [23]. Bulletti et al. (2002) confirmed the presence of uterine contractions during the menstrual phase in both patients with endometriosis (n = 22) and controls (n = 20) [24]. In a case-control study by Kido et al. (2007), by contrast, a difference was found in the presence of uterine contractions throughout the entire menstruation cycle. During the perioviatory phase, statistically significantly fewer patients with endometriosis (n = 26) had uterine contractions compared to controls (n = 12). A trend towards a lower presence during the luteal phase and higher during the menstrual phase compared to controls was suggested but did not prove to be significant [21].

3.4.2.2. Contraction frequency. In three studies, the increase in frequency from early to late follicular phase in healthy controls was also observed amongst women with endometriosis [21,23,24,27]. As reported in several studies, the contraction frequency overall is different in the presence of endometriosis [21,23,24,27]. When the menstrual phases are disregarded, a higher contraction frequency was observed in patients with endometriosis than in controls [23]. Leyendecker et al. (1996) specifically investigated the contraction features through the menstrual cycle phases and found a higher contraction frequency in patients with endometriosis ($n = 111$) than in controls ($n = 94$) across phases. Contraction frequency was especially increased in the follicular and mid-luteal phase [27]. Contradictorily, Kido et al. (2007) found a decreased contraction frequency during the periovulatory phase in patients with endometrial cysts ($n = 26$ vs. $n = 12$) [21]. A controlled prospective study contradicted these outcomes, showing that endometriosis had almost no influence on uterine contractions during the periovulatory phase. Endometriosis severity did not seem to affect contraction frequency [15].

3.4.2.3. Contraction amplitude. Bulletti et al. (1997) described a (non-significant) increased uterine amplitude in patients with endometriosis ($n = 16$) compared to healthy women ($n = 12$) [23]. Further research confirmed statistically significantly increased contraction amplitude in endometriosis patients ($n = 22$ vs. $n = 22$) across menstrual cycle phases [24].

3.4.2.4. Contraction direction. Contraction direction in patients with endometriosis was only examined by two studies. One case-control study stated that patients with endometriosis ($n = 111$) as well as healthy women ($n = 94$) progressing through the menstrual cycle show a similar decrease in cervix-to-fundus directed contractions [27]. A further case-control study focusing on the influence of endometriosis presenting as endometrioma's did report a difference versus healthy women, with statistically significantly fewer uterine contractions from cervix-to-fundus in endometriosis patients during the periovulatory phase [21].

3.4.2.5. Additional peristaltic observations. During the follicular phase, patients with endometriosis ($n = 111$) demonstrated more of these dysperistaltic contractions compared to controls ($n = 94$) [27]. In patients with endometriosis and additional adenomyosis ($n = 24/80$), hyperperistalsis is seen in patients with an focal adenomyosis ($n = 14/80$) whereas dysperistalsis was seen in patients with diffuse adenomyosis ($n = 11/80$) [26].

3.4.3. Congenital uterine anomalies and uterine peristalsis

3.4.3.1. Contraction frequency. One small study investigated women with a bicornuate uterus ($n = 12$) using an IUP catheter, these patients showed a similar contraction frequency when compared to what the literature reveals as normal in controls [25]. In case of dissimilarity of the two parts of the uterus, differences in frequency, characterised by a disorganised pattern of contractions, were noticed in the smaller uterine horn especially in the late-luteal phase.

3.4.4. Chronic endometritis and uterine peristalsis

3.4.4.1. Contraction frequency. A case-control study using TVUS noticed a decreased contraction frequency in patients with chronic endometritis ($n = 45$) compared to healthy controls ($n = 45$), particularly during the periovulatory phase. No further differences were found [28].

3.4.4.2. Contraction direction. Pinto et al. (2015) reported a statistically significant influence by the presence of chronic endometritis on the contraction direction during the periovulatory and midluteal phase. During the periovulatory phase, patients with chronic endometritis presented less cervix-to-fundus contractions compared to healthy controls. During the midluteal phase, patients showed general dysperistalsis [28].

4. Discussion

In summary, the available literature suggests that uterine abnormalities may indeed influence uterine peristalsis even though measurement methods differed across studies. Findings of included studies report that presence of leiomyomas generally lead to a decreased presence of uterine contractions in various menstrual phases, whereas endometriosis/adenomyosis lead to an increased frequency across menstrual phases. No changes in the presence of uterine contractions were noted in patients with a bicornuate uterus or chronic endometritis. Studies were contradictory on the influence of uterine abnormalities on contraction direction. Only patients with chronic endometritis exhibited clearly altered contraction direction was described. The influence of uterine abnormalities on contraction amplitude has not yet been studied extensively. Endometriosis, however, seems produce an increase in contraction amplitude. Dysperistalsis was noted in patients with leiomyomas, endometriosis, adenomyosis and an asymmetric bicornuate uterus. Another observation in patients with leiomyomas was that the treatment of leiomyomas re-established normal uterine contractions, which could confirm the effect of leiomyomas on uterine peristalsis.

Previously published systematic reviews have mainly focused on the influence of uterine contractions on fertility. Kuijsters et al. (2017) briefly described the influence of uterine abnormalities on peristalsis. The results of this systematic review support their reported influence of uterine abnormalities on uterine contraction features [1]. It was postulated that abnormal uterine contractions in patients with uterine abnormalities could be the cause of infertility [1], a hypothesis supported by Hunt et al. (2020). Effects of endometriosis, adenomyosis and leiomyomas on uterine peristalsis were also described by Hunt et al. (2020), with similar conclusions to this review. A clear influence of endometriosis on contraction direction was reported; however, this could not be confirmed in our review [30].

Even though more attention is being given to uterine peristalsis recently, few systematic reviews have been conducted on this subject. This review gives a clear summary of the published studies on the influence of uterine abnormalities on uterine peristalsis up to now. To give an overview of all gathered knowledge, it was chosen to include studies regardless of the method used to assess uterine peristalsis. This, however, does make the results of the various studies difficult to compare. As seen in Tables 1 and 3, four techniques of visualising uterine peristalsis have been used, each with its own limitations. Few can assess all potential parameters and results are often based on subjective assessment of obtained images. To ensure comparability amongst studies, it would be better to eradicate this subjectivity by automating the analysis, as proposed by Sammal et al. (2019) [31,32].

Studies were also difficult to compare due to heterogeneity in study designs, populations and intervention. The moment of measurement in the menstrual cycle seemed to be of major influence on the observed contraction features, however not all studies reported this [23]. Additionally, the sample size of most of the included studies was small. In three studies, participants were divided over the menstrual phases and uterine contractions were only assessed in that particular phase [14,17,21]. As the result of this, only a few participants were assessed per menstrual phase. One might argue whether this is enough to draw conclusions. Furthermore, some included studies are relatively dated. This results from a lack of recent literature on the influence of uterine abnormalities, specifically congenital uterine anomalies, on uterine peristalsis. Besides, reported differences in uterine contractions in endometriosis patients might be influenced by an unreported presence of adenomyosis. Since the sonographic diagnosis of adenomyosis can be difficult, an undiagnosed presence in this endometriosis group could have biased the outcome. Additionally, an article on the influence of endometriosis, presented as endometrial cysts, was included. It could be questioned if this has a comparable effect on uterine peristalsis as in (deep) endometriosis or adenomyosis.

Finally, the included studies use different definitions of uterine peristalsis. Non-propagating contractions were included in the definition

of uterine peristalsis in some, and defined as dysperistalsis, but excluded or unmentioned in other studies. This calls for a standard definition for uterine peristalsis and its various features.

5. Conclusions

Despite the heterogeneity of the included studies, it can be concluded that uterine abnormalities influence uterine peristalsis, often leading to a, menstrual phase-dependent, altered frequency and decreased presence of uterine contractions. The presence of abnormal uterine peristalsis could indicate the presence of underlying uterine pathology. This knowledge could potentially aid in a better diagnosis of uterine abnormalities. More research is needed into objective measurement tools of uterine peristalsis, and into both treatment and clinical implications of abnormal uterine peristalsis in these patients.

Funding statement

No funding.

Disclosure of interest

The authors declare that they have no competing interest.

Author contributions

A.B., C.R., B.S. and J. H. were involved in conceptualisation of this research. A.B. was responsible for data collection. A.B. and C.R. were involved in manuscript writing – original draft preparation and M.M., H. V., J.F and B.S. were involved in manuscript writing – review and editing.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jeud.2023.100038>.

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