

Long-term outcomes in patients with benign central airway stenosis or obstruction following stenting

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Abstract. Although an airway stent is used for central airway stenosis or obstruction due to benign diseases, the long-term outcomes of stenting are unknown. The aim of the present study was to identify the clinical features and outcomes of patients with airway stenosis or obstruction due to benign disease who underwent stenting procedures. For this purpose, clinical data from 136 patients with stents for central airway stenosis or obstruction who underwent treatment at Toho University Omori Medical Center from 1998 to 2018 were retrospectively analyzed. The clinical features, outcomes and complications associated with stenting were evaluated. The clinical features of patients with stents for benign central airway stenosis or obstruction were compared to those of patients with stents for malignant disease. Of the 136 patients with stents, 19 patients had benign disease and 117 had malignant disease. The difference between complications in patients with benign disease compared with those with malignant disease was not significant. The median follow-up time of patients with stents due to benign central airway stenosis or obstruction was 51 (range, 0.164-239) months. Patients with benign disease had a significantly better outcome than patients with malignant disease. For the 19 patients with benign disease, 35 stent procedures were performed as follows: A total of 18 placements, 6 replacements, 3 additional stent placements, 6 removals and 2 stents were repositioned. Patients with benign disease underwent significantly more (≥ 2) stent-related procedures than patients with malignant disease. On the whole, the findings of the present study indicate that patients with benign central airway stenosis or obstruction who undergo stenting may require multiple procedures, and that physicians should plan for multiple treatments following the first stent placement as patients with benign airway disease have good long-term outcomes.

Introduction

In patients with benign central airway stenosis or obstruction, surgical resection/anastomosis is the optimal treatment: However, only 50% of patients can undergo resection (1). Therefore, stenting is required for the treatment of patients with benign airway stenosis or obstruction (1). An airway stent is used to improve symptoms and quality of life. In addition, airway stenting is used as palliative treatment to improve lung function in patients with central airway stenosis or obstruction due to thoracic malignancies (2-4), as central airway stenosis or obstruction can result from tumor invasion or extrinsic tumor compression (5,6). However, the decision for stent placement in an airway should be undertaken carefully, as stenting is associated with serious risks, such as bleeding, airway obstruction during the procedure, or misplacement or migration from the desired location (5). In particular, care should be taken in selecting the types of stenting according to the indications for patients with benign central airway stenosis or obstruction (5). Therefore, the indications for stent placement in patients with benign disease should be based on a risk-benefit analysis.

Reports on stenting for airway stenosis or obstruction due to malignant disease are relatively common; however, limited data are available on stenting for patients with central airway stenosis or obstruction due to benign disease, as there are only a few studies available on the long-term outcomes of patients with benign disease who have undergone airway stenting (1,7). As the outcomes for patients with benign disease may differ from those of patients with malignant disease (7), and a number of issues related to stenting for benign central airway stenosis or obstruction remain unknown (8), the accrual of data on stenting related to benign disease is warranted. The aim of the present study was to identify the clinical features and outcomes of patients with airway stenosis or obstruction due to benign disease who underwent stenting procedures.

Materials and methods

Patients. The present study was approved by the Ethics Committee of Toho University Omori Medical Center (M19151). The present study retrospectively analyzed clinical data from 19 patients with stents for benign airway stenosis or obstruction

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Table I. Characteristics of patients with airway stenosis/obstruction.

Clinical factor	Total no. of patients 136	No. of patients with benign disease 19	No. of patients with malignant disease 117	P-value
Age				
Mean	63	57	64	0.4817
Sex				
Male:female	94:42	8:11	86:31	0.0131
Type of stent				0.2915
Silicon	60	11	49	
Metallic	76	8	68	
Treatment	167	35	132	<0.0001
Placement	135	18	117	
Replacement	10	6	4	
Additional placement	9	3	6	
Removed	9	6	3	
Repositioned	3	2	1	
Cleaned	1	0	1	

who underwent treatment at Toho University Omori Medical Center from 1998 to 2018, and compared the data with those of patients with stents for central airway stenosis or obstruction due to malignant disease. The following parameters were investigated from the medical records obtained from Toho University Omori Medical Center: Sex, age, disease, types of stents, complications, treatment after stenting and patient outcome.

Complications associated with stenting. The following complications were evaluated as positive if treatment via bronchoscopy was required: Granulations, halitosis, infection, mucoid impaction, tumor ingrowth, stent fracture, stent malposition, or stent migration. Bleeding caused by stenting was considered positive if hemostatic agents were administered or bronchoscopic treatment was required. Infections, stent fracture and airway rupture were considered related to stenting if confirmed by bronchoscopy. Halitosis was considered positive if patients did not have halitosis prior to stenting, but developed it after stenting.

Outcomes. The outcomes of patients following stenting for airway stenosis or obstruction due to benign or malignant disease were compared.

Statistical analysis. Fisher's exact test was used to compare binomial proportions in frequency of complication by type. The χ^2 test was used to assess differences between sex, type of stent, treatments in patients' characteristics, complications of stenting, and cases undergoing ≥ 2 procedures. Mann-Whitney U test was used to assess differences in age in the patient characteristics. Survival times were measured from the date of the first stent treatment until the date of death or the last follow-up, and were estimated by the Kaplan-Meier method. Kaplan-Meier graphs were compared by the log-rank test. A P-value <0.05 was considered to indicate a statistically significant difference.

Table II. Reasons for stenting in patients with benign disease.

Group	No. of patients
Benign disease	19
After intubation	8
After tracheostomy	7
Traffic accident	1
After surgery for infection	1
Infection (tuberculosis)	1
Goiter	1

Results

The patient characteristics are presented in Table I. Of the patients with benign disease, a significantly higher proportion were females, whereas this was not the case in patients with malignant disease (Table I). The difference between the types of stents (silicon vs. metallic) used in patients with benign vs. those with malignant disease was not significant.

Of the 19 patients with benign disease, central airway stenosis or obstruction due to long-term intubation, tracheostomy, traffic accident, surgery for infection, tuberculosis and goiter resulted in stenting for 8 patients, 7 patients, 1, 1, 1 and 1 patient, respectively (Table II). The differences between complication rates and types of complication in patients with benign disease vs. those with malignant disease were not significant (Tables III and IV).

The median follow-up times of patients with stents due to benign and malignant central airway stenosis or obstruction were 51 (benign: Range, 0.164-239,) months and 3 (malignant: Range, 0.066-125) months, respectively. The 5-year survival rates were 80.5 and 6.3% in patients with benign and

Table III. Complications of stenting.

Group	Total no. of patients	No. of patients with benign disease	No. of patients with malignant disease	P-value
Positive for complication	33	6	27	0.6077
Negative for complication	103	13	90	

Table IV. Frequency of complication by type.

Group	Total no. of patients	No. of patients with benign disease	No. of patients with malignant disease	P-value
Airway rupture	0	0	0	-
Bleeding	2	0	2	>0.9999
Granulation	9	2	7	0.6129
Halitosis	3	1	2	0.3656
Infection	3	0	3	>0.9999
Mucoid impaction	14	2	12	>0.9999
Stent fracture	0	0	0	-
Stent malposition	2	1	1	0.2608
Stent migration	11	3	8	0.1837
Total	44	9	35	

malignant stenosis or obstruction, respectively. The 10-year survival rates were 58.7 and 3.1% in patients with benign and malignant stenosis or obstruction, respectively. Patients with benign disease had a significantly better outcome than patients with malignant disease (Fig. 1, $P<0.0001$).

For 19 patients with benign disease, 35 stent procedures were performed, which consisted of the following: A total of 18 placements, 6 replacements, 3 additional stent placements, 6 removals and 2 stents repositioned. One patient underwent removal and replacement of the silicon stent in Toho University Omori Medical Center following the placement of the silicon stent in another hospital (Table V, case 4). The differences between the types of treatments for patients with benign disease vs. those with malignant disease were significant (Table I, $P<0.0001$). As regards the number of procedures, 7 out of 19 patients with benign disease had ≥ 2 procedures and 13 out of 117 patients with malignant disease had ≥ 2 procedures; in addition, 6 out of 19 patients with benign disease had ≥ 3 procedures, and only 2 of the 117 patients with malignant disease had ≥ 3 procedures (Table V). Patients with benign disease underwent significantly higher numbers of procedures (≥ 2 and ≥ 3) than patients with malignant disease (Table VI; $P=0.0096$ and $P<0.0001$, respectively).

Discussion

The findings of the present study indicated that patients with benign disease obtained significantly better outcomes after airway stenting than patients with malignant disease, and patients with benign disease had significantly more frequent operations than patients with malignant disease. These results

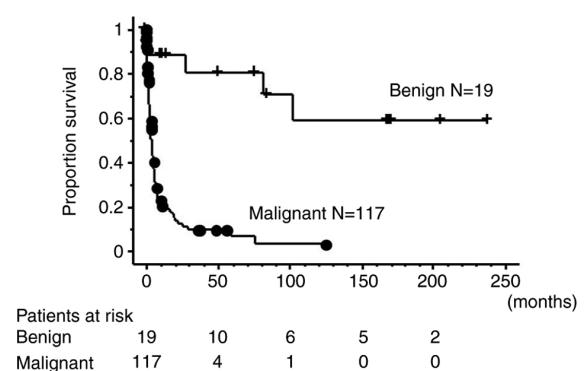


Figure 1. Overall survival curves of 136 patients undergoing stenting for benign central airway stenosis or obstruction and for patients with malignant disease. Patients with benign disease had a significantly better outcome than patients with malignant disease ($P<0.0001$).

indicate that patients with benign central airway stenosis or obstruction who undergo stenting might require multiple procedures, and that physicians should plan for multiple treatments following the first stent placement due to their promising outcomes. Although retrospective studies on airway stenting have revealed risks and complications after stenting (5,6), as there are minimal data available on long-term outcomes, the present study investigated the clinical features and outcomes of patients with airway stenosis or obstruction due to benign disease.

Previous studies on airway stenting for benign central airway obstruction have been retrospective and have included few patients and short follow-up periods, as prospective

Table V. Cases undergoing ≥ 2 procedures.

Group	Reason for obstruction	1st operation	2nd operation	3rd operation	4th operation	5th operation
Benign disease						
Case 1	Traffic accident	Ultraflex	Dumon(ad)	Dumon(re)		
Case 2	Tracheostomy	Dumon	Removal			
Case 3	Infection	Ultraflex	Ultraflex(ad)	Dumon(ad)		
Case 4	Tracheostomy	[Dumon]	Removal	Dumon(re)		
Case 5	Intubation	Dumon	Repositioned	Dumon(re)	Removal	
Case 6	Tracheostomy	Dumon	Removal	Dumon(re)	Dumon(re)	
Case 7	Tracheostomy	Dumon	Repositioned	Removal	T-tube(re)	Removal
Malignant disease						
Case 1	Thyroid cancer	Dumon	Dumon(re)			
Case 2	Lymphoma	Dumon	Ultraflex(ad)			
Case 3	Lung cancer	Ultraflex	Ultraflex(ad)			
Case 4	Lung cancer	Dumon	Removal	Ultraflex(re)		
Case 5	Thyroid cancer	Ultraflex	Ultraflex(ad)	T-tube(ad)		
Case 6	Lung cancer	Dumon	Removal			
Case 7	Lung cancer	Ultraflex	Ultraflex(ad)			
Case 8	Thyroid cancer	Ultraflex	Cleaned			
Case 9	Esophageal cancer	Ultraflex	Ultraflex(ad)			
Case 10	Metastatic cancer	Dumon	Removal			
Case 11	Malignant schwannoma	Dumon	Ultraflex(re)			
Case 12	Lung cancer	Dumon	Repositioned			
Case 13	Esophageal cancer	Dumon	Dumon(re)			

For benign case 4 square brackets '[]' indicate that this procedure was performed in other hospital. (ad), additional placement; (re), replacement. Dumon, Dumon stent; Ultraflex, Ultraflex stent.

Table VI. Differences between patients with benign and malignant disease undergoing ≥ 2 and ≥ 3 procedures.

No. of procedures	Benign disease (n=19)	Malignant disease (n=117)	P-value
Patients with ≥ 2 procedures	7	13	0.0096
Patients with ≥ 3 procedures	6	2	<0.0001

and large-scale studies were difficult to perform for airway stenting (1,5). Saad *et al* examined the clinical features of 21 patients with miscellaneous benign diseases and 11 patients with airway complications following lung transplantation (7). They reported median follow-up durations of 336 days for patients with miscellaneous benign diseases and 329 days for patients following lung transplantation. Husain *et al* performed a retrospective study on the Ultraflex metallic stent, and compared patients with benign airway obstruction with patients with malignant airway obstruction (1). They reported that 10 of 12 patients with benign airway obstruction were alive with a median survival of 1,017 days, ranging from 46 to 1,120 days, but not reaching the 5-year endpoint. Of the 2 patients with benign diseases who passed away, 1 had severe Wegener granulomatosis and the other had the comorbidities of pulmonary fibrosis and cardiac failure (1).

By contrast, Saji *et al* examined 65 patients with advanced lung cancer associated with central airway obstruction and

found a 1-year survival rate of 25.2% and a median survival time of 6.2 months (9). Furukawa *et al* examined 40 patients with advanced lung cancer associated with central airway obstruction and found a 1-year survival rate of 14.3% and median survival time of 94 days (3.1 months) (10). Lemaire *et al* performed a retrospective study on 140 patients with malignant tumor and malignant airway disease and found a 1-year survival rate of 15% and median survival of 3.4 months after stenting (11).

In 2005, the US Food and Drug Administration recommended that metallic stents should be avoided for benign central airway obstruction (5). Although wire stents preserve the mucociliary escalator, permit a larger airway lumen, and are more easily implanted than other stents, some investigators have advised that wire stents should not be used as patients with metallic stents placed for benign tracheobronchial disease have a significantly higher complication rate than patients with metallic stents placed for malignancy (12-14). Wire stents have

also been found to be difficult to remove after they have been in the patients for a long period of time (1). On the other hand, silicon stents have such disadvantages as migration, small internal lumens and impairment of the mucociliary escalator, although they have been easy to remove (1). Although in the present study, no significant differences were found in the complications between silicon and metallic stents, long-term survival and possible multiple stent-related procedures need to be considered for patients with benign airway stenosis or obstruction.

The present study has certain limitations. First, this was a retrospective study. Second, the present study included a small number of patients with benign central airway stenosis or obstruction. However, despite these limitations, the findings were significant.

In conclusion, the present study found that the majority of patients with benign central airway stenosis or obstruction needed multiple stent-related procedures as the patients had better outcomes than patients with malignant disease. Therefore, airway stenting for patients with benign central airway obstruction should be performed, while considering the need for >1 stent-related procedure.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

AI, YA, AS, TS, SK, HO, KI, SS, YH and KT were involved in the conception and design of the study. AI wrote the manuscript. YA, AS, TS, SK, HO, KI, SS and YH collected data. KT supervised the study. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present retrospective study was approved by the Ethics Committee of Toho University Omori Medical Center (M19151).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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