Clinical Success Stenting Distal Bronchi for "Lobar Salvage" in Bronchial Stenosis

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Background: **Airway stents are traditionally used in central airway obstructions to maintain airway patency. Historically, distal bronchial stenting within lobar and segmental bronchi has not been amenable to stenting. In addition, there are questionable benefits to stenting small airways. The Atrium iCast stent is a polytetrafluoroethylene covered stainless steel balloon deployed stent which can be deployed through a flexible bronchoscope under direct visualization. The purpose of this study was to assess the feasibility, complications, and long-term impact of using this stent in patients with lobar bronchial stenosis either secondary to malignancy or benign etiologies.**

Methods: **All records of patients who had the placement of an iCast stent were reviewed over 3.5 years. For each patient the age, sex, location, histology, stent size, duration of stent placement, radiographic improvement, and complications were collected.**

Results: **A total of 122 iCast stents were deployed in 38 patients with lobar bronchial stenosis. The average age was 58 years with 50% male. The etiology included 45% malignant and 55% due to benign conditions. In total, 18.5% patients had stents placed in > 1 segment. There was an average of 4 procedures per patient with a mean time to stent revision or removal of 85 days. All patients had symptomatic or radiographic improvement. Common complications included migration (10%), granulation tissue formation (5%), deployment malfunction (2%), stent dislodgement immediately after deployment (2%), mucous plugging (1%), and tumor occlusion (1%).**

Conclusion: **Stenting small airways with lobar salvage is feasible and improves symptoms and radiographic outcomes.**

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The bronchoscopic management of central airway obstruction dates back to 1914. Airway stents are commonly deployed to reestablish airway luminal patency.[1–3] A variety of stent types and stent materials are available but the ideal stent has yet to be developed. Historically, distal bronchial stenosis within lobar and segmental bronchi has not been amenable to stenting. This is secondary to a multitude of factors including complex distal lobar anatomy and lack of appropriate stent size. In addition, the benefits of stenting distal airways remain questionable.

There have been ample data in the literature regarding the benefits from small expandable stents placed in the biliary tree, urinary tract, and the vasculature (ie, coronary, renal, peripheral vessels, etc.). A routinely used vascular, balloon-expandable, covered, stainless steel stent that is fully encapsulated in 2 layers of polytetrafluoroethylene has recently generated interest for its application within the endobronchial tree. This particular stent has increased flexibility and greater radial strength compared with other types of vascular stents. These stents show promise due to their smaller length and diameter, ease of placement, optimal radial force, and minimal stent foreshortening during deployment.[4] This stent has recently received US Food and Drug Administration approval in the United States for its use in the management of tracheobronchial strictures (Atrium iCAST, Maquet Getinge Group). These stents come in various sizes, from 5 to 10 mm in diameter to 16 to 59 mm in length.

Since 2012, we have been routinely using these stents at the Cleveland Clinic in the management of lobar airway stenosis. Here, we describe our experience with iCAST stent in the management of inoperable lobar airway stenosis.

PATIENTS AND METHODS

We retrospectively analyzed medical charts of patients who underwent an iCAST balloon-expandable stent placement at our institution. All patients had inoperable lobar bronchial stenosis (LBS) confirmed by flexible bronchoscopy. Patients initially had balloon bronchoplasty during bronchoscopy to assess for symptomatic improvement and to avoid stent placement. Patients were only considered for a follow-up bronchoscopy and stenting if they had symptomatic improvement postbronchoplasty and recurrence of their bronchial stricture.

Patients were classified into 4 groups based on the underlying etiology for LBS: (1) complications of radiotherapy, (2) extrinsic compression from primary or metastatic lung carcinoma, (3) complication of lung transplantation, and (4) miscellaneous benign conditions.

We gathered information on patient demographics, clinical presentation, primary diagnosis, location of stenosis, stent size, radiographic findings before and after the stent placement, procedure and/or stent-related complications, number of bronchoscopic procedures since the stent placement, duration of stent therapy and overall follow-up.

Procedure

Before stent deployment, the stenotic airway was gradually dilated using a control radial expansion (CRE) balloon of an appropriate size. The length of the airway to be stented was determined by measuring the distance from the distal to proximal end of the stenotic airway by retracting the bronchoscope and using a tape measure. The diameter of the airway was approximated by the balloon bronchoplasty and size of the bronchoscope that was accommodated by the involved airway. The stent diameter chosen was 10% to 15% larger than the estimated airway diameter to ensure proper apposition to the bronchus and prevent migration. Of note, although the iCAST stent is available in certain diameters, these stents are pliable and not fixed in diameter as other metal or silicone stents. They have the ability to expand beyond their size by ~30% more in diameter and better fit within an airway.

The iCAST stent is folded and premounted on top of a deflated balloon located at the distal end of a multilumen delivery catheter. The main catheter lumen is used for flushing and guidewire introduction. The second lumen is used for inflation and deflation of the balloon to deploy the stent. This stent can easily be deployed through the working channel (2.8 mm or greater) of a flexible bronchoscope under direct visualization. The stent can also accurately be deployed using fluoroscopic guidance over a guidewire using 2 radiopaque markers that are attached to the catheter shaft marking the proximal and distal ends of the loaded stent.

It is our practice to place all iCast stents under direct visualization using a flexible Olympus therapeutic 6.2 mm outer diameter and 2.8 mm working channel bronchoscope (BF-1TH190). All stents were placed under general anesthesia using either a supraglottic airway, an endotracheal tube of >8.5 mm diameter, or a rigid bronchoscope that was already in place.

The stent catheter was inserted through the working channel of the flexible bronchoscope and positioned within the obstructed airway until the proximal portion of the stent was aligned with the lobar carina. Optimal stent placement requires the proximal end of the iCAST stent to be deployed ~2 to 5 mm proximal to the bronchial carina so that the proximal edge can "phalange" over the carina to minimize the risk of migration (Figs. 1–3). After proper positioning of the catheter, the stent is deployed by maximally inflating and then deflating the balloon and gently withdrawing the catheter, leaving the stent in place. Balloon bronchoplasty using an 8-9-10 mm CRE balloon was performed following all iCAST stent placements to attain its largest diameter. If the stent needed to be modified (Fig. 3), the iCAST stent is very pliable. Stent modification included starting with a conventional transbronchial needle aspiration needle to puncture a hole through the stent in the area where the airway is located. This is followed by using a fogarty balloon to find the airway and further expand the opening within the stent. Balloon bronchoplasty is then performed using an 8-9-10 mm CRE balloon.

If required, the fully deployed iCAST stents could easily be removed from the lumen by using flexible forceps. Surveillance bronchoscopy was carried out per our departmental protocol for airway stenting between 6 and 12 weeks after the procedure. Outcome was judged successful if the patient experienced an improvement of symptoms along with radiographic improvement and/or pulmonary function improvement at the first follow-up.

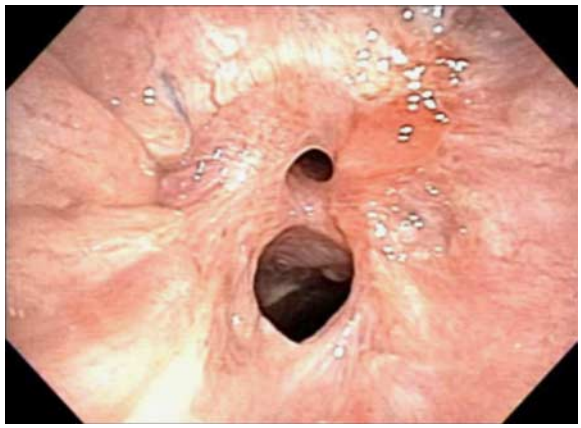

FIGURE 1. Left upper lobe and left lower lobe bronchial stenosis in a double lung transplant recipient.

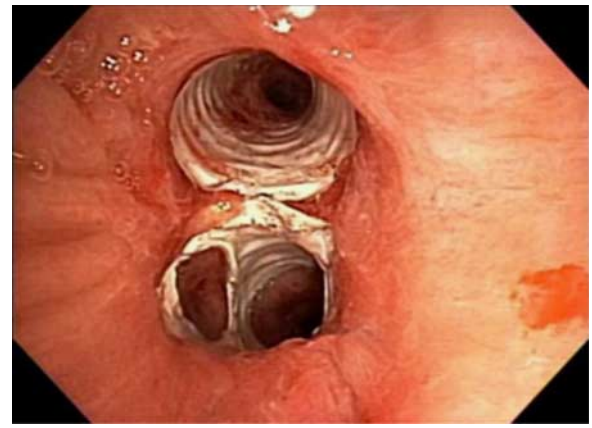

FIGURE 3. iCast stent placed in the left lower lobe and modified as to not cover the superior subsegment.

Complications were reported as device malfunction, procedural-related complications, infection, stent migration, mucous plugging, granulation tissue formation, stent occlusion by the primary process, hemoptysis, or intractable cough. Infectious tracheobronchitis was defined as an acute or subacute process presenting with productive cough, colored sputum, and normal chest radiograph. The overall complication rate was calculated by dividing the total number of complications by the total number of follow-up months of stent use by all patients.

RESULTS

Between January 2012 and June 2015, 38 patients underwent iCAST stent placement for lobar airway stenosis. The overall mean age of the patients was 58 years (range, 28 to 76 y) including 19 women (50%). The indication for lobar stent placement are depicted in Table 1. Of the 14 lung transplant recipients, 2 received a single right lung.

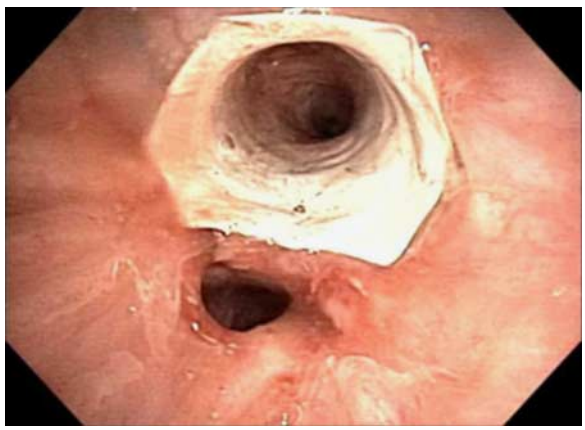

FIGURE 2. iCast stent placed and "phalanged" proximally in the left upper lobe after balloon dilatation.

The most frequent clinical symptoms associated with bronchial stenosis were moderate dyspnea, cough, and those suspicious for post-obstructive pneumonia. This was followed by mild respiratory symptoms including wheezing and sporadic cough. All patients initially had balloon bronchoplasty during a prior bronchoscopy to assess for symptomatic improvement and to avoid stent placement. Patients were only considered for a follow-up bronchoscopy and stenting if they had symptomatic improvement postbronchoplasty and recurrence of their bronchial stricture.

A total of 122 balloon-expandable iCAST stents were deployed. Seven patients (18.5%) had stents placed in >1 segment. In total, 43 stents were placed at the time of initial visit, an additional 2 new stents at the second visit, 4 new stents during the third visit, and 2 new stents during the fourth visit. There were a total of 71 stents replaced over the course of follow-up during the 42 months with an average of 3.2 stents per patient. These were mostly replaced during the second visit (16 stents), followed by the third visit (12 stents), and fourth visit (9 stents). There were a total of 148 procedures in our population, with an average of 4 procedures per patient. These included the initial procedure to place the stent and subsequent procedures as part of routine maintenance and/or stent removal, or patients complaints of new respiratory symptoms (eg, cough, change in sputum, dyspnea).

The location of stent placement is depicted in Table 2. The most common stent size deployed was 7×16 mm (48%), followed by

TABLE 1. Baseline Characteristics, Stent Indication

	Patient Number (%)
Mean age (y)	58 (range, 28-76)
Female	19 (50)
Stent indication	
Malignancy	7 (18.5)
Bronchial stenosis secondary to Radiotherapy	10 (26)
Lung transplantation	14 (37)
Benign etiologies	7 (18.5)
Right middle lobe syndrome	2 (5)
Granulomatosis with polyangiitis	1 (2.7)
Systemic lupus erythematosus	1 (2.7)
Airway Fire	1 (2.7)
Infectious—MAI	1 (2.7)
Mucormycosis	1 (2.7)

7×22 mm (32%), 6×16 mm (14%), 6×22 mm (3%), 5×16 mm (2%), and 8×38 mm (1%).

Outcomes

Symptomatic improvement was observed in 95% of patients (36/38) when they were questioned at their follow-up visit. These questions were similar to what would be found in a formalized quality of life questionnaire. The 2 patients who did not have symptomatic improvement subsequently had their stents bronchoscopically removed. Radiographic evaluation was available for 89% of patients (34/38); in 4 patients radiographic evaluation was not able to be accurately performed because of issues related to their underlying malignancy. Of the 34 evaluable patients, 76% had radiographic improvement on follow-up chest radiograph. Radiographic improvement included resolution of lobar atelectasis and improvement or resolution of lobar infiltrates (Fig. 4). Of the 8 patients without radiographic improvement, all had a normal chest radiograph preprocedure. Seven of these patients were lung transplant recipients, and 1 had lung cancer. The latter patient with lung cancer also experienced no poststent symptomatic improvement and had the stent subsequently removed.

Prestent and poststent placement pulmonary function testing (PFT) were available in 16 patients, 14 of which were lung transplant recipients. In total, 93% (15/16) of these patients showed improvements in their PFT's, with an average improvement in forced expiratory volume (FEV1) of 12.3% (range, 4% to 23%) depicted in Table 3. The 1 patient without PFT improvement also demonstrated no symptomatic improvement, and the stent was subsequently removed; this was a lung transplant recipient who eventually lost his right middle lobe.

TABLE 2. Distribution of Stent Placement

Location	Patient Number (%)
Right middle lobe	19 (37)
Left lower lobe	10 (20)
Right lower lobe	8 (15)
Left upper lobe	7 (14)
Right upper lobe	7 (14)

Complications

The overall complication rate was 20% (25 complications in 122 stents placed), all of which are depicted in Table 4. In total, 22 patients did not have any recorded complications related to stent placement. No death was related to airway stenting complications.

A total of 12 stents migrated (10%). Five stents migrated proximally of which 4 were removed bronchoscopically. One stent was expectorated without any complications. A total of 7 stents migrated distally which were all recovered. Three of the stents migrated distally resulting in granulation tissue formation proximal to the stent, necessitating recapturing the involved airway segment and stent removal. One stent migrated distally resulting in an infectious tracheobronchitis and was successfully treated with oral antibiotics. One stent migrated distally into a large left lower lobe cavitary lesion which occurred after the patient received chemotherapy for primary lung cancer.

Granulation tissue formation either proximal or distal to the stent was the second most frequently observed complication, occurring in 6 instances (5%). Granulation tissue partially obstructed iCAST stents proximally 83% of the time with 67% of the time being an asymptomatic nonobstructive granuloma. On 2 occasions fluoroscopy was necessary to locate and assist in removing the stent due to granulation tissue completely obstructing the proximal airway.

Stent deployment malfunction and stent dislodgement immediately after deployment occurred a total of 5 times. One stent did not deploy and was found to be dislodged inside the bronchoscope; 1 stent did not deploy secondary to balloon rupture. Three stents became dislodged immediately after deployment when they adhered to the outside of the bronchoscope as the bronchoscope was maneuvered within the stent to assess the distal airways.

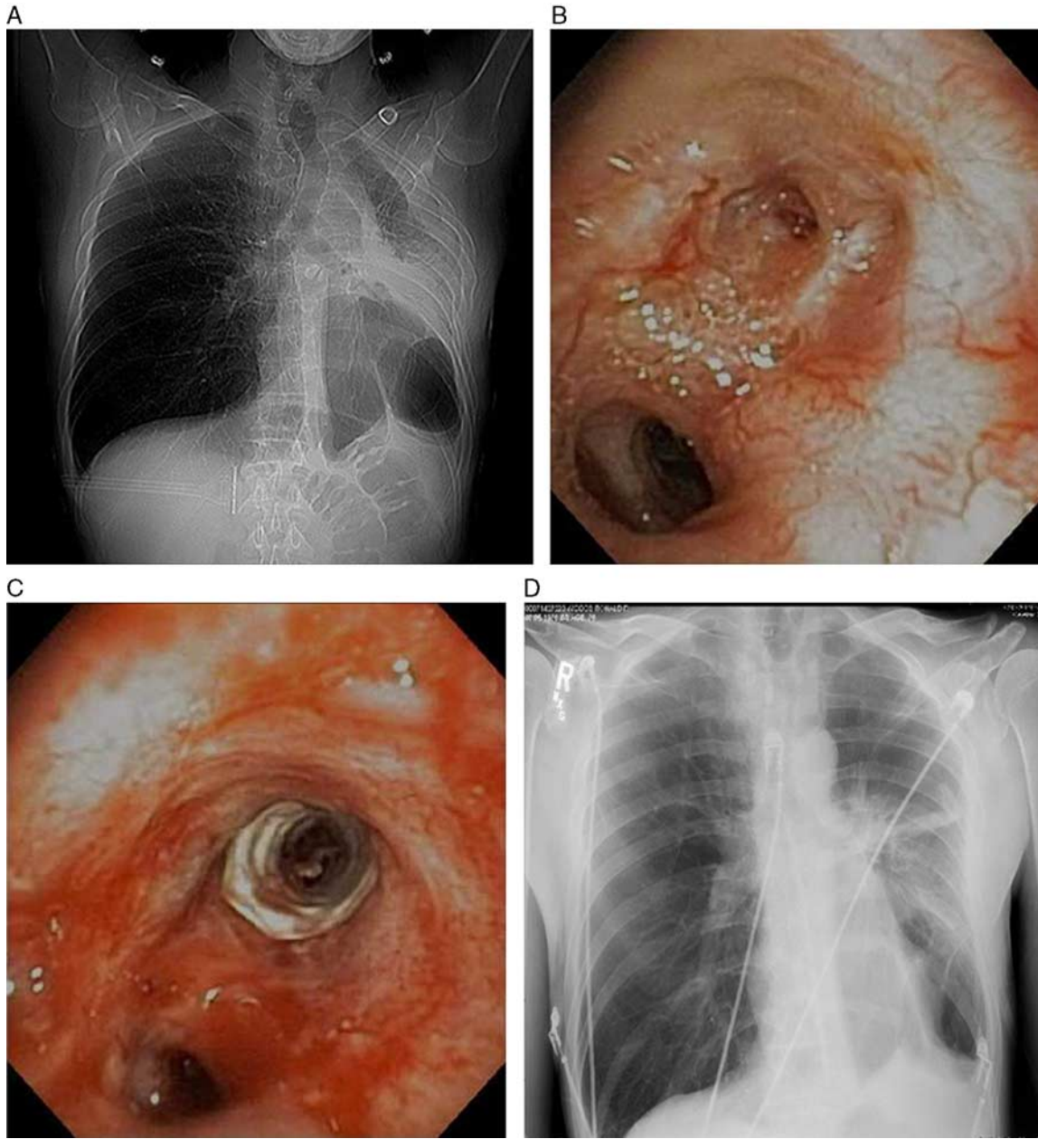

FIGURE 4. LUL bronchial stenosis secondary to radiotherapy. A, Chest radiograph before. B, Bronchoscopic image of LUL stenosis. C, Atrium iCast stent deployment in the LUL. D, Chest radiograph poststent deployment. LUL indicates left upper lobe.

Overall 2 stents were found to be occluded. One stent was 95% occluded with a mucous plug and needed to be replaced. The second stent was occluded with tumor and was removed.

Follow-up

All patients had clinical follow-up after their first intervention between 6 and 12 weeks later. Eight patients eventually had their stents removed; 5 of these patients achieved permanent airway patency without any further need for stent placement. The remaining 3 patients had bronchial restenosis which could not be recaptured on follow-up bronchoscopy. Sixteen patients died secondary to their underlying disease process after the initial follow-up evaluation. The mean time to stent revision or removal was 85 days ranging between 5 days to 525 days. There was never an issue with stent integrity regardless if the stent was left in the airway for long periods of time.

TABLE 3. Distribution of Stent Placement and FEV1 Improvement

Location	Patient Number (%)	Prestent FEV1%	Poststent FEV1%
Right middle lobe	6 (38)	73	82 (↑9)
		67	81 (↑14)
		35	47 (↑12)
		62	62 (no change)
		69*	77 (↑8)*
		96*	106 (↑10)*
Left lower lobe	3 (19)	26	39 (↑13)
		56	74 (↑18)
		70	93 (↑23)
Right lower lobe	4 (25)	23	27 (↑4)
		48	67 (↑19)
		68	75 (↑7)
		53	66 (↑13)
Left upper lobe	1 (6)	87	96 (↑9)
Right upper lobe	2 (12)	46	58 (↑12)
		42	56 (↑14)

*Single lung transplantation.

DISCUSSION

To date, airway stents have been utilized primarily in central airway obstruction to reestablish airway patency.[5–8] This is mostly due to the fact that current pulmonary stents are too large to be deployed in the smaller airways. However, very often patients present with local disease involving lobar bronchi and the secondary carina. Although these patients mainly complain of mild dyspnea, cough, wheeze, or recurrent infections, they are at high risk of "vanishing bronchi" and recurrent postobstructive pneumonias. This study represents a single-center institution experience in the clinical outcomes of stenting lobar bronchi for "lobar salvage" in bronchial stenosis secondary to benign as well as malignant diseases. This the largest study to date describing this technique, and also the only one to offer comparison among different pathologies leading to distal bronchial stenosis and stenting.

iCAST stents can easily be inserted under local or general anesthesia using a flexible bronchoscope with direct visualization. They are flexible and adapt well to airways. Once deployed, their intrinsic radial force keeps them in place secondary to the ability to overexpand. As the stent is fully covered and pliable, they do not embed within the airway and are therefore rather easy and nontraumatic to remove.

Because of the lack of available technology (until now) to address distal airway stenosis, there has been a paucity of studies evaluating the potential palliative benefits of stenting these airways. To address the issue of whether distal bronchial stent insertion provided meaningful palliation, there was a high level of scrutiny in the selection of patients undergoing stenting in our group. Patients were only considered candidates for lobar airway stenting if they experienced symptomatic improvement from a prior bronchoscopy that included aggressive treatment of lobar bronchial strictures with a balloon bronchoplasty and/or endobronchial debridement and subsequently became symptomatic if the stricture recurred. Furthermore, patients were considered candidates for stenting only if prior dilation methods did not result in sustained airway patency. The duration of "sustained airway patency" is not well defined, but in general we considered 30 days as a marker. As a result, not all patients were considered suitable candidates for lobar salvage procedures. Preselecting those patients who were refractory to traditional bronchoscopic techniques in fact makes our outcomes success even more robust; these are patients who would otherwise have remained symptomatic due to refractory stenosis. Although not all patients had prestent and poststent pulmonary function tests and radiographic evaluation, those that did showed a remarkable improvement in these parameters, which paralleled the symptomatic improvement these patients experienced. In evaluable patients, an overall improvement in FEV1 of 12.3% was observed, which exceeds American Thoracic Society standards of what constitutes a minimal clinically important difference in this value. Although not all patients had radiographic improvement, this was primarily due to having a normal study preprocedure. This discrepancy between the radiograph and symptoms is likely due to a severe, but not complete, airway stenosis,

TABLE 4. Complications

Complications	N (%)
Migration	12 (9)
Granulation tissue formation	6 (5)
Stent dislodgement postdeployment	3 (2)
Deployment malfunction	2 (2)
Mucous plugging	1 (1)
Tumor occlusion	1 (1)

resulting in increased work of breathing without frank distal atelectasis.

Almost 20% of stent placements presented with some sort of complication; however, the majority of complications were minor with no escalation in care and included instances of stent migration or development of granulation tissue (which was mostly nonobstructive). Procedural complications included deployment malfunction and dislodgement over the bronchoscope immediately after deployment. It was notable, however, that there is a learning curve associated with deployment of these stents, and as we changed practice, these complication rates dropped significantly.

As stated, migration was the most frequent encountered complication. This occurred more frequently during the initial placement of iCAST stents and seemed to be related to operator experience. As we became more familiar with the procedure, our technique for optimal stent placement improved with "phalanging" the stent over the lobar carina and using a CRE balloon to further radially expand the stent; this resulted in a significantly reduced rate of migration.

Stent-related granulation tissue was on the lower end compared with what is generally reported in the literature (3% to 36%).[3,9] All instances of granulation tissue formation occurred in benign conditions with the majority being lung transplant patients. We believe that stent migration leads to the highest incidence of granulation tissue formation secondary to friction of the stent against the bronchial mucosa.[3] The second most common cause was likely underlying mucosal inflammation from recurrent prior balloon dilations with airway tearing and healing.

Airway colonization after stent placement has been reported by Noppen et al[10] with the occurrence of colonization by pathogenic bacteria in 78% of patients 3 to 4 weeks after stenting. The occurrence of infection was not detected in our experience using the iCAST stent. In fact, our rate of infectious tracheobronchitis was lower than the range reported in the literature (16%).[3] This is most likely secondary to a smaller surface area of the stent which minimizes impairment of mucociliary clearance and expectoration, two important natural defense mechanisms in the prevention of stent infections. Certainly we did not utilize any specific protocol to prove or disprove infection of the stent.

There are indeed major limitations in the present study. One such limitation is the retrospective nature of the study. As such, there may have been selection bias which may have favored successful outcomes. Furthermore, no control group was set up for comparison. Another limitation is that we did not have lung function testing or dyspnea scores available on all patients. However, we only stented patients who self-reportedly had symptomatic improvement after having had a prior therapeutic bronchoscopic dilation. That said, without scoring we are unable to comment on the magnitude of palliation. Another potential limitation is that although all bronchoscopists were well-trained interventional pulmonologists, there were variations in technique with regard to stent revision or removal that may have affected outcomes.

Another important limitation to the present study relates to stent revision/replacement. Given that this is new technology, and that there were multiple operators placing these stents, there was a wide variability in the maintenance of these stents despite a standard institutional surveillance bronchoscopy schedule. Some operator's routinely removed/replaced stents, whereas others were more comfortable with removal/replacement only if a complication developed. Indeed 121 stents were placed in 38 patients. This can somewhat be explained by some patients having >1 area of stenosis, necessitating multiple initial stent placements. In addition, 25 stents were replaced due to migration and granulation. However, these do not account for all of the stents deployed in this analysis, with some patients having their stents replaced "preemptively" by some operators. It is impossible to account for this variability in operator preference in a retrospective study. However, this should spur further prospective studies to address whether routinely removing/replacing stents has any clinical benefit to the outcome of the patient.

In summary, stenting small airways in benign and malignant disease for lobar salvage is safe and effective in improving outcomes with regard to symptoms, radiographic improvement, and pulmonary function tests related to LBS. However, clinical studies are necessary to further identify patients who may have the greatest benefit from stenting. Complication rates are at least similar to, and may be less than, other types of airway stents in larger airways. In addition, balloon-expandable covered iCAST stents have the advantage of easy placement and removability during flexible bronchoscopy even under conscious sedation and local anesthesia. These stents should be a part of every interventional pulmonologists armamentarium for lobar bronchial stenting in the appropriate clinical setting.

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