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Background

- The human ovary is one of the first organs to age.
- Reproductive aging is characterized a decline in oocyte quantity and quality, resulting in infertility, increased pregnancy loss, and diminished endocrine function.
- The ovarian stroma becomes fibrotic with age due to excess collagen and extracellular matrix (ECM) components which translates into a **biomechanically stiffer** organ (Briley et al, 2016; Amargant, 2020).
- Fibrotic stiffening disrupts follicle recruitment and growth, granulosa signaling, ovulation and hormone production (Converse et al, 2025; Pietroforte et al, 2026).
- Despite the broad clinical consequences of ovarian aging, there are currently **no noninvasive modalities** to comprehensively capture this process.

Shear Wave Elastography (SWE)

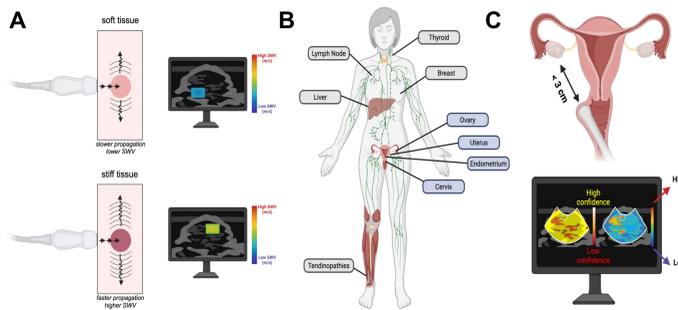


Figure 1. Shear wave elastography (SWE) is an ultrasound-based technology that quantifies tissue stiffness. (A) Slower waves indicate softer tissue, faster waves stiffer tissue (B) SWE has been used clinically in a variety of tissues (Zaniker et al., 2024). (C) SWE performed with transvaginal ultrasound probe (GE Logic Fortis, 7-9 mHz frequency) and up to 12 measurements with a 5mm ROI were taken per ovary in high confidence regions.

OBJECTIVE: To evaluate the association of SWE-measured ovarian stiffness with reproductive age and ART outcomes.

Methods

- This is a single center prospective study of patients presenting for fertility preservation or IVF for non-infertile or presumed age-related diagnoses
- Two age cohorts were recruited; **reproductively young (≤33 years)** and **old (≥37 years)**
- SWE performed by single sonographer in the early follicular phase (cycle days 1-3) at baseline visit prior to gonadotropin stimulation (Figure 1C).
- Ovarian stiffness was examined by age category and ART outcomes

Inclusion Criteria

- Planned fertility cryopreservation
- IVF for unexplained infertility (≥37 years old), male factor, non-infertile reason (same sex), diminished ovarian reserve (DOR)
- BMI 19-29
- First cycle or last oocyte retrieval >1 year ago

Exclusion Criteria

- Random starts, Estrogen priming, or Provera
- Longterm OCPs
- Infertility related to ovarian pathology, unexplained infertility ≤33
- History of ovarian surgery
- Medical fertility preservation or systemic disease
- Smoking or substance use

Results

Treatment Indications:

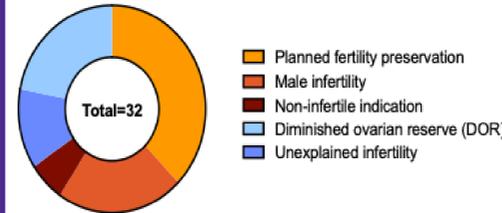


Table 1. Participant Demographics

Characteristic	Reproductively Younger ≤ 33 years (n=16)	Reproductively Older ≥37 years (n=16)	P-value
Age (years)	30.5 ± 1.7	40.3 ± 2.0	<0.00001*
BMI (kg/m ²)	22.5 ± 1.9	24.5 ± 2.6	0.02*
FSH (mIU/ml)	6.2 ± 2.4	7.5 ± 2.9	0.18
AMH (ng/ml)	3.1 ± 1.7	1.7 ± 1.1	0.01
Total AFC	24.4 ± 8.4	12.8 ± 5.1	<0.0001*
Total ovarian volume (ml)	13.9 ± 4.8	10.1 ± 4.9	0.03*
Average probe distance (cm)	0.7 ± 0.4	0.8 ± 0.2	0.68
Total FSH Dose (IU)	3861 ± 1312	4659 ± 1206	0.08
Total retrieved oocytes	20 ± 12	11 ± 7	0.02*
Total mature (MII) oocytes	15 ± 10	8.6 ± 5.6	0.03*

Ovarian Stiffness and Age

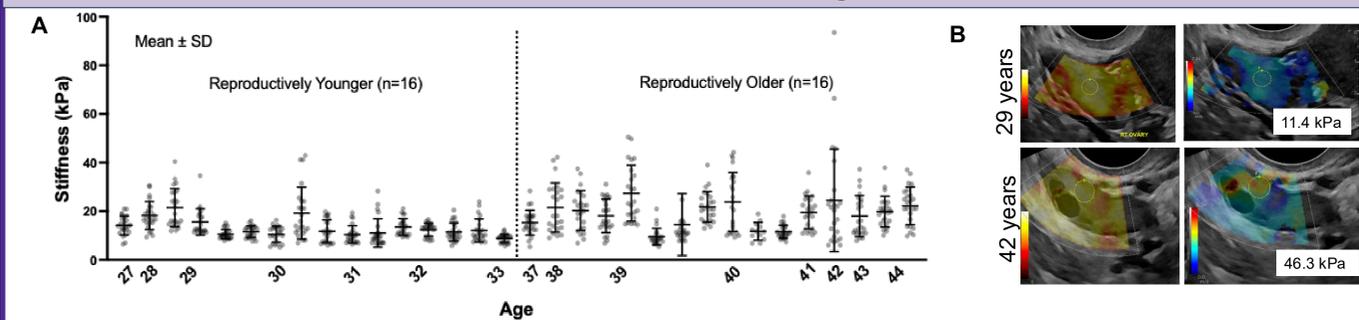


Figure 3. Ovarian stiffness is more heterogenous with older reproductive age. (A) Individual stiffness values of each participant per age group (mean ± SD). (B) Representative SWE confidence map with corresponding stiffness measurement from one ovary from one participant.

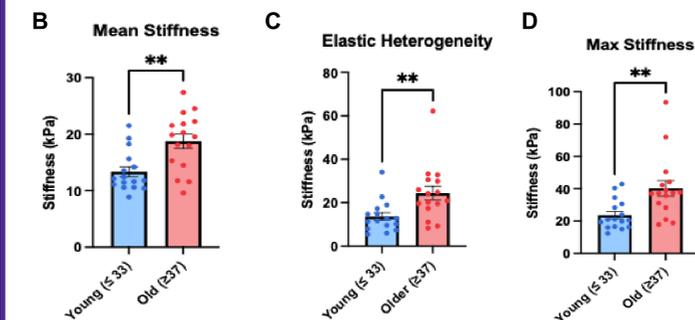
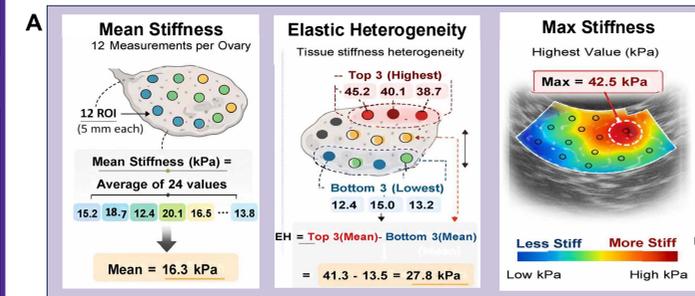


Figure 4. Older age is associated with increased ovarian stiffness. (A) Diagrams of each stromal stiffness parameter calculation. Ovarian stiffness parameters by age group; (B) Mean (C) Elastic heterogeneity and (D) Max stiffness; n=16 per age group, SD± SEM.

Table 2. Multivariable regression analysis reveals positive correlation between “older age” and ovarian stiffness parameters, independent of AMH and BMI.

Mean Stiffness			
Characteristic	Estimate	95% CI	p-value
Age (Young/Old)	7.8	4.1 to 11.5	<0.001*
AMH	0.7	-0.4 to 1.8	0.18
BMI	-0.7	-1.4 to -0.02	0.04*
Elastic Heterogeneity			
Characteristic	Estimate	95% CI	p-value
Age (Young/Old)	14.6	5.8 to 23.4	<0.01*
AMH	0.2	-2.5 to 2.8	0.9
BMI	-1.8	-3.4 to -0.2	0.03*
Maximum Stiffness			
Characteristic	Estimate	95% CI	p-value
Age (Young/Old)	21.6	8.6 to 34.6	<0.01*
AMH	0.2	-3.7 to 4.1	0.92
BMI	-2.4	-4.8 to 0.03	0.05

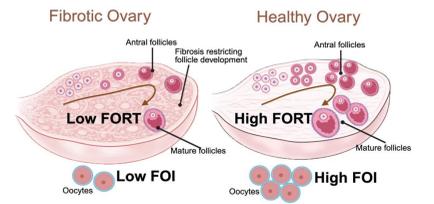
Ovarian Stiffness and ART Performance Indicators

Table 3. Increased mean ovarian stiffness is independently associated with reduced ovarian response and follicular efficiency during ART

Total Oocytes Retrieved			
Characteristic	Estimate	95% CI	p-value
Mean Stiffness	-0.72	-1.5 to -0.03	0.04*
Age (Young/Old)	3.29	-5.6 to 11.9	0.42
AMH	4.99	2.9 to 7.0	<0.0001*
BMI	-0.79	-2.1 to 0.5	0.23
Mature Oocytes Retrieved			
Characteristic	Estimate	95% CI	p-value
Mean Stiffness	-0.61	-1.2 to -0.04	0.04*
Age (Young/Old)	3.60	-3.3 to 10.5	0.29
AMH	3.96	2.3 to 5.6	<0.0001
BMI	-0.69	-1.8 to 0.4	0.19

*Follicular Output Rate (FORT)=
Follicles >15 mm at trigger / AFC

**Follicle-to Oocyte Index (FOI)=
Total oocytes retrieved / AFC



Follicular Output Rate (FORT)*			
Characteristic	Estimate	95% CI	p-value
Mean Stiffness	-2.84	-5.6 to -0.1	0.046*
Age (Young/Old)	34.25	0.001 to 68.5	0.050
AMH	2.77	-5.5 to 11.0	0.50
BMI	-1.10	-6.4 to 4.2	0.67
Follicle-to-Oocyte Index (FOI)**			
Characteristic	Estimate	95% CI	p-value
Mean Stiffness	-5.47	-10.2 to -0.7	0.03*
Age (Young/Old)	55.68	-2.9 to 114.2	0.06
AMH	12.61	-1.4 to 26.7	0.08
BMI	-2.57	-11.6 to 6.4	0.56

Conclusions

- The ovary becomes more stiff and heterogenous with age.
- SWE is the **first noninvasive tool** to quantify human ovarian stiffness.
- Mean ovarian stiffness correlates with the number of mature oocytes retrieved, supporting its potential as a predictive biomarker for ART outcomes.
- Ongoing studies will integrate biologic aging indices (in blood and follicular fluid) in these participants to validate ovarian stiffness as a biomarker of reproductive aging
- Future directions will examine the association ovarian stiffness and ART response, embryo development and live birth outcomes.

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