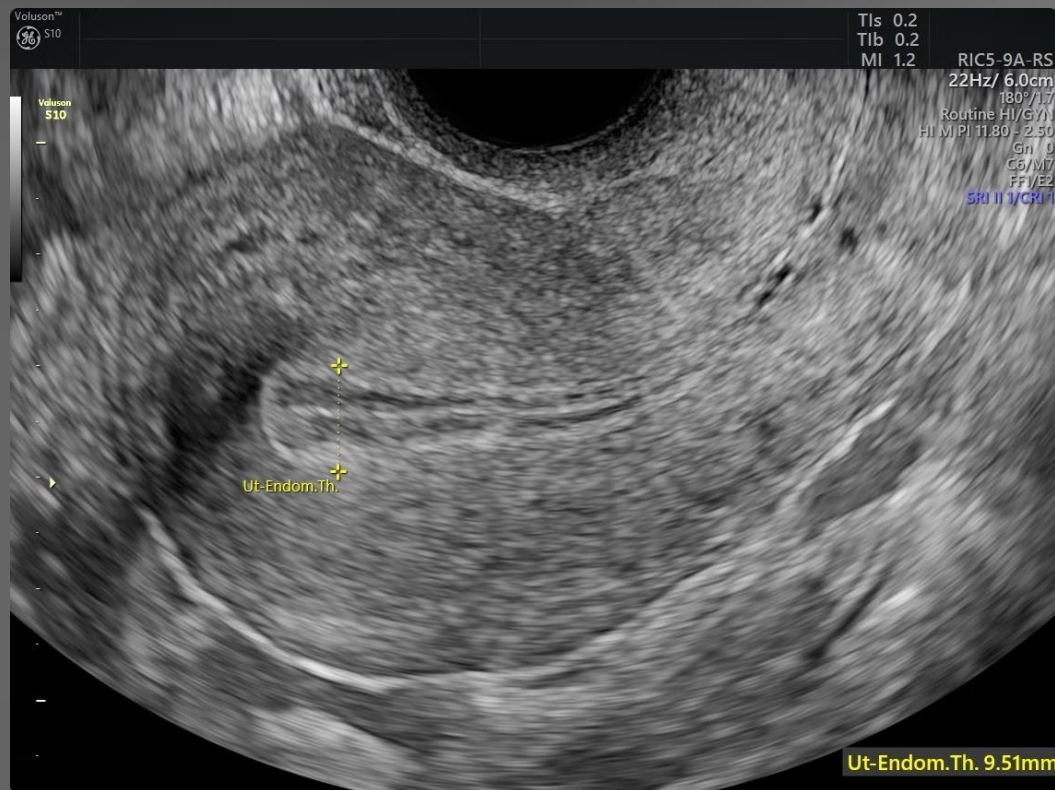


Endometrial Thickness and Placenta Accreta Spectrum Risk in IVF



This study examines the relationship between endometrial thickness (EMT) and the risk of placenta accreta spectrum (PAS) disorders in women undergoing in vitro fertilization (IVF). PAS disorders are a potentially life-threatening condition where the placenta abnormally attaches to the uterine wall. The research aims to evaluate whether thin endometrial lining is associated with increased PAS risk in IVF pregnancies, which could help improve screening and early identification of high-risk cases.



OBSTETRICS

A sonographic endometrial thickness <7 mm in women undergoing in vitro fertilization increases the risk of placenta accreta spectrum

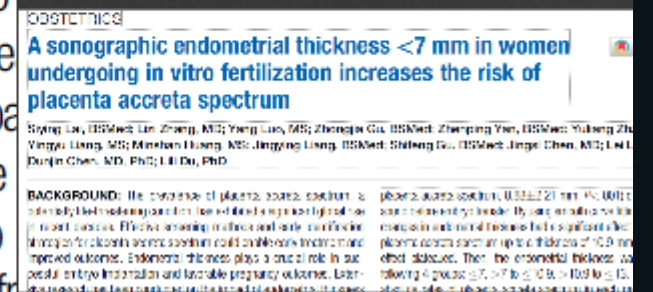


Siying Lai, BSMed; Lizi Zhang, MD; Yang Luo, MS; Zhongjia Gu, BSMed; Zhenping Yan, BSMed; Yuliang Zhang, BSMed; Yingyu Liang, MS; Minshan Huang, MS; Jingying Liang, BSMed; Shifeng Gu, BSMed; Jingsi Chen, MD; Lei Li, PhD; Dunjin Chen, MD, PhD; Lili Du, PhD

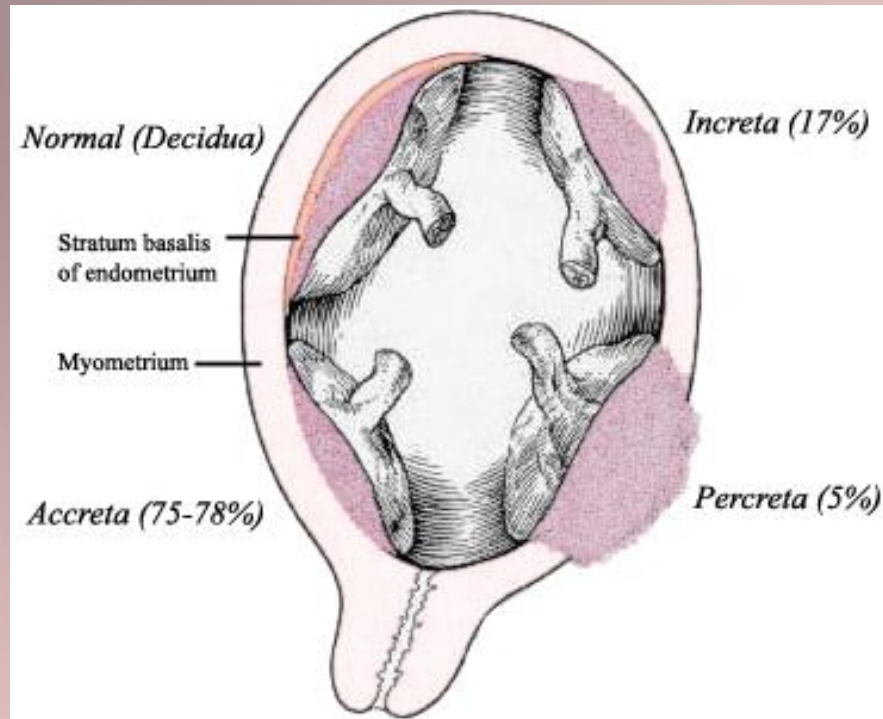
BACKGROUND: The prevalence of placenta accreta spectrum, a potentially life-threatening condition, has exhibited a significant global rise in recent decades. Effective screening methods and early identification strategies for placenta accreta spectrum could enable early treatment and improved outcomes. Endometrial thickness plays a crucial role in successful embryo implantation and favorable pregnancy outcomes. Extensive research has been conducted on the impact of endometrial thickness on assisted reproductive technology cycles, specifically in terms of pregnancy rates, live birth rates, and pregnancy loss rates. However, limited knowledge exists regarding the influence of endometrial thickness on placenta accreta spectrum.

OBJECTIVE: This study aimed to evaluate the association between pre-

placenta accreta spectrum, 8.88 ± 2.21 mm; $P < .001$) during the last ultrasound before embryo transfer. By using smooth curve fitting, it was found that changes in endometrial thickness had a significant effect on the incidence of placenta accreta spectrum up to a thickness of 10.9 mm, beyond which the effect plateaued. Then, the endometrial thickness was divided into the following 4 groups: ≤ 7 , >7 to ≤ 10.9 , >10.9 to absolute rates of placenta accreta spectrum in e 3.73%, 1.35%, and 2.54%, respectively. Compared endometrial thickness from 10.9 to 13 mm, the spectrum increased from an adjusted odds ratio interval, 1.33–3.86) for endometrial thickness fr adjusted odds ratio of 7.15 (95% confidence i



Background on Placenta Accreta Spectrum



Definition

PAS disorders involve abnormal placental attachment to the uterine wall, ranging from placenta accreta to placenta percreta.

Risks

PAS is a leading cause of severe maternal hemorrhage, blood transfusion, and emergency hysterectomy.

Increasing Prevalence

Global incidence of PAS has risen significantly in recent decades due to factors like advanced maternal age and increased cesarean rates.

Role of Endometrial Thickness in IVF

1

Embryo Implantation

EMT plays a crucial role in successful embryo implantation and favorable pregnancy outcomes.

2

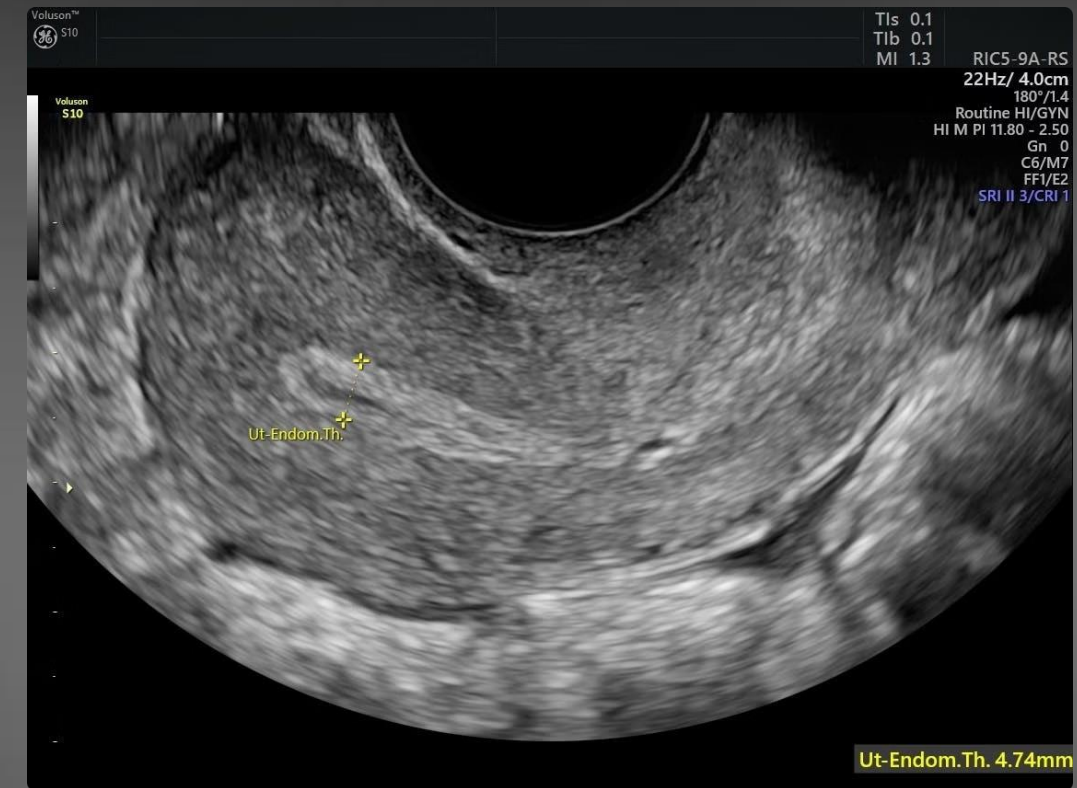
Pregnancy Rates

Extensive research has examined the impact of EMT on pregnancy rates in assisted reproductive technology cycles.

3

Pregnancy Complications

EMT has been associated with various pregnancy complications, but its influence on PAS risk is not well understood.



Study Objectives

1 Primary Aim

To evaluate the association between preimplantation endometrial thickness and occurrence of PAS in women undergoing IVF/ICSI treatment.

2 Hypothesis

Women with thinner endometrial lining may be more susceptible to developing PAS.

3 Clinical Significance

Findings could improve risk assessment and management of PAS in IVF pregnancies.



Study Design and Population

Design

Retrospective cohort study

Setting

Third Affiliated Hospital of
Guangzhou Medical
University, China

Time Period

January 2008 to December
2020

Inclusion Criteria



1

IVF/ICSI Treatment

Women who conceived through IVF or ICSI-embryo transfer

2

Delivery Location

Subsequent delivery at the study hospital

3

Gestational Age

Reached at least 20 weeks of gestation

4

Data Availability

Complete clinical information on EMT, birth history, demographics, and infertility characteristics

Exclusion Criteria

Previous Cesarean Delivery

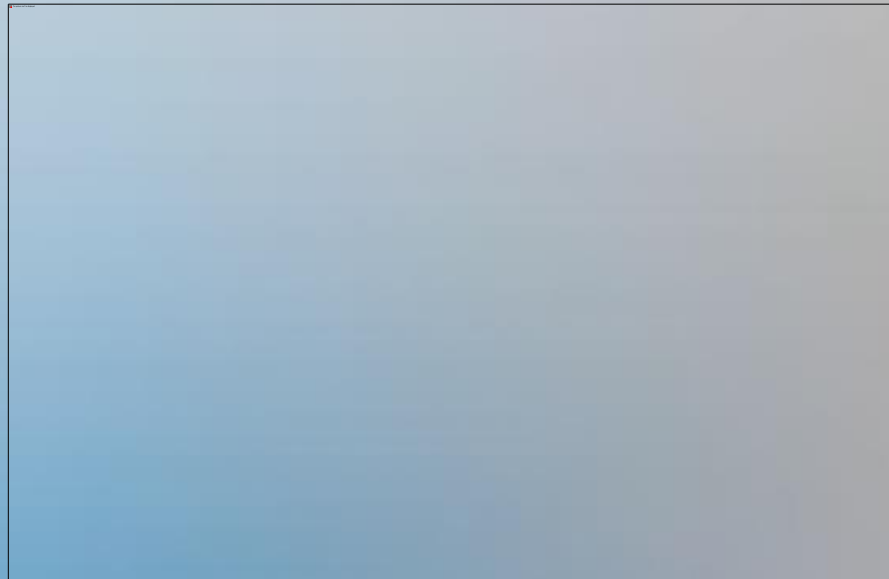
Women with a history of cesarean section were excluded to focus on the independent effect of EMT.

Incomplete Data

Cases without full clinical information were not included in the analysis.



Endometrial Thickness Measurement



1

Fresh IVF Cycles

EMT measured on the day of trigger

2

Frozen Embryo Transfers

EMT measured before progesterone initiation or LH surge/hCG administration

3

Measurement Technique

Maximum anterior-posterior thickness on long-axis transvaginal ultrasound view

Ovarian Stimulation Protocols



GnRH Antagonist

FSH stimulation with antagonist to prevent LH surge



GnRH Agonist

Long, short, and super long protocols



Natural Cycle

No ovarian stimulation medications

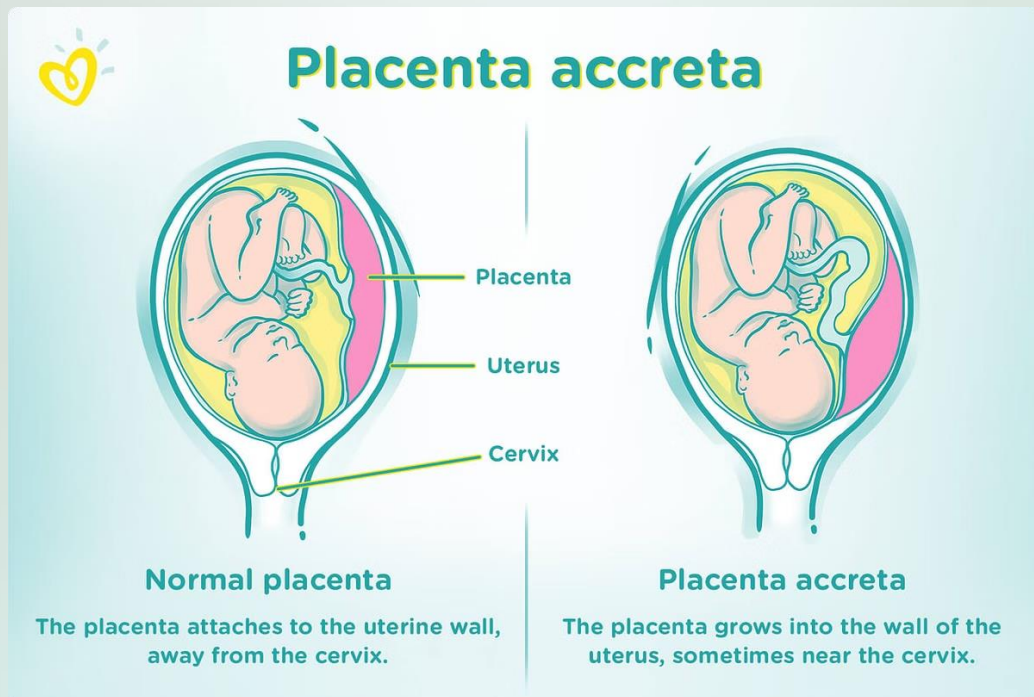


Other Protocols

Includes hormone replacement and mild stimulation



Diagnosis of Placenta Accreta Spectrum



FIGO Guidelines

Diagnosis based on International Federation of Gynecology and Obstetrics criteria

Cesarean Delivery

Direct visualization during laparotomy or histopathologic examination

Vaginal Delivery

Primarily based on clinical criteria

Data Analysis Software



Data Analysis is the process of inspecting, cleaning, transforming, and modeling data with the goal of discovering useful information, suggesting conclusions, and supporting decision making.

Data Analysis Software tool that has the statistical and analytical capability of inspecting, cleaning, transforming, and modelling data with an aim of deriving important information for decision-making purposes.



Data analysis can be classified into descriptive statistics, exploratory data analysis (EDA), and confirmatory data analysis (CDA).

Statistical Analysis Methods

1

Descriptive Statistics

Continuous variables as mean \pm SD, categorical as percentages

2

Group Comparisons

Kruskal-Wallis test for continuous, chi-square for categorical variables

3

Curve Fitting

Smooth curve fitting and generalized additive models for non-linear relationships

4

Regression Analysis

Univariate and multivariate logistic regression to analyze EMT-PAS relationship

Propensity Score Matching

1 Purpose

To reduce selection bias and balance characteristics between PAS and non-PAS groups

2 Method

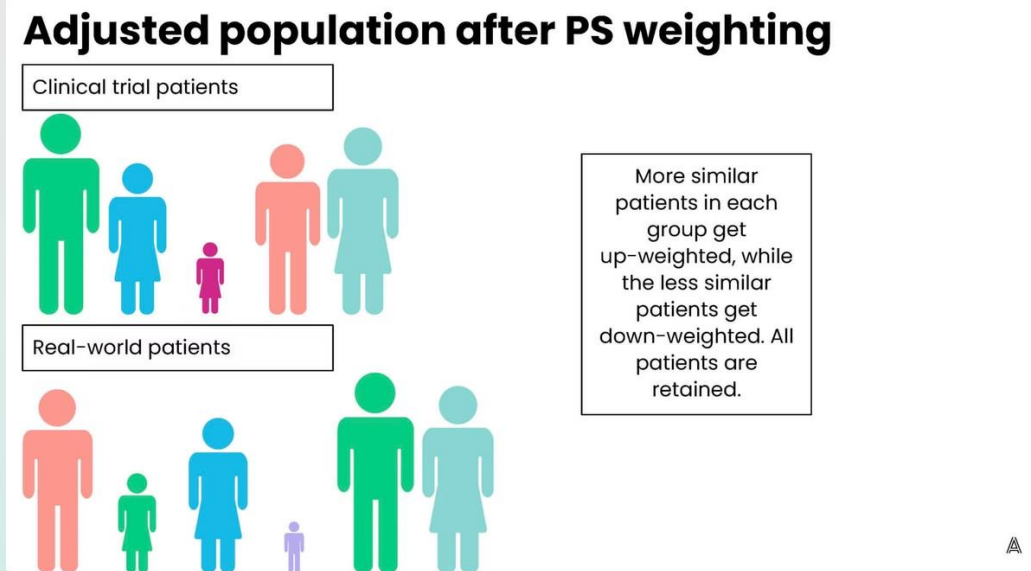
1:1 matching using nearest-neighbor algorithm with 0.05 caliper width

3 Variables

Matched on age, BMI, cycle type, ART indications, and stimulation protocol

4 Evaluation

Balance assessed using standardized differences



Study Population Characteristics



Total IVF/ICSI Cycles	46,799 (2008–2020)
-----------------------	--------------------

Total Deliveries	82,840
------------------	--------

IVF Pregnancies Delivered	6,356
---------------------------	-------

Final Analysis Cohort	4,637
-----------------------	-------

PAS Cases	159 (3.4%)
-----------	------------

Clinical Characteristics of PAS vs Non-PAS Groups

PAS Group

Higher gravidity, more abortion history, more blastocyst transfers, thinner endometrium

Non-PAS Group

Lower gravidity, less abortion history, fewer blastocyst transfers, thicker endometrium

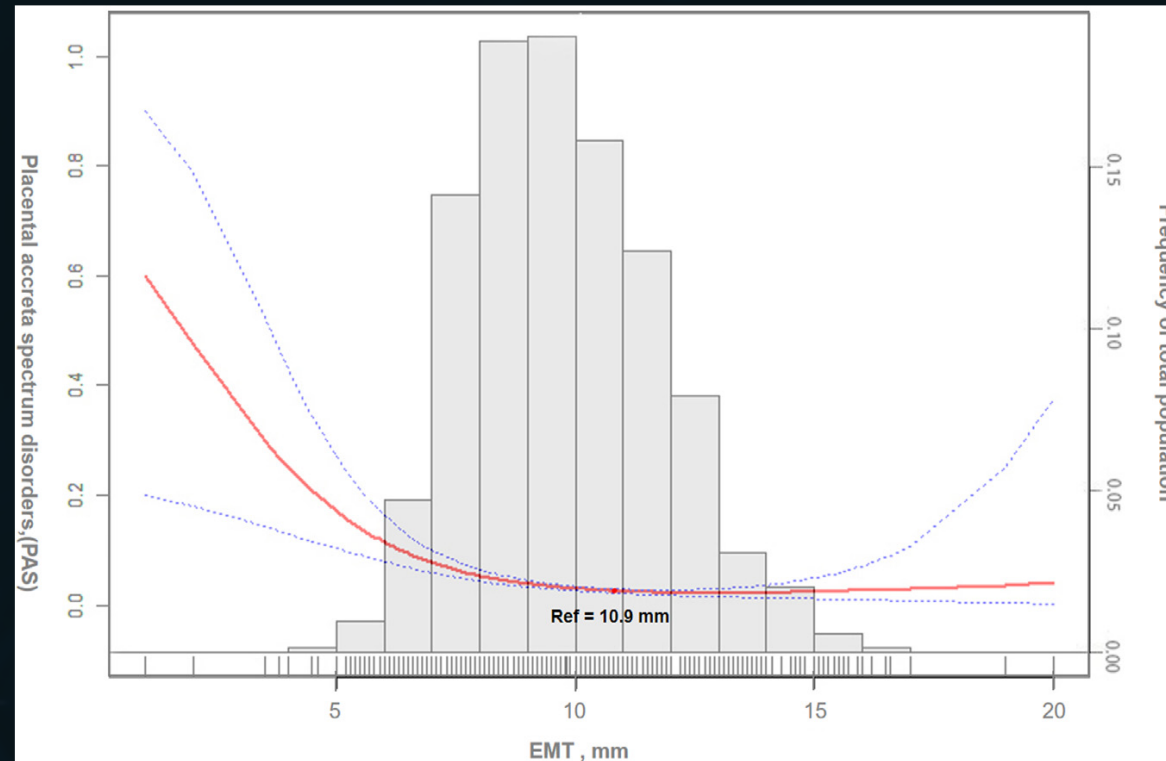
Significant Differences

Infertility type, embryo transfer cycle type, ovarian stimulation protocol

Endometrial Thickness Distribution



Relationship Between EMT and PAS Risk



Non-linear Relationship

Smooth curve fitting revealed a rapid decline in PAS rate with increasing EMT up to 10.9 mm, then plateauing.

Threshold Effect

Below 10.9 mm EMT, each 1 mm increase was associated with a 0.32 decrease in PAS rate ($P < 0.001$).

Placenta Previa as an Independent Risk Factor

Adjusted Odds Ratio

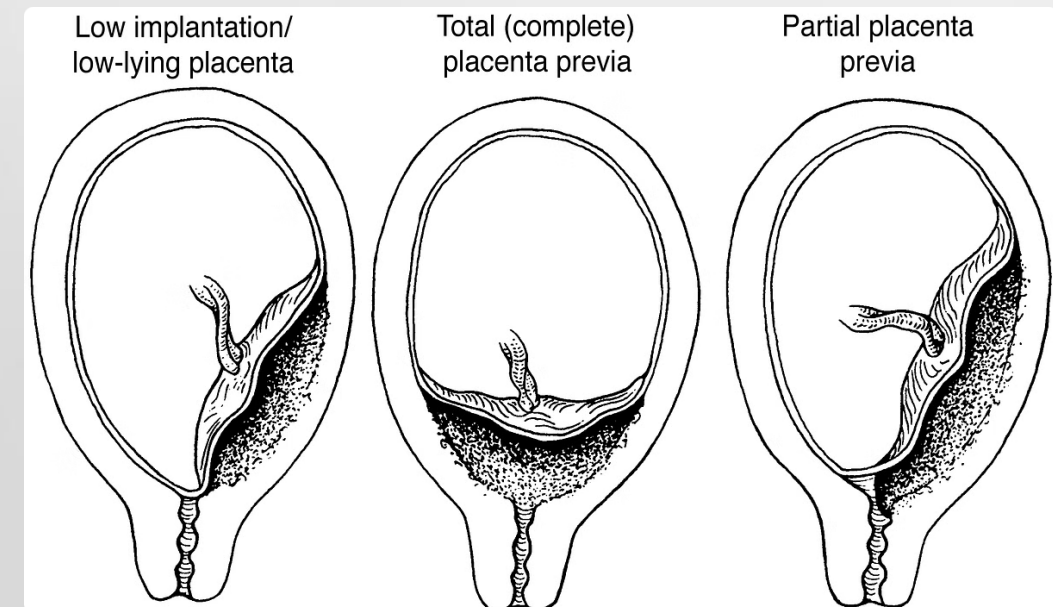
11.80 (95% CI: 7.65–18.19)

Significance

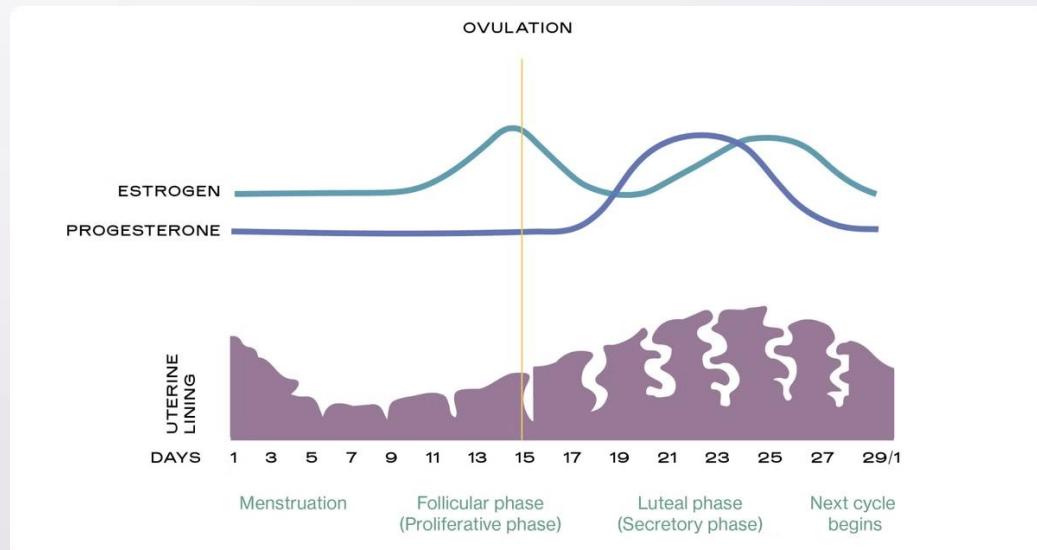
Remained a strong independent risk factor for PAS

Interaction with EMT

1.81% of women with EMT ≤ 7 mm had placenta previa with PAS, significantly higher than other EMT groups



Gravidity and EMT Correlation



1

Observation

Significant correlation between increasing gravidity and thinner EMT

2

Implication

Suggests potential cumulative effect of pregnancies on endometrial thickness

3

Clinical Relevance

May contribute to understanding PAS risk in women with multiple pregnancies

Ovarian Stimulation Protocol and EMT



Shorter Protocols

Associated with thinner endometrium



Longer Protocols

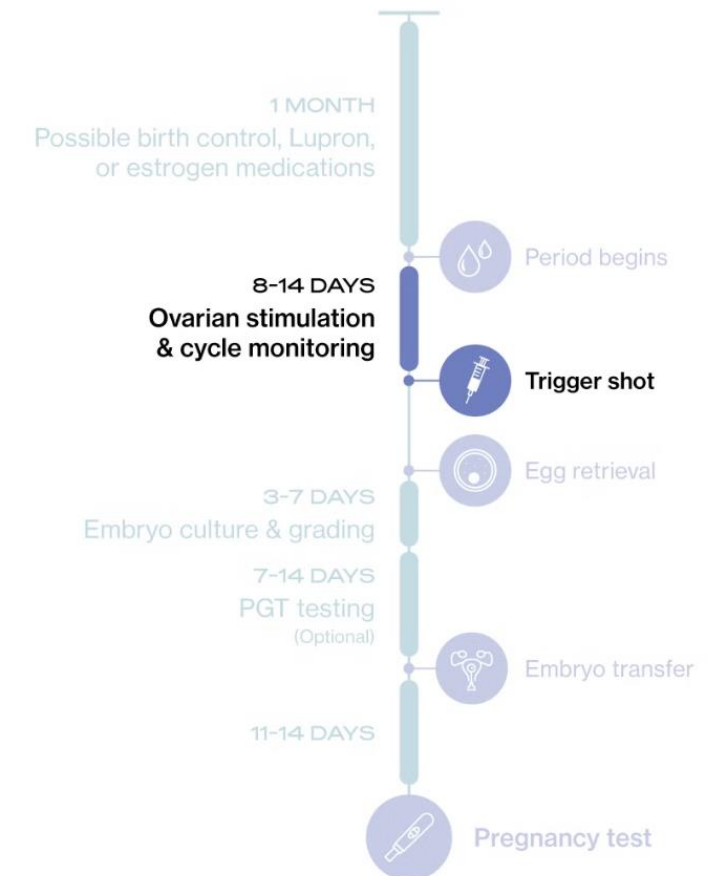
Tended to result in thicker endometrium

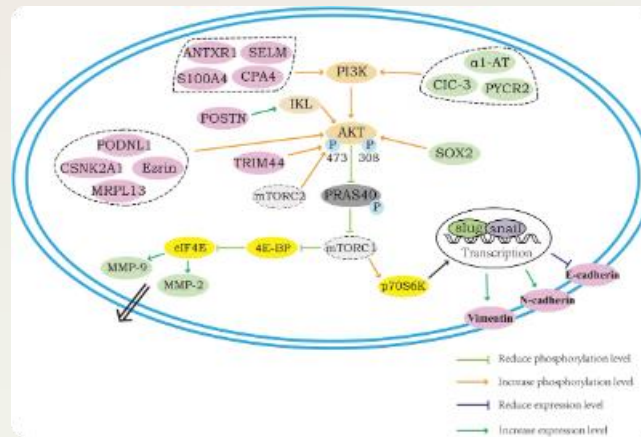


Protocol Duration

Inversely related to EMT

WHERE OVARIAN STIMULATION FITS INTO THE IVF PROCESS





Conclusions: Mediating Role of EMT

Gravidity ——— 1
 EMT mediates 63.9% of gravidity's effect on PAS risk

1

2 ——— Ovarian Stimulation

2

EMT mediates 18.6% of stimulation protocol's effect on PAS risk

Mechanism Insight ——— 3

3

Highlights importance of endometrial factors in PAS pathogenesis

Limitations of the Study

Types of Research Bias



Design Bias



Selection Bias



Procedural Bias



Reporting Bias



Data Collecting Bias

 QuestionPro

1

Retrospective Design

Potential for inherent biases despite PSM analysis

2

Exclusion of Previous CD

Results may not apply to women with prior cesarean deliveries

3

Single Center Study

May limit generalizability to other populations

4

Timing of EMT Measurement

Unclear if EMT at embryo transfer is most relevant for PAS risk

Conclusions: EMT as a Risk Factor

Independent Risk

Thin EMT (≤ 7 mm) is an independent risk factor for PAS in IVF pregnancies

Dose-Response

Risk increases as EMT decreases, with threshold effect at 10.9 mm

Comparison to Placenta Previa

EMT's clinical significance for PAS risk is slightly lower than placenta previa



**What causes
Thin Endometrium?**

Key Takeaways for Clinical Practice



Measure EMT

Routinely assess EMT during IVF cycles



Risk Stratification

Include EMT in PAS risk assessment for IVF pregnancies



Patient Care

Consider closer monitoring for women with $EMT \leq 7$ mm



Further Study

Continue investigating EMT's role in pregnancy outcomes





Future Research Directions

1 Multicenter Studies

Validate findings in diverse populations

2 Prospective Trials

Evaluate interventions to mitigate PAS risk in women with thin endometrium

3 Molecular Mechanisms

Investigate biological pathways linking thin endometrium to PAS

4 Long-term Outcomes

Assess impact of EMT on other pregnancy complications and neonatal outcomes