A Prospective Multicenter Trial of a Self-expanding Hybrid Stent in Malignant Airway Obstruction

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Introduction: There are 2 general classes of stents available for airway obstruction: self-expanding metal and silicone. Metal stents can be placed using flexible bronchoscopy under local anesthesia but may be difficult to remove. Silicone stents require rigid bronchoscopy and general anesthesia to place but they are relatively easy to remove. A new hybrid stent, the AERO stent (Alveolus Inc, Charlotte, NC), has a completely covered nitinol framework. The purpose of this study was to evaluate the efficacy and safety of this new hybrid stent for the treatment of malignant airway obstruction.

Methods: This was a prospective multicenter intention to treat study. Eligible patients with malignant airway obstruction underwent self-expanding hybrid stent placement at 11 centers between June 2005 and December 2006. Patients were evaluated immediately postprocedure and at 7, 30, and 90 days postprocedure. Ease of deployment was assessed on a 4-point Likert scale. Luminal patency was visually assessed preimplant and postimplant by investigators and verified in blinded review of photographs taken during the procedure. Quality of life was measured using the Baseline Dyspnea Index and Transitional Dyspnea Index.

Results: Fifty-six patients (53% male, 47% female, median age 65.7) underwent stent placement. Physicians rated ease of deployment at 3.6 on a 1 to 4 scale with 1 being poor and 4 being excellent. Eighty-eight percent of patients had a lumen patency improvement of $> 50\%$ ($P\& < 0.05$). Dyspnea indices demonstrated quality of life improvement postimplant as compared with baseline values (average improvement in Transitional Dyspnea Index of 2.9 at 7 d and 3.2 at 30 d, $P < 0.05$) Complications included hemoptysis, infection, granulation tissue formation, stent migration, and pain at rates comparable with previously published studies. Stent removal, when clinically indicated, was accomplished without difficulty or complication in 7 patients.

Conclusions: In patients with malignant airway obstruction, self-expanding hybrid stent were easy to deploy and remove and improved luminal patency and quality of life with an acceptable complication rate. Further trials are needed to assess the long-term outcomes of this new stent technology.

Key Words: malignant central airway obstruction, stent, lung cancer

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Tracheobronchial stent placement has become a routine palliative modality for malignant airway obstruction. The goal is to improve airway lumen patency and quality of life. There are in general 2 classes of stents, silicone and metal. Silicone stents have been available and routinely used since the 1980s.[1,2] They are usually placed using a rigid bronchoscope, under general anesthesia, in the operating room. They have both positive and negative attributes. Advantages of silicone stents include the fact that there is much published data on their use. They are efficacious and inexpensive. In addition, these stents can be removed if needed. The disadvantages include: a need for general anesthesia and a trip to the operating room. In addition, granulation tissue formation around the stent and mucous formation within the stent is common.

Self-expanding metal stents, usually made up of nitinol frame that has shape memory, became popular in the 1990s. They have the advantage of being able to be placed in the bronchoscopy suite under local anesthesia under moderate sedation. The disadvantages include difficulty with removal, stent fracture, granulation tissue formation, and infection due to bacterial adherence to the covering.

In an attempt to capture the favorable properties of both classes of stents, a completely covered nitinol (hybrid) stent was designed to reduce stent complications (AERO stent, Alveolus Inc, Charlotte, NC) (Fig. 1).

The purpose of our study was to assess the safety and efficacy of this new hybrid stent.

METHODS

This was a multicenter prospective intention to treat trial. Eleven centers in the United States and Europe

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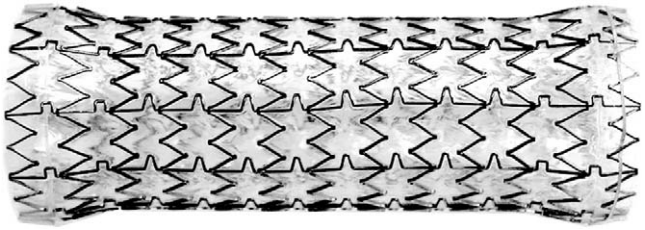
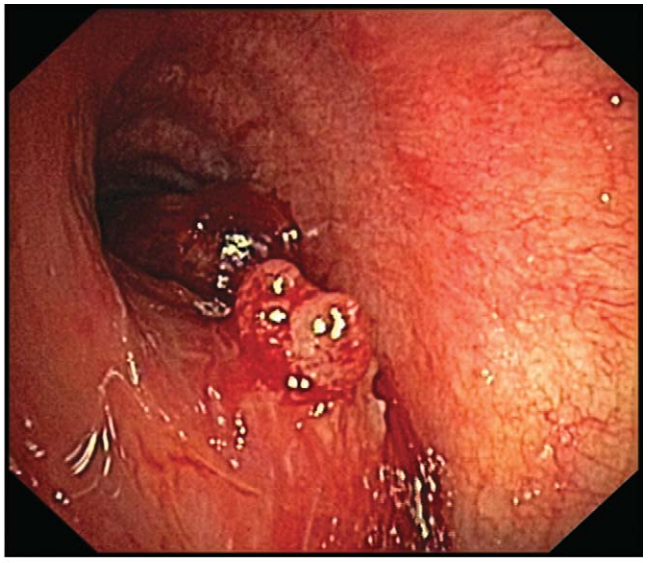


FIGURE 1. The Alveolus AERO stent.

(Appendix I) participated. Inclusion criteria were patients greater than 18 years of age with malignant airway obstruction of the major airways, either extrinsic (Fig. 2) or intrinsic (Fig. 3). Patients needed a predicted life expectancy of greater than 90 days to be included in the study. Exclusion criteria included patients for whom bronchoscopy was contraindicated, those who had benign disease, and those in whom a guidewire could not be passed across the obstruction.



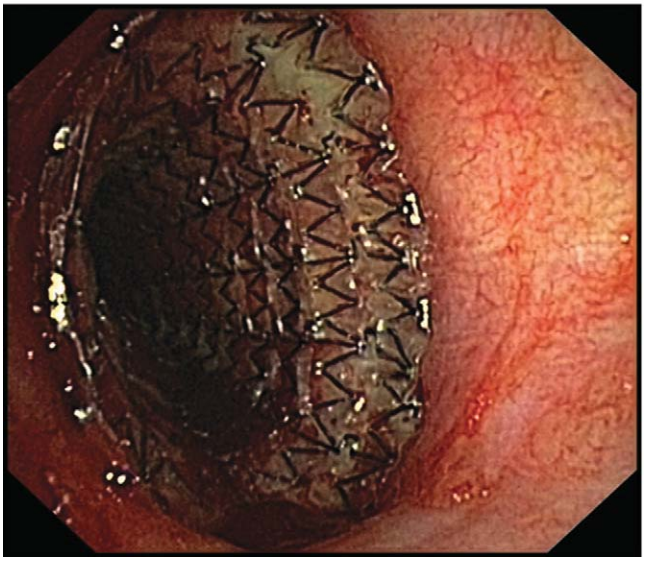


FIGURE 2. Tracheal compression prestent and poststent placement in a 75-year-old female patient.

FIGURE 3. Compression of the left main bronchus prestent and poststent placement in a 61-year-old male patient.

Device Description

The system is comprised of 2 components: a radiopaque self-expanding nitinol stent and the delivery

system. The stent is completely covered with a biocompatible membrane, which minimizes the possibility of tissue in-growth and granuloma formation. A hydrophilic coating in the inner lumen of the stent shall minimize mucous adherence and accumulation. Because the device is cut from a tube of nitinol with a unique design, the stent does not foreshorten or elongate upon delivery. The stent has a slightly larger diameter near the distal and proximal ends (Fig. 1). Both ends are slightly vaulted inwardly to minimize possible airway injury and the formation of granulation tissue at the stent edges.

The stent is deployed with a preloaded dedicated delivery system.

Study End Points

Data were collected before bronchoscopy, immediately postbronchoscopy, and at a 7-day postimplant clinic visit. Telephone interviews were conducted at 30 and 90 days to assess improvement in dyspnea scores.

Improvement in lumen patency was visually assessed by comparison of airway lumen diameter prestent and poststent implant. Success was defined by 50% reduction in stenosis. This assessment was independently confirmed by blinded investigators assessing prebronchoscopy and postbronchoscopy images.

Quality of life was assessed using a Baseline Dyspnea Index (BDI) and Transitional Dyspnea Index (TDI)[3] as a surrogate of quality of life measure. The TDI scores were indicative of improvement (positive integer), no change (score of 0), or deterioration (negative integer) in comparison to the BDI assessed before implant. A change in score of +1 or more indicates a clinically meaningful improvement. A change in score of −1 or more indicates a clinically meaningful worsening of dyspnea.

A 4-point Likert scale to indicate ease of use and deployment performance was also recorded with 1 being difficult to place and 4 being easy to place.

RESULTS

Sixty-one stents were placed in 56 patients. Patient characteristics and stent deployment location are reported in Table 1. Stents were deployed in the central airways. In all cases, palliative effects were observed. The average degree of lumen occlusion before stent placement was 82%. Improvement in luminal patency was noted in 88% of patients as defined by an increase in luminal diameter of $\geq 50\%$ ($P < 0.05$). Success is comparable with images seen in Figures 2 and 3. Dyspnea indices improved after stenting compared with baseline values with an average improvement of 2.9 at 7 days and 3.2 at 30 days ($P < 0.05$). Improvement at 90 days was not clinically significant ($P \geq 0.05$) (Table 2). Physician satisfaction with the deployment of the stent was high. Six aspects of the deployment system, including guidewire passage through the catheter, catheter passage into airway, stent release, catheter removal from airway, visualization, and accuracy of stent placement were rated on a 4-point scale where 4 = excellent and 1 = poor. A final average score between "good" (3) and "excellent" (4) was reported for each aspect with an overall average of 3.57. The stent was determined to be easily deployed.

The major complication of stent placement in this study was migration, which occurred in 28% of patients. Other minor stent-related complications included minimal granulation tissue in 5% (n = 3) and infection in 4% (n = 2). Complications not related to the stent placement included pain in 7% (n = 4) and hemoptysis in 4% (n = 2). Tumor in-growth was not observed in this study.

Survival after stent placement was 54 (96%) at 7, 46 (82%) at 30 and 38 (68%) at 90 days. Seven patients had their stent removed for the following reasons: response to concomitant therapy resulting in tumor response (n = 2), granulation tissue formation (n = 3), tumor growth at the ends of the stent requiring further stent placement (n = 1), and secretion build-up (n = 1).

TABLE 1. Baseline Characteristic

Sex	
Male	59%
Female	41%
Age (mean)	65 (range 45-97)
Stent implant location	
Trachea	12 (20%)
RMS	15 (24%)
RBI	12 (20%)
LMS	20 (33%)
RMS and RBI	2 (3%)
Baseline Dyspnea Index	3.76 (SD = ± 2.2)

LMS indicates left main stem bronchus; RBI, right bronchus intermedius; RMS, right main stem bronchus.

TABLE 2. Post Stent Dyspnea Score Changes

	Worse	Static	Improved	Total
TDI Scores—7 d postimplant				
Observed	5	3	37	45
Expected	15	15	15	45
Total	20	19	51	90
$\chi^2 = 48.5333$		$df = 2$		$P < 0.05$
TDI scores—30 d postimplant				
Observed	7	2	22	31
Expected	10.33	10.33	10.33	31
Total	17	13	32	62
$\chi^2 = 20.9677$		$df = 2$		$P < 0.05$
TDI scores—90 d postimplant				
Observed	5	2	9	16
Expected	5.33	5.33	5.33	16
Total	10	8	14	32
$\chi^2 = 4.625$		$df = 2$		$P \geq 0.05$ not significant

TDI indicates Transitional Dyspnea Index.

DISCUSSION

This is the first prospective, multicenter evaluation of a new hybrid completely covered metallic framed

self-expanding stent. The self-expanding hybrid stent provided immediate palliation in nearly all patients with a reasonable complication rate. It provides some of the strengths of both the silicone and metallic stents while eliminating some of the weaknesses. The self-expanding hybrid stent could be placed in the bronchoscopy laboratory under conscious sedation (a strength of self-expanding metallic stents[4]) but could be easily removed when needed (a strength of the silicone stent[4]). The rate of immediate palliation is consistent with other studies in which metallic stents have been used.[5] Early complication rates are also consistent with published literature. In a study of 82 patients with benign and malignant disease, 54.8% of patients required additional procedures to control granulation tissue formation and disease recurrence (tumor in-growth) postimplant.[6] Another study which included 27 patients had an overall complication rate of 50%. Secretion retention in 18% of the patients required additional interventional procedures and 15% of the patients' experienced recurrent dyspnea from granulation tissue formation at the end of the stent.[7] In this study, we observed 3 instances of slight granulation tissue formation which did not require ablation, no instance of tumor in-growth and no occlusion by secretions, though larger studies are needed to confirm these findings. The rate of migration is higher than what one would see with metallic stents yet, within range of what is found with silicone stents.[5] Since the completion of this trial the stent has been modified and struts have been added to reduce the rate of migration. We have reasons to believe that this goal can be accomplished.

This study has several strengths. First, it was a prospective multicentered study that is rare for a trial, which evaluates airway stent technology. Second, many important clinical end points were captured. Improvement in luminal patency was blindly assessed. Dyspnea, a surrogate of quality of life, as assessed by the BDI/TDI, was evaluated prestent and poststent placement and complications were recorded out to 90 days. The study has some weaknesses, namely, that long-term follow-up beyond 90 days was not assessed. Not surprisingly in this cancer population, a number of patients died before the end of the study, though none were related to stent placement. Transitional dyspnea scores were not available for many of the patients at the 90-day follow-up due to inability to travel, entrance into hospice care, or loss to follow-up. Transitional dyspnea scores were not recorded for some patients at 7 and 30 days due to removal of the device or expiration. Additional studies are needed with a longer follow-up period to accurately assess this new stent technology.

In summary, the initial experience with this new hybrid stent was positive. The device was easy to deploy, effective in palliating symptoms and, when indicated, was easy to remove. The complication rate was comparable with that reported in the literature and repeat procedures were rarely required. Further trials are needed to assess the long-term outcomes of this new hybrid stent. Preferably, a study should be conducted comparing the new modified stent versus other stent types.

APPENDIX 1

Active Site	Approval Date	Patients Enrolled
East Carolina University	25-May-2005	8
M D Anderson	25-May-2005	6
Cleveland Clinic	03-Jun-2005	13
Henry Ford	14-Jul-2005	3
University of Florida	12-Aug-2005	4
U.T. San Antonio	06-Sep-2005	2
University of Washington	28-Dec-2005	1
Marseille, France	31-May-2005	3
Hemer, Germany	17-Jan-2006	5
Heidelberg, Germany	12-Jul-2005	6
Barcelona, Spain	15-Sep-2005	5
Total		56

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