Idiopathic Subglottic Stenosis in Non-Caucasian Women

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Abstract

Objective. To characterize presentation, disease course, and treatment of idiopathic subglottic stenosis (iSGS) in non-Caucasian women and compare this cohort to the predominantly female, Caucasian patient cohorts identified in the literature.

Study Design. Retrospective review. Results are compared to systematic review of demographics.

Setting. Multiple California institutions from 2008 to 2021.

Methods. Patients with intubation within 2 years of disease or who met exclusion criteria listed in prior publications were excluded. A systematic review of iSGS patient demographics was also completed for comparison.

Results. Of 421 patients with iSGS, 58 self-identified as non-Caucasian women, with 50 ultimately included. Mean age of onset was 45.1 years old (95% confidence interval [CI], 41.5-48.8), and mean age at diagnosis was 47.2 years (95% CI, 43.6-50.7). Mean Charlson comorbidity index was 1.06 (n = 49, 95% CI, 0.69-1.44). At diagnosis, Cotton-Meyer severity scores (documented in n = 45) were Cotton-Myer (CM) I (28.9%), CM II (40%), and CM III (31.1%). Mean age at first endoscopic surgery was 47.7 (95% CI, 44.2-51.3) years. 64% experienced disease recurrence with a median of 11 months between their first and second surgery. Our systematic review identified 60 studies that reported demographic features in patients with iSGS. 95% of pooled patients were Caucasian, while other demographic features were similar to the current cohort.

Conclusion. The non-Caucasian population, almost 14% of this Californian cohort, does not differ from the majority Caucasian population detailed in contemporary literature. This cohort supports the presence of some racial and ethnic heterogeneity in this disease population.

Keywords

diversity in literature, idiopathic subglottic stenosis

Idiopathic subglottic stenosis (iSGS) is a rare fibroinflammatory disease that causes progressive upper airway obstruction.[1,2] Diagnosis of iSGS is made through exclusion of other known causes of subglottic stenosis and its treatment can vary from intralesional steroid injection to endoscopic or open airway reconstructive surgery.[2] Although the etiology of the disease is still debated, there is consensus that the patient population is largely limited to Caucasian women.[1-3] Given the disease's rarity of 1 per 400,000 people,[4] extraordinary measures must be employed to accurately study iSGS. The largest multi-institutional cohort of the North American Airway Collaborative (NoAAC) includes 1.7% to 3.0% non-Caucasian women with iSGS from up to 40 institutions.[5,6] If genetic predisposition indicated by consistent racial preponderance in iSGS patient populations influences the

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course of this disease, the small proportion of patients who are not Caucasian may represent a subset that differs from the larger Caucasian cohort.

People of color may incur pathogenic vulnerability when lower representation in research studies negatively affects the health care they receive.[7] In a cross-sectional study of 230 US-based vaccine clinical trials, Caucasian individuals were overrepresented while people of minority groups were underrepresented in comparison to the census.[8] Socioeconomic barriers such as lack of transportation, lower income, and distance from medical centers, which disproportionately affect minority patients, may play a part in their underrepresentation in research[9,10]; however, a significant difference in the types of trials entered by different races raises concerns that recruitment methods may impact minority participation as well.[11] As minority patients may experience more difficulty with participation in prospective studies, different methods may be required to ensure that unintentional underrepresentation does not result in exclusion from the benefits of ongoing research or timely diagnosis.

As iSGS has been definitively characterized in a larger population comprised almost exclusively of Caucasian patients the objective of this study was to determine if disease and patient characteristics in non-Caucasian patients significantly differ from those in Caucasian patients. To accomplish this, we compared our own retrospective multi-institution cohort of non-Caucasian women to a larger, predominantly Caucasian cohort that has already been published in the literature through systematic review.

Materials and Methods

Retrospective Review

A retrospective observational study was conducted across 6 tertiary care hospital systems in California. All the contributors are members of the NoAAC. Institutional Review Board (IRB) approval was sought and awarded according to the protocol for each participating institution. Informed consent was not required, and data are not publicly available per IRB directive.

Non-Caucasian women with iSGS were identified through review of medical records from 2008 to 2021. The team at each institution identified and quantified patients with idiopathic stenosis limited to the subglottis based on their diagnostic workup and exclusion of other causes of airway stenosis. The patients were categorized by race or ethnicity in accordance with their self-identification and the National Institute of Health's definitions of race and ethnicity.[12] The term "Caucasian" included those of European or Middle Eastern descent as well as those who identified as non-Hispanic white.[12] These patients were excluded from consideration. Subjects were also excluded if they had been intubated within 2 years of disease onset or had history of neck irradiation, significant laryngotracheal traumatic injury, clinically diagnosed vasculitis or collagen vascular disease, positive antinuclear cytoplasmic antibody titers, or positive family history of autoimmune diseases.[13] Patient age at symptom onset, diagnosis, and first surgery, race, Cotton-Myer (CM) grade of stenosis,[14] stenosis length and distance from glottis, body mass index (BMI), comorbidities, pharmacologic interventions, treatment with serial intralesional steroid injections (SILSI), date and type of each surgery, and occupation were collected from patient charts.

Statistics

R version 4.1.0 (2021-05-18) was used to calculate the means, CIs, and medians of the collected data. The packages tidyverse, lubridate, and readr were used.

Systematic Review

Search strategy

Many of the Caucasian patients from our cohort have been included in prior NoAAC studies, thus characteristics of this group have already been published. To capture these patients and a wider cohort of predominantly Caucasian patients with iSGS, a systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (**Figure 1**).[15] To identify studies for inclusion in this review, a research librarian with expertise in conducting systematic reviews developed detailed search strategies in the following 4 databases: PubMed (US National Library of Medicine, National Institutes of Health), Embase (Elsevier), Web of Science (Clarivate), and CENTRAL (Cochrane Library). The search strategies used a combination of keywords for iSGS. Full search terms and results can be found in Supplemental Table S1, available online. The databases were searched from database inception through September 27, 2023, with an English and Chinese language filter. Deduplication was conducted using the methodology established by Bramer et al.[16]

Inclusion and exclusion criteria of studies

Articles were analyzed using the review management software Rayyan.[17] The eligibility criteria for inclusion in the review are outlined in **Table 1**. Following the initial search, abstracts were reviewed by 2 authors (N.P. and E.S.). For the abstracts that were not excluded, full-text articles were independently assessed for eligibility by the same 2 reviewers. Conflicts were resolved with discussion and consensus.

Data extraction and quality assessment

Variables to be extracted were defined a priori. Two authors (N.P. and E.S.) independently extracted data from each publication and then compared results to optimize accuracy. Discrepancies were addressed by discussion and consensus. Among the studies included in the analysis, we collected data regarding study information, participant

demographics, comorbidities, CM grading, and frequency of surgical treatment. For categorical variables, pooled proportions were calculated by summing the number of patients from each study together. For continuous variables, pooled averages and standard deviations were calculated by combining the average and variance of each study weighted by sample size. Quality assessment was conducted by 2 authors (N.P. and E.S.) using The Joanna Briggs Institute Prevalence Critical Appraisal Tool.[18] Studies were assigned an overall appraisal decision of "include," "exclude," or "seek more information" based on

the answers to the 9 questions in this tool. Discrepancies were addressed by discussion and consensus.

Results

Participants

Four hundred and twenty-one patients with iSGS were identified from all sites over the study period. Many of these patients were offered the opportunity to participate in NoAAC prospectively and some joined those study cohorts. Consequently, these patients are already represented in the published literature. Fifty-eight of these did not identify as Caucasian. Eight were excluded due to insufficient data. The range of 2008 to 2021 was decreased for several of the contributors reflecting a shorter period practicing at the participating institution. Of the 50 women included in the study, 43 self-identified as Hispanic, 4 Asian, 1 African American, 1 non-Hispanic/mixed race, and 1 other. The cohort had an average Charlson comorbidity index of 1.06 (n = 49, 95% CI, 0.68-1.44). Of the 50 patients, 2 (4%) were prediabetic, 10 (20%) were diabetic, 15 (30%) had hypertension, and 26 (52%) were obese (mean BMI $31.1 \pm 1.92 \, kg/m^2$). **Table 2** lists all 60 studies that met inclusion for the systematic review.[1-6,19-71] **Tables 3** and **4** displays findings from this cohort alongside the results from the included studies. Four studies reported different variables extracted from the same 810-patient NoAAC cohort.[5,6,46,48] These studies were combined into 1 entry for our analysis. Similarly, 2 other studies that were based on the same patient cohort were combined.[66,69] As a result, there were 56 unique patient cohorts examined. **Table 5** compares the findings from the retrospective cohort to the pooled results from the systematic review. The studies identified in the systematic review capture a predominantly Caucasian iSGS population (95.9%) while the current total multi-institutional iSGS patient group from which this cohort was derived was only 86.2% Caucasian. Our cohort had more patients with diabetes (20% vs 7.4%, $P = .001$) but fewer patients diagnosed with gastroesophageal reflux disease (GERD) (4% vs 35%, $P < .001$) than in the pooled studies.
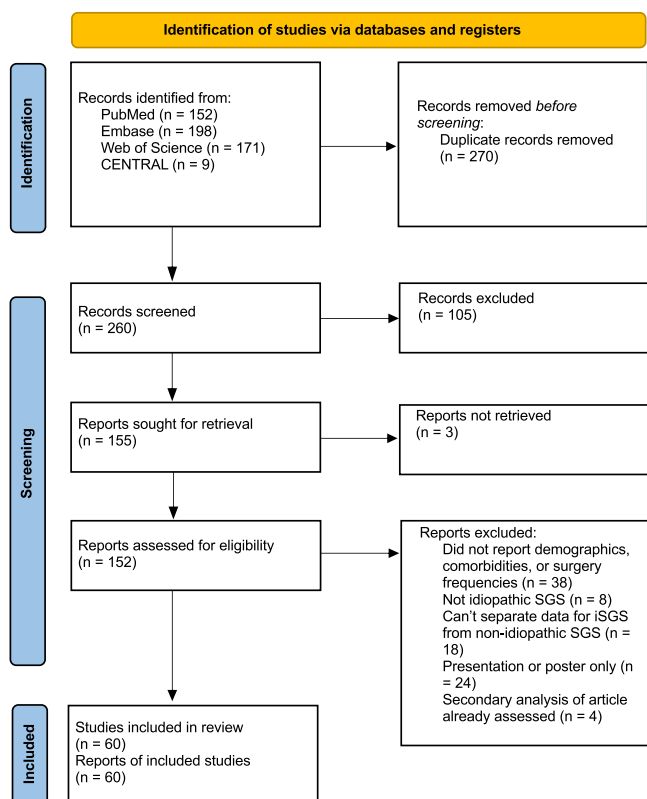
Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses diagram for study selection. iSGS, idiopathic subglottic stenosis.

Table 1. Inclusion and Exclusion Criteria for Systematic Review

Study inclusion criteria	Study exclusion criteria
(1) Original peer-reviewed publications	(1) Pooled nonidiopathic SGS data with iSGS data
	(2) Did not report on demographics, comorbidities, Cotton-Myer Grade, or frequency of surgical treatments
(2) Included patients with iSGS	
	(3) Review articles, case reports, or conference abstracts
	(4) Duplication of studies or secondary analysis of the same group of patients
(3) Reported demographics (sex distribution, age, race/ethnicity), comorbidities, Cotton-Myer Grade, or frequency of surgical treatments (endoscopic or open)	(5) No full text available for review

Abbreviations: iSGS, idiopathic subglottic stenosis; SGS, subglottic stenosis.

Table 2. List of Included Studies

First author	Year	Country	Sample size
Current	2023	USA	50
Aarnæs	2017	Norway	38
Anderson	2020	International	544
Benjamin	1997	Australia	15
Berges	2021	USA	124
Blumin	2011	USA	22
Carpenter	2019	USA	42
Carpenter	2018	USA	61
Case	2022	USA	46
Chan	2021	Canada	201
Compton	2021	Canada	33
D'Oto	2022	USA	107
Davis	2020	USA	8
Davis	2021	USA	9
Dedo	2001	USA	50
Dwyer	2020	Canada	72
Fang	2018	USA	41
Fiz	2018	Italy	44
Gadkaree	2016	USA	74
Gelbard	2020	USA	25
Gelbard	2016	USA	479
Giudice	2003	Italy	30
Gnagi	2015	International	2015
Grillo	2003	USA	73
Guo	2020	China	15
Hall	2016	USA	69
Hintze	2022	Ireland	10
Hoffman	2019	USA	16
Hoffman	2017	USA	19
Holmes	2022	Canada	36
Jindal	1994	USA	7
Kraft	2014	USA	25
Lina	2022	USA	9
Liu	2020	USA	16
Lu	2023	USA	51
Maldonado	2013	USA	116
Maronian	2001	USA	9
Menapace	2019	USA	186
Menapace	2017	USA	33
Morcillo	2013	USA	60
Motz	2017	USA	8
NoAAC	2015-2017	International	810
Nouraei	2019	UK	22
Nouraei	2013	UK	54
Ospino	2022	USA	8
Park	1995	USA	10
Rohlfing	2023	mUSA	37
Schoeff	2020	USA	12
Schoeff	2023	USA	64
Shabani	2016	USA	37
Singh	2023	USA	41
Taylor	2013	USA	24

Table 2. (continued)

First author	Year	Country	Sample size
Valdez	2002	USA	16
Wang, Tapias	2015, 2020	USA	263
Woliansky	2019	Australia	37
Zhang	2022	USA	22

Presentation and Disease Course

Mean age of symptom onset in this study cohort was 45.1 years old (95% CI, 41.5-48.8). Mean age at diagnosis was 47.2 years (95% CI, 43.6-50.7). Distribution of iSGS severity at diagnosis was CM I (28.9%), CM II (40%), and CM III (31.1%), n = 45. These findings were similar to the pooled results from the systematic review (**Table 5**).

Treatment

Mean age at first surgery was 47.7 years (95% CI, 44.2-51.3), significantly younger than the average age of 49.4 years from the systematic review (P = .014). Nineteen underwent SILSI. While treatment type varied in this retrospective study, none of the 50 women underwent open airway reconstruction during the study period, in contrast to the 23.9% of patients who underwent open surgery from the systematic review (P = .001). 84.5% of patients represented in the systematic review underwent endoscopic surgery, as opposed to 100% from this cohort (P = .003). In the current study, 64% experienced disease recurrence after their first surgery with a median of 3 surgeries documented (range, 2-10). Excluding 1 patient whose first surgery date was not recorded, patients who experienced recurrence had a median of 11 months between their first and second surgery with a range of 6 days to 3 years. Forty patients received additional medical treatment for their iSGS, including prescription of an inhaler (44%), reflux medication (48%), antibiotics (10%), or oral steroids (6%).

Quality Assessment

None of the studies were excluded based on the risk of bias assessment. Some studies showed potential bias in their sampling methodology (ie, taking convenience samples from iSGS online patient forums, not specifying patient inclusion/exclusion criteria). However, we did not exclude any studies due to issues with sampling quality, as we aimed to capture sampling bias since it may contribute to the low number of non-Caucasian iSGS patients represented in the literature. Otherwise, the included studies were of adequate quality.

Discussion

This study compared patient and disease characteristics of 50 non-Caucasian patients with iSGS to a

Table 3. Demographics and Comorbidities From All Included Studies

	Demographics						Comorbidities					
Author (n)	Female, n (%)	Caucasian, n (%)	African American, n (%)	Asian, n (%)	Hispanic, n (%)	Other, n (%)	BMI, mean (SD), kg/m²	CCI, mean (SD)	None, n (%)	HTN, n (%)	Diabetes mellitus, n (%)	GERD, n (%)
Current (50)	50 (100)	0	1 (2)	4 (8)	43 (86)	2 (4)	31 (1)	1.1 (0.2)	19 (38)	15 (30)	10 (20)	2 (4)
Aarnæs (38)	38 (100)	na	na	na	na	na	na	na	25 (66)	6 (16)	6 (16)	4 (11)
Anderson (544)	543 (99)	521 (98)	2 (<1)	3 (1)	5 (1)	2 (<1)	na	na	na	na	na	na
Benjamin (15)	15 (100)	na	na	na	na	na	na	na	na	na	na	na
Berges (124)	122 (99)	120 (97)	1 (<1)	2 (2)	1 (<1)	na	27 (9)	1.1 (1.4)	na	na	na	na
Blumin (22)	22 (100)	na	na	na	na	0	na	na	na	na	na	12 (55)
Carpenter (42)	42 (100)	41 (98)	0	0	1 (2)	0	na	na	na	na	na	na
Carpenter (61)	59 (97)	na	na	na	na	na	na	na	na	7 (11)	3 (5)	38 (62)
Case (46)	46 (100)	46 (100)	0	0	0	0	na	na	na	na	na	na
Chan (201)	192 (95)	na	na	na	na	na	na	0.3 (0.9)	na	42 (21)	15 (7)	65 (32)
Compton (33)	32 (97)	na	na	na	na	na	29 (7)	na	na	na	na	na
D'Oto (107)	105 (98)	93 (87)	6 (6)	1 (1)	7 (7)	0	29	na	na	na	8 (8)	53 (50)
Davis (8)	8 (100)	7 (88)	na	na	na	1 (13)	na	na	na	na	2 (25)	na
Davis (9)	8 (89)	9 (100)	0	0	0	0	30 (5)	1.0 (1.0)	na	na	1 (11)	4 (44)
Dedo (50)	49 (98)	na	na	na	na	na	na	na	na	na	na	6 (16) (n = 37)
Dwyer (72)	71 (99)	na	na	na	na	na	na	1.2	na	17 (24)	11 (15)	28 (39)
Fang (41)	40 (98)	na	na	na	na	na	31 (9)	na	na	na	na	19 (46)
Fiz (44)	44 (100)	na	na	na	na	na	na	na	na	na	na	na
Gadkaree (74)	73 (98)	70 (95)	3 (4)	0	1 (1)	0	31 (10)	0.7 (0.9)	na	15 (21)	8 (11)	24 (34)
Gelbard (25)	25 (100)	25 (100)	0	0	0	0	na	na	na	na	na	na
Gelbard (479)	471 (98)	466 (97)	4 (1)	0	9 (2)	0	na	1.6 (0.1)	na	na	20 (4)	103 (22)
Giudice (30)	30 (100)	30 (100)	0	0	0	0	na	na	na	na	na	na
Gnagi (132)	129 (98)	na	na	na	na	na	na	na	na	na	5 (4)	55 (42)
Grillo (73)	71 (97)	na	na	na	na	na	na	na	na	na	na	15 (21)
Guo (15)	11 (73)	0	0	15 (100)	0	0	na	na	na	na	na	na
Hall (69)	65 (94)	64 (96)	0	0	1 (2)	2 (3)	28 (7)	na	na	na	6 (9)	36 (52)
Hintze (10)	9 (90)	10 (100)	0	0	0	0	na	na	na	1 (10)	1 (10)	na
Hoffman (16)	16 (100)	16 (100)	0	0	0	0	na	na	na	na	2 (11)	11 (58)
Hoffman (19)	19 (100)	19 (100)	0	0	0	0	na	na	na	7 (37)	na	11 (31)
Holmes (36)	36 (100)	36 (100)	na	na	na	na	na	na	na	na	na	na
Jindal (7)	7 (100)	na	na	na	na	na	na	na	na	na	na	3 (43)
Kraft (25)	25 (100)	23 (92)	0	0	2 (8)	0	na	na	na	na	na	na

(continued)

Table 3. (continued)

	Demographics								Comorbidities			
Author (n)	Female, n (%)	Caucasian, n (%)	African American, n (%)	Asian, n (%)	Hispanic, n (%)	Other, n (%)	BMI, mean (SD), kg/m²	CCI, mean (SD)	None, n (%)	HTN, n (%)	Diabetes mellitus, n (%)	GERD, n (%)
Lina (9)	9 (100)	na	na	na	na	na	32	1.6 (range: 0-5)	na	4 (44)	1 (11)	4 (44)
Liu (16)	16 (100)	16 (100)	0	0	0	0	31 (8)	na	na	na	na	na
Lu (51)	50 (98)	na	na	na	na	na	na	na	42 (82)	na	3 (6)	na
Maldonado (116)	115 (99)	na	na	na	na	na	na	na	na	na	na	43 (37)
Maronian (9)	8 (89)	na	na	na	na	na	na	na	na	na	na	5 (71) (n = 7)
Menapace (186)	182 (98)	na	na	na	na	na	na	na	na	66 (36) (n = 185)	16 (9)	78 (42) (n = 185)
Menapace (33)	32 (97)	na	na	na	na	na	na	na	na	na	na	na
Morcillo (60)	55 (91)	na	na	na	na	na	na	na	na	na	na	na
Motz (8)	7 (87)	8 (100)	0	0	0	0	na	na	na	na	na	na
NoAAC (810)	798 (98)	787 (97)	1 (<1)	na	17 (2)	5 (1)	na	na	na	na	na	280 (38)
Nouraei (22)	22 (100)	na	na	na	na	na	30 (9)	na	na	na	na	14 (64)
Nouraei (54)	54 (100)	na	na	na	na	na	na	na	na	na	na	30 (56)
Ospino (8)	8 (100)	na	na	na	na	na	29 (7)	1.3 (1.2)	1 (2)	3 (6)	na	na
Park (10)	8 (80)	na	na	na	na	na	na	na	na	na	na	na
Rohlfing (37)	36 (100)	36 (100)	na	na	na	na	na	na	na	na	na	na
Schoeff (12)	12 (100)	12 (100)	na	na	na	na	na	na	na	na	na	6 (50)
Schoeff (64)	64 (100)	62 (97)	0	0	0	2 (3)	na	na	na	na	na	na
Shabani (37)	37 (100)	na	na	na	na	na	30 (7)	na	na	na	na	24 (65)
Singh (41)	37 (90)	na	na	na	na	na	29 (8)	na	na	na	6 (15)	na
Taylor (24)	24 (100)	23 (96)	0	0	1 (4)	0	na	na	na	na	na	12 (50)
Valdez (16)	14 (88)	na	na	na	na	na	na	na	na	na	na	na
Wang, Tapias (263)	261 (99)	252 (96)	na	na	na	na	na	na	na	53 (20)	20 (8)	78 (30)
Woliansky (37)	36 (97)	na	na	na	na	na	na	na	na	na	na	Median (IQR): 9 (24)
Zhang (22)	22 (100)	na	na	na	na	na	30 (range: 21-47)	na	na	7 (32)	3 (14)	8 (36)

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; GERD, gastroesophageal reflux disease; HTN, hypertension; SD, standard deviation.

Table 4. Disease Course, Cotton-Myer Grade, and Treatment From All Included Studies

	Disease course			Cotton-Myer grade				Treatment			
	Age at onset, mean (SD), years	Age at diagnosis, mean (SD), years	Time from symptom onset to diagnosis, mean (SD), years	CM I, n (%)	CM II, n (%)	CM III, n (%)	CM IV, n (%)	Age at first surgery, mean (SD, range)	Open surgery, n (%)	Endoscopic surgery, n (%)	Required multiple surgeries, (%)
Current (50)	45 (2)	47 (2)	2 (1)	13 (29) (n = 45)	18 (40) (n = 45)	14 (31) (n = 45)	0 (n = 45)	48 (2)	0	50 (100)	32 (64)
Aarnaes (38)	na	54 (range: 20-85)	3	na	na	na	na	na	na	38 (100)	30 (79)
Anderson (544)	na	na	na	na	na	na	na	na	na	na	na
Benjamin (15)	na	43 (17)	3 (3)	na	na	na	na	na	2 (13)	15 (100)	3 (20)
Berges (124)	na	49 (14)	median: 2	39 (31)	33 (27)	52 (42)	0	na	na	na	na
Blumin (22)	na	na	na	na	na	na	na	na	na	na	na
Carpenter (42)	na	52 (10)	na	1 (2) (n = 50)	27 (54) (n = 50)	22 (44) (n = 50)	0	na	0	42 (100)	41 (98)
Carpenter (61)	na	na	2	na	na	na	na	na	61 (100)	na	na
Case (46)	na	na	na	na	na	na	na	na	na	na	na
Chan (201)	na	48 (13)	na	na	na	na	na	na	na	na	na
Compton (33)	na	na	na	na	na	na	na	na	33 (100)	0	na
D'Oto (107)	na	na	median: 2	na	na	na	na	na	na	na	na
Davis (8)	na	na	na	na	na	na	na	na	na	na	na
Davis (9)	na	na	na	na	na	na	na	na	3 (33)	9 (100)	9 (100)
Dedo (50)	na	44 (range: 15-77)	na	na	na	na	na	na	3 (6)	50 (100)	49 (98)
Dwyer (72)	na	50 (14)	3 (3)	I-II: 38 (53) (n = 53)	na	III-IV: 15 (28) (n = 53)	na	na	31 (43)	53 (74)	43 (60)
Fang (41)	na	na	na	na	na	na	na	na	na	na	na
Fiz (44)	na	na	na	na	na	na	na	na	44 (100)	na	26 (59)
Gadkaree (74)	na	na	na	19 (30) (n = 64)	30 (47) (n = 64)	15 (23) (n = 64)	0	na	na	na	na
Gelbard (25)	na	na	na	na	na	na	na	na	na	na	na
Gelbard (479)	na	na	na	na	na	na	na	50 (1)	95 (20)	384 (80)	185 (23)
Giudice (30)	na	53 (range: 22-81)	4 (range: <1-17)	0	26 (87)	4 (13.3)	0	na	5 (17)	30 (100)	na
Gnagi (132)	na	na	> 2	na	na	na	na	na	34 (36)	na	na
Grillo (73)	na	na	4 (range: <1-32)	na	na	na	na	na	na	na	na

(continued)

Table 4. (continued)

	Disease course			Cotton-Myer grade				Treatment			
Study (n)	Age at onset, mean (SD), years	Age at diagnosis, mean (SD), years	Time from symptom onset to diagnosis, mean (SD), years	CM I, n (%)	CM II, n (%)	CM III, n (%)	CM IV, n (%)	Age at first surgery, mean (SD, range)	Open surgery, n (%)	Endoscopic surgery, n (%)	Required multiple surgeries, (%)
Guo (15)	na	na	na	0	8 (53)	4 (27)	3 (20)	35 (16) (n = 9)	13 (87)	na	na
Hall (69)	43 (12)	na	na	na	na	na	na	na	na	na	na
Hintze (10)	na	na	na	3 (30)	6 (60)	1 (10)	0	na	0	10 (100)	5 (50)
Hoffman (16)	na	na	na	na	na	na	na	na	na	14 (88)	9 (56)
Hoffman (19)	na	na	na	17 (90)	2 (11)	0	0	na	na	na	na
Holmes (36)	na	~50	na	na	na	na	na	na	na	na	na
Jindal (7)	na	46 (10)	na	na	na	na	na	na	na	na	5 (71)
Kraft (25)	na	na	na	4 (16)	17 (68)	4 (16)	0	Median (IQR): 45 (39-67)	0	25 (100)	13 (52)
Lina (9)	na	na	na	1 (11)	6 (67)	2 (22)	0	na	na	na	na
Liu (16)	na	na	na	na	na	na	na	55 (12)	na	na	na
Lu (51)	na	na	na	na	na	na	na	na	na	na	na
Maldonado (116)	na	na	na	na	na	na	na	na	10 (9)	116 (100)	na
Maronian (9)	na	57 (range: 35-83)	na	na	na	na	na	na	na	na	na
Menapace (186)	Median (IQR): 46 (36-57) (n = 151)	na	na	na	na	na	na	Median (IQR): 51 (41-60)			na
Menapace (33)	na	na	na	na	na	na	na	na	33 (100)	21 (63)	na
Morcillo (60)	na	na	na	na	na	na	na	na	60 (100)	0	38 (59)
Motz (8)	na	na	na	na	na	na	na	na	na	na	na
NoAAC (810)	na	na	na	na	na	na	na	Median (IQR): 50 (43-58)	86 (11)	724 (89)	na
Nouraei (22)	na	na	na	na	na	na	na	46 (7)	4 (18)	22 (100)	18 (82)
Nouraei (54)	na	48 (12)	2 (2)	5 (9)	19 (37)	27 (48)	3 (6)	na	12 (22)	54 (100)	na
Ospino (8)	na	na	na	4 (50)	4 (50)	0	0	na	2 (20)	8 (80)	na
Park (10)	38 (range: 25-60)	na	1 (range: <1-3)	na	na	na	na	42 (11) (n = 8)	na	na	5 (50)

Table 4. (continued)

	Disease course			Cotton-Myer grade				Treatment			
	Age at onset, mean (SD), years	Age at diagnosis, mean (SD), years	Time from symptom onset to diagnosis, mean (SD), years	CM I, n (%)	CM II, n (%)	CM III, n (%)	CM IV, n (%)	Age at first surgery, mean (SD, range)	Open surgery, n (%)	Endoscopic surgery, n (%)	Required multiple surgeries, (%)
Rohlfing (37)	na	na	na	na	na	na	na	Median (IQR): 50 (44-56)	na	na	na
Schoeff (12)	na	na	na	na	na	na	na	na	na	na	17 (27)
Schoeff (64)	na	48 (11)	na	na	na	na	na	na	3 (5)	54 (84)	21 (33)
Shabani (37)	na	46 (15)	na	na	na	na	na	48 (SD: 14)	4 (11)	37 (100)	31 (84)
Singh (41)	na	52 (14)	na	28 (68)	10 (24)	2 (5)	1 (3)	na	na	na	na
Taylor (24)	na	na	na	2 (4)	14 (28)	34 (68)	0	na	na	23 (96)	na
Valdez (16)	na	40 (13)	na	na	na	na	na	na	2 (13)	14 (88)	8 (50)
Wang, Tapias (263)	na	na	Median: 3	na	na	na	na	na	na	na	na
Woliansky (37)	na	na	Median (IQR): 29 (25-34)	0	27 (73)	na	na	na	na	na	na
Zhang (22)	na	na	na	na	na	na	na	54 (range: 37-66)	0	21 (96)	10 (46)

Abbreviations: CCI, Charlson Comorbidity Index; CM, Cotton-Myer; IQR, interquartile range; SD, standard deviation.

Table 5. Comparison of the Current Cohort to Pooled Data From the Systematic Review

	Current study (n = 50)	Pooled SR data	Pooled n; # of studies	P value
Female	100%	97.9%	4423; 56	.301
Caucasian	0%	95.9%	2912; 26	**<.001***
African American	2%	0.7%	2612; 24	.283
Asian	8%	0.8%	2612; 24	**<.001***
Hispanic	86%	1.7%	2612; 24	**<.001***
Other	4%	0.5%	2612; 24	**.001***
Age at onset, years	45.1 (1.8)	43.3 (11.5)	69; 1	.275
Age at diagnosis, years	47.2 (1.8)	48.3 (13.2)	673; 11	.555
Time from symptom onset and diagnosis, years	2.1 (0.5)	2.3 (2.3)	141; 3	.561
BMI, kg/m^2	31.1 (1.0)	29.1 (9.2)	1284; 12	.124
CCI	1.1 (0.2)	1.1 (0.7)	895; 6	.532
None	38%	47.6%	143; 3	.244
Hypertension	30%	22.5%	1008; 12	.219
Diabetes mellitus	20%	7.4%	1851; 19	**.001***
GERD	4%	35.0%	3040; 29	**<.001**
CM I	29% (n = 45)	26.0%	473; 13	.662
CM II	40% (n = 45)	44.9%	510; 14	.526
CM III	31% (n = 45)	35.3%	473; 13	.564
CM IV	0% (n = 45)	1.5%	473; 13	.409
Age at first surgery, years	47.7 (1.8)	49.4 (4.9)	571; 6	**.014**
Open surgery	0%	23.9%	2261; 25	**.001**
Endoscopic surgery	100%	84.5%	2087; 24	**.003**
Required multiple operations	64%	52.3%	1083; 21	.104

Proportions or means (standard deviation) are presented.

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CM, Cotton-Myer; GERD, gastroesophageal reflux disease; SR, systematic review.

predominantly Caucasian cohort identified through systematic review of the literature. Overall, patient characteristics and disease presentation, course, and treatment were similar between the groups. Current literature has established iSGS as a disease primarily affecting perimenopausal Caucasian women.[1,3,13,72] That the features of this non-Caucasian iSGS cohort resemble other large cohorts of Caucasian iSGS patients serves to reassure physicians that they may reasonably provide the same treatment options and disease course expectations to both groups.

While treatment type varied in this study, none of the 50 women in this cohort underwent open reconstruction. Other published majority Caucasian cohorts demonstrate a pooled open surgery rate of 23.9% as shown in **Table 5**. This difference may reflect patient preference, surgeon preference, lower disease severity, or resources available at their institution.[1] A recent systematic review investigating only endoscopic techniques in iSGS patients was unable to produce a meta-analysis due to disunity in treatment over time, intrapopulation variation in treatment, and lack of reporting about specific treatments employed in existing literature.[73] Adding open treatment only exacerbates these difficulties and highlights the need for additional investigation in this area. Larger multi-institutional studies must be undertaken to understand the factors influencing surgical decision-making for these patients. While age at first surgery was lower in the non-Caucasian cohort, no

difference in age was seen at the time of diagnosis or disease onset, suggesting this finding may also be due to practice preference.

Comorbidities also varied between Caucasian and non-Caucasian patients. A significantly higher proportion of non-Caucasian patients were diagnosed with diabetes mellitus, while a lower proportion had GERD. Both of these pathologies have been implicated in the pathogenesis of iSGS. The chronic inflammation caused by hyperglycemia in diabetes is known to interfere with wound-healing, which may explain its association with iSGS.[74] These results may suggest that diabetes is a more significant contributing factor in non-Caucasian patients while GERD is a more important risk factor in Caucasian populations. However, rates of diabetes have been shown to be 22.1% for Hispanic and 19.1% for Asian populations, while they are only 12.1% for non-Hispanic white populations.[75] These demographic differences may also be responsible for the variation in diabetes we observed. More studies are needed to elucidate the influence of diabetes on iSGS in non-Caucasian populations.

This study details a non-Caucasian population that represents 13.78% of the patients with iSGS treated at the participating institutions. Recent prospective NoAAC publications have included no more than 3% non-Caucasian iSGS patients.[5,6,72] The results suggest that more non-Caucasian patients with iSGS have yet to be captured by ongoing research efforts. The region where

this study was conducted (California) has a significantly larger population of people of Hispanic or Asian descent as compared to the rest of the United States.[76] This likely explains why these groups were more heavily represented in the sample. However, it also highlights the need for more studies in other regions with large non-Caucasian populations, which would likely capture more non-Caucasian patients with iSGS. To date, very few studies have examined iSGS in regions with large non-Caucasian populations. A study of iSGS conducted in China included only 15 patients.[39] Excluding European, North American and Australian studies, other studies of iSGS are limited to case reports.[73–78] As these cases are rare, multi-institutional studies are likely to be needed.

Minorities may have unique challenges to participating in research. The factors that prevent each minority group from participating can vary from language barriers to employment restrictions to socioeconomic factors, time restraints, lack of trust in the medical establishment, and recruitment methods that unintentionally exclude minorities.[7] Five of our sites did offer the opportunity to participate in the NoAAC trial but most non-Caucasian patients did not enroll and no effort was made to follow patients with iSGS to determine why they did or did not.

As iSGS is a rare disease, attempts to study it are limited by the number of patients who are eligible for inclusion. Because this is a retrospective study, patients received variable treatment and we were unable to categorize patients into more specific races and ethnicities beyond how each self-identified in the chart. Comparison with other studies was difficult to perform due to the diversity of reported outcomes and differences in the types of studies performed (retrospective reviews with wide-ranging follow-up periods, surveys, prospective studies, and others). Future studies should utilize established outcomes to facilitate continued collaboration and improved understanding of this rare condition.

Conclusion

This multi-institutional retrospective study of 50 non-Caucasian women with iSGS confirmed that their presentation, disease course, and treatment did not differ significantly from those of Caucasian women with iSGS. Given the contemporary acceptance of iSGS as a rare condition primarily affecting Caucasian women, the size of this study cohort supports preserving this diagnosis in the differential for non-Caucasian patients with breathing symptoms.

Author Contributions

Amber Suk, design, conduct, analysis, presentation; **Salem Dehom,** design, analysis, presentation; **Nihal Punjabi,** design, conduct, analysis, presentation; **VyVy N. Young,** design, conduct, analysis, presentation; **Priya D. Krishna,** conduct, analysis, presentation; **Lindsay Reder,** conduct, analysis, presentation; **Karla O'Dell,** conduct, analysis, presentation; **Grant E. Gochman,** conduct, presentation; **Ethan Simmons,** conduct, analysis, presentation; **Sunil P. Verma,** conduct, presentation; **Matthew Harmon,** conduct, presentation; **Philip A. Weissbrod,** conduct, presentation; **Jin Yang,** conduct, analysis, presentation; **Shanalee Tamares,** design, conduct, presentation; **Brianna K. Crawley,** design, conduct, analysis, presentation.

Disclosures

Data Availability

In order to maintain patient privacy, data are available upon reasonable request from the authors.

Supplemental Material

Additional supporting information is available in the online version of the article.

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References

1. Gelbard A, Donovan DT, Ongkasuwan J, et al. Disease homogeneity and treatment heterogeneity in idiopathic subglottic stenosis. *Laryngoscope.* 2016;126(6):1390-1396. doi:10.1002/lary.25708

2. Giudice M, Piazza C, Foccoli P, Toninelli C, Cavaliere S, Peretti G. Idiopathic subglottic stenosis: management by endoscopic and open-neck surgery in a series of 30 patients. *Eur Arch Otrhinolaryngol.* 2003;260(5):235-238. doi:10.1007/s00405-002-0554-y

3. Dwyer CD, Qiabi M, Fortin D, et al. Idiopathic subglottic stenosis: an institutional review of outcomes with a multi-modality surgical approach. *Otolaryngol Head Neck Surg.* 2021;164(5):1068-1076. doi:10.1177/0194599820966978

4. Maldonado F, Loiselle A, DePew ZS, et al. Idiopathic subglottic stenosis: an evolving therapeutic algorithm: idiopathic subglottic stenosis. *Laryngoscope.* 2014;124(2):498-503. doi:10.1002/lary.24287

5. Gelbard A, Anderson C, Berry LD, et al. Comparative treatment outcomes for patients with idiopathic subglottic stenosis. *JAMA Otolaryngol Head Neck Surg.* 2020;146(1):20. doi:10.1001/jamaoto.2019.3022

6. Drake VE, Gelbard A, Sobriera N, et al. Familial aggregation in idiopathic subglottic stenosis. *Otolaryngol Head Neck Surg.* 2020;163(5):1011-1017. doi:10.1177/0194599820935402

7. Rogers W, Lange MM. Rethinking the vulnerability of minority populations in research. *Am J Public Health*. 2013;103(12):2141-2146. doi:10.2105/AJPH.2012.301200

8. Flores LE, Frontera WR, Andrasik MP, et al. Assessment of the inclusion of racial/ethnic minority, female, and older individuals in vaccine clinical trials. *JAMA Netw Open*. 2021;4(2):e2037640. doi:10.1001/jamanetworkopen.2020.37640

9. Guidry JJ, Aday LA, Zhang D, Winn RJ. Transportation as a barrier to cancer treatment. *Cancer Pract*. 1997;5(6):361-366.

10. Silver D, Blustein J, Weitzman BC. Transportation to clinic: findings from a pilot clinic-based survey of low-income suburbanites. *J Immigr Minor Health*. 2012;14(2):350-355. doi:10.1007/s10903-010-9410-0

11. Loree JM, Anand S, Dasari A, et al. Disparity of race reporting and representation in clinical trials leading to cancer drug approvals from 2008 to 2018. *JAMA Oncol*. 2019;5(10):e191870. doi:10.1001/jamaoncol.2019.1870

12. Racial and ethnic categories and definitions for nih diversity programs and for other reporting purposes. National Institute of Health. April 8, 2015. Accessed June 1, 2023. https://grants.nih.gov/grants/guide/notice-files/not-od-15-089.html

13. Aravena C, Almeida FA, Mukhopadhyay S, et al. Idiopathic subglottic stenosis: a review. *J Thorac Dis*. 2020;12(3):1100-1111. doi:10.21037/jtd.2019.11.43

14. Myer CM, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. *Ann Otol Rhinol Laryngol*. 1994;103(4 pt 1):319-323. doi:10.1177/000348949410300410

15. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097

16. Bramer WM, Giustini D, de Jonge GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc*. 2016;104(3):240-243. doi:10.5195/jmla.2016.24

17. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. doi:10.1186/s13643-016-0384-4

18. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. *Int J Health Policy Manag*. 2014;3(3):123-128. doi:10.15171/ijhpm.2014.71

19. Aarnæs MT, Sandvik L, Brøndbo K. Idiopathic subglottic stenosis: an epidemiological single-center study. *Eur Arch Otrhinolaryngol*. 2017;274(5):2225-2228. doi:10.1007/s00405-017-4512-0

20. Anderson C, Sandhu G, Al Yaghchi C. Impact of the COVID-19 pandemic on patients with idiopathic subglottic stenosis. *Ear Nose Throat J*. 2021;100(2_suppl):122S-130S. doi:10.1177/0145561320977467

21. Benjamin B, Jacobson I, Eckstein R. Idiopathic subglottic stenosis: diagnosis and endoscopic laser treatment. *Ann Otol Rhinol Laryngol*. 1997;106(9):770-774. doi:10.1177/000348949710600911

22. Berges AJ, Lina IA, Chen L, Ospino R, Davis R, Hillel AT. Delayed diagnosis of idiopathic subglottic stenosis. *Laryngoscope*. 2022;132(2):413-418. doi:10.1002/lary.29783

23. Blumin JH, Johnston N. Evidence of extraesophageal reflux in idiopathic subglottic stenosis. *Laryngoscope*. 2011;121(6):1266-1273. doi:10.1002/lary.21776

24. Carpenter DJ, Ferrante S, Bakos SR, Clary MS, Gelbard AH, Daniero JJ. Utility of routine spirometry measures for surveillance of idiopathic subglottic stenosis. *JAMA Otolaryngol Head Neck Surg*. 2019;145(1):21-26. doi:10.1001/jamaoto.2018.2717

25. Carpenter PS, Pierce JL, Smith ME. Outcomes after cricotracheal resection for idiopathic subglottic stenosis. *Laryngoscope*. 2018;128(10):2268-2272. doi:10.1002/lary.27263

26. Case HF, Lott DG, Do ALR. Anxiety and depression in patients with idiopathic subglottic stenosis. *J Voice*. 2022;S0892-1997(22)00059-5. doi:10.1016/j.jvoice.2022.02.020

27. Chan RK, Ahrens B, MacEachern P, Bosch JD, Randall DR. Prevalence and incidence of idiopathic subglottic stenosis in southern and central Alberta: a retrospective cohort study. *J Otolaryngol Head Neck Surg*. 2021;50(1):64. doi:10.1186/s40463-021-00544-8

28. Compton EC, Beveridge S, Andreassen M, et al. Long-term voice outcomes following cricotracheal resection for subglottic stenosis: a retrospective analysis. *Laryngoscope*. 2022;132(5):1054-1060. doi:10.1002/lary.29827

29. D'Oto A, Baker H, Mau T, Childs LF, Tibbetts KM. Characteristics of idiopathic subglottic stenosis in the elderly. *Laryngoscope*. 2023;133:3075-3079. doi:10.1002/lary.30742

30. Davis RJ, Lina I, Ding D, et al. Increased expression of PD-1 and PD-L1 in Patients with laryngotracheal stenosis. *Laryngoscope*. 2021;131(5):967-974. doi:10.1002/lary.28790

31. Davis RJ, Lina I, Motz K, et al. Endoscopic resection and mucosal reconstitution with epidermal grafting: a pilot study in idiopathic subglottic stenosis. *Otolaryngol Head Neck Surg*. 2022;166(5):917-926. doi:10.1177/01945998211028163

32. Dedo HH, Catten MD. Idiopathic progressive subglottic stenosis: findings and treatment in 52 patients. *Ann Otol Rhinol Laryngol*. 2001;110(4):305-311. doi:10.1177/000348940111000403

33. Fang H, Codipilly DC, Ravi K, Ekbom DC, Kasperbauer JL, Halland M. Gastroesophageal reflux characteristics and patterns in patients with idiopathic subglottic stenosis. *Gastroenterol Res Pract*. 2018;2018:1-5. doi:10.1155/2018/8563697

34. Fiz I, Koelmel JC, Piazza C, et al. Predictors of recurrence after surgical treatment of idiopathic progressive subglottic stenosis. *Acta Otorhinolaryngol Ital*. 2018;38(5):417-423. doi:10.14639/0392-100X-1872

35. Gadkaree SK, Pandian V, Best S, et al. Laryngotracheal stenosis: risk factors for tracheostomy dependence and dilation interval. *Otolaryngol Head Neck Surg*. 2017;156(2):321-328. doi:10.1177/0194599816675323

36. Gelbard A, Wanjalla C, Wootten CT, et al. The proximal airway is a reservoir for adaptive immunologic memory in idiopathic subglottic stenosis. *Laryngoscope*. 2021;131(3):610-617. doi:10.1002/lary.28840

37. Gnagi SH, Howard BE, Anderson C, Lott DG. Idiopathic subglottic and tracheal stenosis: a survey of the patient experience. *Ann Otol Rhinol Laryngol.* 2015;124(9):734-739. doi:10.1177/0003489415582255

38. Grillo HC, Mathisen DJ, Wright CD, Ashiku SK, Wain JC. Successful treatment of idiopathic laryngotracheal stenosis by resection and primary anastomosis. *Ann Otol Rhinol Laryngol.* 2003;112(9):798-800. doi:10.1177/000348940311200909

39. Guo Z, Cui P, Zhao D, et al. Diagnosis and treatment of 15 cases of idiopathic subglottic stenosis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.* 2020;34(2):173-176. doi:10.13201/j.issn.1001-1781.2020.02.018

40. Hall SR, Allen CT, Merati AL, Mayerhoff RM. Evaluating the utility of serological testing in laryngotracheal stenosis. *Laryngoscope.* 2017;127(6):1408-1412. doi:10.1002/lary.26385

41. Hintze JM, Fitzgerald CW, O'Riordan I, Keane E, Kinsella J, Timon C. Idiopathic subglottic stenosis—a familial association and review of practice. *J Laryngol Otol.* 2022; 136(12):1275-1277. doi:10.1017/S0022215122001049

42. Hoffman MR, Coughlin AR, Dailey SH. Serial office-based steroid injections for treatment of idiopathic subglottic stenosis. *Laryngoscope.* 2017;127(11):2475-2481. doi:10.1002/lary.26682

43. Hoffman MR, Francis DO, Mai JP, Dailey SH. Office-based steroid injections for idiopathic subglottic stenosis: patient-reported outcomes, effect on stenosis, and side effects. *Ann Otol Rhinol Laryngol.* 2020;129(4):361-368. doi:10.1177/0003489419889066

44. Holmes C, Aravinthan K, Murphy RA, Gore-Hickman R, Nair SP, Sharma AR. Idiopathic subglottic stenosis in Saskatchewan Hutterite population. *J Laryngol Otol.* 2022;136(6):554-558. doi:10.1017/S0022215122000445

45. Jindal JR, Milbrath MM, Hogan WJ, Shaker R, Toohill RJ. Gastroesophageal reflux disease as a likely cause of "idiopathic" subglottic stenosis. *Ann Otol Rhinol Laryngol.* 1994;103(3):186-191. doi:10.1177/000348949410300304

46. Kimura K, Du L, Berry LD, et al. Modeling recurrence in idiopathic subglottic stenosis with mobile peak expiratory flow. *Laryngoscope.* 2021;131(12):E2841-E2848. doi:10.1002/lary.29760

47. Kraft SM, Sykes K, Palmer A, Schindler J. Using pulmonary function data to assess outcomes in the endoscopic management of subglottic stenosis. *Ann Otol Rhinol Laryngol.* 2015;124(2):137-142. doi:10.1177/0003489414548915

48. Lee J, Huang LC, Berry LD, et al. Association of social determinants of health with time to diagnosis and treatment outcomes in idiopathic subglottic stenosis. *Ann Otol Rhinol Laryngol.* 2021;130(10):1116-1124. doi:10.1177/0003489421995283

49. Lina IA, Tsai HW, Berges AJ, et al. Phenotypic epithelial changes in laryngotracheal stenosis. *Laryngoscope.* 2022; 132(11):2194-2201. doi:10.1002/lary.30040

50. Liu MM, Motz KM, Murphy MK, et al. Laryngotracheal mucosal surface expression of candidate biomarkers in idiopathic subglottic stenosis. *Laryngoscope.* 2021;131(2): 342-349. doi:10.1002/lary.28712

51. Lu RJ, Hijaz B, Naunheim MR, Stevenson L, Franco RA. The subglottic stenosis 6 questionnaire. *Chest.* 2024;165: 161-171. doi:10.1016/j.chest.2023.07.4217

52. Maronian NC, Waugh P, Azadeh H, Hillel A. Association of laryngopharyngeal reflux disease and subglottic stenosis. *Ann Otol Rhinol Laryngol.* 2001;110(7):606-612. doi:10.1177/000348940111000703

53. Menapace DC, Ekbom DC, Larson DP, Lalich IJ, Edell ES, Kasperbauer JL. Evaluating the association of clinical factors with symptomatic recurrence of idiopathic subglottic stenosis. *JAMA Otolaryngol Head Neck Surg.* 2019;145(6): 524. doi:10.1001/jamaoto.2019.0707

54. Menapace DC, Modest MC, Ekbom DC, Moore EJ, Edell ES, Kasperbauer JL. Idiopathic subglottic stenosis: long-term outcomes of open surgical techniques. *Otolaryngol Head Neck Surg.* 2017;156(5):906-911. doi:10.1177/0194599817691955

55. Morcillo A, Wins R, Gómez-Caro A, Paradela M, Molins L, Tarrazona V. Single-staged laryngotracheal reconstruction for idiopathic tracheal stenosis. *Ann Thorac Surg.* 2013;95(2):433-439. doi:10.1016/j.athoracsur.2012.09.093

56. Motz KM, Yin LX, Samad I, et al. Quantification of inflammatory markers in laryngotracheal stenosis. *Otolaryngol Head Neck Surg.* 2017;157(3):466-472. doi:10.1177/0194599817706930

57. Nouraei SAR, Dorman EB, Johnston J, Vokes DE. Vocal fold fixation due to proximal stenosis progression complicating idiopathic subglottic stenosis. *Eur Arch Otrhinolaryngol.* 2019;276(8):2293-2300. doi:10.1007/s00405-019-05494-6

58. Nouraei SaR, Sandhu GS. Outcome of a multimodality approach to the management of idiopathic subglottic stenosis. *Laryngoscope.* 2013;123(10):2474-2484. doi:10.1002/lary.23949

59. Ospino R, Berges A, Mafla L, et al. Characterizing the macrophage population in patients with idiopathic subglottic stenosis. *Laryngoscope.* 2023;133(9):2308-2316. doi:10.1002/lary.30524

60. Park SS, Streitz, Jr. JM, Rebeiz EE, Shapshay SM. Idiopathic subglottic stenosis. *Arch Otolaryngol Head Neck Surg.* 1995;121(8):894-897. doi:10.1001/archotol.1995.01890080062012

61. Rohlfing ML, Hillel AT, Wohler E, et al. Human leukocyte antigen genotyping of idiopathic subglottic stenosis. *Laryngoscope.* 2023;133(10):2533-2539. doi:10.1002/lary.30580

62. Schoeff S, Hoffman MR, Zhang Y, Yang Q, Dailey SH. Long-term follow-up of 64 patients with idiopathic subglottic stenosis: treatment pathways, outcomes, and impact of serial intralesional steroid injections. *Ann Otol Rhinol Laryngol.* 2023;132(11):1341-1348. doi:10.1177/00034894231156122

63. Schoeff SS, Shi X, Young WG, et al. Proteomic and genomic methylation signatures of idiopathic subglottic stenosis. *Laryngoscope.* 2021;131(2):E540-E546. doi:10.1002/lary.28851

64. Shabani S, Hoffman MR, Brand WT, Dailey SH. Endoscopic management of idiopathic subglottic stenosis: factors affecting inter-dilation interval. *Ann Otol Rhinol*

Laryngol. 2017;126(2):96-102. doi:10.1177/00034894166 75357

65. Singh E, Hullfish H, Fils A, Ma R, Rosow D. Predictors of clinical outcomes in adult laryngotracheal stenosis. *Laryngoscope.* 2024;134:257-263. doi:10.1002/lary.30908

66. Tapias LF, Rogan TJ, Wright CD, Mathisen DJ. Pregnancy-associated idiopathic laryngotracheal stenosis: presentation, management and results of surgical treatment. *Eur J Cardiothorac Surg.* 2021;59(1):122-129. doi:10.1093/ ejcts/ezaa296

67. Taylor SC, Clayburgh DR, Rosenbaum JT, Schindler JS. Clinical manifestations and treatment of idiopathic and wegener granulomatosis–associated subglottic stenosis. *JAMA Otolaryngol Head Neck Surg.* 2013;139(1):76. doi:10.1001/jamaoto.2013.1135

68. Valdez TA, Shapshay SM. Idiopathic subglottic stenosis revisited. *Ann Otol Rhinol Laryngol.* 2002;111(8):690-695. doi:10.1177/000348940211100806

69. Wang H, Wright CD, Wain JC, Ott HC, Mathisen DJ. Idiopathic subglottic stenosis: factors affecting outcome after single-stage repair. *Ann Thorac Surg.* 2015;100(5):1804-1811. doi:10.1016/j.athoracsur.2015.05.079

70. Woliansky J, Paddle P, Phyland D. Laryngotracheal stenosis management: a 16-year experience. *Ear Nose Throat J.* 2021; 100(5):360-367. doi:10.1177/0145561319873593

71. Zhang C, Wang S, Casal Moura M, et al. RNA sequencing of idiopathic subglottic stenosis tissues uncovers putative profibrotic mechanisms and identifies a prognostic bio-marker. *Am J Pathol.* 2022;192(11):1506-1530. doi:10.1016/j. ajpath.2022.07.005

72. Gelbard A, Shyr Y, Berry L, et al. Treatment options in idiopathic subglottic stenosis: protocol for a prospective international multicentre pragmatic trial. *BMJ Open.* 2018;8(4):e022243. doi:10.1136/bmjopen-2018-022243

73. Hatta C, Terada T, Kakibuchi M, Ogasawara H, Nakasho K, Sakagami M. A case of idiopathic tracheal stenosis. *Auris Nasus Larynx.* 2003;30(4):435-438. doi:10.1016/s0385-8146(03)00094-4

74. To M, Sano Y, Hata E. A case of idiopathic subglottic stenosis successfully treated with endoscopic laser treatment. *Nihon Kokyuki Gakkai Zasshi.* 2000;38(7):545-550.

75. Yamada S, Kikuchi K, Kosaka A, Inoue H, Umemura S. Surgical management of idiopathic tracheal stenosis. *Jpn J Thorac Cardiovasc Surg.* 1999;47(7):335-338. doi:10.1007/ BF03218021

76. Dezfouli AA, Shadmehr MB, Sheikhy K. Idiopathic subglottic tracheal stenosis in identical twin sisters. *Iran J Otorhinolaryngol.* 2019;31(105):243-245.

77. Lavrysen E, Hens G, Delaere P, Meulemans J. Endoscopic treatment of idiopathic subglottic stenosis: a systematic review. *Front Surg.* 2020;6:75. doi:10.3389/fsurg.2019. 00075

78. Abbasi Dezfouli A, Shadmehr MB, Sheikhy K. Idiopathic subglottic tracheal stenosis in identical twin sisters. *Iran J Otorhinolaryngol.* 2019;31(105):243-245.