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A Systematic Review on Surgical Treatments for Sulcus Vocalis and Vocal Fold Scar

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Objectives/Hypothesis: Vocal fold sulcus and scars are benign vocal fold lesions that present as a challenge to the laryngologist. A number of different surgical techniques have been proposed, aiming at restoring the lamina propria (LP), closing the glottal gap, or both. This study aimed to provide a systematic review of surgical treatment for sulcus and scar and to propose a new classification for these techniques.

Study Design: A literature search using MEDLINE and Google Scholar through August 2020.

Methods: Data on study design were retrieved and outcomes were classified as acoustic, aerodynamic, self-reported, perceptual, and stroboscopic. Methodological quality was assessed using the MINORs criteria. Each technique was classified as direct, indirect, or combined.

Results: Our search included 31 studies with a total of 617 patients. Direct techniques included dissection, graft interposition, or LP regeneration/scar degradation while indirect techniques aimed for glottal gap closure. Only one article performed a comparison between different types of techniques and only eight studied the five types of outcomes. No superiority of any technique was noted in our analysis. Self-reported outcomes were the most frequently improved.

Conclusions: There seems to not exist a one-fits-all treatment for this clinical picture and no clear decision-making pattern. A recent trend toward sequential approaches, starting with less invasive procedures, can be observed.

Key Words: Sulcus vocalis, vocal scar, glottal gap, mucosal wave, surgical techniques.

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INTRODUCTION

Vocal fold sulcus and scars are benign vocal fold lesions with fibrotic changes to the vocal fold mucosa.[1] Vocal fold sulcus represents an indentation parallel to the free edge of the vocal fold, in which the epithelium invaginates into the other layers of the lamina propria (LP).[2] These may be divided into three types as proposed by Ford[3]: type I is a physiological sulcus, whereas types II and III are pathologic. Type II, also known as *sulcus vergeture*, represents as a groove with atrophy of the superficial layer of the lamina propria (SLP). In type III, or sulcus vocalis (SV), there is an absence of the SLP with epithelium adherent to the vocal ligament or vocalis muscle.[4] Vocal fold scar present with deposition of fibrous tissue within the LP.

These two entities modify the pliability of the mucosa, causing an impaired mucosal wave with glottic incompetence during phonation,[5] bowing of the vocal folds, and excessive ventricular fold adduction.[4,6,7] Patients present with a variable degree of hoarseness, associated with vocal fatigue, breathiness, and vocal strain.[8]

The heterogeneity in clinical appearance makes the diagnosis and treatment of these entities a challenge.[4] Many different surgical treatments have been proposed, with no current gold standard.[3,9] These treatments may focus on glottal gap closure, direct treatment of the lesion, or both. We can, therefore, divide our treatments into "direct" treatments to the sulcus, which will endeavor to improve the mucosal wave as well as possibly correct some degree of glottic gap, and "indirect" treatments, which focus mainly on the correction of glottic gap, not addressing the LP defect. In many studies, combinations of both of these treatments are used to enhance good results.

The purpose of the current study was to answer the following research question "In adults with vocal fold sulcus or scar, are there different outcomes for patients treated with direct approaches, indirect approaches or a combination of both, in terms of perceptual, acoustic, aerodynamic, self-reported, and stroboscopic outcomes?" As a secondary objective, we propose a new classification for these techniques.

METHODS

Protocol and Registration

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[10] The following PICO question was formulated (Population, Intervention, Comparison, Outcome): "In adults

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with vocal fold sulcus or scar, are there different outcomes for patients treated with direct approaches, indirect approaches or a combination of both, in terms of perceptual, acoustic, aerodynamic, self-reported, and stroboscopic outcomes?" Separate forms for data collection and quality assessment were produced, which were not published or registered.

Data Collection Process

Database search included MEDLINE and Google Scholar. MEDLINE search query was: ("sulcus vocalis"[tiab] OR "vocal fold sulcus"[tiab] OR "sulcus vergeture"[tiab] OR "vocal scar"[tiab] OR "vocal fold scar"[tiab] OR "vocal cord scar"[tiab] OR "vocal fold atrophy"[tiab]) AND ("treatment"[tiab] OR "surgery"[tiab] OR "Surgical Procedures, Operative"[mh]). Figure 1 outlines the steps taken: following the elimination of the duplicate entries, 324 abstracts were reviewed. The full text of the remaining citations was obtained and reviewed in full. Inclusion criteria included the following: 1) vocal scar and/or vocal sulcus surgical treatment; 2) human studies; 3) English, Dutch, French, Spanish, Italian, or Portuguese language; and 4) full-text articles. Review articles and case reports were excluded. Following this step, 63 full-text articles were analyzed for eligibility. These were read in full by two authors (N.M., G.D.). Each author then independently decided whether a study should be included or excluded from the study. There were no cases of disagreement between the authors regarding which studies met inclusion criteria. Noneligible studies were excluded—specifically, those that did not provide data on treatments or outcomes and those that did not distinguish between patients with sulcus/scar and other benign vocal fold lesions. To make sure that studies were not missed, the references of all of the identified full-text articles were reviewed to try to further identify any eligible studies. The last search was completed in August 2020.

Data Extraction and Statistical Analysis

One researcher extracted the data from articles and another checked this data. The following data were recorded: author/yr, number of patients, mean age, surgical treatment, perceptual outcomes, aerodynamic outcomes, acoustic outcomes, self-reported outcomes, stroboscopic outcomes, and complications. Different surgical treatment procedures were compared. A descriptive analysis of the outcomes was performed. Statistical analysis was conducted with the Cochrane RevMan software. Clinical heterogeneity was analyzed by two authors (N.M., G.D.), with meta-analysis only conducted where both agreed that study participants, interventions, and outcomes were sufficiently similar. Statistical heterogeneity was assessed therefore using the Chi-squared statistic. A P value of $<.05$ was the cut-off considered for high heterogeneity.

Risk of Bias in Individual Studies

MINORs criteria were used to evaluate the quality and level of bias.[11] MINORs criteria are a validated instrument to assess for bias among observational studies, especially studies involving surgical intervention. There are two sets of criteria for MINORs criteria: noncomparative studies include eight items; comparative studies include additional four items. Items are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The global maximum score is 16 for noncomparative studies and 24 for comparative studies.

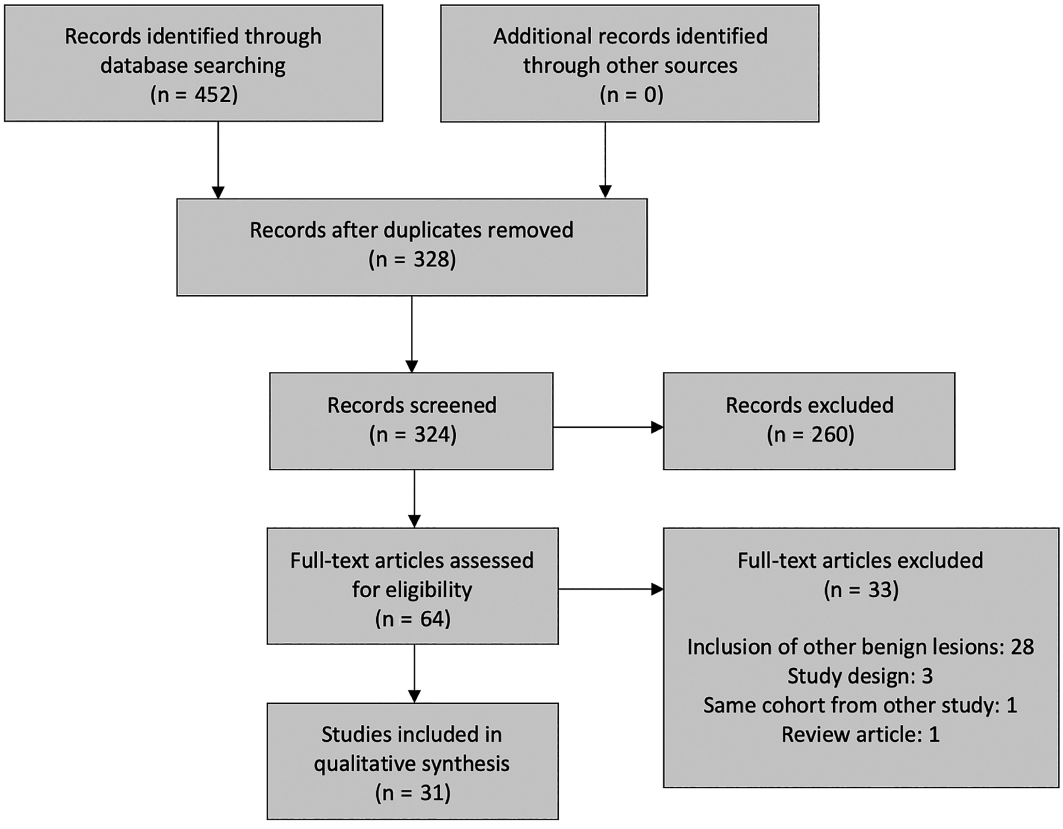

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram with reasons of exclusion.

Each article was assigned a score based on the level of bias. A value of ≥11 was considered to have a low level of bias, where a value of <11 was considered to have a high level of bias.

RESULTS

The techniques described in each article were organized by classification in Table I, according to the principle of treatment. Techniques focusing on the LP of the affected vocal fold were classified as "direct," while glottal gap closure techniques with no intervention in the LP were classified as "indirect."

The main characteristics of these 31 articles included in the analysis are seen in Table II (direct techniques), Table III (indirect techniques), and Table IV (combined techniques). Selection and information bias, lack of uniform reporting, and inclusion of low methodological quality studies configured enough clinical and methodological heterogeneity to prevent a formal meta-analysis.

Publication years of included articles ranged between 1993 and 2020. Four included studies (12.9%) were randomized controlled trials[25–28] (one of them including a placebo arm), one (3.2%)[9] was a quasi-experimental clinical trial, five (16.1%)[22,35–37,41] were prospective cohorts, and the remaining (67.8%) were retrospective cohorts. Fifteen (48.4%) of the included studies had a high level of bias (MINORs score <11 points).

In total, 617 operated patients were included. In four selected studies, other benign vocal fold lesions were included, but it was possible to isolate data for sulcus/scar. Fifteen studies focused solely on sulcus, five studies focused solely on scars, and the remaining included a combination of benign vocal fold pathologies. Eleven studies[12,13,15–17,21–23,32,37,38] included patients <18 years old. Most studies included unilateral and bilateral interventions all together. Three studies[14,19,21] included exclusively unilateral procedures, and five others only bilateral procedures.[20,26,27,33,34]

Sixteen studies[9,16,17,20,22–25,28,32–35,38–40] (51.6%) included follow-ups greater than 6 months, and only in two studies[9,16] (6.5%) follow-up was longer than 1 year, for every patient. Of the 31 articles, 23 (74.2%)[9,13,17,21,24,25,27–30,32–36,39,40] outlined self-reported outcomes, 24 (77.4%)[9,12,17,18,21–25,27,29–41] acoustic outcomes, 20[13,16,18,21–25,27,29–31,33–38,41] (64.5%) aerodynamic outcomes, 22 (71.0%)[9,12,14,17,19,21–31,33–35,38,40,41] perceptual outcomes, and 22 (71.0%)[9,12–19,21–23,25,27–30,32,36–38,40] stroboscopic outcomes. Only eight articles (25.8%)[21–23,25,27,29,30,38] explicitly studied these five domains.

TABLE I.
Tested Treatments in the Included Articles, Separated by Direct or Indirect, According to the Principle of Treatment.

Direct Treatment (MW ± GG)	Indirect Treatment (GG)
Dissection (cold or laser CO_2) ±	Medialization
• Excision	• Injection laryngoplasty (TA muscle)
• Internal section of vocal ligament	• Type I thyroplasty
• Slicing mucosa	
Graft interposition	
• Temporal fascia	
• Autologous fat injection	
• Gray's minithyrotomy	
• Atelocollagen sheet	
• Gelatin sponge	
LP regenaration/scar degradation	
• GCT	
• Collagen	
• Angiolytic lasers (PDL, KTP)	
• FGF, HGF	
• Autologous fibroblasts	
• (Grafts?)	

FGF = fibroblast growth factor; GG = glottal gap; HGF = recombinant hepatocit growth factor; KTP = potassium titanyl phosphate; MW = mucosal wave; PDL = pulsed dye laser.

Direct Treatments

Dissection techniques. Different dissection techniques were the only mainstay of therapy in four of our evaluated papers.[12–15] A 2019 retrospective cohort (n = 16) by Andreadis et al.[15] evaluated the effect of excision without reconstruction on SV type 3. Only stroboscopic outcomes were considered, having a significant improvement in amplitude, mucosal wave, nonvibrating portion, erythema, and vascularity (but not regularity). Gonzalez-Herranz et al. published a retrospective series (n = 35) on microflap with or without fibrin glue, showing a significant improvement in voice handicap index (VHI)-10 and glottal space on closed phase in both groups, with improvement in open phase as well for the fibrin glue group. A slicing mucosa technique was proposed in a retrospective series of 10 patients with SV, by Pontes et al.[12] Nine of the 10 patients had satisfactory results in the studied outcomes. One retrospective series of 12 patients by Filho et al.[13] proposes the transversal sections of the vocal ligament where there was a statistically significant increase of the mean phonatory time (MPT). No complications are described in these studies.

Graft implantation. Seven of the included articles[9,16–21] performed uniquely graft implantation. Temporal fascia was used in five of them. In these studies, aerodynamic, stroboscopic, self-reported, and perceptual outcomes seemed to significantly increase in the postsurgical period, but the acoustic parameters did not achieve statistical significance. Complications described in the articles included extrusion of the graft material,[17,21] herniation of the graft material,[16] and granuloma.[17] Kishimoto et al.[18] used an atelocollagen sheet (n = 6), with variable results, but with an overall improvement in aerodynamic and acoustic parameters. One included study[19] described a specific technique for subepithelial fat grafting, called "Gray minithyrotomy." The study failed to improve VHI-10 as a whole in the group of 12 patients, and improvements in mucosal wave only occurred in seven of the patients. On the other hand, complications were described in five patients, namely neck ecchymosis, wound dehiscence, subcutaneous emphysema with abscess, tongue numbness and taste changes, and aspiration pneumonia.

TABLE II.
Included "Direct Treatment" Studies and Their Characteristics.

Reference	Study Design	Diagnosis	Treatment	n	MINORs	Gender (M:F)	Mean of Age (yr)	Follow-Up	Perceptual	Acoustic	Aerodynamic	Self-reported	Endoscopic
Dissection techniques													
Pontes et al.[12]	Cohort (retrospective)	Sulcus	Slicing mucosa	10	6/16	7:3	23.8	–	B†, Pitch	F0†	–	Vocal fatigue†	GC†, MW†
Filho et al.[13]	Cohort (retrospective)	Sulcus	Internal section of the vocal ligament	12	5/16	1:3	31.5	1 mo	GRB†	–	MPT*	–	GC†, MW†
González-Herranz et al.[14]	Cohort (retrospective)	Sulcus + scar	Microflap	32	16/24	0:1	32.3	6 mo	–	–	–	VHI-10*	GC*, MW*
Andreadis et al.[15]	Cohort (retrospective)	Sulcus	Excision (+ GCT)	13	12/16	5:8	28.9	2 mo	–	–	–	–	GC*, MW*
Graft interposition													
Tsunoda et al.[16]	Cohort (retrospective)	Sulcus	Temporalis fascia	10	10/16	4:1	46.5	3 yr	–	–	MPT*	–	GC*, MW*
Pinto et al.[17]	Cohort (retrospective)	Sulcus	Temporalis fáscia ± fat	32	11/16	15:19	34.8	12 mo	G	Jitt, Shim, F0	–	Self-evaluation*(1–5 scale)	GC†, MW†
Kishimoto et al.[18]	Cohort (retrospective)	Sulcus + scar	Atelocolagen sheet (direct)	6	9/16	1:1	52.3	6 mo	-	Jitt†, Shim†, NHR†	MPT†, MFR†	-	GC†, MW†
Welham et al.[9]	Clinical trial	Sulcus + scar	Temporalis fascia	28	20/24	11:17	54.5	18 mo	GRBAS	Jitt, Shim, SNR, F0	-	VHI-10*	MW
Mallur et al.[19]	Cohort (retrospective)	Sulcus + scar	Gray minithyrotomy	13	9/16	7:5	57.6	6 mo	–	–	–	VHI-10	GC, MW
Karle et al.[20]	Cohort (retrospective)	Sulcus + scar	Temporalis fascia	21	10/16	19:31	–	6 mo	G*R*B*A*S*	–	–	VHI-10* Specific survey*	–
Gonzalez-Herranz et al.[21]	Cohort (retrospective)	Sulcus + scar	Temporalis fascia	10	9/16	–	–	6 mo	G*R*A*S*B	Jitt, Shim, NHR, F0	MPT*S/Z Ratio*	VHI-10*	GC*, MW*
LP regenaration/scar degradation													
Mortensen et al.[22]	Cohort (prospective)	Scar	PDL laser	11	13/16	8:3	60.5	6 mo	–	Jitt, Shim, NHR	MPF*	VHI-30* other survey*	GC*
Hwang et al.[12]	Cohort (prospective)	Sulcus	PDL laser	25	13/16	17:8	37.6	12 mo	G*R*B*	Jitt*, Shim NHR, F0*	MPT, MFR*, Psub*	VHI-30*	GC†, MW†
Park et al.[23]	Cohort (retrospective)	Sulcus	PDL/KTP laser	79	11/16	55:24	41	12 mo	G*R*B*A*S*	Jitt*,Shim*, NHR*, F0*	MPT*, MFR*	VHI-30*	GC†, MW†
Hirano et al.[24]	Cohort (retrospective)	Sulcus + scar	FGF with/without flap elevation	15	17/24	3:2	54	6 mo	G*R*B*A*S*	Jitt, Shim	MPT	VHI-10*	–
Jin Ban et al.[25]	Clinical trial	Scar	FGF	17	11/16	4:13	50.4	12 mo	G*R*B*A*S*	Jitt, Shim, NHR	MPT*	VHI-10*	GC*, MW*
Takeharu et al.[26]	Clinical trial	Sulcus	bFGF	12	10/16	1:1	51.6	3 mo	–	Jitt, Shim, F0*, NHR*	MPT*, MFR	VHI-10*	–
Hirano et al.[27]	Clinical trial	Sulcus + scar	dHGF	18	Rand	1: 5/1 2: 1/5 3: 1/5	1: 38.2 + 12.5 2: 45.7 + 14.9 3: 44.7 + 10.5	6 mo	G*R*B*A*S*	Jitt	MPT	VHI-10*	GC*, MW*

(Continues)

TABLE II.
Continued

Reference	Study Design	Diagnosis	Treatment	n	MINORs	Gender (M:F)	Mean of Age (yr)	Follow-Up	Perceptual	Acoustic	Aerodynamic	Self-reported	Endoscopic
Ma et al.[28]	Clinical trial	Scar	Autologous fibroblasts	8	Rand	5:3	53	12 mo	G	–	–	VHI-30 other survey*	GC*MW*
Young et al.[29]	Cohort (retrospective)	Scar	GCT injection	25	11/16	12:13	53.3	3 mo	GRBAS	Jitt, F0*	MPT* Psub	VHI-30	GC*, MW
Martínez Arias et al.[30]	Cohort (retrospective)	Scar	Collagen injection + laser CO_2	12	5/16	1:5	45.3	2 mo	G*	F0	MPT*	VHI-30*	GC†, MW†

Only the most frequently analyzed outcomes for each subset are included. Welham et al.[9] study appears in both direct and indirect therapies, as both analyses are made in the same study.

dHGF = recombinant hepatocit growth factor; FGF = fibroblast growth factor; GC = glottal closure; GRBAS = grade, roughness, breathiness, asteny, strain; Jitt = jitter; KTP = potassium titanyl phosphate; NHR = noise to harmonic ratio; MFR = mean flow rate; MPT = mean phonatory time; MW = mucosal wave; PDL = pulsed dye laser; Psub = subglottic pressure; Rand = randomized studies; Shim = shimmer; SNR = sound to noise ratio; F0 – fundamental frequency; VHI = voice handicap index.

*Outcomes that achieved statistical significance.

†No values on statistical significance.

TABLE III.
Included "Indirect Treatment" Studies and Their Characteristics.

Reference	Study Design	Diagnosis	Treatment	n	MINORs	Gender (M:F)	Mean of Age (yr)	Follow-Up	Perceptual	Acoustic	Aerodynamic	Self-Reported	Endoscopic
Kandogan et al.[31]	Cohort (retrospective)	Sulcus	Type I thyroplasty	6	8/16	5:1	26.7	2 mo	RB†	Jitt†	MPT†	VHI-30*	-
Al Dousary et al.[32]	Cohort (retrospective)	Sulcus	Fat	19	6/16	9:10	32.6	12 mo	GRBAS†	Jitt†, Shim†, SNR†, F0†	-	-	GC†, MW†
Welham et al.[9]	Clinical trial	Sulcus + scar	Type I Thyroplasty OR injection	28	20/24	11:17	54.5	18 mo	GRBAS	Jitt, Shim, F0	-	VHI-10 (thyroplasty*, injection)	MW
Van den Broek et al.[33]	Cohort (retrospective)	Sulcus	Injection	9	12/16	0:1	39.5	12 mo	G	F0	MPT	VHI-30*	-
Van den Broek et al.[34]	Cohort (retrospective)	Sulcus	Type I thyroplasty	15	12/16	12:17	50.5	12 mo	G	F0 (male*)	MPT	VHI-30*	-
Salmeron-Gonzalez et al.[35]	Cohort (prospective)	Scar	Injection	21	13/16	17:4	57.2	8 mo	G*R*B*A*S*	Jitt*, Shim*, NHR*	MPT*	VHI-10*	-

Only the most frequently analyzed outcomes for each subset are included. Welham et al.'s[9] study appears in both direct and indirect therapies, as both analyses are made in the same study.

F0 = fundamental frequency; GRBAS = grade, roughness, breathiness, asteny, strain; GC = glottal closure; Jitt = jitter; MPT = mean phonatory time; MW = mucosal wave; NHR = noise to harmonic ratio; Shim = shimmer; SNR = sound to noise ratio; VHI = voice handicap index.

*Outcomes that achieved statistical significance.

†No values on statistical significance.

LP regeneration/scar degradation. Three of the included articles[22,23,41] performed glottoplasty with angiolytic lasers (PDL[22,23,41] and/or KTP[23]). Statistical significant changes were achieved in self-reported, endoscopic, and perceptual outcomes, while some acoustic (shimmer, noise to harmonic ratio [NHR])[22] and aerodynamic outcomes (MPT) did not achieve this. Complications included the formation of vocal cord cysts in five patients.[23] One of the studies was a preliminary report, with no publication of results of all the enrolled patients. Three of the analyzed studies[24–26] used basic fibroblast growth factor (FGF) as the mainstay of therapy for sulcus and/or scar (total n = 44). This was either directly injected or soaked in a sponge with a previous detachment of the sulcus/scar. A 2018 clinical trial (n = 12) on SV patients showed significant improvement in MPT, VHI, pitch range, NHR, and F0 after one injection of FGF, with additional significant gains on MPT and VHI after multiple injections. Another 2017 clinical trial (n = 17) showed improvements on grade, roughness, breathiness, asteny, strain (GRBAS), VHI-10, glottal closure, mucosal wave, MPT, and voice range profile. Acoustic parameters did not significantly change at 12 months postprocedure. One retrospective series (n = 12) compared the injection alone with injection associated with dissection. Both groups had a statistically significant improvement in VHI-10 and GRBAS, with the dissection group achieving statistical significance in the improvement of MPT. Differences between groups were not statistical significant. A 2018 phase I/II trial by Hirano et al.[27] (n = 18) used recombinant hepatocyte growth factor (HGF) for scar and sulcus treatment. This study compared three different doses of the product on different subjects, demonstrating whole-group improvement in stroboscopic, perceptual (GRBAS), and self-reported (VHI-10) analysis, with no improvement of MPT or jitter. No complications were described with either of these products. Other attempted injection products included autologous fibroblasts,[28] glicocorticoids,[29] and collagen[30] with variable results, as stated in Table II.

Indirect treatments

Sole indirect treatments as a mainstay for sulcus and/or scar were performed in six of our reviewed studies[9,31–35] (Table III). These studies included two different techniques: type I thyroplasty[9,31,34] and fat injection augmentation.[9,32,33,35] Self-reported outcomes had general significant improvement in most studies. A prospective study of 21 patients by Salmeron-Gonzalez et al.[35] reported a significant improvement in acoustic and aerodynamic outcomes as well as perceptual and self-reported. Only one of these studies[32] analyzed stroboscopic outcomes, reporting a significant improvement in glottic gap at 3 months post-op.

Combined therapies

Combined simultaneous techniques were used in five studies[36–40] (Table IV). These studies used a dissection technique and/or graft interposition associated

TABLE IV.
Included "Combined Treatment" Studies and Their Characteristics.

Reference	Study Design	Diagnosis	Treatment	n	MINORs	Gender (M:F)	Mean of Age (yr)	Follow-up	Perceptual	Acoustic	Aerodynamic	Self-reported	Endoscopic
Hsiung et al.[36]	Cohort (prospective)	Sulcus	Fascia + injection laryngoplasty	22	10/16	1:2	33.1	6 mo	G*R*B*	Jitt, Shim, F0, NHR	MPT*	-	GC*, MW*
Zhang et al.[37]	Cohort (prospective)	Sulcus	Gelatin sponge + injection laryngoplasty	12	19/24	7:5	25.2	6 mo	-	Jitt*, Shim*, F0*	MPT*	-	GC†, MW†
Yilmaz et al.[38]	Cohort (retrospective)	Sulcus	Excision + (injection OR thyroplasty)	44	8/16	9:13	37	1 yr	G*R*B*AS	Jitt*, Shim*, F0, NHR*	MPT*, MFR*, Psub*	VHI-30*	GC*, MW*
Miaskiewicz et al.[39]	Cohort (retrospective)	Sulcus	Dissection + injection laryngoplasty	24	10/16	11:13	38.7	8 mo	G*R*B*AS*	Jitt, Shim, F0, NHR	-	-	GC†, MW†
Miaskiewicz et al.[40]	Cohort (retrospective)	Sulcus	Laser CO_2 + injection laryngoplasty	36	10/16	13:23	44.2	12 mo	G*R*B*A*S*	Jitt, Shim*, F0, NHR	-	VHI-30*	GC*, MW*

Only the most frequently analyzed outcomes for each subset are included.
F0 = fundamental frequency; GRBAS = grade, roughness, breathiness, asteny, strain; GC = glottal closure; Jitt = jitter; NHR = noise to harmonic ratio; MFR = mean flow rate; MPT = mean phonatory time; MW = mucosal wave; Psub = subglottic pressure; Shim = shimmer; VHI = voice handicap index.
*Outcomes that achieved statistical significance.
†No values on statistical significance.

with injection laryngoplasty. Perceptual, self-reported, and aerodynamic outcomes achieved statistical difference in all studies, with exception of astheny[38,39] and strain.[38] Stroboscopic outcomes also improved in all studies, albeit some[37,39] not presenting statistical data to confirm it. Acoustic changes were noted in some studies.[37,38,40]

DISCUSSION

The primary objective of our systematic review identified a heterogeneity between study designs, employed techniques, and measured outcomes. These characteristics did not allow, therefore, to conclude with the existing published evidence, a predominance of a specific technique over the others. The level of evidence is NA because the mixed study designs are included. Regarding the secondary objective of our study and knowing that not every technique addresses both glottal gap and mucosal wave, we managed to propose a new classification of techniques. No previous classification was found in the revised literature. The authors feel that intervening in Reinke's space is substantially different as a procedure, in comparison with medialization laryngoplasty by injection or type I thyroplasty. Direct treatments act on the LP of the affected vocal fold while indirect treatments focus on glottal gap closure, without addressing directly the mucosal wave component. The authors also feel that the rationale of each MW technique has different objectives: plain dissection, graft interposition, or LP regeneration/scar degradation. Therefore, the proposed new classification can both promote the creation of clearer pathways of treatment and also direct future comparative studies that are lacking at the moment.

The mentioned direct treatments act through different pathways. They might attempt to simply free the mucosa from the vocal ligament or they might try to produce a normal Reinke's space, by either grafting, degrading scar tissue, or promoting its regeneration by growth factors. Directly addressing the SV has the advantage of possibly freeing the epithelium from the LP and/or removing cicatricial tissue, but it might cause the appearance of another scar. The vocal ligament section tries to decrease the glottic tension and glottic gap while the slicing mucosa technique tries to release the lesion's tension lines. Graft materials try to mimetize the characteristics of SLP. In gray minithyrotomy, a drill is used for opening a window in the thyroid cartilage, which is used for fat placement, without epithelial disruption. Angiolytic lasers have selective phototermolysis and the rationale beyond this usage comes from extrapolation of its utilization in other areas, like hypertrophic scars or keloids. The mechanism is not fully understood, but it may reduce scar-related angiogenesis, helping in scar remodeling and, possibly, repairing the existing defect of the SLP. FGF produces histological recovery of HA with reduced disorganization of collagen bundles while HGF is a peptide with antifibrotic, organogenic, and angiogenic properties, already studied for therapeutical potential in other organs.

Indirect treatments as type I thyroplasty or injection laryngoplasty might not correct the mucosal wave per se, but the improvement in vocal quality and consequent reduction of strain and fatigue might be just enough to meet patient's needs. These techniques are used frequently for correcting glottal gaps in other clinical pictures. Combined simultaneous therapies address both components. Some recent papers[33,34] seem to favor a sequential approach, with medialization techniques used as the first approach, based on the European Laryngeal Society recommendation for being the least invasive possible on the treatment of scar.[42]

Outcomes that most consistently improve are self-reported outcomes, with few exceptions,[9,19,28] that include experimental techniques not reproduced in other studies. Stroboscopic outcomes are variable and many of the studies mention improvement, while not giving statistical analysis of its magnitude (as seen in Table II). It is also noteworthy that these were not included in most of the indirect therapy studies, as they do not act on the mucosal wave directly. Acoustic outcomes are infrequently improved, and statistically significant difference is found in less than half of the studies, with no evident difference for each technique. Aerodynamic outcomes are more often improved than not. Only one indirect therapy reports significant acoustic improvement[35] although these techniques would theoretically act on glottal insufficiency. Perceptual outcome variation is also variable, with grade, roughness, and breathiness being more frequently improved than astheny or strain. Most indirect techniques do not present, however, enough data on these outcomes for them to be compared with other techniques.

The comparison of outcomes between studies has to be done carefully. As stated in the MINORs statement,[11] subjective outcomes must be double-blinded and objective outcomes must be blinded, to reduce the risk of bias. Moreover, interrater reliability of perceptual outcomes like the GRBAS scale may vary, being greater for overall grade and weaker for asthenia and strain.[43] Some studies[36,44] use other scales outside the 0 to 3 scoring, which also limits comparisons. Self-reported outcomes use most of the times standardized scales like the VHI-30, or more recently, the VHI-10. However, some studies apply personal scales[17,20,41] that lack validation and difficult comparisons. The acoustic and aerodynamic outcomes used in each study vary greatly, with the five most cited being MPT, mean flow rate, jitter, shimmer, and f0, which goes in line with studies about most cited in the literature for other pathologies, such as unilateral vocal fold paralysis.[45]

Voice therapy is considered previously to attempting surgical treatment, with a variable degree of success.[4] It can also be used postsurgically to improve outcomes. However, implementation reports in the included studies were inconsistent, with only 10 studies mentioning preoperative therapy, while 14 studies mentioned its utilization postoperatively, with different initiation periods (from 2 weeks to 3 months postoperation). As stated by some of the analyzed studies, this fact can also add to the variability of results, with none of the studies accounting for its effect separately.

From the reviewed studies, it seems clear that there is no "one-fits-all" treatment for sulcus/scar. Most of them present and defend only one technique. Some studies

mention an individual algorithm for a decision between techniques: Welham et al.[9] perform injection laryngoplasty in patients with small volumetric deficiencies and limited scar contraction, and thyroplasty in patients with larger deficiencies where preoperative manual compression of the thyroid yielded perceptive improvement of voice and graft implantation for extensive scar/deep sulci. Hsiung et al.[36] mentioned the combined fascia transplantation associated with indirect fat injection only for patients with perceptible atrophy and bowing; It is, however, noteworthy to mention that in every study where a decision is detailed about different procedures, the cited criteria are subjective rather than objective. Some other parameters, such as mean airflow, have been proven valuable in glottal incompetence assessment, in particular with unilateral vocal fold paralysis.[46] Future incorporation of other objective criteria in the decision-making process, after the failure of a conservative approach, might be useful.

In our systematic review, we found only one study that attempted to compare outcomes between direct and indirect treatments for vocal sulcus/scar.[9] This study by Welham et al. (n = 18) directly compared outcomes between graft implantation, fat injection (in the paraglottic space), and type I thyroplasty. The study is, however, nonrandomized, as every technique was selected for the patient based on preoperatory stroboscopic findings of glottal closure and mucosal wave pliability. In this study, there was no obvious superior technique although the fat injection failed to improve any of the studied outcomes. Graft material was also not the same for every patient in that subgroup (temporal fascia or acellular dermal matrix).

One of the limitations of our study, as well as the comprised studies within it, is the inclusion of both scars and vocal sulcus on the same analysis. Another aspect to consider is the possibility of types 2 and 3 sulcus having relevant histologic differences[3,15,47]: there seems to exist an inflammatory reaction accompanying SV type 3, which does not exist in the other types. This may explain some differences in outcomes and may favor different techniques for different processes. It should also be clarified that the utilization of the term "sulcus vocalis" is reserved for type 3 sulcus in some studies, while in others it is used interchangeably for all types of sulcus. Only a few studies mention comparisons of results between types 2 and 3 of sulcus[32,36]: they were not able to demonstrate statistical differences between outcomes in both groups.

This study, as a systematic review, is limited by the quality of the included studies. Because it is a collection of findings from various other studies, it provides an overview of the direction of the literature but is unable to show new findings. Therefore, we have to account for possible bias. MINORs criteria[11] were used to evaluate each study, and due to the observational nature of most of them, conclusions are limited. This study is not a meta-analysis, and study results have not been statistically combined for more powerful results. In addition, some studies in languages not included in our analysis were forcefully excluded, namely multiple Chinese and Korean studies who could have yielded different results.

Several of these series are from referral centers that use a very specific and sometimes challenging technique. This makes a widespread application of the results less likely and limits external validity. An intervention may be chosen based on an individual surgeon or patient preference, rather than a risk-severity scale, patient-specific characteristics, or other means of allocation. This precludes conclusions for which treatment is best, as compared to randomized control trials or studies from a prospectively collected database that would be more likely to definitively prove one treatment is better than another. Overall, standardized study protocols outlining outcome measures, method of reporting measurements, and follow-up intervals would facilitate future analysis of data, including meta-analyses.

CONCLUSION

In our study, we suggest a classification for the different proposed treatments, based on the pathophysiology of sulcus and scar, in order to improve data presentation. Our evidence suggests that there probably is no one-fits-all treatment for this clinical picture. There is still no clear decision-making pattern in the literature, although there is a recent trend toward sequential approaches, starting with less invasive procedures. More decision-making tools, subjective and objective ones, should be sought and validated.

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