Prognostic Factors for Endotracheal Silicone Stenting in the Management of Inoperable Post-Intubation Tracheal Stenosis

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Purpose: Stenting has been developed to deal with airway stenosis and is applicable in patients with post-intubation tracheal stenosis (PITS) in whom surgery would not be indicated. The purpose of this study was to investigate the prognostic factors in inoperable patients in whom a silicone stent was inserted due to PITS. **Materials and Methods:** We retrospectively evaluated 55 PITS patients undergoing silicone stenting between January 2001 and December 2009. **Results:** Silicone stent was inserted to narrowed trachea after the combination of pre-dilatation including laser cauterization, mechanical bougienation and ballooning. Following airway stabilization, the stent could be removed successfully in 40% (22/55) of the patients after median 12 months of stenting. However, in 60% (33/55) of patients, the stent could not be removed successfully and surgical management was needed after initial stabilization. Multivariate analysis revealed that the stent could be successfully removed more frequently in those who do not have cardiovascular disease [odds ratio (OR)=12.195; p=0.036] and the intervention was performed within 6 months after intubation (OR=13.029; p=0.031). **Conclusion:** Among those patients undergoing silicone stenting due to PITS, the stent could be successfully removed when patients do not have cardiovascular disease and stented within 6 months after intubation.

Key Words: Intervention, post-intubation tracheal stenosis, prognosis, rigid bronchoscopy, silicone stent

INTRODUCTION

Tracheal stenosis (narrowing of the trachea) is a life-threatening, emergent disease with an increasing frequency.[1,2] One of the most common etiologies of benign tracheal stenosis is post-procedural tracheal stenosis, such as that following long-term tracheal intubation or following tracheostomy. Although the use of low pressure cuffs has reduced the incidence of post-intubation tracheal stenosis (PITS) by 10-fold, the occurrence of PITS has increased, due to early application of tracheostomy in the intensive care unit.[2,3]

The management of PITS is a complex problem that requires a multi-disciplined approach. Generally, the preferred management is open resection and re-

anastomosis.[2] However, stenting is recommended in patients with PITS in whom surgery is not indicated due to poor general condition or long involvement of the trachea.[2,3] There is an increasing need to investigate the factors that favor stenting in the management of patients with PITS, because the stent can successfully be removed in only 30-40% of stented patients. Therefore, we investigated such prognostic factors in initially inoperable patients in whom stenting was performed.

MATERIALS AND METHODS

Patients

Among 59 patients who underwent bronchoscopic silicone stenting for the treatment of initially inoperable PITS at the Samsung Medical Center, Seoul, Korea between January 2001 and December 2009, 4 patients lost follow-up within 3 months, and 55 patients who had complex type stenotic lesion were included in this study. Twenty-two patients were had already been studied in the prior study by Park, et al.[3] Bronchoscopic intervention in patients with PITS was indicated when all of the following conditions were met: 1) The degree of dyspnea was greater than American Thoracic Society grade 3; 2) obstruction in tracheal lumen exceeded 25%; 3) general condition was tolerable for intervention, and 4) distal airways were patent.

The Institutional Review Board of the Samsung Medical Center approved this study. Written informed consent was obtained from each patient.

Definitions

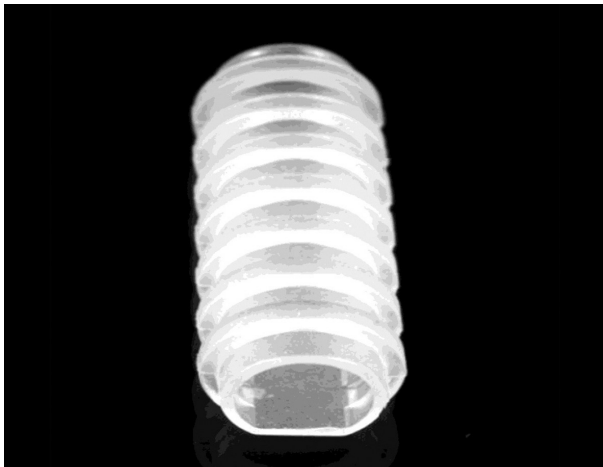The Myer-Cotton stenosis grading system was initially pro-

Fig. 1. A natural silicone stent.

posed for subglottic stenosis, although it has been used with other airway site assessment. It was defined as follows: Grade I: ≤50% lumen stenosis; Grade II: 51-70% lumen stenosis; Grade III: 71-99% lumen stenosis; Grade IV: no lumen.[4] "Successful group" was defined as the group of the stent being removed successfully (usually after 6-12 months) without re-insertion or tracheostomy during the follow-up. "Unsuccessful group" was defined when the stent removal was intolerable and following re-stenting or surgical intervention was needed.

Stents

A Natural (M1S Co., Seoul, Korea) stent of 12-14 mm outer diameter was used for tracheal stenosis (Fig. 1). A new silicone stent, named the Natural stent, was developed by the TNO Company in 2001. This stent is composed of molded silicone and is straight in shape.[3,5] It features regularly placed 'C' circular ribs on its outer surface.[3,5] These stent designs increase stent-to-wall contact due to 'C' shaped studs, and have a theoretical advantage to reduce the stent migration and granulation tissue overgrowth.[3,5] An adequate size and type of stent were selected and used according to the interventionist's decision.

Airway intervention techniques and follow-up

Airway intervention was performed following standard techniques, as described by Dumon.[6,7] Briefly, under general anesthesia, patients were intubated with a rigid bronchoscope tube (Hopkins, Karl-Storz, Germany), and a flexible bronchoscope (EVIS BF 1T240, Olympus, Tokyo, Japan) was introduced through this rigid bronchoscope tube and airway narrowing was examined. The length of stenotic lesion was measured by a scale mark of flexible bronchoscope and a stent of appropriate size (1 cm longer than the stenotic length) was selected by the interventionist. Patients underwent mechanical dilatation prior to stenting, such as dilatation with rigid tubes, ballooning (Boston Scientific, Boston, MA, USA), and laser cauterization (LaserSonics, Mipiltas, CA, USA). A stent of an appropriate size was folded longitudinally, introduced into a stent pusher (BryanCorp., Woburn, MA, USA), and re-positioned using alligator forceps.

Patients were discharged from hospital one to three days following the procedure. We assessed the symptomatic relief as interviewing the patients in the next morning of the bronchoscopic intervention. Patients were followed at 1, 3, 6, 9 and 12 months after intervention with chest radiography and spirometry, and three-dimensional CT and flexible

bronchoscopy were performed before stent removal. Stent removal was planned 12 months after the intervention when the patients were stable and airway related problem did not develop at least for 6 months.

Statistical analysis

For statistical analysis, PAWS 17.0 (SPSS Inc., Chicago, IL, USA) was used. Group comparisons of categorical variables were made using the Pearson chi-square test or Fisher's exact test. To assess the relationship between continuous variables, the Mann-Whitney U test was used. Multivariate logistic regression analysis was used to determine independent predictors of failure to attain a stent-free airway. Among the variables used in this model, predictive factors with a p-value less than 0.15 were selected for multivariate logistic regression analysis. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics of patients

Total 55 patients were included. The stent insertion at first

Table 1. Baseline Characteristics of the Study Population (n=55)

Variable	Number (% or range)
Age (yrs)	60 (16-84)
Gender (male)	22 (40)
Cause of intubation	
Medical	
Respiratory failure	20 (36.4)
Cardiac failure	7 (12.7)
Neurological problem	8 (14.5)
Burn	1 (1.8)
Drug intoxication	5 (9.1)
Surgical	
Operation	5 (9.1)
Trauma	8 (14.5)
Suicide	1 (1.8)
Cause of tracheal stenosis	
Post-intubation	40 (72.7)
Post-tracheostomy	15 (27.3)
Intubation-to-intervention time, months	4 (0.5-480)
Tracheostomized state at the first visit	20 (36.3)
Baseline spirometer data (n=20)	
FEV_1 (% predicted)	61 (18-113)
FVC (% predicted)	68 (22-123)
FEV_1/FVC (% predicted)	64 (23-89)

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
Data are presented as n (%) or median (range).

intervention was conducted in 48 patients, and 7 patients underwent stenting at second intervention after first mechanical dilatation. Their median age was 60 years (range, 16-84), and 22 patients (40%) were males (Table 1). The intubation-to-intervention time was median 4 months (range, 0.5-480 months). The causes of the tracheal stenosis were post-intubation (72.7%) and post-tracheostomy (27.3%). Baseline spirometry data were available for 20 patients (36.4%); the forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), and FEV_1/FVC were 61% (18-113%), 68% (22-123%), and 64% (23-89%), respectively.

Bronchoscopic findings and interventions

Bronchoscopic findings and interventions are summarized in Table 2. The luminal narrowing was classified by the Myer and Cotton grading system.[4] Grade I was observed in 5 patients (9.1%), grade II was evident in 26 patients (47.3%), grade III in 17 patients (30.9%), and grade IV in 7 patients (12.7%).

Outcomes and complications

The overall clinical outcomes are shown in Fig. 2. Success-

Table 2. Bronchoscopic Findings and Parameters of Intervention (n=55)

Variable	Number (% or range)
Stenosis site, overlapped (n=67)	
Subglottis	9 (16.4)
Upper trachea	39 (70.9)
Mid-trachea	13 (23.6)
Lower trachea	6 (10.9)
Stenosis type	
Fibrous stricture	50 (90.9)
Malacia	1 (1.8)
Fibrous stricture+malacia	4 (7.3)
Characteristics of the lesion at first bronchoscopy	
Myer and Cotton Grade	
I	5 (9.1)
II	26 (47.3)
III	17 (30.9)
IV	7 (12.7)
Luminal diameter before procedure, mm	5 (0-10)
Luminal diameter after procedure, mm	12 (9-14)
Length of stent, mm	50 (30-85)
Method of airway dilatation (overlapped)	
Ballooning	7 (12.7)
Nd-YAG laser	13 (23.6)
Bougienation	50 (90.9)

Nd-YAG, neodymium-yttrium aluminum garnet.
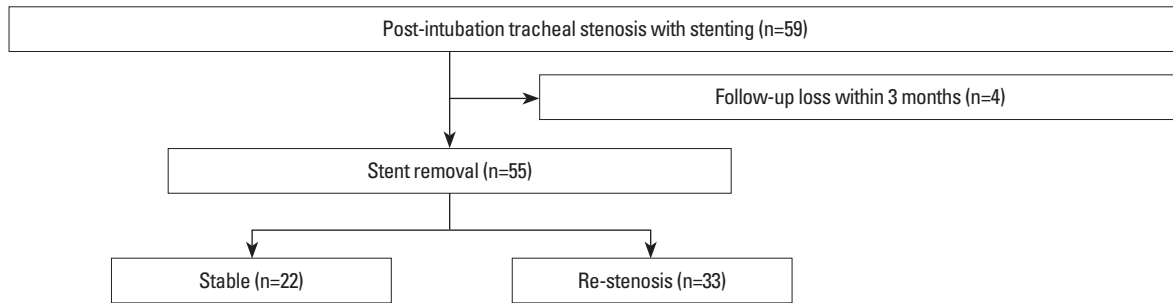Data are presented as n (%) or median (range).

Fig. 2. Outcomes of bronchoscopic interventions in 59 post-intubation tracheal stenosis patients.
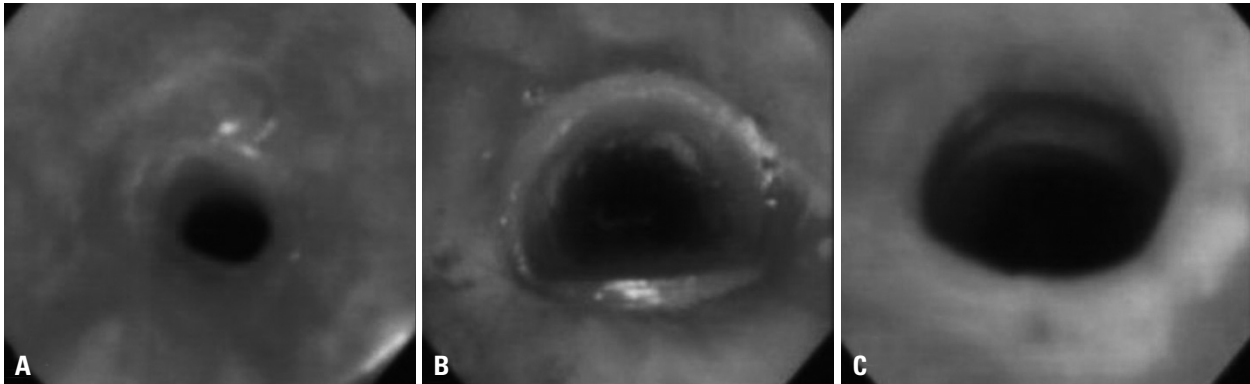

Fig. 3. A representative case of temporary stenting for post-intubation tracheal stenosis. (A) Marked narrowing of the trachea was noted in a 59-year-old male patient after neurosurgical operation. (B) After silicone stent was inserted, the trachea was widened. (C) The stent was removed 1 year after the intervention. The widened diameter of trachea was maintained successfully.

ful stent removal occurred in 22 patients (40%), and duration of stent placement was median 12 months (Fig. 3). However, re-stenosis was done in 33 patients (60%). Among them, persistent stent placement occurred in 23 patients (41.8%). Surgical management, such as tracheal resection with end-to-end anastomosis, occurred in 10 patients (18.2%).

Pneumothorax occurred in one patient. Late complications including stent migration (36.4%), mucostasis (21.8%), and granulation tissues formation at the end of the stent (49.1%) were observed, and repeated bronchoscopic interventions were required to treat these complications.

Comparison of the "successful group" and "unsuccessful group"

Patients were grouped according to whether the stent could be successfully removed (successful group) or whether the stent remained or received surgical intervention (unsuccessful group) (Table 3). The patients of unsuccessful group had cardiovascular disease ($p=0.008$), neurological sequelae ($p=0.018$), high Myer and Cotton grade ($p=0.075$), and the delay of treatment more than 6 months ($p=0.005$). Multivariate logistic regression model was used to determine independent predictors of the successful removal of the stent. Among the variables used in the model, no cardiovascular disease (OR=12.195; $p=0.036$; 95% CI=1.179-125.012) and initiation of treatment within 6 months (13.029; 0.031; 1.257-135.082) were independently associated with successful stent removal (Table 4).

DISCUSSION

The treatment of initially inoperable PITS requires a multidisciplinary approach, including initial conservative treatment, interventional bronchoscopy, and surgical management such as tracheal resection and end to end anastomosis, slide tracheoplasty, and open expansion tracheoplasty with stent fixation, especially for long segment tracheal stenosis.[8] Surgical resection and re-anastomosis have been the first choice of treatment when the patients' condition is tolerable, and interventional bronchoscopy has been applied if the general condition is impossible for an operation.[9] However, even with developments in the management of critically ill patients, surgical treatment is still not indicated in PITS patients with poor neurological, cardiovascular, or respiratory condition.[10] In these patients, interventional bronchoscopy is a good alternative and has led to satisfactory

results in selected patients with benign airway stenosis. A positive outcome of interventional bronchoscopy was reported in 32 PITS patients by Park, et al.[3]

The current study was conducted to reveal prognostic factors for tracheal stenting in initially inoperable post-intuba-

tion tracheal stenosis and was performed in one of the largest centers for interventional bronchoscopy in Asia. We demonstrated that the factors contributing to successful stent removal included no history of cardiovascular disease and initiation of treatment within 6 months after intubation. To our best

Table 3. Subgroup Analysis between "Successful group" (Stable after Removal) and "Unsuccessful group" (Restented or Operated Patients)

Variables	Successful group (% or range) (n=22)	Unsuccessful group (% or range) (n=33)	p value
Age, yrs (range)	60 (24-84)	61 (16-80)	0.286
Gender, male	9 (40.9)	13 (39.4)	1.000
Cardiovascular disease	1 (4.5)	12 (36.4)	0.008
Neurologic sequelae	1 (4.5)	11 (33.3)	0.018
Presence of tracheostomy	5 (22.7)	11 (33.3)	0.547
FEV$_1$, predicted %			
Before stenting (n=17)	67 (18-84)	47 (20-113)	0.753
After stenting (n=39)	92.5 (40-126)	89 (22-124)	0.364
After removal of stent (n=14)	92.5 (38-127)	-	-
Change after removal of stent	26 (1-44)	-	-
Stenotic site			1.000
Subglottis	2 (9)	7 (21.2)	
Upper trachea	15 (68.2)	24 (72.7)	
Mid trachea	5 (22.7)	9 (27.3)	
Lower trachea	2 (9)	4 (12.1)	
Characteristics of the lesion at first bronchoscopy			
Myer and Cotton Grade			0.075
I	3 (13.6)	2 (6.1)	
II	14 (63.6)	12 (36.4)	
III	3 (9.1)	14 (42.4)	
IV	2 (9.1)	5 (15.2)	
Luminal diameter before procedure, mm	5 (0-6)	4 (0-10)	0.609
Luminal diameter after procedure, mm	12 (9-14)	12 (9-14)	0.536
Stenosis type			
Fibrous stricture	21 (95.5)	30 (90.9)	1.000
Fibrous stricture and malacia	1 (4.5)	3 (9.1)	0.522
Length of the stent	4.5 (3.5-6)	5 (3-8.5)	0.145
Stenosis-to-intervention time	3 (1-10)	5 (1-60)	0.110
Intervention within 6 months	20 (90.9)	20 (60.6)	0.005
Visit of emergency room	13 (59)	21 (63.6)	0.570
Emergent bronchoscopy	10 (45.5)	16 (48.5)	0.782
Duration of follow-up	13 (6-156)	20 (7-97)	0.918

FEV$_1$, forced expiratory volume in 1 second.
Data are presented as n (%) or median (range).

Table 4. Multivariate Logistic Regression Analysis for Determining the Factors of Successful Stent Removal

Variables	Odds ratio	95% confidence intervals	p value
Neurologic sequelae	0.197	0.017-2.306	0.196
Cardiovascular disease	12.195	1.179-125.012	0.036
Myer and Cotton Grade	0.513	0.181-1.455	0.210
Length of stent	0.684	0.239-1.954	0.478
Intervention within 6 months after intubation	13.029	1.257-135.082	0.031

knowledge, this is the first reported study on the prognosis of PITS, managed by bronchoscopic intervention with silicone stenting. In this study, the silicone stent could be successfully removed in 40% of patients. In 60% of patients, the stent could not be removed and they received surgical management, demonstrating that the stent can be removed successfully only in a limited number of patients. The poor prognosis reflects not only the need for advances in bronchoscopic intervention, but also the shortage in the pathophysiological understanding and early diagnosis of PITS.

In this study, cardiovascular disease had a relevance to unfavorable prognosis. For good prognosis, stent should promote healing of de-epithelialization of the stenotic lesions by allowing mucosal to grow and should not impede airway mucocilliary clearance, resisting bacterial contamination and avoiding excessive pressure that would impede capillary circulation.[11] However, cardiovascular disease may cause defect of good blood supply to the mucosa of trachea. Also, symptomatic dyspnea might be increased when the patients had underlying cardiovascular disease. In addition, many co-morbidities and sequelae result in a poor general condition. These problems may lead to difficulties in both coughing and stent-related complications such as mucostasis.

Another important prognostic factor of successful stent removal in this study was the initiation of intervention within 6 months after intubation. In the early phase, PITS is initiated by mucosal ulceration and perichondritis, followed by granulation tissue formation.[12-14] In the later phase, cartilaginous tracheal rings are damaged and resorbed, leading to the circumferential loss of mechanical support coupled with scar contracture, resulting in the collapse of the whole tracheal segment.[15] Because stents provide resistance to scar contracture and provide support in areas of structural weakness because of cartilage loss, this severe stenosis is often indicated to surgical intervention.[11] Thus, a favorable outcome would be predicted when the patients were referred prior to damage in the airway cartilages. Consistent with this, we found in the present study that it was an unfavorable factor for the successful stent removal, when the initiation of treatment exceeds 6 months.

There are clear limitations in this study. It is a retrospective review of small sample size, which needs a large scaled prospective study to avoid the lack of statistical significance in some potentially important confounders. Therefore, the decision to remove a stent will be made by considering the prognostic factors being discussed in this study (no cardiovascular disease and initiation of treatment within 6 months) and

other undisclosed factors, which should be revealed by future studies. Second, in majority of patients (35 patients, 64%), spirometer data were missing due to patients' condition. Other objective measurements should be sought in future study.

In conclusion, among patients undergoing silicone stenting due to initially inoperable PITS, the stent could be successfully removed when the patients did not have cardiovascular disease and stented less than 6 months after intubation.

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