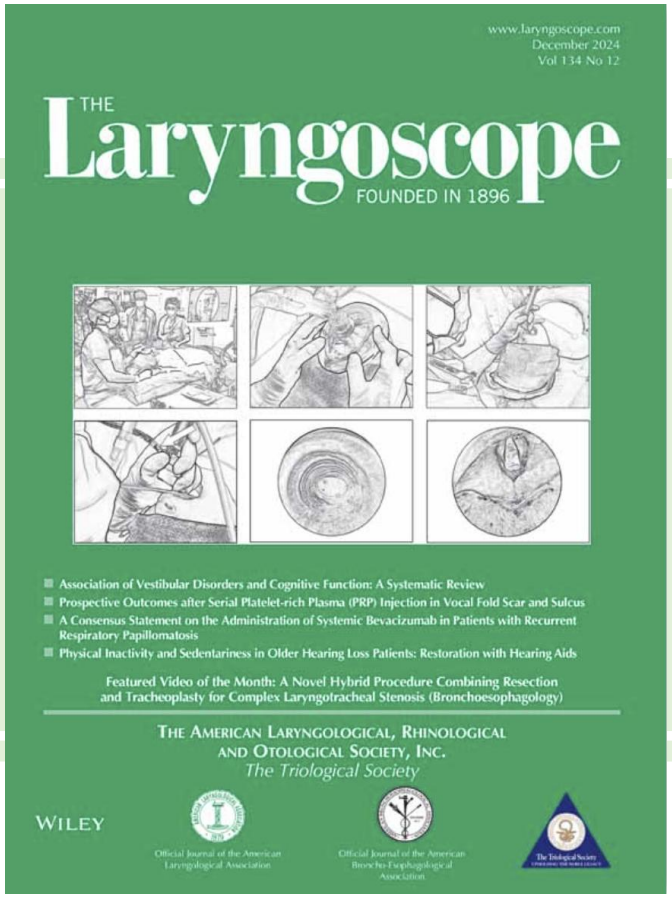

2024 journal Impact factor: 2.0

Prospective Outcomes After Serial Platelet-Rich Plasma (PRP) Injection in Vocal Fold Scar and Sulcus

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Introduction- Superficial lamina propria (SLP) disorders

- **Vocal Fold Scar**
  - Fibrous tissue deposition in the SLP after injury
- **Vocal Fold Sulcus**
  - SLP layer deficiency causing epithelial invagination at the vocal fold's free edge.
- Both disrupt SLP structure, resulting in **abnormal mucosal wave, glottic insufficiency, and dysphonia.**

Introduction- SLP Structure and Function

- SLP contains organized extracellular matrix proteins (ECMPs), including type III collagen, elastin, reticular collagen fibrils, hyaluronic acid (HA), fibronectin, and proteoglycans.
- These components **determine vocal fold pliability and viscosity**, critical for **vibration**.

Introduction- Treatment Challenges

- Difficulty in reconstructing SLP's complex structure and function.
- Traditional surgeries may cause inflammation, remodeling, or additional scarring, failing to adequately improve acoustic, aerodynamic, auditory-perceptual, or stroboscopic outcomes.
- Current treatments are largely experimental, with no method fully restoring SLP structure or function.

Introduction- Platelet-Rich Plasma (PRP)

- **PRP Characteristics**
  - Autologous high-concentration platelet sample rich in growth factors, cytokines, chemokines, and fibrinogen.
  - Promotes tissue regeneration in fields like hair restoration, skin rejuvenation, and scar treatment via angiogenesis and new collagen formation.

→ Potential in vocal cord disorders that have SLP and collagen deficiency

Introduction- Existing Literature

- Limited studies on PRP for vocal fold disorders, with few exploring its potential for scar and sulcus.
- **No prospective, multi-blinded rater studies have evaluated auditory-perceptual or videostroboscopic outcomes.**

Introduction- Study Objectives

- A **prospective cohort study with blinded analysis** across **USC Keck School of Medicine and UCLA David Geffen School of Medicine**
- To evaluate the results **after serial PRP injections**
  - **short-term voice**
  - **Videostroboscopic**
  - **patient-reported outcomes**

Introduction- Study Objectives

- **Expected Outcomes**
  1. Post-serial PRP improvements
     - Voice Handicap Index(VHI-10)
     - Vocal Fatigue Index (VFI)
     - Dyspnea Index (DI)
     - Auditory-perceptual measures
     - Videostroboscopic findings
  2. Treatment response may vary with scar severity

Materials and Methods- Inclusion Criteria

- **Age ≥18 years + diagnosed with vocal fold scar or sulcus**
- Prior interventions or voice therapy did not exclude participation
- Total: 15 subjects

TABLE I.
Demographic Data for the Prospective Platelet-Rich Plasma Cohort.

Variable	Frequency (%)/Mean (SD)
Age (years)	64.2 (12.5) range = 44–81
Gender	12 (80.0%)
Male	3 (20.0%)
Female	
Severity	8 (53.3%)
Mild	3 (20%)
Moderate	4 (26.7%)
Severe	
Side	9 (60%)
Left	6 (40%)
Right	

Materials and Methods- Protocol

- **Baseline Assessment**
  - Standardized voice recordings: CAPE-V sentences
  - Videostroboscopy
  - Patient-Reported Outcome Measures (PROMs): VHI-10, VFI, DI

Materials and Methods- Protocol

- **PRP preparation**
  - 11 mL blood sample centrifuged at 3500 rpm for 10 minutes, with autologous conditioned plasma (ACP) transferred to 1 mL or 3 mL syringes.

    → might be 1.8× concentration fold
  - **Four injections, one month apart**

2 Ways to Collect Eclipse PRP

High & Lower Concentration Methods

Cell Count & Growth Factor Statistics

Eclipse PRP	
Platelet concentration fold*	1.8x
RBC (10^6/ul)	0.0
WBC (10^3/ul)	0.2
Granulocytes %	8.5
Mononuclear cells %	86.2

*An average of several independent, validated tests using the collection method outlined in this guide for the 11mL Eclipse PRP tube without the removal of PPP.

Eclipse PRP HC	
Platelet concentration fold*	3.2x
RBC (10^6/ul)	0.0
WBC (10^3/ul)	0.2
Granulocytes %	8.5
Mononuclear cells %	86.2

*STD DEV. Mean concentration using 22ml tube, removing 6-7ml of platelet poor plasma (PPP) in patients with whole blood platelet counts ranging from 169,000 to 356,000 per microliter.

We recommend using the 22mL kit for the High Concentration Method.

Use the 11mL tube for the lower concentration method.

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1. Rappl LM et al., Int Wound J 2011; 8:187-195.
2. Weibrich G et al., Bone 2004; 34:665-671.
3. Yamaguchi R et al., J Surg Res 2012; 173(2): 258-266.
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6. Belcher et al., Antioxidants & Redox Signaling 2010; 12(2): 233-48.
7. Kumar et al., Toxicol lett 2005; 157 (3): 175-188.
8. Tidball, Am J Physiol Regul Integr Comp Physiol 2005; 288: R345-353.
9. Muylle, Transfusion 1993; 33(3): 195-199.
10. Mei-Dan, Br J Sports Med 2010; 44: 618-619.

ECLIPSE PRP®

Materials and Methods- Injection Technique

- **Injection Method**
  - **Transcervical thyrohyoid or transnasal approach** into the **subepithelial plane**
- **Dosage**
  - **Typically require 1 mL**

    (0.5-1.5 mL)
  - unilateral on the affected side

Materials and Methods- Evaluations

- **Blinded stroboscopic evalution**
  - 15 participants recorded **pre-injection and one month post-fourth injection**, with 2 repeated (17 pairs).
  - 2 external laryngologists rated **pre-injection severity (mild/moderate/severe), mucosal lateral wave excursion, glottic closure (complete/incomplete),** and selected **perceptually better exam.**

Materials and Methods- Evaluations

- **Blinded voice evalution**
  - Pre- and post-serial injection recordings, randomized and blinded, with 2 repeated.
  - 2 speech-language pathologists **rated CAPE-V sentence severity (out of 100)** and **select perceptually better recordings.**

VHI-10

- Assess the psychosocial and functional impact of voice disorders
- Scored from 0–4 (higher scores indicate greater impairment)

Rosen CA, Lee AS, Osborne J, Zullo T, Murry T. Development and validation of the voice handicap index-10. *Laryngoscope*. 2004;114(9):1549-1556. doi:10.1097/00005537-200409000-00009

VHI-10

Voice Handicap Index-10.

My voice makes it difficult for people to hear me.	0	1	2	3	4
People have difficulty understanding me in a noisy room.	0	1	2	3	4
My voice difficulties restrict personal and social life.	0	1	2	3	4
I feel left out of conversations because of my voice.	0	1	2	3	4
My voice problem causes me to lose income.	0	1	2	3	4
I feel as though I have to strain to produce voice.	0	1	2	3	4
The clarity of my voice is unpredictable.	0	1	2	3	4
My voice problem upsets me.	0	1	2	3	4
My voice makes me feel handicapped.	0	1	2	3	4
People ask, “What’s wrong with your voice?”	0	1	2	3	4

Rosen CA, Lee AS, Osborne J, Zullo T, Murry T. Development and validation of the voice handicap index-10. *Laryngoscope*. 2004;114(9):1549-1556. doi:10.1097/00005537-200409000-00009

VFI

- VFI-1 (fatigue and voice limitation)
- VFI-2 (pain/discomfort)
- VFI-3 (improvement with rest)
- Scored from 0–4 (higher scores indicate greater fatigue)

Nanjundeswaran C, Jacobson BH, Gartner-Schmidt J, Verdolini Abbott K. Vocal Fatigue Index (VFI): Development and Validation. *J Voice*. 2015;29(4):433-440. doi:10.1016/j.jvoice.2014.09.012

VFI-1

Part 1					
1. I don't feel like talking after a period of voice use	0	1	2	3	4
2. My voice feels tired when I talk more	0	1	2	3	4
3. I experience increased sense of effort with talking	0	1	2	3	4
4. My voice gets hoarse with voice use	0	1	2	3	4
5. It feels like work to use my voice	0	1	2	3	4
6. I tend to generally limit my talking after a period of voice use	0	1	2	3	4
7. I avoid social situations when I know I have to talk more	0	1	2	3	4
8. I feel I cannot talk to my family after a work day	0	1	2	3	4
9. It is effortful to produce my voice after a period of voice use	0	1	2	3	4
10. I find it difficult to project my voice with voice use	0	1	2	3	4
11. My voice feels weak after a period of voice use	0	1	2	3	4

Nanjundeswaran C, Jacobson BH, Gartner-Schmidt J, Verdolini Abbott K. Vocal Fatigue Index (VFI): Development and Validation. *J Voice*. 2015;29(4):433-440. doi:10.1016/j.jvoice.2014.09.012

VFI-2

Part 2					
12. I experience pain in the neck at the end of the day with voice use	0	1	2	3	4
13. I experience throat pain at the end of the day with voice use	0	1	2	3	4
14. My voice feels sore when I talk more	0	1	2	3	4
15. My throat aches with voice use	0	1	2	3	4
16. I experience discomfort in my neck with voice use	0	1	2	3	4

Nanjundeswaran C, Jacobson BH, Gartner-Schmidt J, Verdolini Abbott K. Vocal Fatigue Index (VFI): Development and Validation. *J Voice*. 2015;29(4):433-440. doi:10.1016/j.jvoice.2014.09.012

VFI-3

Part 3					
17. My voice feels better after I have rested	0	1	2	3	4
18. The effort to produce my voice decreases with rest	0	1	2	3	4
19. The hoarseness of my voice gets better with rest	0	1	2	3	4

Nanjundeswaran C, Jacobson BH, Gartner-Schmidt J, Verdolini Abbott K. Vocal Fatigue Index (VFI): Development and Validation. *J Voice*. 2015;29(4):433-440. doi:10.1016/j.jvoice.2014.09.012

DI

- Evaluating dyspnea's impact on daily life
- Scored from 0–4 (higher scores indicate greater severity)

Dyspnea Index (DI)*

Name: _____

Date: ___/___/___

Date of Birth: ___/___/___

These are some symptoms that you may be feeling. Please circle the response that indicates how frequently you experience the same symptoms (0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, 4 = always)

1. I have trouble getting air in.	0	1	2	3	4
2. I feel tightness in my throat when I am having my breathing problem.	0	1	2	3	4
3. It takes more effort to breathe than it used to.	0	1	2	3	4
4. Changes in weather affect my breathing problem.	0	1	2	3	4
5. My breathing gets worse with stress.	0	1	2	3	4
6. I make sound/noise breathing in.	0	1	2	3	4
7. I have to strain to breathe.	0	1	2	3	4
8. My shortness of breath gets worse with exercise or physical activity.	0	1	2	3	4
9. My breathing problem makes me feel stressed.	0	1	2	3	4
10. My breathing problem causes me to restrict my personal and social life.	0	1	2	3	4

Gartner-Schmidt JL, Shembel AC, Zullo TG, Rosen CA. Development and validation of the Dyspnea Index (DI): a severity index for upper airway-related dyspnea. *J Voice*. 2014;28(6):775-782. doi:10.1016/j.jvoice.2013.12.017

CAPE-V

- A set of six standardized English sentences for auditory-perceptual evaluation of voice quality in dysphonia.
- Overall severity, roughness, breathiness, strain, pitch, loudness
- Scored from 0–100

Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V)

Voice Sample #:_____

The following parameters of voice quality will be rated upon completion of the following tasks:
1. Sustained vowels, /a/ and /i/ for 3-5 seconds duration each.
2. Sentence production:
   a. The blue spot is on the key again.
   b. How hard did he hit him?
   c. We were away a year ago.
   d. We eat eggs every Easter.
   e. My mama makes lemon muffins.
   f. Peter will keep at the peak.
3. Spontaneous speech in response to: "Tell me about your voice problem." or "Tell me how your voice is functioning."

Legend: C = Consistent I = Intermittent
MI = Mildly Deviant
MO =Moderately Deviant
SE = Severely Deviant

			SCORE
Overall Severity	MI MO SE	C I	/100
Roughness	MI MO SE	C I	/100
Breathiness	MI MO SE	C I	/100
Strain	MI MO SE	C I	/100
Pitch	(Indicate the nature of the abnormality): _____ MI MO SE	C I	/100
Loudness	(Indicate the nature of the abnormality): _____ MI MO SE	C I	/100
_____	MI MO SE	C I	/100
_____	MI MO SE	C I	/100

COMMENTS ABOUT RESONANCE: NORMAL OTHER (Provide description):_____

ADDITIONAL FEATURES (for example, diplophonia, fry, falsetto, asthenia, aphonia, pitch instability, tremor, wet/gurgly, or other relevant terms):

Clinician:_____

Kempster GB, Gerratt BR, Verdolini Abbott K, Barkmeier-Kraemer J, Hillman RE. Consensus auditory-perceptual evaluation of voice: development of a standardized clinical protocol. *Am J Speech Lang Pathol*. 2009;18(2):124-132. doi:10.1044/1058-0360(2008/08-0017)

CAPE-V sentences

2. Sentence production:
   a. The blue spot is on the key again.
   b. How hard did he hit him?
   c. We were away a year ago.
   d. We eat eggs every Easter.
   e. My mama makes lemon muffins.
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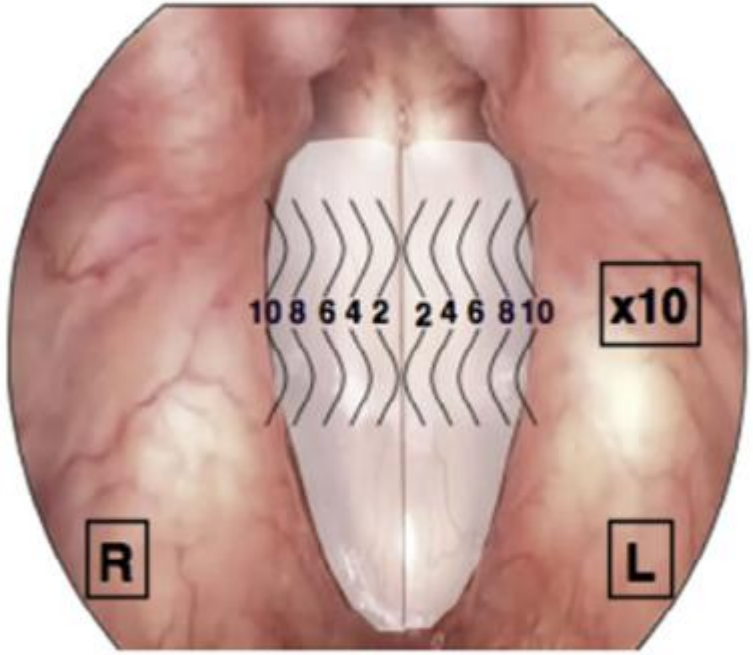
Vibratory Assessment with Laryngeal Imaging (VALI) Scale

Glottal Closure	
Definition:	Appearance of glottis during the most closed portion of the glottal cycle
Rating:	Rate at normal pitch and loudness.

Poburka BJ, Patel RR, Bless DM. Voice-Vibratory Assessment With Laryngeal Imaging (VALI) Form: Reliability of Rating Stroboscopy and High-speed Videoendoscopy. *J Voice*. 2017;31(4):513.e1-513.e14. doi:10.1016/j.jvoice.2016.12.003

Vibratory Assessment with Laryngeal Imaging (VALI) Scale

Mucosal Wave	
Definition:	Magnitude of movement of the muc. membrane.
Rating:	Rate at normal pitch and loudness.



Right:_____ Left:_____

F0:_____ (Hz.)

Poburka BJ, Patel RR, Bless DM. Voice-Vibratory Assessment With Laryngeal Imaging (VALI) Form: Reliability of Rating Stroboscopy and High-speed Videoendoscopy. *J Voice*. 2017;31(4):513.e1-513.e14. doi:10.1016/j.jvoice.2016.12.003

Results-Patient-Reported Outcome Measures (PROMs)

- **Adjusted mean reduction(unrelated to age or severity)**
  - **VHI-10:** ↓8.67 points
  - **VFI-1:** ↓ 10.5 points
  - **DI:** ↓ 6.26 points

TABLE II.
Patient Reported Outcome Measures Pre- and Post-Serial Platelet-Rich Plasma Injection.

Variable	Pre-injection	Post-injection	*p*-value
VHI-10 ($n = 15$)	30.0 (15.0)	20.0 (21.0)	**0.007***
VFI-1 ($n = 10$)	26.0 (19.5)	11.0 (17.2)	**0.020***
VFI-2 ($n = 10$)	2.5 (5.8)	0.0 (0)	0.104
VFI-3 ($n = 10$)	8.5 (7.8)	1.0 (7.5)	0.063
DI	10.0 (18.0)	3.0 (7.3)	**0.024***

Scores represent median (IQR). *p*-values reflect adjustments for age and severity of scar. Bolded values represent p value < 0.05.
*Significant at $p < 0.05$ (Wilcoxon signed rank test).

Results-Auditory-Perceptual Measures (CAPE-V)

- **Adjusted mean reduction(unrelated to age or severity)**: ↓ 18.8 points (95% CI [0.32–0.03], p=0.036)
- **Higher age associated with higher CAPE-V scores**

  (0.02, 95% CI [0.01–0.03], p=0.026)

Results-Auditory-Perceptual Measures (CAPE-V)

TABLE III.
Voice Quality and Videostroboscopy Perceptual Rating Stratified by Severity.

Variable	Severity	Rater		Average
		Rater A ($n = 15$)	Rater B ($n = 15$)	
Post-injection voice rated as better	All exams	10/15 (66.7%)	12/15 (80%)	73.4%
	Mild	7/8 (87.5%)	5/8 (62.5%)	75.0%
	Moderate	1/3 (33.3%)	3/3 (100%)	66.7%
	Severe	2/4 (50.0%)	4/4 (100%)	75.0%

Results-Videostroboscopic Assessment

- Mucosal wave magnitude increased (**median 2.0 → 4.0**,p=0.026), but remained below normal (<5 considered stiff).

TABLE IV.
Change in Glottic Closure After Serial Platelet-Rich Plasma Injection.

Variable		Rater C (n = 15)	Rater D (n = 15)
Glottic Closure	Pre-injection videostroboscopy rated as incomplete closure	8/15 (53.3%)	13/15 (86.7%)
	Changed from incomplete to complete	4/8 (50%)	5/13 (38.5%)

Results-Videostroboscopic Assessment

TABLE III.
Voice Quality and Videostroboscopy Perceptual Rating Stratified by Severity.

Post-injection videostroboscopy rated as better	All exams	10/15 (66.7%)	7/15 (46.7%)	56.7%
	Mild	6/8 (75.0%)	2/8 (25.0%)	50.0%
	Moderate	2/3 (66.7%)	2/3 (66.7%)	66.7%
	Severe	2/4 (50.0%)	3/4 (75.0%)	62.5%

Discussion-Study Findings

	Expected Outcomes
VHI-10	Improvements
Vocal Fatigue Index (VFI)	
Dyspnea Index (DI)	
Auditory-perceptual measures	
Videostroboscopic findings	
Scar severity and outcomes	Outcome may vary with scar severity

Discussion-Study Findings

Expected Outcomes	Final outcome
VHI-10	PROM significant reductions
Vocal Fatigue Index (VFI)	
Dyspnea Index (DI)	
Auditory-perceptual measures	Objective blinded data high variability mismatches with PROM
Videostroboscopic findings	
Scar severity and outcomes	No correlation

Discussion-Study Findings

TABLE III. Voice Quality and Videostroboscopy Perceptual Rating Stratified by Severity.

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Discussion-Study Findings

Voice

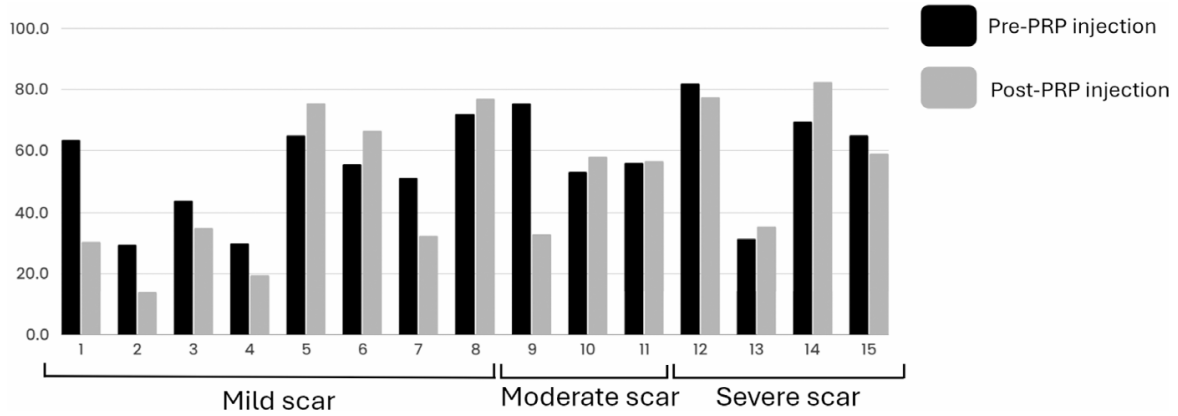


Fig. 2. Change in auditory-perceptual measures of voice using the CAPE-V assessments in each patient after serial platelet-rich plasma injection, by scar severity. Highlights average overall perceived severity ofvoice recording (out of 100) as rated by blinded voice specializingspeech-language pathologists, pre and post PRP injection, shown by scarseverity. Higher numbers reflect worse dysphonia.

Videostroboscopic

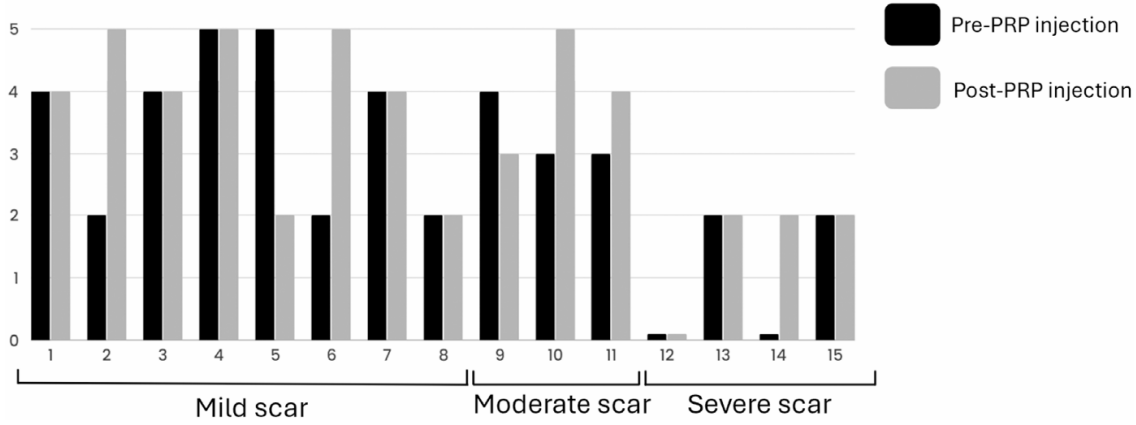
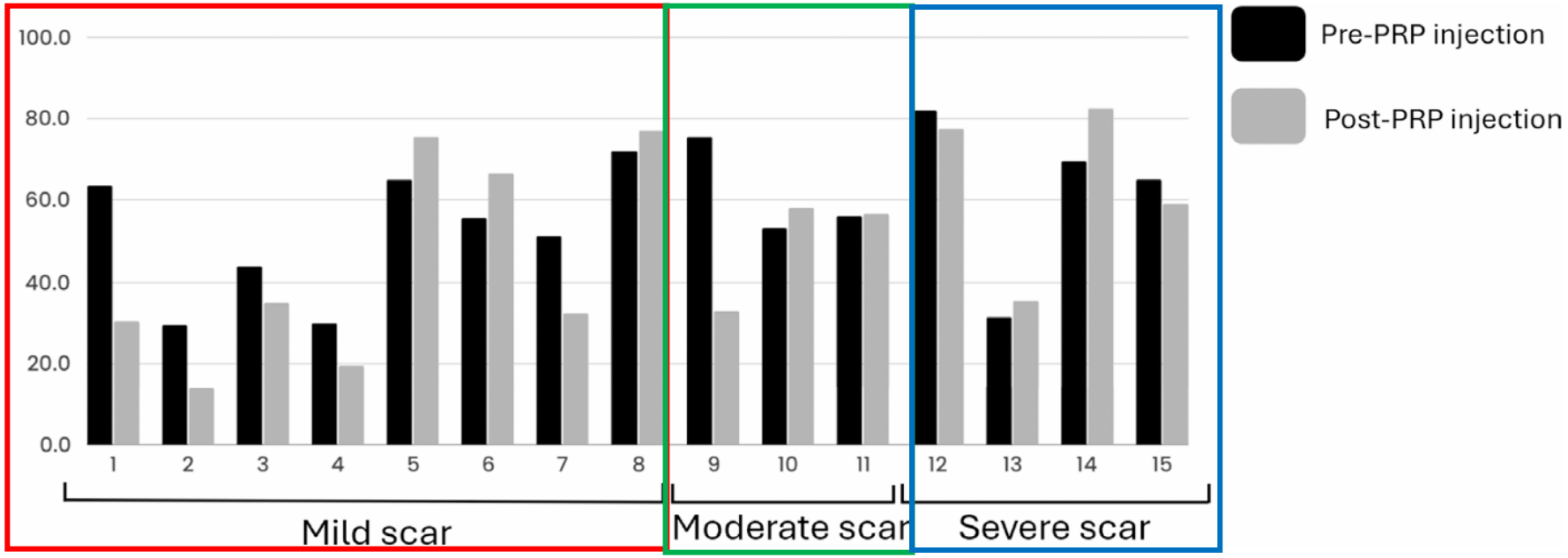


Fig. 3. Change in Vibratory Assessment with Laryngeal Imaging (VALI) magnitude of movement of the mucosal membrane in each patient after serial platelet-rich plasma injection, by scar severity. Highlights average mucosal wave onvideostroboscopy, as rated by blinded laryngologists, pre and post PRPinjection, shown by scar severity. Lower numbers reflect less mucosalpliability.

Discussion-Study Findings



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Discussion-PRP Advantages and Limitations

- Widely used and safe in vocal folds, easily integrated into practice with simple, minimally invasive injections.
- Positive but variable results with mixed objective outcomes
- Study limited to short-term results, unable to assess durability.

Conclusion

- Serial PRP injections improved patient-reported outcomes and auditory-perceptual measures
- Videostroboscopic mucosal wave magnitude results were more variable


SEE YOU