



# Safety of hybrid bronchial stents in transplant airway complications: a single center experience

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**Background:** Tracheobronchial stents are often used to manage lung transplant airway complications. In 2005, the Food and Drug Administration (FDA) issued a warning against the use of metallic stents for benign airway disease. Since that time, fully covered hybrid metallic stents have been developed and are increasingly used due to their ease of insertion and removal. There is limited data to support their safe utilization for transplant airway complications. This is the largest analysis to date of the safety of hybrid metallic stents for transplant airway complications.

**Methods:** We performed a retrospective study of patients who had covered metallic stents placed for transplant airway complications between April 2016 to April 2021. Information obtained from chart review included demographics, procedure notes and stent data including indication for placement, type, size, location, duration, and complications.

**Results:** We identified 50 patients who had a combined 376 stents placed for a total of 15,711 stent days. The most common minor complication and reason for removal was mucus plugging affecting 193 stents. There were only two cases of major stent associated complications. Among minor complications, there was an increased risk of stent fracture with Bonastent<sup>®</sup> (P=0.04).

**Conclusions:** Our data shows that hybrid metallic stents are a safe intervention for patients with transplant airway complications. Most complications were minor and managed with repeat bronchoscopy. There were only two major complications over a 5-year period. Given the wide spectrum of possible airway complications, further research is needed to determine the optimal use of stents for patients with transplant airway complications.

**Keywords:** Lung transplant; tracheobronchial stents; airway complications; bronchial stenosis

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## Introduction

Lung transplant airway complications, including bronchial stenosis, anastomotic dehiscence, excess granulation tissue and bronchomalacia, are common with a reported incidence

of 15–20% and an associated attributable mortality of 2–4% (1-4). The diagnosis of an airway complication has also been associated with an overall reduced survival measured at 30 days, 1 year and 5 years (5). For patients who do survive,

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**Table 1** Properties of hybrid bronchial stents

Stents	iCAST	Bonastent	AERO
Description	Stainless steel frame encapsulated in expanded PTFE  Originally a vascular stent but has a license for bronchial stent	Woven Nitinol stent frame lined with a silicone cover	Nitinol stent with a polyurethane coating  Anti-migration struts
Sizes diameter × length, mm	10×30.8; 6.9×15; 6.9×20.1	10, 12, 14, 16, 18, 20 mm diameter; variety of lengths	8, 10, 12, 14 mm diameter; variety of lengths down as short as 10 mm
Deployment	Balloon mounted can be deployed through the 2.8 mm working channel of the bronchoscope or over a guide wire	Delivery catheter with distal deployment  Ability to re-capture stent prior >70% deployment  10 mm diameter stents can be deployed through the working channel 8 Fr delivery catheter	Gun type deployment system
Properties	Easy to deploy  Easy to deploy	Easy to deploy especially through the bronchoscope  Flared ends anchor the stents well but do create granulation tissue  Conforms to airway  Fracture risk with excessive pressure	2 deployment methods over the scope or via guidewire
Advantages	Helpful for smaller airways  Customizable in the airway	Easy to place and remove  Conforms to airway shape	–

PTFE, polytetrafluoroethylene.

airway complications can lead to a significant reduction in quality of life due to increased need for medications, procedures and hospital admissions which contribute to temporal and financial constraints. Lung transplant airway complications have a wide spectrum of severity and variable response to intervention, over a third of patients will suffer a complication recurrence after intervention and nearly 70% of those will have a third (2). Bronchial stenosis is the most common post-transplant airway complication and management requires a stepwise approach with potential interventions including dilation of the stenosis, ablation of excess tissue and stent placement (6).

Management of airway stenosis with tracheobronchial stents has increased over the last three decades. Stenting is a potential intervention for recurrent stenosis after other techniques like balloon dilation have failed (7). Initial stents were comprised of silicone and required rigid bronchoscopies for placement. However, the advent of self-expandable metallic stents (SEMS) allowed stents

to be placed with flexible bronchoscopy, assisted by guidewires and fluoroscopy (8,9). Unfortunately, providers noted more complications over time with metallic stents including restenosis, bacterial colonization, granulation tissue formation, stent fracture and epithelialization into the airway wall (10,11). These issues led the United States Food and Drug Administration (FDA) to issue a black box warning in 2005 against the use of SEMS in benign tracheal disease. This warning was specific to benign disease processes because of prolonged survival in this group, increasing time of implantation as well as risk of complication compared to malignant airway disease (12).

Since the 2005 FDA warning, metallic stents have evolved. The third and newest generation was designed specifically to address issues related to removal; these stents are self-expandable or balloon expandable and are fully covered (*Table 1*). There is limited data evaluating the safety and efficacy of third generation stents in benign airway disease, with even less data specific to transplant airway

complications (13-15). Our institution has multiple years of experience utilizing covered metallic stents for post-transplant airway complications. This is the largest analysis to date of covered metallic stents in transplant airway complications; we hypothesize that covered metallic stents placed by flexible bronchoscopy have an acceptable safety profile with a low risk of major morbidity and mortality. We present the following article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-2003/rc>).

## Methods

This is a single center retrospective cohort study using patient data collected between April 2016 and April 2021 at Temple University Hospital in Philadelphia, Pennsylvania. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Research Ethics Board at Temple University Hospital, protocol 28636, and individual consent for this retrospective analysis was waived. We reviewed the electronic medical record, specifically the bronchoscopy procedure notes, of all lung transplant patients who had covered metal stents placed for bronchial stenosis or anastomotic dehiscence. All stents were placed and removed with general anesthesia using flexible bronchoscopy by two proceduralists. Most of these patients (88%, n=44) were also treated with balloon dilation and some form of tissue ablation. Data specific to these ablative interventions is not included in this analysis. Follow up bronchoscopy was scheduled on a case-by-case basis or performed as needed. All patients were encouraged to perform regular airway clearance maneuvers and prescribed twice daily inhaled mucolytics. The specific covered metallic stents included in this analysis are the Bonastent<sup>®</sup> (EndoChoice Inc., Alpharetta, GA, USA), the AERO<sup>®</sup> (Merit Medical Systems, South Jordan, UT, USA), and the Atrium iCAST<sup>™</sup> (Atrium Medical, Hudson, NH, USA). Of note, the Atrium iCAST<sup>™</sup> is not self-expandable like the Bonastent<sup>®</sup> or the AERO<sup>®</sup>; but it is a fully covered metallic stent or hybrid metallic stent. See *Table 1* for specific details about each stent type.

Information obtained from the electronic medical record include patient gender, patient age at transplantation, patient BMI at transplantation, date of lung transplant, lung transplant laterality (right, left, double), underlying diagnosis leading to lung transplant, bronchoscopy intervention date, bronchoscopy procedure description, date

of stent placement, date of stent removal, type of stent, stent size, stent location, stent removal reason and any potential procedural complications. The potential etiologies for stent removal and stent complications included secretions, granulation tissue, stent migration or malposition, stent fracture or stent hemorrhage. Complications were defined as minor if they were able to managed with bronchoscopy and did not require further intervention. Complications were defined as major if they required intervention beyond bronchoscopy for management or led to direct morbidity or mortality.

## Statistical analysis

The primary objective of this study is to assess the safety profile of covered hybrid metallic stents in the management of transplant airway disease. This was done by determining the incidence of each procedural complication and etiology for stent removal, the incidence of major stent related complication and by determining the total and average number of stent days each patient tolerated. More than one etiology for stent removal was allowed. Descriptive statistics including mean, median, standard deviation and range were utilized to determine the incidence of stent related complications and the number of stent days tolerated. Chi square analysis was used to determine the statistical significance of complications by stent.

## Results

We identified a total of 50 patients with transplant airway disease who underwent stent placement with a covered metal stent between April 2016 and April 2021. Baseline characteristics are shown in *Table 2*. During this time 645 transplants were performed at our center. The mean age at time of transplantation was 63 years old. The majority of patients were male (n=35, 70%) and the most common indication for lung transplantation was interstitial lung disease (n=29, 58%). More than half of the patients (n=26, 52%) were deceased at the time of analysis. The most frequent indication for intervention was bronchial stenosis (n=44, 88%) rather than anastomotic dehiscence (n=6, 12%).

A total of 376 stents were placed or manipulated in 50 patients for a total of 15,711 stent days (*Table 3*) over the course of 774 bronchoscopies. The average patient had a median total of 176 stent days (IQR, 45.5–351.25). The median duration per stent was 22.5 days (IQR, 13–29). The most frequent reasons for stent removal were secretions

**Table 2** Patient demographics

Patient characteristics	Values
Total patients	50
Age at transplantation, years	63.44±7.90
Male	35 (70%)
Female	15 (30%)
BMI at transplantation, kg/m <sup>2</sup>	26.91±4.88
Primary diagnosis	
Chronic obstructive pulmonary disease	10 (20%)
Interstitial lung disease	29 (58%)
Pulmonary hypertension	1 (2%)
Combined pulmonary fibrosis and emphysema	10 (20%)
Deceased at time of analysis	26 (52%)
Alive at time of analysis	24 (48%)
Right lung transplant	16 (32%)
Left lung transplant	11 (22%)
Double lung transplant	23 (46%)
Redo lung transplant	4 (8%)
Indication for intervention	
Bronchial stenosis	44 (88%)
Anastomotic dehiscence	6 (12%)

Values presented as mean ± standard deviation or n (%).

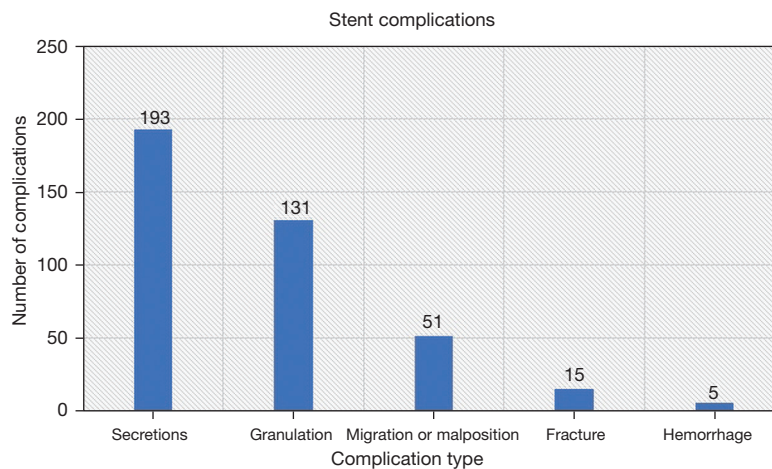
(n=193), granulation tissue (n=131) and migration or malposition (n=51) as described in *Figure 1*. There were two major complications related to hemorrhage with one case of stent related mortality from major hemorrhage after removal; in that case there was concern that the tissue in the bronchus intermedius had thinned and there was direct bleeding from the pulmonary artery after the stent was removed. The second case involved major bleeding after a left mainstem stent was removed and balloon dilation was done. That patient went into hemorrhagic shock and ultimately required a pneumonectomy.

The Bonastent<sup>®</sup> was the most frequent utilized covered metal stent in our analysis (n=219, 58.24%), the least

**Table 3** Stent characteristics

Stent characteristics	Values
Total stents	376
Total bronchoscopies involving stents	774
Bonastent <sup>®</sup>	219 (58.24%)
Bonastent <sup>®</sup> length, mm	30+10
#Diameter 10	69
#Diameter 12	125
#Diameter 14	25
Atrium iCAST <sup>™</sup>	130 (34.57%)
Atrium iCAST <sup>™</sup> length, mm	16+22
#Diameter 6	4
#Diameter 7	84
#Diameter 10	42
AERO <sup>®</sup>	27 (7.18%)
AERO <sup>®</sup> length, mm	15+15
#Diameter 8	4
#Diameter 10	4
#Diameter 12	16
#Diameter 14	3
Days per stent	22.5+22.9
Stents per patient	4+8.75
Stent location	
RMSB	147 (39.10%)
RUL	33 (8.78%)
BI	77 (20.48%)
RLL	14 (3.72%)
RML	8 (2.13%)
LMSB	82 (21.81%)
LUL	7 (1.86%)
LLL	8 (2.13%)

Values presented as median + IQR or n (%). #, number of stents. RMSB, right mainstem bronchus; RUL, right upper lobe; BI, bronchus intermedius; RLL, right lower lobe; RML, right middle lobe; LMSB, left mainstem bronchus; LUL, left upper lobe; LLL, left lower lobe.



**Figure 1** The most common complication and reason for stent removal was secretions (n=193), followed by formation of excessive granulation tissue (n=131), migration or malposition (n=51), stent fracture (n=15) and hemorrhage (n=5). There were two cases of major hemorrhage; one case led to cardiac arrest from hemorrhagic shock. The other case resulted in the patient receiving a pneumonectomy. More than one complication and reason for removal was allowed for some stents. Stents that were left in place at end analysis, planned removals or left in deceased patients are not included in this figure.

**Table 4** Complications by stent

Complication	Stent	N (%)	P value
Secretions (n=193)	Bonastent®	112 (51.14)	0.462
	Atrium iCAST™	70 (53.85)	
	AERO®	11 (40.74)	
Granulation (n=131)	Bonastent®	72 (32.88)	0.235
	Atrium iCAST™	46 (35.38)	
	AERO®	13 (48.15)	
Migration (n=51)	Bonastent®	29 (13.24)	0.869
	Atrium iCAST™	19 (14.62)	
	AERO®	3 (11.11)	
Fracture (n=15)	Bonastent®	15 (6.52)	0.04
	Atrium iCAST™	0	
	AERO®	0	

More than one complication was allowed for some stents. The percentage is the incidence of the complication for each stent type. Chi square analysis was used to determine statistical significance.

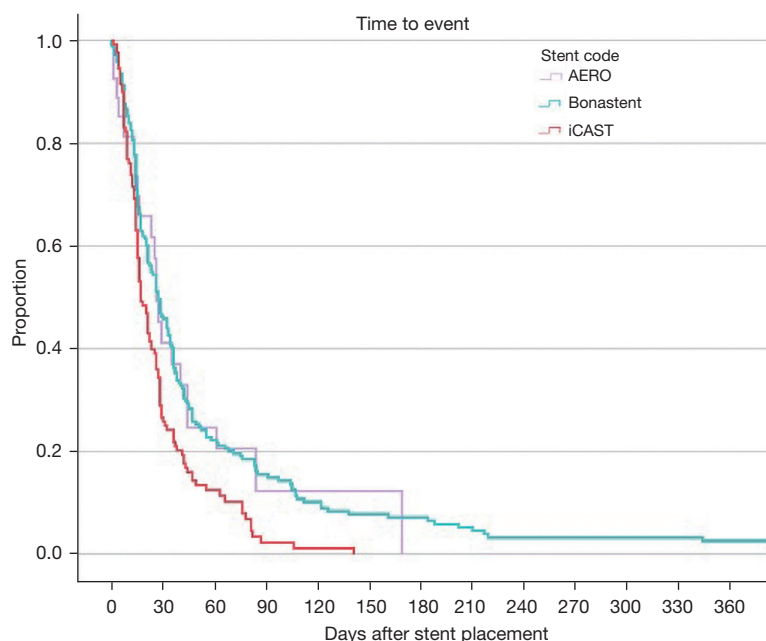
utilized was the AERO® (n=27, 7.18%). Stents were placed most frequently in the right mainstem bronchus (n=147, 39.10%) followed by the left mainstem bronchus (n=82, 21.81%) and the bronchus intermedius (n=77, 20.48%).

See *Table 3* for further details. Analysis of complication by stent demonstrated that each stent's individual complication rate was similar to the overall complication rate with the exception of stent fracture which only occurred more frequently in the Bonastent® subgroup (P=0.04). See *Table 4* for further details.

## Discussion

The United States FDA warned against the safety of SEMS in benign airway primarily due to concerns about safe removal after prolonged implantation (12). There were only two major complications out of the 376 stents that were placed over a total of 15,711 stent days. The average patient had a median total of 176 stent days (IQR, 45.5–351.25). The median duration per stent was 22.5 days (IQR, 13–29). See *Figure 2* for more details. Mucus plugging around the stents was the most frequent reason why stents were removed in our patients (n=193). Despite differences in stent diameter (see *Table 3*), there was no difference in incidence of stents removed due to secretions among the different stent types (see *Table 4*). Although patients are instructed to perform airway clearance techniques after stent placement, mucus plugging of stents is an inevitable minor complication that can easily be treated with repeat bronchoscopy. Granulation tissue was the second most common indication for stent removal, the decision to treat





**Figure 2** Time to stent removal for each stent subtype. The Atrium iCAST<sup>TM</sup> (red, median: 17 + IQR: 19.75) had a shorter duration than the AERO<sup>®</sup> (purple, median: 26 + IQR: 30.5) or Bonastent<sup>®</sup> (blue, median: 26 + IQR: 33).

granulation tissue or exchange a stent was at the discretion of the proceduralist. Subgroup analysis of complications by stent type demonstrated that individual complication rates for each stent were consistent with the overall complication rate. The exception was stent fracture which only occurred in the Bonastent<sup>®</sup> subgroup ( $n=15$ ,  $P=0.04$ ). However, this occurred infrequently and was not associated with major morbidity or mortality. An increased incidence of stent fracture with Bonastent<sup>®</sup> has previously been described in the management of gastric outlet obstructions (16).

In this retrospective study, we provide the largest analysis to date demonstrating the safety of hybrid covered metallic stents in transplant airway disease. Unlike prior studies reviewing metallic stents in benign airway disease, which primarily used rigid bronchoscopy, we utilized flexible bronchoscopy for placement and removal of all stents. We also have a significantly larger number of stents in our analysis, 376, as compared to 20, 40 and 47 in the papers by Dooms *et al.*, Fortin *et al.* and Ma *et al.* respectively (13-15). One major difference in our study is that we have a significantly shorter average duration of stent placement (median: 22.5 + IQR: 29) as compared to Fortin *et al.* (median: 77.0±96.6 days) and Ma *et al.* (median: 258 + IQR: 308). We attribute this difference to multiple factors. Our entire cohort of 50 patients consists of lung transplant

patients unlike Fortin *et al.* (14) who had only 8 post-transplant patients. Transplant patients may be more prone to mucus plugging in the immediate post operative period due to sloughing of ischemic mucosa and transplant specific medications may interfere mucociliary clearance. Secondly, stent variation between studies may account for some differences. All the stents in our cohort were covered metal stents unlike Ma *et al.* (15), who primarily utilized silicone stents. We would have anticipated less mucus plugging with the covered metal stent versus the silicone stents and cannot explain the contrary. The average stent duration for covered metal stents in Ma *et al.* (15) was shorter (median: 108 + IQR: 107) than for silicone stents (median: 296 + IQR: 317) demonstrating that stent duration is not equivalent for metallic and silicone stents. Additionally, Ma *et al.* study only evaluated stenting for anastomotic pathology and the majority of stents placed in Fortin *et al.* were placed in proximal airways (14,15). Nearly half of our stents were placed in distal airways (Table 3), the smaller lumen size may account for worse mucus plugging and may have contributed to the intensity of surveillance and revision. We believe that based on the number of hybrid metallic stents included in our cohort and use of flexible bronchoscopy, our data adds valuable evidence that this intervention can be safely utilized for lung transplant airway complications.

Our study does have several limitations. This is a retrospective cohort analysis with data that is reliant on interpretation of procedural documentation. Ideally, this would have been performed as a prospective analysis with predefined complication outcomes as well as a defined protocol for intervention and follow up bronchoscopy. Decisions regarding stent placement and other complementary procedures were at the discretion of the performing proceduralists. Furthermore, this is a single center experience and the practice patterns of our institution and the performing bronchoscopists likely impacted the results, specifically our stent duration which is shorter than what has previously been reported. It is hard to grade the severity of complications retrospectively. Additionally, our analysis does not account for variations in patient's baseline comorbidities or for synchronous interventions that were performed to treat airway complications which certainly could have impacted the safety profile of the covered metal stents. Complementary interventions for bronchial stenosis including dilation and tissue ablation procedures like argon plasma coagulation (APC) are generally regarded as safe but can cause airway perforation and hemorrhage in rare circumstances (17).

While our study contributes significantly to the safety profile of stents, it does not include a distinct measure of clinical efficacy. Prior studies have utilized changes in spirometry, frequency of bronchoscopy and lack of follow-up after removal as markers of clinical success (13-15). Unfortunately, this data can easily be confounded by other acute complications in lung transplant patients. Given that stent placement for bronchial stenosis is largely a palliative intervention, future prospective studies should include a validated dyspnea or quality of life questionnaire to assess the true benefit of each intervention.

In conclusion, we provide the largest analysis to date of the safety of covered metal stents. Prior warnings against SEMs should be updated to reflect the enhanced safety of hybrid covered metallic bronchial stents for transplant airway complications. Future studies should account for patient specific comorbidities and the impact of other interventions, while also objectively measuring the benefit of each intervention for patients with airway complications after lung transplantation.

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### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-2003/rc>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-2003/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Research Ethics Board of Temple University Hospital, protocol 28636, and individual consent for this retrospective analysis was waived.

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