College of Human Medicine
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Sex Differences in Paradoxical Vocal Fold Motion: Is Estrogen the Missing Link?

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Clinical Vignette

23-year-old female collegiate rower with a prior diagnosis of exercise-induced asthma and normal PFTs presented with recurrent episodes of breathing distress during intense exercise.

🔪 After treadmill exertion to elevate heart and respiratory rates and provoke symptoms, flexible laryngoscopy demonstrated inappropriate inspiratory vocal fold adduction, confirming PVFM.

♀Considering the predominance of female patients with PVFM, could estrogen play a role in disease susceptibility?

Background & Significance

What is PVFM?

🫁 **Paradoxical vocal fold motion (PVFM)**, also known as vocal cord dysfunction or inducible laryngeal obstruction, is a functional airway disorder characterized by inappropriate inspiratory vocal fold adduction, leading to episodic upper airway obstruction.

🚨 Because symptoms overlap with asthma, PVFM is frequently misdiagnosed, resulting in ineffective bronchodilator therapy.

A Striking Clinical Pattern!

- **70–80%** of PVFM patients are female, with female-to-male ratios of 2:1 to 3:1
- The biological explanation for female predominance remains unclear ❗
- Current proposed mechanisms do not fully explain the strong sex distribution

Current Treatment

🎯 Speech-Language Pathology (SLP) – Guided Respiratory Retraining

Significance

💡 Understanding whether estrogen exposure contributes to PVFM could:

- Clarify disease pathophysiology
- Identify hormonally mediated subgroups
- Improve diagnostic accuracy
- Inform individualized management strategies

PICO ❓

In female patients, does standard or higher estrogen exposure increase likelihood or severity of paradoxical vocal fold motion compared with lower and/or avoiding estrogen exposure?

Literature Search Strategy

📚 Database: PubMed (MEDLINE)

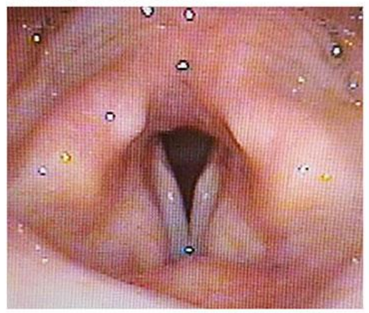
🔑 Search Terms and 🔗 Boolean Strategy
("paradoxical vocal fold motion" OR "vocal cord dysfunction" OR "inducible laryngeal obstruction")
AND
(estrogen OR "menstrual cycle" OR pregnancy OR contraception)

⚙️ Filters Applied
Publication date: 1980 to present
Article types: Clinical studies, physiologic studies, reviews

Figure 1. Normal Vocal Cord Function During Inspiration



Figure 2. Paradoxical Adduction of Vocal Cords During Inspiration



Vocal cords showing the loss of available airflow capability; this motion can vary in severity.

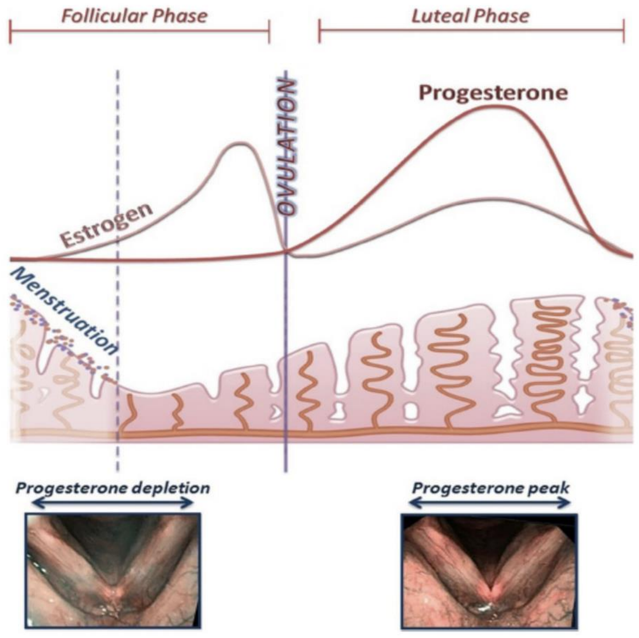


Figure 3. Different events of the menstrual cycle and corresponding laryngeal changes as seen by narrow band imaging

Search Results

Study ID	Study Aim	Study Design	Population	Intervention	Outcomes Measured	Results
Forrest et al., 2012	Classify PVFM via scope; assess treatment response	Prospective observational cohort	~50 adult ENT patients with PVFM; majority female	Speech therapy / respiratory retraining	Symptom change; scope patterns	Significant sx improvement with behavioral therapy; female predominance observed
Newman et al., 2000	Determine ER/PR expression in vocal folds	Immunohisto-chemical tissue study	Normal adult vocal fold specimens	ER and PR staining	Receptor presence/ localization	ER and PR identified in epithelium and glandular structures
Abitbol et al., 1999	Evaluate menstrual cycle effects on voice	Prospective physiologic voice study	Premenopausal women; non-PVFM	Voice/acoustic analysis across cycle phases	Edema, mucosal pliability, F0	Low-estrogen phases associated with increased edema and measurable acoustic changes

Conclusion

Emerging evidence suggests the larynx is hormonally responsive:

🔬 Estrogen and progesterone receptors are present in normal vocal fold tissue

🔬 Vocal fold edema, mucosal pliability, and acoustic parameters vary across the menstrual cycle

🔬 Postmenopausal atrophy improves with hormone therapy

🔬 Estrogen modulates airway sensory receptors involved in laryngeal hypersensitivity

Together, these findings suggest estrogen may influence vocal fold biomechanics and airway reflex sensitivity — both central to PVFM pathophysiology.

Limitation: The absence of randomized controlled trials limits the ability to establish causality and reduces the overall strength of evidence guiding clinical recommendations.

References

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