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Restenosis Following Bronchoscopic Airway Stenting for Complex Tracheal Stenosis

Ara A. Chrissian, MD, Javier Diaz-Mendoza, MD,†‡ and Michael J. Simoff, MD†*

Background: **Nonsurgical patients with complex post-intubation tracheal stenosis (PITS) and tracheostomy-associated tracheal stenosis (PTTS) often require airway stenting. However, the optimal approach is unknown. Identifying patients at higher risk for restenosis after stent removal may allow the treating physician to individualize the vigilance and duration of airway stenting, and help optimize outcomes.**

Methods: **This was a single-center retrospective analysis of prospectively collected data on all patients with complex PITS and/or PTTS treated with protocolized bronchoscopic airway stenting over a consecutive 16-year period. The primary outcome analyzed was restenosis rate at 1 year after stent removal. Predictors for restenosis and factors influencing risk for death during stent therapy were also assessed.**

Results: **Of the 181 subjects treated with silicone airway stenting, 128 were available for analysis of the primary outcome. Restenosis by 1 year after stent removal occurred in 58%. Independent predictors for restenosis were coexisting diabetes [odd ratio (OR) = 3.10, 95% confidence interval (CI) = 1.04-9.24; $P = 0.04$], morbid obesity (OR = 3.13, 95% CI = 1.20-8.17; $P = 0.02$), and occurrence of stent-associated complications requiring bronchoscopic management (OR = 2.13, 95% CI = 1.12-4.03; $P = 0.02$). The overall mortality during the initial stenting period was 14%, and a silicone Y-stent was associated with a higher risk of death (OR = 3.58, 95% CI = 1.40-9.14; $P = 0.008$).**

Conclusion: **Tracheal restenosis after silicone stent therapy for complex PITS and PTTS is common and more likely to occur in patients with diabetes, morbid obesity, and frequent stent-associated complications. Mortality risk during stent therapy is not negligible, and a Y-stent should be utilized only after careful consideration. These findings may be incorporated into the approach to bronchoscopic airway stenting in these patients.**

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Nonmalignant tracheal stenosis is a relatively rare yet debilitating and life-threatening disease resulting from local injury and ischemia of the airway wall. Endotracheal intubation [post-intubation tracheal stenosis (PITS)] or placement of a tracheostomy tube [post-tracheostomy tracheal stenosis (PTTS)] is often implicated. The type and extent of the stenosis may be related to the severity of insult, loss of cartilaginous integrity, and underlying disease. A complex lesion is often described as involving the full thickness of the tracheal wall, measuring >1 cm in length, or exhibiting associated malacia.[1,2] The definitive treatment for complex tracheal stenosis is surgical resection and tracheal reconstruction.[3]

Unfortunately, comorbid conditions in patients with complex PITS/PTTS often preclude surgical intervention. Bronchoscopic approaches including airway stenting can be offered to individuals with limited options.[2,4–10] Stenting aims to stabilize and protect the diseased tracheal segment while appropriate re-epithelialization and remodeling occurs. In a proportion of patients, the stent may be removed allowing for long-term airway stability, while in others recurrent narrowing necessitates re-intervention. Stent-related complications include migration, airway obstruction and infection.[11,12] These may interfere with healing and expose the patient to additional risk, including death.[13] The heterogeneity and relative paucity of the available literature studying this patient population prevents reliable conclusions on predictors of initial stent therapy success.

The primary purpose of this study was to analyze the rate of tracheal restenosis after airway stent therapy in patients with complex PITS and PTTS. Secondary goals were to identify predictors of restenosis and predictors of death during the initial stenting period. The sample

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source is a referral center that manages tracheal stenosis not amenable to surgical correction. It has a long-standing protocolized approach to these patients, including indications for stenting, scheduled bronchoscopic surveillance, duration of therapy, and management of complications. Consequently, the study database offers a valuable tool for assessing the utility of bronchoscopic management of complex PITS and PTTS treated with airway stenting.

METHODS

Design

This was a retrospective analysis of prospectively collected data on all patients with PITS and PTTS treated with airway stenting over a consecutive 16-year period. The utilized database catalogs all bronchoscopic interventions by multiple patient, procedure, and outcome-related characteristics. The study hospital's Institutional Review Board provided its approval (#11450).

Data Collection

All patient, procedural, and outcome variables were predefined and a data extraction form was created a priori. All data extraction and primary analysis was performed by investigators not involved in any of the procedures performed during the study period. Each subject's medical record was reviewed in detail and compared with the existing prospective database to ensure accuracy. Relevant missing data points were added as needed, if available.

Outcomes

The primary outcome was tracheal restenosis at 1 year after stent removal. Restenosis was definitively diagnosed and characterized by bronchoscopy, and defined as a re-narrowing of the airway requiring any intervention. As secondary outcomes, we analyzed predictors of restenosis after stent removal, and predictors of death during the initial stenting period.

Patient Assessment for Airway Stenting

Airway stenting for PITS/PTTS was considered for a clinically significant complex lesion or for a simple lesion that recurred more than once despite conservative measures. We defined a stenosis as clinically significant if there was more than 50% cross-sectional obstruction or if there was dyspnea, regardless of extent of endoluminal compromise. Simple lesions were those without any complex features: they were <1 cm in length, had only mucosal involvement and no associated malacia.[1,2] Conservative measures used to treat simple stenoses included LASER-assisted mechanical dilation (LAMD) using either a rigid bronchoscope or airway balloon, with or without mucosal application of steroid or mitomycin-C. For all cases, airway stenting was offered after evaluating the potential for surgical reconstruction or tracheostomy tube placement/revision. This assessment was based on disease-specific, anatomic, comorbid, and patient-centered factors.

Airway Stenting Protocol

Only silicone stents were used, and in all cases were deployed using rigid bronchoscopy. The type and dimensions of the initial prosthesis was at the discretion of the treating physician and was one of a straight silicone stent (Bryan Corp or Endoxane-Novatech; Aubagne, France), a Y-shaped silicone stent (Bryan Corp or Endoxane-Novatech; Aubagne) or a Montgomery T-tube (Hood Laboratories; Pembroke, MA). Supplemental LAMD was performed as indicated. The type of LASER used was one of neodymium-doped yttrium aluminum garnet (Nd:YAG), potassium titanyl phosphate, or Holmium. If LAMD was performed at the time of stent placement, mucosal therapy with steroid or mitomycin-C was applied per discretion of the treating physician. After stent insertion, each patient was given a stent clearance regimen and scheduled for surveillance bronchoscopy at 1 month and 3 months poststent placement. Additional bronchoscopies to manage complications were performed as needed.

The goal of stent therapy was to promote and allow time for airway remodeling. During the first 8 years of the study period, the stent was removed after maintaining 6 months of a stable airway, defined as a continuously stent-covered lesion. During the latter 8 years, the stent was removed after 4 months of a stable airway. This change in practice was because of apparent similar outcomes between the 2 approaches found during an internal quality review (unpublished data). Reasons for stent removal before completion of protocolized indwelling time included recurrent complications or patient noncompliance. After stent removal, all patients were evaluated with bronchoscopy 1 week and then 1-month postremoval. They were then followed at 3, 6, and 12 months using a combination of clinical assessment, spirometry, computed tomography scanning, and bronchoscopy as needed.

Statistical Analysis

Statistical analysis was performed using SPSS software (IBM SPSS Statistics, Chicago, IL) and R Cran version 3.5.1 (R Core Team, 2019). Simple

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bivariate analyses were conducted to evaluate differences between restenosis or death status (the Pearson χ^2 or the Fisher exact tests for categorical variables and 2 sample t test or Mann-Whitney U test for continuous variables). Multivariate logistic regression analysis was used to determine predictors of restenosis and death. Variables chosen for these models were based on clinical relevance and/or suggestion of significant group differences during bivariate analysis.

RESULTS

A total of 346 patients treated for PITS or PTTS over the consecutive 16-year study period were identified. Of these, 198 were managed with airway stenting, with 181 having follow-up for at least 6 months after stent placement or until removal (Fig. 1). Acuity was high, with 47% of subjects hospitalized at time of diagnosis. A large majority (94%) of stented stenoses were complex, 48% percent had severe (Cotton-Myer ≥ 3) tracheal narrowing, and 40% were longer than 2 cm. Most lesions (84%) were located in the proximal trachea, and 64% were associated with current or past tracheostomy (PTTS).

A straight silicone stent was the most common initial stent placed (69%). In 45 subjects (25%), a silicone Y-stent was chosen for initial intervention. At least 1 delayed stent-associated complication occurred in 69% of subjects (Table 1). Granulation (39%) and migration (34%) were most common. To manage these, 2.5 bronchoscopies in addition to those performed for routine stent surveillance were required. Overall, excluding the procedures required for initial stent placement and final removal, patients received an average of 3.4 bronchoscopies during their initial stenting period. This translated to 0.86 bronchoscopies per stent-month (a bronchoscopy every 1.2 mo). Twenty-six subjects (14%) died during the initial stenting period.

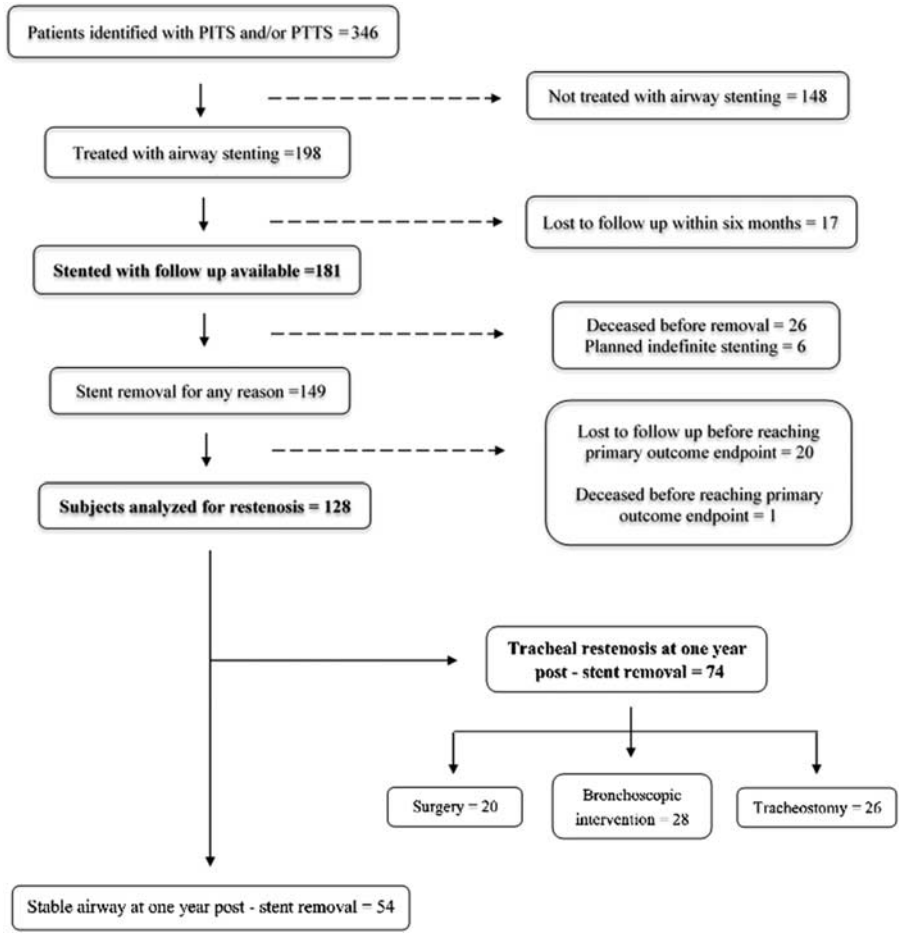

FIGURE 1. Flow diagram summarizing subject selection and outcomes. PITS indicates postintubation tracheal stenosis; PTTS, post-tracheostomy tracheal stenosis.

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TABLE 1. Delayed Stent-associated Complications and Secondary Bronchoscopic Management Burden Among 181 Subjects With at Least 6 Months Follow-up Available After Initial Stenting

Complication	Incidence, n (%)	Median Time to First Event, Weeks (Interquartile Range)	Number of Nonprotocolized Bronchoscopies* Required for Management, Per Patient
Granulation	71 (39.2)	4.5 (10)	1.6
Migration	62 (34.3)	4 (6)	1.7
Mucostasis	51 (28.2)	3.5 (7)	1.4
Malfunction†	14 (7.7)	4 (12)	1.4
Overall	125 (69.1)	4 (5)	2.5

*Bronchoscopies performed in addition to those of the 1-month and 3-month stent surveillance protocol.
†Stent tear or malfolding.

Ultimately, 149 subjects underwent stent removal, with 128 available for analysis of the primary outcome. Their characteristics are shown in Table 2. Mean indwelling stent duration was 25.2 weeks (±21.1). Forty-six subjects (36%) had their stents removed because of intolerance before reaching planned protocolized indwelling duration goal. The most common single motive for premature stent removal was recurrent stent migration

TABLE 2. Characteristics of Subjects With and Without Restenosis at 1-year After Stent Removal

Patient Characteristics	Overall (n = 128), n (%)	Restenosis (n = 74), n (%)	No Restenosis (n = 54), n (%)	*P*
Age at diagnosis, years, mean (SD)	52.2 (15.8)	51.1 (15.4)	53.6 (16.3)	0.262
Female	84 (65.6)	51 (68.9)	33 (61.1)	0.451
Diagnosis				
PITS	46 (35.9)	26 (35.1)	20 (37.0)	0.854
PTTS	82 (64.1)	48 (64.9)	34 (63.0)	
Hospitalized at time of diagnosis	60 (46.9)	39 (52.7)	21 (38.9)	0.152
Respiratory failure at time of diagnosis	28 (21.9)	13 (17.6)	15 (27.8)	0.197
Comorbid conditions				
Hypertension	74 (57.8)	42 (56.8)	32 (59.3)	0.857
Diabetes	59 (46.1)	38 (51.4)	21 (38.9)	0.209
Morbid obesity	51 (39.8)	36 (48.7)	15 (27.8)	0.019
Gastroesophageal reflux disease	50 (39.1)	31 (41.9)	19 (35.2)	0.469
Chronic lung disease	44 (34.4)	29 (39.2)	15 (27.8)	0.193
Coronary disease	40 (31.2)	22 (29.7)	18 (33.3)	0.702
Chronic renal disease	22 (17.2)	12 (16.2)	10 (18.5)	0.814
Dependent functional status	17 (13.3)	10 (13.5)	7 (13.0)	0.999
Lesion and procedure characteristics				
Proximal tracheal location	108 (84.4)	61 (82.4)	47 (87.0)	0.62
Cotton-Myer ≥3 obstruction	62 (48.4)	38 (51.4)	24 (44.4)	0.714
Length >2 cm	52 (40.6)	36 (48.6)	16 (29.6)	0.045
Pseudoglottic ("A-shape") configuration	46 (35.9)	24 (32.4)	22 (40.7)	0.356
Associated malacia	43 (33.6)	21 (28.4)	22 (40.7)	0.185
Previous airway intervention	37 (28.9)	28 (38.4)	9 (17.0)	0.01
LAMD+mucosal therapy at time of initial stent placement*	57 (44.5)	38 (51.4)	19 (34.5)	0.073
Initial stent type = silicone Y	26 (20.3)	11 (14.9)	15 (27.8)	0.08
Stent therapy characteristics				
6-month stent protocol group (vs. 4-month)	64 (50.0)	38 (51.4)	26 (48.2)	0.858
Total indwelling stent time, weeks, mean (SD)	25.19 (21.1)	24.73 (23.1)	25.81 (18.2)	0.236
Revision of first stent for any complication	52 (40.6)	38 (51.4)	14 (25.9)	0.006
Number of bronchoscopies† required to manage stent complications, per stent-month, mean (SD)	0.54 (0.97)	0.72 (1.12)	0.29 (0.64)	0.005
Stent removed per protocol	82 (64.1)	40 (54.1)	42 (77.8)	0.009

*Laser-assisted mechanical dilation with mucosal steroid or antifibrotic therapy.
†In addition to those performed as part of stent surveillance protocol, as outlined in text.
PITS indicates postintubation tracheal stenosis; PTTS, post-tracheostomy tracheal stenosis.

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TABLE 3. Multivariate Analysis Determining Predictors of Restenosis at 1-year Poststent Removal

Variable	OR	2.50%	97.50%	*P*
Diabetes	3.10	1.04	9.24	0.042
Coronary disease	0.50	0.16	1.53	0.223
Renal disease	0.87	0.27	2.80	0.810
Gastroesophageal reflux disease	1.30	0.52	3.26	0.571
Lung disease	1.72	0.66	4.47	0.263
Morbid obesity	3.13	1.20	8.17	0.020
Previous airway intervention	2.53	0.89	7.19	0.081
Length of stenosis >2 cm (vs. 2 cm or shorter)	2.61	0.92	7.36	0.07
Cotton-Myer ≥grade 3 obstruction (vs. less severe)	1.28	0.52	3.16	0.593
Pseudoglottic ("A-shape") configuration (vs. all others)	0.45	0.14	1.41	0.172
6-month stent duration protocol group (vs. 4-month)	1.12	0.46	2.69	0.808
Silicone Y-stent (vs. others)	0.19	0.06	0.62	0.006
LAMD+mucosal therapy at time of initial stent placement*	0.48	0.16	1.37	0.168
Bronchoscopies required† to manage complications, per stent-month	2.13	1.12	4.03	0.021

*Laser-assisted mechanical dilation with mucosal steroid or antifibrotic therapy.
†In addition to those performed as part of stent surveillance protocol, as outlined in text.
LAMD indicates LASER-assisted mechanical dilation; OR, odds ratio.

(12 subjects), which occurred exclusively with straight silicone stents.

The overall tracheal restenosis rate at 1 year was 58% (74 subjects) and occurred at a median of 1 week after stent removal (interquartile range = 0 to 4). Bivariate analysis identified multiple factors associated with restenosis (Table 2). Twenty subjects with restenosis became surgically operable and were treated with resection. The remaining 54 subjects were managed with either tracheostomy or various bronchoscopic applications, such as dilation, mucosal therapies, and/or re-stenting (Fig. 1). Restenosis risk was similar between stenting duration protocol groups (6 vs. 4 months, $P = 0.86$).

Multivariate analysis of patient, lesion, and stent-related characteristics identified coexisting diabetes and morbid obesity, as well as occurrence of stent-associated complications requiring bronchoscopic management as independent predictors for restenosis (Table 3). While the placement of a silicone Y-stent had a protective effect against eventual restenosis compared with other stent types [odd ratio (OR = 0.19, 95% confidence interval (CI) = 0.06-0.62, $P = 0.006$], Y-stent therapy was also associated with death during the

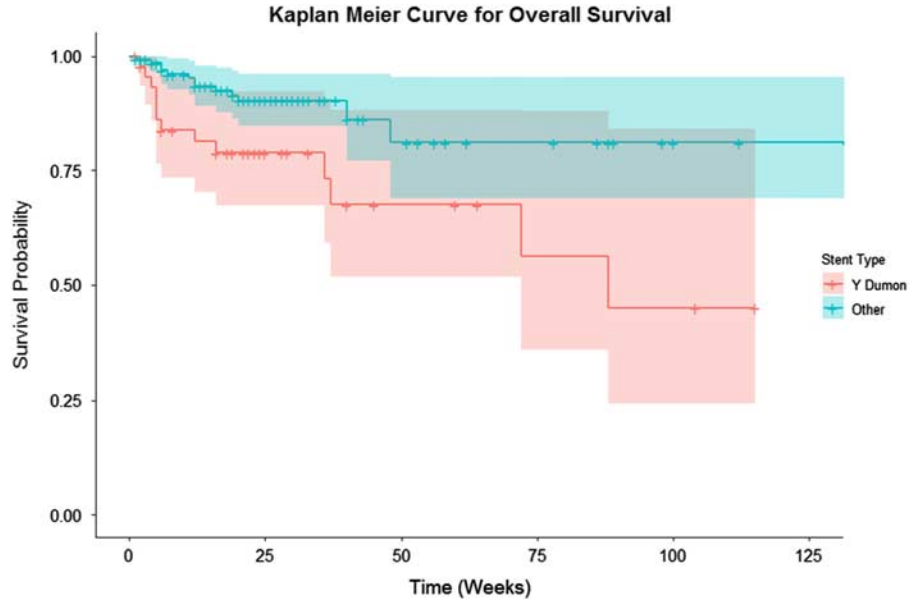

FIGURE 2. Survival probability during airway stenting: subjects with silicone Y-stents and all others; $P = 0.008$.

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initial stenting period (OR = 3.58, 95% CI = 1.40-9.14, $P = 0.008$; Fig. 2).

DISCUSSION

To our knowledge, this is the largest analysis to date assessing the outcome of patients with complex postintubation and tracheostomy-associated tracheal stenosis treated with bronchoscopic airway stenting. We found that restenosis at 1 year after stent removal was common overall (58%), and in a large majority of subjects (85%) occurred within 1 month. Adjusted analysis revealed restenosis was more likely in those with diabetes and morbid obesity. It also occurred more in subjects who had experienced stent-associated complications requiring additional intervention.

Success of airway stenting may depend on multiple factors affecting the healing process, including patient comorbidities, lesional features, and therapeutic approach. Our findings are consistent with the underlying pathogenesis of PITS/PTTS, which results from mucosal injury, exuberant inflammation, and dysregulated tissue repair and remodeling.[14–16] Local ischemia triggers expression of hypoxia-inducible factor-1α and its various target growth factors, resulting in activation of myofibroblasts, deposition of extracellular matrix and scar formation.[17] Diabetes is an established marker of microvascular disease and a known predictor of poorer wound healing because of compromised tissue blood flow and oxygen delivery. For example, diabetic PITS patients treated surgically are at higher risk for anastomotic complications.[18–20] The diabetics in our cohort also had a suboptimal outcome with stent therapy. Aggressive glycemic control and lifestyle modification is of utmost importance for these patients during their stenting period to optimize candidacy for potential future operability.

We found morbid obesity was also associated with a higher likelihood for restenosis. While morbid obesity often coexists with other chronic medical conditions, such as diabetes, coronary disease, and gastroesophageal reflux, after adjusting for these variables it remained an independent risk factor for eventual restenosis. This may be because of the presence of confounders not factored into our model. However, obesity also represents an independent marker of compromised wound healing because of multiple factors such as alterations in immunoregulation, tissue repair mechanisms, resistance to oxidative stress, and nutrient utilization.[21] As with glycemic control, weight loss should be an integral component of the management of these patients.

Other microvascular disease-equivalents, such as coronary insufficiency and chronic renal failure, may also influence likelihood for restenosis. Lim et al[6] reported higher success of stent removal in PITS patients who did not have cardiovascular disease (OR = 12.20, $P = 0.036$). In contrast, our model did not predict restenosis in those with cardiac or renal comorbidity, and other studies have not reported on this association. This may be because demonstrating coexistent cardiovascular illness in study design is more difficult than establishing presence of diabetes. In addition, patients with renal disease are relatively uncommon in patients with PITS, limiting the sample size available for analysis. Within our study only 19% of subjects had evidence of renal failure of any stage, while 52% had diabetes. Therefore, the impact of cardiac or renal disorders on tracheal restenosis after stent therapy remains unclear.

Our analysis did not reveal any lesional characteristics to be convincingly predictive of restenosis. Complex injuries of longer length theoretically may represent a poorer template for successful healing because of more severe inflammation, increased chance for multilevel cartilaginous compromise, and a higher likelihood of bacterial colonization with stenting. Lesional length (and by extension, length of resected trachea) is a recognized predictor for poorer outcome after tracheal reconstruction.[20] However, in our study the adjusted association of longitudinal extent with restenosis after stent removal approached, but did not reach, statistical significance. Similarly, other investigations of complex PITS patients treated with stenting have not shown such an association.[6,9,10] We also found restenosis occurred with similar frequency in PITS and PTTS subjects. That these and other features such as severity of intraluminal compromise, location, configuration, or associated malacia failed to predict restenosis underscores the complexity and heterogeneity of the disease. Furthermore, detailing these characteristics during bronchoscopic evaluation remains subjective and proceduralist dependent. Therefore, given the data available, we caution against using lesion-associated features to forecast potential outcomes of stent therapy.

Among factors associated with stent therapy, we found that subjects who had frequent stent-related complications requiring bronchoscopic

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intervention were more likely to have restenosis. Of these complications, stent migration likely contributed most to eventual stent therapy failure. Migration occurred in 34% of our cohort, and its recurrence was the most frequent reason for stent revisions and premature stent removal. Not surprisingly, these patients had a significantly higher risk of restenosis than those who tolerated their stents until the target protocolized removal date (74% vs. 49%, $P = 0.009$). A consistently stable airway during stent therapy is likely an important factor in promoting healing. Recurrent migrations lead to lesion re-exposure, potential reinjury because of additional intervention, and a resetting of remodeling. Supporting this theory is that in our cohort migration did not occur with Y-stents, and the use of a Y-stent protected against restenosis even though these patients still required interventions to manage other complications. The "stable" Y-stent may have optimized chances for healing by more consistently protecting the lesion and minimizing recurrent local insult. Unfortunately, predicting which straight stent types are more likely to migrate is challenging. To our knowledge, other studies have not adequately evaluated the impact of stent-associated complications on stent therapy outcomes in this patient population.

While a reasonable conclusion then could be to manage these patients preferentially with Y-stents, we also found Y-stent therapy to be associated with death during the stenting period. This was after adjusting for multiple variables including comorbidities, stenosis length, severity of luminal obstruction, and need for bronchoscopic interventions. This result, which negated the benefit on restenosis rate, has several potential explanations. Y-stents for PITS/PTTS usually require a long tracheal limb to ensure proper coverage of proximally located lesions. This substantially reduces the surface area of otherwise normal trachea and can increase the risk for tenacious mucostasis and secondary airway obstruction or respiratory infection. Indeed, when reviewing the profile of deceased subjects in our cohort, 16 of 26 (62%) died either as a direct result of or in association with a respiratory issue. Eleven of these subjects (69%) had Y-stents in place at time of death. Furthermore, the relatively fixed proximal aspect of the Y-stent in the subglottis can hinder endotracheal intubation, especially in an emergent or uncontrolled situation. At least 3 deaths in our cohort were preceded by a difficult intubation, all in subjects with Y-stents. Reasons for utilizing a Y-stent for a particular PITS/PTTS patient include presence of long segment, mixed, and/or distal tracheal disease, extensive airway malacia, high chance for straight stent migration, or failed straight stent therapy. On the basis of our findings, Y-stents should be carefully chosen and reserved for patients who understand associated risks, are able to strictly comply with stent clearance techniques, and have ready access to appropriate medical care.

While such stent-related risks emphasize the importance of minimizing stenting duration as much as possible in patients with PITS/PTTS, the influence of indwelling stent time on eventual therapeutic success remains unclear. Several experts advocate for a prolonged stenting period, up to 18 to 24 months or more.[7,22,23] This intuitively makes sense, as a longer stenting duration may maximize chances for airway remodeling and healing. However, the available literature provides heterogeneous and inconsistent results from a fairly small sample size, limiting conclusions. For example, in one of the larger reports available, restenosis occurred in 18 of 81 subjects (22%) with PITS or PTTS treated with stenting for a minimum of 52 weeks.[9] In contrast, in a separate study, restenosis was seen in 33 of 55 subjects (60%) with complex PITS after silicone stenting for a similar time period.[6] This latter restenosis rate is nearly identical to our findings, but indwelling stent time in our cohort was substantially shorter, at 25 weeks. Other studies report restenosis risk ranging from 0% to 70% with indwelling stent times between 24 and 128 weeks.[2–9] However, these are of smaller samples and with inconsistently reported criteria for stent removal (Table 4). We did not find stenting duration predicted restenosis. Nevertheless, it remains unclear whether longer or even indefinite stent therapy is needed in patients with the risk factors for restenosis identified in our analysis, and further investigation is needed.

The main limitation of our study is its retrospective and single institution design, though the analysis was conducted on a large, prospectively maintained database. Twenty of the 149 subjects who had their stents eventually removed were lost to follow-up before reaching the 1-year analysis point, with their clinical outcome unknown. While some of these individuals may have had restenosis and sought therapy elsewhere, others may have felt "cured" and decided to defer further clinical care. Nevertheless, we consider the 87% follow-up

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TABLE 4. Selected Literature Review of Restenosis Risk After Stent Therapy for Complex Postintubation and Tracheostomy-associated Tracheal Stenosis

Study	Criteria for Stent Removal	Indwelling Stent Time (Approx. weeks)	Restenosis/Total Stents Removed (%)
Brichet et al[2]	Operative candidacy at 6 mo	At least 24	7/10 (70)
Puma et al[7]	Epithelialization, adequate airway patency, lack of malacia	128	6/14 (43)
Schmidt et al[8]	Reduced inflammation, adequate airway patency	80	0/12 (0)
Galluccio et al[5]	Individualized	72	12/33 (36)
Lim et al[6]	Minimum 12-month indwelling time, stable airway for 6 mo	52	33/55 (60)
Terra et al[10]	Clinical stability, adequate airway patency, lack of inflammation, bleeding, granulation, malacia	NR	2/21 (10)
Shin et al[9]	Stable airway for one year, presence of peristent air	At least 52	18/81 (22)
Freitas et al[4]	Individualized; adequate airway patency	88	7/14 (50)
This study	Stable airway for either 4 or 6 mo	25	74/128 (58)
Total		Median = 76*	159/368 (43)

*The median indwelling stent time calculation does not include data from references 2, 9, and 10.
NR indicates not reported.

rate in our cohort acceptable for reaching our conclusions. Finally, our study should not be interpreted as an analysis of long-term stent therapy success for complex PITS, since we chose restenosis after first stent removal as the primary outcome. It is possible that such patients who require re-stenting for a longer duration may have their stents permanently removed at a later time or be managed successfully with indefinite stenting.

In summary, we provide a comprehensive assessment of bronchoscopic airway stenting in patients with complex PITS and PTTS. We highlight several potential risk factors for failure that may be used to guide initial stent therapy and outcome expectations. The management of these patients remains problematic owing to an inadequately studied and heterogeneous population that has many medical comorbidities, and should be pursued within a multidisciplinary context. Further investigation is needed to identify the optimal approach.

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