REVIEW

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Lower pregnancy rate in women with high uterine peristalsis before embryo transfer: a systematic review and meta-analysis



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Abstract

Background Uterine contractions, also known as peristalsis, have been shown to affect fertility. However, despite previous studies, most clinicians have not paid sufficient attention to uterine peristalsis. Recent studies have recognised its importance and evaluated contractility parameters prior to embryo transfer.

Method A systematic literature search was conducted in Medline, Embase and Cochrane CENTRAL up to January 2024. Inclusion criteria were studies involving patients undergoing in vitro fertilization (IVF) or other infertility treatments in which uterine contractility was assessed. Studies were excluded if they included therapeutic interventions that affected contractility, or if they focused on uterine pathologies such as adenomyosis or fibroids. The meta-analysis included trials with IVF treatments that compared clinical pregnancy rates in women with high versus low frequent uterine contractions.

Results A total of 2587 women (17 studies) were included in the systematic review, of whom 1134 (43.1%) (5 studies) underwent embryo transfer and were eligible for meta-analysis. The review found that elevated contractility on the day of embryo transfer is associated with a negative impact on pregnancy rates. The meta-analysis showed that women with two or more uterine contractions at the time of the embryo transfer had a significantly lower clinical pregnancy rate than with women with two or fewer contractions (OR 0.52, 95% Cl: 0.38- 0.69). There was moderate heterogeneity between studies ($l^2 = 55$, p < 0.01).

Conclusions The lower clinical pregnancy rate in women with high uterine contractility, highlights the role of uterine peristalsis around the time of embryo implantation. However, due to the limited and heterogeneous data available, the influence of uterine peristalsis on reproductive outcomes such as live birth rates remains unclear.

Keywords Uterine peristalsis, Uterine contractility, Implantation rate, Pregnancy rate, Embryo transfer

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Introduction

Infertility is a significant problem affecting 17% of couples of reproductive age [1]. Half of those experiencing subfertility eventually seek assisted reproductive treatments. However, despite recent advances, the success rate of these treatments is still limited.

One of the key phases in reproduction is the implantation phase, which is characterised by a complex interaction between the embryo and the receptive endometrium. Histological and immunological factors are of fundamental importance in facilitating the acceptance



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and hence successful implantation of the embryo. Although all of these factors are highly relevant, another factor also appears to be relevant but has been less intensively studied and is less well known: uterine peristalsis (UP) [2, 3]. Uterine peristals was first described in 1973 [4] and is defined as myometrial uterine contractions (UC) of variable frequency, amplitude and direction that appear to have an effect on implantation [5–9].

Animal studies have shown that UCs play a role in the correct positioning of the embryo in the uterine cavity [10]. Indirect evidence in humans suggests that UCs help to create the right conditions for embryo implantation [11-13]. This hypothesis is supported by the observation that uterine contractility typically decreases during the luteal phase of the menstrual cycle [8, 11, 12].

Recent studies have shown an association between excessive uterine activity and a reduced likelihood of clinical pregnancy and implantation. Treatments to reduce uterine contractions, such as oxytocin antagonists, have been proposed and tested. However, the results of the trials have been controversial [13]. Therefore, more knowledge and a better understanding of the physiology of UP is needed to better understand its impact on fertility and to apply UC reducing treatments only to those who might benefit most.

UP is primarily assessed using transvaginal ultrasound, a non-invasive method that visualizes the frequency, direction, and amplitude of myometrial contractions. In clinical practice, both 2D and 3D ultrasound are currently used to quantify these contractions, typically measuring their frequency per minute at different stages of the menstrual cycle and during assisted reproduction treatments. Previously, transabdominal ultrasound was more common. More advanced techniques, such as electrohysterography, which measures myometrial electrical activity, and magnetic resonance imaging, have also been explored, though their use is limited by cost and availability [14–16]. Evaluating UP is crucial in in vitro fertilization (IVF), as excessive uterine activity at the time of embryo transfer has been linked to lower implantation rates [17]. However, standardizing measurement methods remains a challenge, and their integration into clinical decision-making requires further validation.

We therefore conducted a review to analyze the characteristics of UP and its impact on fertility treatments, especially before embryo transfer, and performed a metaanalysis of the study results.

Materials and methods

Registration of protocols

The study protocol was registered under the Prospective International Registry of Systematic Reviews, PROSPERO (registry number CRD42024514500). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used [18].

Search strategy

A systematic literature search was conducted using the Medline, Embase, and Cochrane CENTRAL databases in January 2024. An initial MEDLINE search strategy was developed by a medical information specialist and tested with a list of basic references. After refinement and querying, complex search strategies were established for each information source based on database-specific controlled vocabulary (thesaurus terms/subject headings) and text words. Synonyms, acronyms and similar terms were included in the text word search. The search was limited to publications from 1946 to the present. The search terms included "uterine contractions", "uterine peristalsis", "junctional contractions", "in vitro fertilization", "embryo transfer", and "embryo implantation". We incorporated respective thesaurus terms and used synonyms, acronyms, and similar terms for all concepts in the text word search.Animal-only studies were excluded from the MEDLINE and Embase searches using a double negative search strategy based on Ovid "humans only" filters. The detailed final search strategies are presented as a supplementary file (S1). In addition to searching the electronic databases, reference lists and bibliographies of relevant publications were checked for relevant studies. All identified citations were imported into Covidence and duplicates were removed automatically.

Inclusion and exclusion criteria

Investigators AV and VT independently assessed studies for inclusion using the Covidence software (www.covid ence.org). Eligibility was based on original papers revealing information about the frequency of uterine contractility per minute performed by transvaginal ultrasound (2D or 3D) and the reproductive outcome to establish the relationship between frequency and embryo implantation. Only clinical studies that used ultrasound to measure uterine contractility were included. We excluded studies involving therapeutic interventions affecting contractility (such as various pharmacological treatments like progesterone, prostaglandins, anticholinergic agents, beta-adrenergic receptor antagonists, oxytocin receptor antagonists, prostaglandin synthetase inhibitors, nitric oxide donors and others), uterine pathologies like adenomyosis or myomas, as well as those studies with an inadequate design or based on animals.

Data extraction

Two investigators (AV and VT), independently summarized and reviewed the extracted data in detail. The primary variables of interest included the characteristics of the study populations such as the patients' age, cause and duration of infertility/sterility, the sort of treatment cycle used, parameters related to uterine contractility like the method of measurement, endometrial thickness, and frequency of contractions per minute, as well as reproductive outcomes, primarily the clinical pregnancy rate. Discrepancies were discussed and resolved by consensus.

Quality assessment

The Newcastle-Ottawa scale (NOS) was utilized to evaluate the quality of the individual studies [19]. Three parameters were considered for individual study scoring: subject selection (0-4 stars), comparability (0-2)stars), and study outcome (0-3 stars). The scoring was composed as follows: Good quality (=3 or 4 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain), fair quality (=2 stars in the selection domain) AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain), and poor quality (=0 or 1 star in the selection domain OR 0 stars in the comparability domain OR 0 or 1 stars in the outcome/ exposure domain).All included studies were reviewed by AV and VT to independently assess risk of bias. Disagreements were resolved by consensus.

Data synthesis

The primary outcome of our systematic review was the association between the frequency of contractility and pregnancy rate. For dichotomous data, we used the numbers of pregnancy in the group of high (i.e. > 2) vs. low (i.e. ≤ 2) uterine contractions per minute of each study to calculate Mantel-Haenszel odds ratios (ORs) using a fixed and random-effects model. For the pooled ORs, statistical analyses were performed with the "metafor" function of the R software (R Core Team, Vienna, Austria, 2013). Heterogeneity was examined using Cohen's Q statistic and the I2 statistic. In the presence of high heterogeneity, random-effects models were used. Furthermore, a prediction interval was calculated as an indicator of the anticipated uncertainty in the summary effect.

Results

Results of the systematic review

After screening the abstracts and the full text of the study topic, 103 studies remained. However, we excluded 86 of these studies as they did not fit our predetermined inclusion criteria. Therefore, we included 17 articles in the systematic review (Fig. 1).

Study characteristics

The characteristics of the study populations are summarized in Table 1. Fifteen studies were prospective and two retrospective. The population was women with infertility without uterine pathology.

The patients included in the 17 studies were mainly European (ten studies) and 7 studies evaluated Asian population. In total, 2587 women were included in the review, of whom 1134 (43.83%) (5 studies) were eligible for meta-analysis. The sample sizes of the studies varied considerably, ranging from six to 635 patients.

Six good-quality studies were identified [9, 14, 26, 28, 29, 31]. The methodological quality of the majority of these studies was rated as either poor (n=4) or fair (n=7), primarily due to the absence of a comparison group (Table 2).

Results of individual studies

The timing of contractility measurement varies across studies: Three studies evaluated UP on the trigger day [8, 12, 21], four assessed it on the day of oocyte retrieval [6, 8, 26, 33], 12 studies investigated UP just before embryo transfer in the cleavage stage [6, 9, 12, 20, 23, 25, 28, 29, 31, 32, 34] and two on day 5 [14, 25]. Another key issue is interpreting contractility in different IVF cycles, both fresh and frozen. This interpretation must be differentiated and evaluated in order to draw conclusions about uterine contractility. The duration of ultrasound-recorded uterine contractility in the majority of studies ranged from 3 to 5 min and was analysed based on contractions per minute.

Contraction frequency

A balance of increased uterine frequency (not exceeding 2 uterine contractions (UC) /min), combined with lower amplitude of uterine activity, may promote successful embryo implantation. This is particularly observed in blastocyst transfer, where a lower frequency of UCs tends to be linked with higher pregnancy rates [6, 14, 28]. Consistent with these findings, studies on the impact of uterine peristalsis in IVF have demonstrated a negative correlation between elevated contraction activity (>3 waves per minute) and clinical pregnancy rates [12, 32].

Contraction amplitude

Vlaisavljevic et al. [25] stated that the contraction amplitude does not contribute to pregnancy outcomes. Blank et al. [14] suggested that a combination of higher frequency (up to 2 UC/min) and lower amplitude of uterine activity could potentially facilitate successful embryo implantation.

Direction of contraction

Fanchin et al. [5] examined the pattern of UC in patients, including the relative prevalence of retrograde, anterograde, antagonistic, and non-propagated UC. They concluded that these patterns did not influence the outcome



Fig. 1 PRISMA flow chart. Flowchart of the bibliography search and selection process

of embryo transfer [7]. Chung et al. [28] similarly found that approximately 40% of contractions, both before and after transfer, were directed as retrograde and anterograde waves, respectively. They also did not find a significant correlation between the wave direction at -5 min and +5 min, with either pregnancy outcome or progesterone level. However, a significant difference was found for live birth rates (LBR) among different wave directions at +60 min after the transfer procedure. The highest rate was among women with no contractions/direction or

those with an indeterminate direction. This suggests that a uterus that is either at rest or has contractions of indeterminate direction may provide a more stable environment for embryo implantation.

Impact of progesterone concentration on contractions

Fanchin et al., [7] described a significant inverse relationship between progesterone plasma levels and the frequency of UCs. As progesterone levels decreased, contraction frequency increased. In line with this in case of

Table 1 Cha	iracteristic	s of include	d studies									
First author, Year of publication	Country	Study design	Population	Age, yrs (mean ±SD)	Cause of sterility	Treatment cycle	CPR	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) (ng/ml) (ng/ml) (Day 5)
Narayan et al., 1994 [20]	Kingdom	prospec- tive	11	Concep- tion group: 34.1 ± 4.23 Non-concep- tion group: 34.2 ± 4.59	Tubal (48.2%) Male factor (11.6%) Unex- plained infertility (25.9%) Endometri- osis (7.1%) PCOS (4.5%) PCOS (4.5%) Premature menopause (2.7%)	INF: COH and FET cycles	30.36%	not reported	COH: 1.59± 1.08 FET: 1.74±0.86 HRIVFET cycles: 1.44±1.29	COH: Retrograde 37.1% Antegrade 35.7% Indetermi- nate 27.2% FET: Antegrade: Antegrade: a3.3% Antegrade: Indetermi- nate: 20.0% Indetermi- nate: 20.0%	not reported	not reported
Ayoubi et al.,2003 [6]	France and Swit- zerland	prospec- tive crossover trial	Q	28–35 (31.8)	Male factor (100%)	Group A: Natural Cycle (without IVF Treatment) Group B: IVF: COH Long protocol	33.33%	not reported	A: 5.3 ± 0.7 B: 0.5 ± 1	reported	not reported	not reported
ljland et al.,1998 [21]	Nether- lands	prospec- tive	19	26–36 (32)	not reported	D	not reported	not reported	not reported	not reported	not reported	not reported

Table 1 (co.	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean±SD)	Cause of sterility	Treatment cycle	CPR.	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (IU/L) Serum LH (IU/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Fanchin et al.,1998 [22]	France	prospec- tive	509	23-38	Tubal (40%) Male factor (45%) Unex- plained infertility (12%) Endome- triosis (3%)	nist Protocol	not reported	≤3 UC/min: 9.8 ± 0.3 9.2 ± 0.3 9.2 ± 0.4 9.4 ± 0.4 > 5 UC/min: 9.9 ± 0.3 9.9 ± 0.3	4 .3 ± 0.1	Retrograde 15% Antegrade 28% Antagonis- tic 11% Non-propa- gated 6%	CP: Serum P (ng/ ml) < 3.0 UC/min group: 0.96 ng/ ml; 3.1-4.0 UC/min group: 0.81 ng/ ml sroup: 0.81 ng/ ml sroup: 0.81 ng/ ml sroup: 0.81 ng/ ml sroup: 0.7 ng/ ml group: 0.7 ng/ ml 3.1-4.0 UC/ min group: 2589 pg/ml 3.1-5.0 UC/ min group: 250 UC/ min group: 250 UC/ min group: 2376 pg/ml	not reported

Table 1 (co	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean±SD)	Cause of sterility	Cycle cycle	СРК	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Ijland et al.,1999 [23]	Nether- lands	prospec- tive	28	25-38 (32)	Tubal (35.7%) Endometri- osis (3.5%) Male factor (13.28%) Unex- plained subfertility (46.4%)	IVF: COH Agonist Long- protocol	39%	13.4±3.9	CF waves: 7.11 ±4 (on hCG -6) 6, 9.4±5.7 on the (day of hCG) 10.1±5.0 (day of ET) FC waves: 8.12±4.5 (on hCG -6) 7.15±5.2 (day of hCG)	Absent FC: P: 35.7% NCP: 14.3% Present FC: P: 3.5% NCP: 25%	not reported	not reported

Table 1 (co	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean±SD)	Cause of sterility	Treatment cycle	CPR	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (IU/L) Serum LH (IU/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Fanchin et al., 2000 [24]	France	prospec- tive	ξ.	23-38	Tubal abnormali- ties (39%) Sperm abnormali- Unex- plained infertility (5%) Endome- triosis (2%)	nist Protocol	Low P group: 27% high P group: 46% CPR: 35%	not reported	Day HCG: 4.6±0.2 Day ET: 4.2±0.2	Day of hCG administra- tion: Retrograde (CF) 62% Antegrade (FC) 27% non-propa- gated, 2% Antegrade (CF) 61% Antegrade (FC) 24% Antegrade (FC) 24% antagonis- tic 14% non-propa- gated 1%	hCG adminis- tration: Serum E2 Low P: 2 150 \pm 124 pg/ ml Serum Proges- terone Low P: 1065 \pm 76 pg/ ml On the day of embryo transfer: Serum E2 Low P: 1189 \pm 86 pg/ ml High P: 1189 \pm 86 pg/ ml High P: 1189 \pm 86 pg/ ml High P: 1189 \pm 86 pg/ ml High P: 128.8 ng/ml (102.9-232.0)	not reported

Table 1 (co	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean±SD)	Cause of sterility	Treatment cycle	CPR	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) Serum P (ng/ml) (ng/ml) (ng/ml)
Vlaisavljevic et al.,2001 [25]	Slovenia	prospec- tive	122	not reported	reported	INTER COH	23.8%	P: 12.2 ± 2.2 NCP: 11.9 ± 2.7	not reported	Day of cycle + 6: antegrade 11.1 retrograde 18.5 both 15.2	CP: Bay of cycle+2 Serum P (imol / L) 115.4±57.6 Serum E2 (mol / L) 1.8±1.4 NCP: Day of cycle+2 Serum P(nmol / L) 102.6±55.1 / L) 2.5±5.5	CP: Day of cycle+6 Serum P (nmol/L) 147.5±45.5 Serum P (nmol/L) 3.1±2.3 Day of cycle+12 Serum P (nmol/L) 131.3±65.4* Serum P (nmol/L) 131.3±65.4* Serum P (nmol/L) 134.1±48.5 Cnmol/L) 3.5±3.8 Day NCP: nmol/L) 3.5±3.8 Day Serum P (nmol/L) 3.5±3.3 Day Serum P (nmol/L) 134.1±48.5 Serum P (nmol/L) 134.1±48.5 Serum P (nmol/L) 3.5±3.8 Day NCP: 134.1±48.5 Serum P (nmol/L) 3.5±3.8 Day NCP: 134.1±48.5 Serum P (nmol/L) 3.5±3.8 Day NCP: 0 of cycle+12 (nmol/L) 3.5±3.8 Day Serum P (nmol/L) 3.5±3.8 Day Serum P (nmol/L) 3.5±3.8 Day NCP: 17.4±33.7 Serum P (nmol/L) 3.5±3.8 Serum P (nmol/L) 3.5 Serum P (nmol/L) 3.5 Serum P (nmol/L) 3.5 Serum P (nmol/L) 3.5 Serum P (nmol/L) 3.5 Serum P (nmol/L) 3.5 Serum P

Table 1 (cor	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean ± SD)	Cause of sterility	Treatment cycle	ъ.	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Vangestel et al.,2005 [26]	Nether- lands	prospec- tive	8	22-41 (33)	Tubal pathology (13.33%) endo- metriosis (2.22%) male factor infertility (58.88%) unex- plained subfertility (25.55%)	IVF: COH	30.23%	not reported	not reported	FC 55.9% FC 55.9%	not reported	not reported
Kim et al., 2013 [27]	Korea	Obser- vational study	243	Conception group (49): 31.43 ±3.06 Non- conception group (192): 32.86 ±3.56	unex- plained infertility (100%)	CC 100 mg, IUI	NP: 79,66% P: 20.33%	not reported	NCP: 3.46 ± 1.89 P: 4.02 ± 1.44	NCP: CF: 75.5% FC: 89.8% P: CF: 24.5% FC: 10.2%	not reported	not reported
Zhu et al.,2014 (Nov 2013) [9]	China	prospec- tive	112	not reported	not reported	IVF: COH	44.9%	not reported	2.24±0.74 waves/min	not reported	not reported	not reported

Table 1 (co	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean ± SD)	Cause of sterility	Treatment cycle	La contra c	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) Serum P (ng/ml) (ng/ml) (ng/ml)
2014 [9]	China	prospec- tive	292	20-35 291±35	reported	IVF: COH long agonist protocol Natural FET HRT FET	53.42%	CP: 11.3 + 2.7 NCP: 11.2 + 3.0	Fresh cycles: 1.80 ± 0.77 Natural FET: 2.05 ± 0.80 HRT FET: 2.15 ± 0.81 2.15 ± 0.81	reported	CP: Serum E2 (pg/ml) 1068.3 + 973.0 Serum P (ng/ ml) 56.3 + 11.5 Fresh cycle Fresh cycle Fresh cycle Artificial FET cycle 53.2 + 13.6 Artificial FET cycle 53.2 + 13.6 Artificial FET cycle 43.6 + 16.4 P (ng/ ml) 52.8 + 15.2 Fresh cycle 59.0 + 7.2 Fresh cycle 59.0 + 7.2 Natural FET Cycle 43.8 + 16.4 Artificial FET Cycle 43.8 + 20.0	not reported

Table 1 (cor	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean ±SD)	Cause of sterility	Treatment cycle	CPR	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (IU/L) Serum LH (IU/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Chung et al., 2017 [28]	China	prospec- tive	586	CP: 346±3.0 NCP: 35.1±3.4	Ovulatory problem (4.6%) Tubal (50.5%) Male factor (28.9%) Endometri- osis (7.1%) Unex- plained (8.8%)	COH: Long protocol vs antagonist protocol	42% 1% (ectopic pregnancy) 32.5% (LBR)	CP: 11 ± 0.2 NCP: 11 ± 0.3	-5 min: 1.8 ± 1.1 + 6 min: 2.0 ± 1.1 + 60 min: 1.8 ± 1.1 1.8 ± 1.1	-5 min Retrograde: 41.3% Antegrade: 43.5% Indetermi- nate: 38.8% NII: 44.4% + 5 min Retrograde: 39.5% NII: 61.5% NII: 61.5% Antegrade: 32.1% NII: 61.5% NII: 60.5% NII: 60.5%NII: 60.5% NII: 60.5% NII: 60.5%NII: 60.5%NII: 60.5% NII: 60.5%NII: 60.5%NII: 60.5% NII: 60.5%NII: 60.5%NI	CP: Serum E2 (pmo/L1) 5928.8 ± 3030.8 Serum Proges- terone (nmo/L) 304.2 ± 140.3 NCP: Serum E2 (pmo/L) (pmo/L) 562.9.1 ± 3720.5 Serum Proges- terone (nmo/L) 261.2 ± 133.5	not reported
Samara et al., 2019 [29]	Israel	retrospec- tive	224	Control: 35.1±3.7 MatrisTM scoring: 35.2±3.7	not reported	FET cycles	44.3% (Con- trol) 42% (MatrisTM scoring) 38.2% (Waves Group)	Control: 9.3 ± 1.8 Waves group: 9.4 ± 2.5 MatrisTM scor- ing: 9.4 ± 2	not reported	reported	not reported	not reported

Table 1 (co	ntinued)											
First author, Year of publication	Country	Study design	Population	Age, yrs (mean±SD)	Cause of sterility	Treatment cycle	а К	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (IU/L) Serum LH (IU/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Blank et al.,2020 [14]	Nether- lands	prospec- tive	<u>ب</u>	Ongoing pregnancy: 29:9±3.9 No ongoing pregnancy: 33.9±4.6	Male factor (50%) Tubal (12.5%) Unex- plained plained infertility (25%) Recurrent miscarriage (6.25%)	COH: Agonist vs antagonist Protocol	43.8% (fresh SET with a day-5 embryo) 56.3% (posi- tional age on 6 weeks, implanta- tion)	Overall: 9.2 ± 2.8 nancy: 8.8 ± 1.6 No ongoing pregnancy: 9.4 ± 3.9	1 h before ET: Ongoing implan- tation group: 1.35 ± 0.44 Ongoing preg- nancy group: 1.45 ± 0.42 No ongoing implanta- timp and tage- nancy group: 0.91 ± 0.19 No ongo- ing preg- nancy group: 0.050 Hz± 0.004 No ongoing implan- tation group: 0.050 Hz± 0.004 No ongoing preg- nancy group: 0.050 Hz± 0.004 No ongoing preg- nancy group: 0.051 Hz± 0.004 No ongo- nancy group: 0.045 Hz± 0.004 No ongo- No ongo-	reported	E2: Total: 1115 (210-2630) Ongoing preg- nancy: 1240 (1030-2630) No ongoing pregnancy: 842 (210-1450) Progesterone: Total: 0.3 (0.15-1.23) No ongoing pregnancy: 0.3 (0.15-1.23) (0.15-1.23)	 E2: Total: 153 (25-486) Ongoing pregnancy: 326 (70-486) No ongoing pregnancy: 25 (25-44) Progester- one: Total: 15 (8-71) Ongoing pregnancy: 13 (8-71)
Anshikha et al., 2021 [30]	India	prospec- tive	60	20-45 33.33±5.22	Poor ovar- ian reserve (45%) Tubal (18.3%)	COH:Antagonist protocol FET HRT	38.3%	not reported	56.7%:>3/2 min 20%:<3/2 min	not reported	not reported	not reported

First author, Year of publication	Country	Study design	Population	Age, yrs (mean ±SD)	Cause of sterility	Treatment cycle	CPR	Endometrium thickness on embryo transfer day (mm)	Frequency (contr./min)	Direction	Serum E2 (pg/ ml) Serum P (ng/ ml) (ET on day 2–3)	Serum FSH (1U/L) Serum LH (1U/L) Serum E2 (pg/ml) Serum P (ng/ml) (Day 5)
Masroor et al.,2023 [31]	Iran	prospec- tive	68	25-40	not reported	FET HRT cycle	36.8%	7−15 9.02±2.2	PR: 2.2±1.6 NPR: 3.3±1.2	not reported	not reported	not reported
Li et al.,2023	China	prospec- tive	230	20-35	Unex- plained infertility (0.9%) Male factor (6.1%) Female fac- tor (46.1%) Male and female factor (47%)	СОН	68.7%	Total: 11.26±2.14 NPR: 11.44±2.28 PR: 11.18±2.08	Total: 2.90 ± 1.44 NPR: 2.86 ± 1.56 PR: 2.92 ± 1.38	reported	not reported	not reported
Summary of co Abbreviations: LBR (live birth r minute)	hort studies i /VF In vitro feu ate), PCOS (Pc	investigating t rtilization, <i>COI</i> olycystic ovary	uterine contractil H Controlled ova y syndrome), CF (ity and implantat rian hyperstimula (cervix fundus), Fl	ion rate and m ition, <i>FET</i> frozer C (fundus cervi:	ale outcomes 1 embryo transfer, IU X), E2 (estrogen), P (p	l (insemination), rogesterone), FS	HRT (Hormone repla 5H (follicle stimulatin	cement therapy), CP . g hormone), LH (Lutei	clinical pregna nizing hormor	incy), NCP (no clinica ie) UC/min (uterine c	l pregnancy), contractions/

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Table 1 (continued)

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Table	

	Selection				Comparability		Outcome					
First author, Year of publication	Representativeness of exposed cohort	Selection of non- exposed cohort	Ascertainment of exposure	Outcome of interest not present at study start	Comparability of cohorts in main factors	Comparability of cohorts in additional factors	Assessment of outcome	Sufficient length of follow-up for outcomes to occur	Adequacy of follow-up of cohorts	Total	Quality Assessment	Comments
Narayan et al.,1994 [20]	*		*		*	*	*	1	*	6/9	Fair	
ljland et al.,1997 [8]		ī	*	*			*	ı	*	4/9	Poor	No state- ment of compari-
Fanchin et al.,1998 [22]	*		*		*	ı	*	*	*	6/9	Fair	son group
jjland et al., 1998 [71]	*	I	*	*	ı	ı	*	*	*	6/9	Poor	No compari- son group
رت حیا jjand et al.,1999 [23]	*	I	*	*	ı	*	*	I	I	5/9	Fair	No statment in follow up
Fanchin et al.,2000 [24]	*	ı	*	*			*	1	1	4/9	Poor	No compari- son group; No statment
Vlaisavljevic et al.,2001 [25]	*	ı	*	ı	*	*	*	I	*	6/9	Fair	
Ayoubi et al.,2003 [6]	*	1	*		*	*	*	*	*	6/2	Fair	
Vangestel et al.,2005 [26]	*	ı	*	*	*	*	*	ī	*	6/2	Good	
Kim et al., 2013 [<mark>27</mark>]	*		*	*	ı	*	*	*	*	6/2	Fair	
Zhu et al., 2014 (March) [32]	*	I	*	*	*	*	*	*	*	8/9	Good	

	Selection				Comparability		Outcome					
First author, Year of publication	Representativeness of exposed cohort	Selection of non- exposed cohort	Ascertainment of exposure	Outcome of interest not present at study start	Comparability of cohorts in main factors	Comparability of cohorts in additional factors	Assessment of outcome	Sufficient length of follow-up for outcomes to occur	Adequacy of follow-up of cohorts	Total	Quality Assessment	Comments
Zhu et al.,2014 (Nov 2013) [9]	*	1	*	*	1	1	*	1	1	4/9	Fair	No statment in follow up
Chung et al.,2017 [28]	*	*	*	*	*	*	*	*	*	6/6	Good	
Samara et al., 2019 [<mark>29</mark>]	*	*	*	ı	*	I	*	ı	*	6/9	Good	
Blank et al.,2020 [14]	*	*	*	*	*	*	*	*	*	6/6	Good	
Anshikha et al., 2021 [30]	*	I	*	*	ı	1	*	*	*	6/9	Poor	No compari- son group
Li et al.,2023	*	*	*	*	*	*	*	*	*	6/6	Fair	
Masroor et al.,2023 [31]	*	T	*	*	*	ı	*	*	*	6/2	Good	

Table 2 (continued)

ovarian stimulation, progesterone levels were negatively correlated with the amplitude of UCs [14, 24]. However, other studies found that serum progesterone level on the day of embryo transfer did not influence clinical pregnancy rate [14, 25, 32].

Meta-analysis results

Global uterine contractility and pregnancy rate

Five studies were eligible for meta-analysis, comparing pregnancy rates between women with high vs. low- uterine contractility after different In vitro fertilization (IVF) treatments followed by cleavage-stage embryo transfer. Women with more than two uterine contractions (UC)/ min had a significantly lower clinical pregnancy rate compared to women with lower uterine contractility (OR 0.52, 95% CI: 0.38- 0.69). There was moderate heterogeneity between studies ($I^2 = 55\%$, p < 0.01). The prevalence of each of these studies, the summary prevalence and the prediction interval are shown in Fig. 2.

Discussion

The aim of this systematic review was to analyze data on UP and the association with clinical pregnancy rates, focusing on UP before embryo transfer in patients undergoing fertility treatment, particularly IVF. Our data suggest a lower pregnancy rate in women with high uterine peristalsis before embryo transfer. The strengths of the study is that we not only performed a systematic review but also a meta-analysis. The meta-analysis showed that having more than two contractions per minute at the time of embryo transfer reduces the pregnancy rate by half (OR: 0.52; 95% CI: 0.38-0.69).

Their weakness is that all included trials transferred embryos at cleavage, 2-3 days after egg retrieval. This approach did not cover the implantation window. Furthermore, only one study explicitly excluded patients with uterine pathology [28], a crucial variable in the assessment of contractile dysfunction. Another point to consider is that ultrasound technology has developed and improved considerably over the years [17, 35]. This may have an impact on the quality of data obtained in previous studies. Therefore, although this issue was extensively studied in the 1990s [7, 23, 36], it is essential to revisit it with today's technology and it is therefore necessary to address this issue. This approach is particularly relevant to better interpret the effect of uterine contractility on implantation, for which the development of imaging accuracy and quality will be crucial. Finally, because the meta-analysis was performed on mixed study cohorts, it is difficult to interpret the effects of various external factors such as IVF treatment, progesterone treatment and its route of administration, and patients with recurrent implantation failure. Notably, the heterogeneity among the included studies is a key limitation, as variations in





Heterogeneity: $I^2 = 55\%$, $\tau^2 = 0.0092$, $\chi_4^2 = 8.82$ (p = 0.07)

Fig. 2 *Pooled global uterine contractility and implantation rate.* Forest plot of odds ratios (OR) and 95% confidence intervals (CI) for studies evaluating uterine peristalsis and clinical pregnancy. The blue squares in each study indicate the OR, the size of the squares indicates the study weight, and the horizontal lines indicate the 95% CI. The data in blue diamond represent the pooled OR in patients with high vs. low uterine contractility and 95% CI. Overall estimates are presented in the fixed- and random-effects models. The prediction interval is defined as the interval within which the effect size of a new study would fall if this study were selected at random from the same population of studies already included in the meta-analysis

study design, patient populations, stimulation protocols, and contractility assessment methods may have influenced the findings. Despite applying statistical methods to quantify heterogeneity, the limited number of studies (n=5) reduces the robustness of the evidence.

Based on previous research on UP during natural menstrual cycles, UP of the 'uterine myometrial (subendometrial) unit' is characterized by differences in frequency, amplitude and direction of contractions (Table 3). The uterine contraction frequency limit of two contractions per minute, which serves to distinguish between low and high contractility, was selected on the basis of established physiological findings from studies of the late luteal phase. Specifically, significant contributions to this field were provided by van Gestel et al. [37]. Therefore, these findings reflect the natural decline in uterine contractility during the luteal phase, which is essential for embryo implantation. The highest frequency of uterine contractility often occurs with cervical-fundal wave direction just before ovulation [8, 32] (Supplement 2). This change in orientation allows efficient transport of sperm to the fallopian tubes [8, 23, 36, 38, 39, 39]. Asymmetric UP is induced by local hormone production in dominant follicles [36]. As a result, contractile activity decreases, creating a favorable environment for implantation. During the luteal phase, the uterus remains inactive, providing an ideal environment for embryo implantation [7, 40]. As physiological UP appears to have specific fertility functions, dysfunctional contractions could contribute to infertility [21, 38].

However, uterine peristalsis is defined as wave movements in the subendometrial layer that can be detected by ultrasound [41]. Assessing the frequency of uterine contractions at different times in the menstrual cycle has implications for embryo implantation rates. The frequency of contractions is one to two per minute with small amplitudes at the beginning of the follicular phase [7, 8, 12]. Then, around the time of ovulation, the frequency increases to around 3–4 per minute. During the luteal phase, both the frequency and amplitude of contractions decrease to facilitate implantation of the embryo. Independently of observations made earlier in the menstrual cycle, the high frequency of uterine contractions on the day of transfer is still associated with a lower implantationsrate. Measurement of uterine contractility closer to the time of embryo transfer has a more significant effect on implantation success [17].

In line with this studies of the impact of UP on IVFs have shown a negative correlation between high estimated contraction activity (>3 wave/min) and clinical pregnancy [7, 9]. Chung et al. [28] investigated the measurement of UP and its frequency before and after embryo transfer (ET) (+5,+60 min) using 2D ultrasound. Notably, the increased UP observed 5 min after ET was only significant in the non-pregnant group (14.7%) and not in the pregnant group (8.5%). The frequency of contractions also returned to its original rate 60 min after ET. These results suggest that a prolonged high uterine frequency may have a negative effect on the pregnancy rate. In addition, women who had more than five contractions after ET were found to have a significantly lower live birth rate. A positive association between pregnancy rates and low pre-ET UP (less than 4 waves per minute) was found by Masroor et al. (2023) in a similar study [31]. Conversely, high frequency, low amplitude post-ET uterine activity may actually enhance embryo implantation, as suggested in a pilot study by Blank et al. [14]. Current evidence suggests a potential association between excessive uterine contractility and recurrent implantation failure (RIF). A recent study by Dong et al. (2023) identified abnormalities in uterine muscle contractions, along with inflammation and impaired vascularization, as key factors in the pathogenesis of RIF [42]. These findings support the hypothesis that increased uterine contractility could contribute to implantation failure, highlighting the need for further research to establish a direct causal relationship between RIF and uterine activity.

 Table 3
 Characteristics of UP frequency, direction and amplitude of UC in different phases of the menstrual cycle (van Gestel et al., 2003) [37]

Phase	Subphase	Frequency (contractions/min)	Amplitude (mmHg)	Direction
Menstruation		0.33–3.0	13.6	FC
Follicular phase Luteal phase	Mild	1.5–3.3	5.2	FC/CF
	Late	3.0-6.0	2.9	CF
	Early	2.0-4.0	Amplitude rises	
	Late	0.8–1.8	CF/opposing	Opposing/ no contrac- tions

Abbreviations: CF cervix to fundus, FC fundus to cervix, opposing = Contractions are initiating both in the cervical and fundal regions, UP uterine peristalsis, UC uterine contraction

The direction of UCs after ET is a critical factor for implantation and consequently has a significant impact on the reproductive outcome [32, 43]. Lesny et al. [44] warned of the risk of excessive contractions leading to expulsion of the transferred fluid. Also, the pregnancy rate had been correlated with the movements of the endometrium, the amount of UP, the cervicofundal direction and the hyperechoic change, with a higher cervicofundal movement being observed in the pregnant group [45].

Current evidence suggests that uterine contractility differs significantly between fresh and frozen IVF cycles, with potential implications for implantation rates and reproductive success. Research conducted by Zhu et al. [32] and Chung et al. [28] has identified increased uterine contractility in fresh cycles; this phenomenon is likely influenced by hormonal fluctuations resulting from ovarian stimulation [28, 32]. These fluctuations have been demonstrated to compromise endometrial receptivity and reduce pregnancy rates. However, Masroor et al. [31] and Fanchin et al. [12] have demonstrated that uterine contractility is lower in frozen cycles, where endometrial preparation is more stable and less affected by hormonal variations, potentially facilitating embryo implantation. These findings underscore the importance of considering cycle type when evaluating uterine contractility and its impact on IVF outcomes, highlighting the need for individualised strategies to optimize the uterine environment for successful implantation.

The prevalence of UCs may be influenced by several factors, including hormonal factors such as progesterone. Progesterone has been suggested to be negatively correlated with the amplitude of UCs [7, 14]. However, some studies show no significant differences between pregnant and non-pregnant women [25, 28]. Observational studies suggest a reduction in UP [17]. Further clinical research is required to investigate the relationship between progesterone levels and uterine activity on day 5 of ET. The effect of progesterone or route of progesterone supplementation also require critical investigation.

The impact of uterine pathology on UC was evaluated by a recent study by Rees et al. [46] evaluated uterine contractility during different phases of the menstrual cycle in patients with adenomyosis compared to a healthy control group. This study found that women with adenomyosis had dysfunctional uterine contractility, particularly in the luteal phase, characterised by higher amplitude, slower velocity and less coordinated contractions. Boer's review [47] indicates that despite the heterogeneity of the studies reviewed, uterine abnormalities typically resulted in altered and reduced UCs. However, there is a very limited amount of good quality research on this topic, despite its clinical importance.

The method of measuring uterine contractility is a key point of discussion. A definitive method of measuring contractions has not been identified, because of limitations in all the diagnostic tools currently in use, although many studies have been conducted on UP over the years. Intrauterine pressure measurement is not the optimal diagnostic tool during IVF cycles, as its invasive character potentially affects the characteristics of the UC and making it impractical for ET. A further issue is the subjective and operator dependent nature of transvaginal (2D) ultrasound, which makes it problematic. Although other methods such as 3D and 4D transvaginal ultrasound have gained popularity in recent years, the need for operator expertise remains. Transabdominal ultrasound is another option, but presents challenges due to external factors such as bladder fullness and body mass index (BMI) during ET [28]. More objective alternatives, such as magnetic resonance imaging (MRI), are costly and inappropriate for procedures close to ET. Alternatively, a novel technique, electrohysterography (EHG), may offer an objective, user-friendly and non-invasive measurement tool that can provide information on the most electrically active regions during different phases of the menstrual cycle [35].

The findings from this review and meta-analysis highlight the need to consider UP assessment as part of clinical practice, particularly in women undergoing IVF. The strong association between increased UP and reduced pregnancy rates suggests that evaluating UP could provide valuable diagnostic insight. However, while interventions such as oxytocin antagonists have been explored to mitigate excessive uterine activity, clinical trials have yielded inconsistent results [48]. Although it is still premature, the integration of UC assessment into the diagnostic workup for women with RIF prior to any subsequent embryo transfers should be considered. The use of newer and more precise measurement tools could facilitate a more accurate evaluation of uterine activity, allowing for targeted interventions only in cases of elevated UP. Further studies are needed to validate these findings and determine whether reducing UP in selected patients can improve pregnancy and live birth rates, ultimately optimizing IVF outcomes.

The standardization of uterine contractility measurement is a critical aspect of research on its impact on embryo implantation and pregnancy rates in assisted reproductive treatments. The reviewed evidence suggests that a higher frequency of uterine contractions at the time of embryo transfer is associated with a reduced success rate, highlighting the need for more precise and uniform evaluation methods. The implementation of advanced techniques, such as 2D and 3D transvaginal ultrasound, along with emerging tools like electrohysterography, would allow for more reliable and reproducible data, facilitating the integration of uterine contractility as a key factor in clinical practice. In the future, studies adopting standardized methodologies could not only enhance the understanding of uterine physiology in the context of in vitro fertilization but also contribute to the development of targeted therapeutic strategies, ultimately optimizing implantation and pregnancy rates in patients undergoing fertility treatments.

Despite strictly following the recommendations for high-quality systematic reviews and meta-analyses, our study has some limitations. First, the sample sizes in several included trials were small, preventing subgroup analyses, such as those focusing on women with recurrent implantation failure or specific uterine pathologies like fibroids or adenomyosis. Additionally, the heterogeneity among studies in terms of patient characteristics, stimulation protocols, and embryo transfer techniques makes it challenging to draw definitive conclusions about the direct impact of uterine contractility on implantation. Moreover, contractility was assessed exclusively through transvaginal ultrasound, a method highly dependent on the operator, which may have introduced variability in the results. Finally, since most of the included studies analyzed cleavage-stage transfers (day 2-3), our findings may not be fully generalizable to blastocyst transfers (day 5), which are increasingly used in clinical practice. Future studies with prospective designs and more objective measurement methods are needed to better understand the influence of uterine contractility on reproductive outcomes.

In conclusion, the lower clinical pregnancy rate in women with high uterine contractility highlights the role of uterine peristalsis around the time of embryo implantation. However, due to the limited and heterogeneous data available, the influence of uterine peristalsis on reproductive outcomes such as live birth rates remains unclear. Further research is required to improve our understanding of the role of UP on infertility and IVF. Further research should be based on a user-friendly, objective measurement tool for the interpretation of UCs.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12958-025-01380-5.

Additional file 1: Supplement S1 Database Searching Strategies. Systematic literature search in Medline, Embase, and Cochrane.

Additional file 2: Supplement S2 Video Uterine contractility is assessed through a 2D transvaginal ultrasound five days after ovulation during the luteal phase.

Acknowledgements

Centre Suisse d'Électronique et de Microtechnique (CSEM)

Author's contributions

Conceptualization: Angela Vidal, Valery Trejos, Y. Gürkan, Michael von Wolff. Data curation: Angela Vidal, Valery Trejos. Formal analysis: Janna Pape, Angela Vidal, Valery Trejos. Research: Angela Vidal, Valery Trejos. Methodology: Angela Vidal, Valery Trejos Tanya Karrer. Statistics: Janna Pape. Editing and proofreading: Angela Vidal, Michael von Wolff, Janna Pape. Supervision: Michael von Wolff. All authors reviewed the results and approved the final version of the manuscript.

Funding

No specific financial support was received for the review.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 21 May 2024 Accepted: 8 March 2025 Published online: 29 March 2025

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