CHEST

Therapeutic Bronchoscopy for Malignant Central Airway Obstruction

Success Rates and Impact on Dyspnea and Quality of Life

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BACKGROUND: There is significant variation between physicians in terms of how they perform therapeutic bronchoscopy, but there are few data on whether these differences impact effectiveness.

METHODS: This was a multicenter registry study of patients undergoing therapeutic bronchoscopy for malignant central airway obstruction. The primary outcome was technical success, defined as reopening the airway lumen to > 50% of normal. Secondary outcomes were dyspnea as measured by the Borg score and health-related quality of life (HRQOL) as measured by the SF-6D.

RESULTS: Fifteen centers performed 1,115 procedures on 947 patients. Technical success was achieved in 93% of procedures. Center success rates ranged from 90% to 98% ($P = .02$). Endobronchial obstruction and stent placement were associated with success, whereas American Society of Anesthesiology (ASA) score > 3, renal failure, primary lung cancer, left mainstem disease, and tracheoesophageal fistula were associated with failure. Clinically significant improvements in dyspnea occurred in 90 of 187 patients measured (48%). Greater baseline dyspnea was associated with greater improvements in dyspnea, whereas smoking, having multiple cancers, and lobar obstruction were associated with smaller improvements. Clinically significant improvements in HRQOL occurred in 76 of 183 patients measured (42%). Greater baseline dyspnea was associated with greater improvements in HRQOL, and lobar obstruction was associated with smaller improvements.

CONCLUSIONS: Technical success rates were high overall, with the highest success rates associated with stent placement and endobronchial obstruction. Therapeutic bronchoscopy should not be withheld from patients based solely on an assessment of risk, since patients with the most dyspnea and lowest functional status benefitted the most. CHEST 2015; 147(5):1282-1298

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ABBREVIATIONS: APC = argon plasma coagulation; AQuIRE = American College of Chest Physicians Quality Improvement Registry, Evaluation, and Education; ASA = American Society of Anesthesiology score; ΔBorg = postprocedure − preprocedure Borg score; Δutility = postprocedure − preprocedure utility; HRQOL = health-related quality of life; MCID = minimal clinically important difference

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Malignant airway obstruction occurs frequently in patients with lung cancer and in patients with pulmonary metastases from other malignancies, including breast, colon, and renal cell cancer.[1] There are three main types of malignant airway obstruction: endobronchial, extrinsic compression, and a mixed pattern. Ablative techniques that destroy tissue are useful for endobronchial obstruction. Ablative techniques include lasers, electrocautery, argon plasma coagulation (APC), photodynamic therapy, microdebriders, and cryotherapy. Stents are the primary modality used for patients with extrinsic compression. For mixed patterns, multiple modalities are usually required. Practice patterns vary significantly between bronchoscopists in terms of the type of bronchoscopy used (flexible vs rigid), ablative technique preferred (eg, laser vs electrocautery), and stent strategy and preference (eg, silicone vs metal). Whether these practice variations impact effectiveness is unknown.

Prior studies of therapeutic bronchoscopy for central airway obstruction[2-6] have included both malignant and benign cases, and most were done retrospectively. However, outcomes and complications differ significantly depending upon the indication (eg, malignant airway obstruction vs postintubation tracheal stenosis). In many studies there was significant heterogeneity in terms of patient population and indications.[1,3,4] Other studies have focused on individual technologies, such as microdebriders[3] or APC.[7] These studies are useful for evaluating new technologies, but they are not designed to show comparative effectiveness. In clinical practice, a multimodality approach using a variety of technologies is the norm, but there is relatively scant evidence comparing techniques. In addition, the impact of interventions on quality of life has not always been quantified with validated instruments. This makes clinical decision-making more difficult, since physicians must be able to quantify the potential benefits and weigh them against the risks. Finally, most of these studies were performed at centers of excellence as part of clinical research studies and used relatively small and highly selected patient populations. Whether these results can be generalized to everyday clinical practice is unknown.[8,9]

We used the American College of Chest Physicians Quality Improvement Registry, Evaluation, and Education (AQuIRE) program to evaluate therapeutic bronchoscopy for malignant central airway obstruction. Registries offer the benefit of providing clinical effectiveness data that are more generalizable than those obtained from more focused clinical trials.[8,9] Our primary objective was to quantify the technical success rate of therapeutic bronchoscopy, defined as anatomic reopening of the airways, and to identify techniques and factors associated with technical success. Secondary objectives were to assess the impact of therapeutic bronchoscopy on dyspnea and changes in health-related quality of life (HRQOL) in a subset of these patients. Data on complications are presented separately.

Materials and Methods

Patients undergoing therapeutic bronchoscopy from January 2009 to February 2013 were entered into AQuIRE.[10] Not all centers started participating at the same time; some centers participated for the entire duration, and others participated for ≥ 1 year. However, participating physicians agreed to enter all consecutive patients for the duration of their participation. Institutional review board approval was obtained from The University of Texas MD Anderson institutional review board committee 4, protocol DR09-0101 (e-Appendix 1). The principal investigator for each site was primarily responsible for data quality for that site. Informed consent or a waiver of consent was obtained in accordance with institutional guidelines. Data were entered via the AQuIRE web-based interface using standardized definitions, quality control checks, and protocols as previously described.[8,9,11]

Patients undergoing therapeutic flexible or rigid bronchoscopy for malignant central airway obstruction were included. Central airway obstruction was defined as occlusion of $\geq 50\%$ of the trachea, mainstem bronchi, bronchus intermedius, or a lobar bronchus. All clinical

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decisions, including type of interventions used, were left to the discretion of the attending bronchoscopist.

Information extracted from AQuIRE included patient demographics, clinical characteristics, physician and hospital information, sedation information, procedural information, and technical success of the procedure. Technical success was based on anatomic criteria and was defined bronchoscopically as reopening the airway lumen to >50% of the normal diameter. The airway also had to connect to a viable area of distal lung. If a physician successfully reopened a proximal airway, only to discover that there was distal disease that occluded all the segmental and subsegmental levels, this was classified as a technical failure. All clinical outcomes were assessed by the attending physician using standardized definitions from a code book. See e-Appendix 1 for additional details on definitions. Center volume was determined by calculating the average number of cases per month for each center, and this was used as a center-level variable in hierarchical models. A subset of centers agreed prospectively to collect preprocedure and 30-day postprocedure data on dyspnea and self-reported HRQOL. Dyspnea was measured using the Borg score, and HRQOL was measured using the SF-6D.[12] The SF-6D provides a means to estimate a preference-based single index measure for health using general population data.

The primary outcome was technical success of the procedure. All centers decided in advance whether to collect additional data on dyspnea and HRQOL, since this was an optional module within AQuIRE because most centers do not collect these data as part of their routine clinical care. A secondary analysis was conducted to analyze the outcomes of change in dyspnea as measured by the Borg score and changes in utility as derived from the SF-6D, only using the data from those centers that agreed in advance to participate in that module.

Statistical Analysis

For binary outcomes, the association of the outcome with each of the covariates was checked by χ^2 test or Fisher exact test or Wilcoxon-Mann-Whitney two-sample test or Wilcoxon signed-rank test as appropriate. For continuous outcomes, the association of the outcome with each of the covariates was checked by *F* test in analysis of variance models or *t* test in linear regression models, as appropriate. Change in dyspnea was calculated as postprocedure − preprocedure Borg score (ΔBorg). For responder analysis we used a ΔBorg of ≤ −1 to define patients having a clinically significant improvement in dyspnea. This was based on the minimal clinically important difference (MCID) of the Borg score, which is a one-unit change.[13,14] Change in utility was calculated as postprocedure − preprocedure utility (Δutility) among patients alive 30 days after the procedure. For responder analysis we used a Δutility of + 0.033 to define patients having a clinically significant improvement in utility. This was based on the MCID of the SF-6D.[15] Variables that had *P* values < .20 on univariate analyses were candidates for multivariate models. Predictive models used only clinical information available preprocedure; explanatory models used all available information. Multivariate models used backward selection to retain only variables with *P* values < .05. To control for regression to the mean when analyzing ΔBorg, we included baseline Borg in the multivariate models.[16] Additional information on models and controlling for regression to the mean are in e-Appendix 1. We used hierarchical models to evaluate the impact of center-level variation on homogeneity. Logistic regression using the maximum likelihood approach was used. For continuous outcomes, an analysis of covariance model was used. *P* values < .05 were considered to be significant; all tests were two-sided. All statistical analyses were performed in SAS version 9.3 (SAS Institute Inc).

Results

Fifteen centers with 26 physicians enrolled 947 patients who had 1,115 procedures. Baseline patient and clinical characteristics are shown in Table 1. There were significant variations in practice patterns between centers in location of care ($P < .001$), anesthesia ($P < .001$), ventilation ($P < .001$), rigid bronchoscopy ($P < .001$), ablative techniques ($P < .001$), stent use ($P < .001$), and types of stents used ($P < .001$).

Technical Success of the Procedure

Out of the 1,115 procedures, 1,039 (93%) were technically successful (>50% success) (Table 2). On multivariate analysis, endobronchial obstruction and stent placement were associated with higher technical success rates, whereas American Society of Anesthesiology (ASA) score > 3, renal failure, primary lung cancer, left mainstem disease, and tracheoesophageal fistula were associated with lower technical success rates. Among the eight centers that had data on 25 or more cases (n = 1,052), success rates ranged from 90% to 98% ($P = .02$). We evaluated center-level impact on homogeneity, but the model did not converge if smaller centers were included. When we used only larger centers, we failed to find evidence of heterogeneity, and we did not find evidence of a relationship between center volume and success rates. This is not to say that centers had the same outcomes, but rather that after evaluating for other covariates the between-center variance was negligible.

Dyspnea

A total of 187 patients had pre- and post-Borg scores measured. We compared this dyspnea assessment subset to other patients from the same centers who did not have dyspnea data collected. We found that the dyspnea assessment subsets were more likely to have elective procedures ($P = .006$), be inpatients ($P < .001$), and have rigid bronchoscopy ($P < .001$). In all other regards they were similar (e-Table 1).

Dyspnea decreased following intervention (mean ΔBorg, -0.9 ± 2.2; Wilcoxon signed-rank test, $P < .0001$). Note that since lower Borg scores indicate less dyspnea, if ΔBorg is negative, then there has been a decrease in dyspnea from preprocedure to postprocedure. On multivariate analysis, a one-unit increase of baseline Borg score was found to be associated with a 0.63-unit decrease in ΔBorg ($P < .0001$), indicating that higher baseline Borg scores were associated with greater improvements in dyspnea (Table 3). Conversely, smokers, patients with another primary solid tumor, and patients with lobar obstruction tended to have a higher ΔBorg, indicating that these

TABLE 1] Patient and Clinical Characteristics of Procedures

Characteristics	Frequency (N = 1,115)
Age, mean ± SD, y	62.8 ± 13.3
Baseline Borg score, mean ± SD	3.6 ± 2.4
Male sex	620 (55.6)
Inpatient	366 (32.8)
Race	
Nonwhite	202 (18.1)
White	913 (81.9)
Urgency of the procedure	
Elective	767 (68.8)
Emergent	104 (9.3)
Urgent	244 (21.9)
Zubrod score	
≤ 1	469 (42.1)
> 1	646 (57.9)
ASA score	
≤ 3	701 (62.9)
> 3	414 (37.1)
Therapeutic bronchoscopy	
First therapeutic bronchoscopy	800 (71.7)
Redo bronchoscopy (second or later)	315 (28.3)
Comorbidities[a]	
Asthma	55 (4.9)
COPD	339 (30.4)
Cardiovascular disease	566 (50.8)
Diabetes	175 (15.7)
GERD	65 (5.8)
Hematologic malignancy	5 (0.4)
Second primary solid tumor present[b]	7 (0.6)
Renal failure creatinine > 2 or on HD	17 (1.5)
Bleeding risk high medications	81 (7.3)
Current or prior tobacco use	872 (78.2)
Cancer related	
Primary lung cancer	800 (71.7)
Time from cancer diagnosis > 75 d	556 (49.9)
Location(s) of disease[a]	
Trachea	255 (22.9)
Left main	416 (37.3)
Right main	459 (41.2)
Bronchus intermedius	268 (24)
Lobar	323 (29)
Any tracheoesophageal fistula	9 (0.8)
Type(s) of obstruction present[a]	
Any endobronchial	549 (49.2)
Any extrinsic	161 (14.4)
Any mixed	485 (43.5)
Procedural variables	
Anesthesia	
Moderate sedation	154 (13.8)
Deep or general	961 (86.2)
Paralysis	
No	283 (25.4)
Yes	832 (74.6)
Type of ventilation	
Volume cycled	714 (64)
Jet	230 (20.6)
Spontaneous	171 (15.3)
Type of bronchoscopy	
Flexible	382 (34.3)
Rigid	733 (65.7)
Ablative techniques used	
Any laser used	262 (23.5)
Any electrocautery used	238 (21.3)
Any APC used	393 (35.2)
Any cryotherapy used	89 (8)
Any dilation done	448 (40.2)
Stent(s) placed[a]	
Any stent placed	406 (36.4)
Any metal stent	298 (26.7)
Any silicone tube stent	36 (3.2)
Any tube stent[c]	331 (29.7)
Any Y stent	85 (7.6)

Data are given as No. (%) unless otherwise indicated. APC = argon plasma coagulation; ASA = American Society of Anesthesiology; GERD = gastroesophageal reflux disease; HD = hemodialysis.

[a]Patients could have multiple comorbidities, disease locations, types of obstruction, and interventions during the same procedure. Therefore, these are not mutually exclusive.

[b]Patients having a second primary cancer present other than the one causing obstruction.

[c]If a patient had any non-Y-shaped stent placed, whether metal or silicone, it was considered a tube stent. See e-Appendix 1 for interpretation of ORs related to stent type.

groups were less likely to have improvements in dyspnea. There was no difference between predictive and explanatory models.

In a responder analysis, 90 of the 187 patients (48%) had a clinically significant improvement in dyspnea, 81 (43%) stayed the same, and 16 (9%) worsened (e-Table 2). On

TABLE 2] Patient and Clinic Characteristics by Technical Success of the Procedure (> 50% Successful)

Characteristic	Univariate Analysis			Multivariate Analysis	
	No Technical Success (n = 76)	Yes Technical Success (n = 1,039)	*P* Value	Multivariate OR (95% CI)[a]	*P* Value
Age, mean, y	62.5	62.9	.88[b]	…	…
Inpatient					
No	53 (7.1)	696 (92.9)	…	…	…
Yes	23 (6.3)	343 (93.7)	.62	…	…
Urgency of the procedure					
Elective	53 (6.9)	714 (93.1)	…	…	…
Emergent	5 (4.8)	99 (95.2)	…	…	…
Urgent	18 (7.4)	226 (92.6)	.73[c]	…	…
Zubrod score					
≤ 1	32 (6.8)	437 (93.2)	…	…	…
> 1	44 (6.8)	602 (93.2)	.99	…	…
ASA score					
≤ 3	38 (5.4)	663 (94.6)	…	Reference	…
> 3	38 (9.2)	376 (90.8)	.02	0.55 (0.33-0.9)	.018
Therapeutic bronchoscopy					
First therapeutic bronchoscopy	54 (6.8)	746 (93.3)	.90	…	…
Redo bronchoscopy (second or later)	22 (7.0)	293 (93.0)	…	…	…
Comorbidities					
Asthma					
No	75 (7.1)	985 (92.9)	…	…	…
Yes	1 (1.8)	54 (98.2)	.17[c]	…	…
COPD					
No	46 (5.9)	730 (94.1)	…	…	…
Yes	30 (8.8)	309 (91.2)	.08	…	…
Cardiovascular disease					
No	42 (7.7)	507 (92.3)	…	…	…
Yes	34 (6)	532 (94)	.28	…	…
Second primary solid tumor					
No	76 (6.9)	1,032 (93.1)	…	…	…
Yes	0 (0)	7 (100)	1.0[c]	…	…
Renal failure creatinine > 2 or HD					
No	72 (6.6)	1,026 (93.4)	…	Reference	…
Yes	4 (23.5)	13 (76.5)	.02[c]	0.17 (0.04-0.66)	.011
Bleeding risk high medications					
No	72 (7)	962 (93)	…	…	…
Yes	4 (4.9)	77 (95.1)	.65[c]	…	…
Tobacco use					
Never user	10 (4.1)	233 (95.9)	…	…	…
Current or prior use	66 (7.6)	806 (92.4)	.06	…	…
Cancer related					
Time from cancer diagnosis					

(Continued)

TABLE 2] *(continued)*

Characteristic	Univariate Analysis			Multivariate Analysis	
	No Technical Success (n = 76)	Yes Technical Success (n = 1,039)	*P* Value	Multivariate OR (95% CI)[a]	*P* Value
≤75 d	44 (7.9)	515 (92.1)	…	…	…
>75 d	32 (5.8)	524 (94.2)	.16	…	…
Primary lung cancer					
No	13 (4.1)	302 (95.9)	…	Reference	…
Yes	63 (7.9)	737 (92.1)	.02	0.45 (0.23-0.88)	.019
Location of disease					
Trachea					
No	71 (8.3)	789 (91.7)	…	…	…
Yes	5 (2)	250 (98)	.0002[c]	…	…
Left main					
No	38 (5.4)	661 (94.6)	…	Reference	…
Yes	38 (9.1)	378 (90.9)	.02	0.51 (0.31-0.83)	.007
Right main					
No	52 (7.9)	604 (92.1)	…	…	…
Yes	24 (5.2)	435 (94.8)	.08	…	…
Bronchus intermedius					
No	60 (7.1)	787 (92.9)	…	…	…
Yes	16 (6)	252 (94)	.53	…	…
Lobar					
No	50 (6.3)	742 (93.7)	…	…	…
Yes	26 (8)	297 (92)	.30	…	…
Any tracheoesophageal fistula					
No	74 (6.7)	1,032 (93.3)	…	Reference	…
Yes	2 (22.2)	7 (77.8)	.12[c]	0.03 (0-0.17)	<.0001
Type of obstruction					
Any endobronchial					
No	51 (9)	515 (91)	…	Reference	…
Yes	25 (4.6)	524 (95.4)	.003	2.62 (1.56-4.39)	.0003
Any extrinsic					
No	69 (7.2)	885 (92.8)	…	…	…
Yes	7 (4.3)	154 (95.7)	.18	…	…
Any mixed					
No	30 (4.8)	600 (95.2)	…	…	…
Yes	46 (9.5)	439 (90.5)	.001	…	…
Procedural variables					
Anesthesia					
Moderate sedation	15 (9.7)	139 (90.3)	…	…	…
Deep or general anesthesia	61 (6.3)	900 (93.7)	.12	…	…
Paralysis					
No	24 (8.5)	259 (91.5)	…	…	…
Yes	52 (6.3)	780 (93.8)	.20	…	…

(Continued)

TABLE 2] *(continued)*

Characteristic	Univariate Analysis			Multivariate Analysis	
	No Technical Success (n = 76)	Yes Technical Success (n = 1,039)	*P* Value	Multivariate OR (95% CI)[a]	*P* Value
Type of ventilation					
Volume cycled	51 (7.1)	663 (92.9)	…	…	…
Jet	9 (3.9)	221 (96.1)	…	…	…
Spontaneous	16 (9.4)	155 (90.6)	.08	…	…
Type of bronchoscopy					
Flexible	28 (7.3)	354 (92.7)	…	…	…
Rigid	48 (6.5)	685 (93.5)	.62	…	…
Any laser used					
No	53 (6.2)	800 (93.8)	…	…	…
Yes	23 (8.8)	239 (91.2)	.15	…	…
Any electrocautery used					
No	58 (6.6)	819 (93.4)	…	…	…
Yes	18 (7.6)	220 (92.4)	.60	…	…
Any APC used					
No	59 (8.2)	663 (91.8)	…	…	…
Yes	17 (4.3)	376 (95.7)	.014	…	…
Any cryotherapy used					
No	65 (6.3)	961 (93.7)	…	…	…
Yes	11 (12.4)	78 (87.6)	.03	…	…
Any dilation done					
No	48 (7.2)	619 (92.8)	…	…	…
Yes	28 (6.3)	420 (93.8)	.54	…	…
Stent					
Stent placed					
No	69 (9.7)	640 (90.3)	…	Reference	…
Yes	7 (1.7)	399 (98.3)	< .0001	11.90 (5.1-27.8)	< .0001
Metal stent					
No	69 (8.4)	748 (91.6)	…	…	…
Yes	7 (2.3)	291 (97.7)	.0004	…	…
Silicone stent					
No	76 (7)	1,003 (93)	…	…	…
Yes	0 (0)	36 (100)	.17[c]	…	…
Tube stent					
No	69 (8.8)	715 (91.2)	…	…	…
Yes	7 (2.1)	324 (97.9)	.0001	…	…
Y stent					
No	76 (7.4)	954 (92.6)	…	…	…

Data are given as No. (%) unless otherwise indicated. See Table 1 legend for expansion of abbreviations.
[a]Firth penalized likelihood approach used for rare events.
[b]Wilcoxon two-sample test.
[c]Fisher exact test.

TABLE 3] Patient and Clinical Characteristics by Difference of Borg Score (Post − Pre)

Characteristic	No.	Univariate Analysis		Multivariate Analysis	
		Mean (SD) of Difference of Borg Score	*P* Value (*F* Test)	Coefficient Estimate (Error)	*P* Value
Baseline Borg score, coefficient[a] (SD)	187	−0.61 (0.05)[a]	<.0001[b]	−0.63 (0.05)	<.0001
Age, coefficient[a] (SD), y	187	0.024 (0.012)[a]	.04[b]	…	…
Inpatient, No. (%)					
No	143	−0.7 (1.8)	…	…	…
Yes	44	−1.4 (3)	.08	…	…
Urgency of the procedure, No. (%)					
Elective	153	−0.7 (2.1)	…	…	…
Emergent	3	−4.7 (1.5)	…	…	…
Urgent	31	−1.3 (2.3)	.004	…	…
Zubrod score					
≤1	85	−0.6 (2.2)	…	…	…
>1	102	−1.1 (2.1)	.08	…	…
ASA score, No. (%)					
≤3	148	−0.7 (2)	…	…	…
>3	39	−1.4 (2.7)	.1	…	…
Therapeutic bronchoscopy, No. (%)					
First therapeutic bronchoscopy	126	−1.1 (2.3)	…	…	…
Redo bronchoscopy, second or later	61	−0.4 (1.7)	.023	…	…
Comorbidities, No. (%)					
Asthma					
No	177	−0.8 (2.2)	…	…	…
Yes	10	−2 (2)	.11	…	…
COPD					
No	136	−0.8 (2.2)	…	…	…
Yes	51	−1 (2)	.64	…	…
Cardiovascular disease					
No	100	−0.8 (2.4)	…	…	…
Yes	87	−1 (1.9)	.63	…	…
Second primary solid tumor					
No	183	−0.9 (2.1)	…	Reference	…
Yes	4	0.6 (3.7)	.16	2.19 (0.82)	.008
Renal failure creatinine>2 or HD					
No	183	−0.9 (2.2)	…	…	…
Yes	4	−0.3 (0.5)	.56	…	…
Bleeding risk high medications					
No	186	−0.9 (2.2)	…	…	…
Yes	1	0 (.)	.69	…	…
Tobacco use					
Never user	50	−1.1 (2.3)	…	Reference	…
Current or prior use	137	−0.8 (2.1)	.46	0.52 (0.27)	.05
Cancer related					
Time from cancer diagnosis					

(Continued)

TABLE 3] *(continued)*

Characteristic	No.	Univariate Analysis		Multivariate Analysis	
		Mean (SD) of Difference of Borg Score	*P* Value (*F* Test)	Coefficient Estimate (Error)	*P* Value
≤75 d	59	−1.4 (2.5)	…	…	…
>75 d	128	−0.6 (2)	.034	…	…
Primary lung cancer, No. (%)					
No	76	−0.6 (2.3)	…	…	…
Yes	111	−1.1 (2.1)	.16	…	…
Location of disease, No. (%)					
Trachea					
No	154	−0.8 (2.1)	…	…	…
Yes	33	−1.1 (2.7)	.53	…	…
Left main			…		
No	114	−0.8 (2.3)		…	…
Yes	73	−1 (1.9)	.66	…	…
Right main					
No	126	−0.8 (1.9)	…	…	…
Yes	61	−1.1 (2.7)	.25	…	…
Bronchus intermedius					
No	118	−0.9 (2.1)	…	…	…
Yes	69	−0.8 (2.3)	.81	…	…
Lobar					
No	116	−1.1 (2.2)	…	Reference	…
Yes	71	−0.6 (2.1)	.13	0.51 (0.24)	.04
Any tracheoesophageal fistula					
No	187	−0.9 (2.2)	…	…	…
Yes	0		NA	…	…
Type of obstruction, No. (%)					
Any endobronchial					
No	58	−1 (2.4)	…	…	…
Yes	129	−0.8 (2)	.63	…	…
Any extrinsic					
No	166	−0.9 (2)	…	…	…
Yes	21	−0.3 (3.3)	.22	…	…
Any mixed					
No	137	−0.8 (2.1)	…	…	…
Yes	50	−1.1 (2.3)	.51	…	…
Procedural variables					
Anesthesia, No. (%)					
Moderate sedation	45	−1.1 (2)	…	…	…
Deep or general	142	−0.8 (2.2)	.5	…	…
Paralysis, No. (%)					
No	76	−1.2 (2)	…	…	…
Yes	111	−0.7 (2.2)	.1	…	…
Type of ventilation, No. (%)					

(Continued)

TABLE 3] *(continued)*

Characteristic	No.	Univariate Analysis		Multivariate Analysis	
		Mean (SD) of Difference of Borg Score	*P* Value (*F* Test)	Coefficient Estimate (Error)	*P* Value
Volume cycled	58	−1 (2.6)	…	…	…
Jet	80	−0.7 (1.9)	…	…	…
Spontaneous	49	−1 (2)	.7	…	…
Type of bronchoscopy					
Flexible	66	−1.2 (2.3)	…	…	…
Rigid	121	−0.7 (2.1)	.19	…	…
Any laser used					
No	149	−0.9 (2.1)	…	…	…
Yes	38	−0.8 (2.4)	.85	…	…
Any electrocautery used					
No	143	−1 (2.1)	…	…	…
Yes	44	−0.4 (2.3)	.08	…	…
Any APC used					
No	102	−1.2 (2.4)	…	…	…
Yes	85	−0.5 (1.8)	.045	…	…
Any cryotherapy used					
No	151	−0.8 (2.2)	…	…	…
Yes	36	−1 (2)	.64	…	…
Any dilation done					
No	150	−0.8 (2.1)	…	…	…
Yes	37	−1.2 (2.4)	.37	…	…
Stent					
Stent placed					
No	128	−0.7 (1.9)	…	…	…
Yes	59	−1.2 (2.7)	.17	…	…
Metal stent					
No	143	−0.8 (1.8)	…	…	…
Yes	44	−1.2 (3)	.27	…	…
Silicone stent					
No	178	−0.9 (2.2)	…	…	…
Yes	9	−1.1 (2)	.74	…	…
Tube stent					
No	134	−0.8 (1.8)	…	…	…
Yes	53	−1.2 (2.9)	.23	…	…
Y stent					
No	180	−0.9 (2.2)	…	…	…
Yes	7	−0.4 (2.6)	.58	…	…

Data are given as mean (SD) unless otherwise indicated. NA = not applicable. See Table 1 legend for expansion of other abbreviations.
[a]Coefficient of linear regression with dependent variable being continuous change in Borg score. Note that lower Borg scores indicate less dyspnea, so a negative post−pre score indicates improvements in dyspnea. Therefore, negative coefficients indicate factors that are associated with improvements in dyspnea from pre to post, whereas positive coefficients indicate factors that are associated with worsening dyspnea from pre to post.
[b]*t* test.

multivariate responder analysis, only higher baseline Borg score and never smoking were associated with clinical improvements in dyspnea.

Quality of Life and Utility

Mean baseline HRQOL was 0.65 ± 0.13 utiles. Pre- and post-utility scores were measured in 183 patients. HRQOL improved following intervention (mean Δutility, 0.023 ± 0.107 utiles; paired *t* test, $P = .004$). In multivariate predictive analysis, higher baseline Borg score and not having lobar obstruction were associated with greater improvements in HRQOL (Table 4). In an explanatory multivariate analysis (e-Table 3), lower baseline utility, absence of tracheal obstruction, absence of bronchus intermedius obstruction, and greater improvements in dyspnea postprocedure (ie, more negative ΔBorg) were associated with greater improvements in utility. A one-unit increase in ΔBorg (ie, more dyspnea) resulted in a decrease in Δutility of 0.020 utiles ($P < .0001$).

In a responder analysis, 76 of the 183 patients (42%) had a clinically significant improvement in utility, 61 (33%) stayed the same, and 46 (25%) worsened (e-Table 4). In a multivariate predictive analysis, Zubrod score > 1, not having extrinsic airway compression, and flexible bronchoscopy were associated with clinically significant improvements in utility.

Adverse Events

Complication occurred in 44 of the 1,115 procedures (3.9%). There was significant variation between centers (range, 0.9%-11.7%; $P = .002$) in complication rates. Six patients (0.5%) died secondary to procedural complications. Factors associated with complications included ASA > 3 ($P = .0002$) and Zubrod > 1 ($P = .02$). The 30-day mortality was 14.8%. There was significant variation between centers (range, 7.7%-20.2%; $P = .02$). Risk factors for 30-day mortality included ASA > 3 ($P \leq 0.0001$) and Zubrod > 1 ($P < .0001$). Detailed data and analysis of risk factors for complications and 30-day mortality are presented separately.

Discussion

Therapeutic bronchoscopy for malignant central airway obstruction is essentially a palliative intervention, since most patients have advanced disease that is incurable. Although therapeutic bronchoscopy in this setting may indeed prolong life modestly for some patients (eg, enable them to get off the ventilator), the majority of patients benefit from changes in quality of life rather than duration. When comparing the effectiveness of various therapeutic bronchoscopy techniques, it is therefore important to consider technical success and the subsequent impact on dyspnea and HRQOL. The potential benefits in HRQOL must then be weighed against the risks associated with the intervention. In this study, we found that although there were significant differences in technique between centers, technical success was usually achieved. There were differences between centers in the rate of technical success, but these were relatively modest. However, technical success did not always result in a meaningful improvement in dyspnea. Patients who were more short of breath at baseline were more likely to experience improvements in dyspnea, whereas those with lobar disease were less likely to improve. Similarly, HRQOL improvements were greatest in patients with more dyspnea at baseline, whereas those with lobar disease were less likely to improve. HRQOL improvement was also associated with higher ASA score and lower functional status. Thus, patients at the highest risk for complications also had the greatest potential for benefit.

Our study is consistent with and adds to the existing body of evidence by comparing alternative technologies and quantifying the nature and magnitude of the benefits of therapeutic bronchoscopy more precisely.[1,2,4,5,17-24] Prior studies often involved single centers and focused on particular technologies. Because of this, the populations were highly selected and not large enough to compare alternative approaches. Consistent with prior studies, we found a high rate of technical success (93%) with a modest amount of variation in success rates between centers. In addition, because of the number of centers and physicians involved, we were able to compare alternative techniques. We found there was no single best method in terms of ablative techniques. In addition, we found that stenting was associated with higher technical success rates. This association is not necessarily causal, since some patients may prove to have extensive disease beyond the central airways, such that the physician may deem that stenting is of no benefit. Hence there may be confounding by indication present, so caution is warranted when analyzing the factors associated with technical success.

However, measuring technical success alone is not sufficient, since palliation of dyspnea and improvement in HRQOL is the primary clinical goal. Many prior studies were case series and focused on feasibility, proof of concept, and quantifying risks with less emphasis on quantifying impact on HRQOL.[1,2,4,5,17-23] In our subset analysis, 48% of patients had a clinically significant

TABLE 4] Patient and Clinical Characteristics by Difference in Utility (Post − Pre)

		Univariate Analysis		Predictive Multivariate Analysis	
	No.	Mean (SD) of Difference of Utility	*P* Value (*F* test)	Coefficient Estimate (Error)	*P* Value
Baseline utility, coefficient[a] (SD)	183	−0.314 (0.057)[a]	<.0001[b]	…	…
Baseline Borg score, coefficient[a] (SD)	179	0.009 (0.003)[a]	.007[b]	0.010 (0.003)	.005
Post−pre Borg score difference, coefficient[a] (SD)	173	−0.022 (0.004)[a]	<.0001[b]	…	…
Age, coefficient[a] (SD), y	183	−0.00006 (0.0006)	.92[b]	…	…
Inpatient, No. (%)					
No	142	0.02 (0.1)	…	…	…
Yes	41	0.05 (0.12)	.13	…	…
Urgency of the procedure, No. (%)					
Elective	150	0.02 (0.11)	…	…	…
Emergent	3	0.09 (0.05)	…	…	…
Urgent	30	0.05 (0.1)	.18	…	…
Zubrod score					
≤1	88	0 (0.11)	…	…	…
>1	95	0.04 (0.1)	.023	…	…
ASA score, No. (%)					
≤3	148	0.01 (0.11)	…	…	…
>3	35	0.06 (0.11)	.017	…	…
Therapeutic bronchoscopy, No. (%)					
First therapeutic bronchoscopy	124	0.02 (0.11)	…	…	…
Redo bronchoscopy, second or later	59	0.02 (0.11)	.94	…	…
Comorbidities, No. (%)					
Asthma					
No	174	0.02 (0.11)	…	…	…
Yes	9	0.08 (0.08)	.11	…	…
COPD					
No	131	0.01 (0.11)	…	…	…
Yes	52	0.05 (0.11)	.08	…	…
Cardiovascular disease					
No	98	0.02 (0.11)	…	…	…
Yes	85	0.02 (0.11)	.85	…	…
Second primary solid tumor					
No	180	0.02 (0.11)	…	…	…
Yes	3	−0.05 (0.09)	.25	…	…
Renal failure creatinine>2 or HD					
No	179	0.02 (0.11)	…	…	…
Yes	4	0.09 (0.08)	.19	…	…
Bleeding risk high medications					
No	183	0.02 (0.11)	…	…	…
Yes	0		NA	…	…
Tobacco use					
Never user	52	0.01 (0.12)	…	…	…

(Continued)

TABLE 4] *(continued)*

		Univariate Analysis		Predictive Multivariate Analysis	
	No.	Mean (SD) of Difference of Utility	*P* Value (*F* test)	Coefficient Estimate (Error)	*P* Value
Current or prior use	131	0.03 (0.1)	.42	…	…
Cancer related					
Time from cancer diagnosis					
≤75 d	58	0.03 (0.12)	…	…	…
>75 d	125	0.02 (0.1)	.33	…	…
Primary lung cancer, No. (%)					
No	72	0.02 (0.11)	…	…	…
Yes	111	0.03 (0.1)	.43	…	…
Location of disease, No. (%)					
Trachea					
No	151	0.03 (0.1)	…	…	…
Yes	32	−0.01 (0.13)	.08	…	…
Left main					
No	115	0.02 (0.11)	…	…	…
Yes	68	0.04 (0.1)	.22	…	…
Right main					
No	125	0.02 (0.1)	…	…	…
Yes	58	0.03 (0.12)	.56	…	…
Bronchus intermedius					
No	116	0.03 (0.1)	…	…	…
Yes	67	0.01 (0.12)	.2	…	…
Lobar					
No	113	0.03 (0.11)	…	Reference	…
Yes	70	0.01 (0.11)	.07	−0.036 (0.016)	.02
Any tracheoesophageal fistula					
No	183	0.02 (0.11)	…	…	…
Yes	0	…	NA	…	…
Type of obstruction, No. (%)					
Any endobronchial					
No	52	0.03 (0.1)	…	…	…
Yes	131	0.02 (0.11)	.71	…	…
Any extrinsic					
No	165	0.03 (0.11)	…	…	…
Yes	18	0 (0.12)	.4	…	…
Any mixed					
No	137	0.02 (0.11)	…	…	…
Yes	46	0.03 (0.1)	.75	…	…
Procedural variables					
Anesthesia, No. (%)					
Moderate sedation	47	0.04 (0.1)	…	…	…
Deep or general anesthesia	136	0.02 (0.11)	.21	…	…

(Continued)

TABLE 4] *(continued)*

		Univariate Analysis		Predictive Multivariate Analysis	
	No.	Mean (SD) of Difference of Utility	*P* Value (*F* test)	Coefficient Estimate (Error)	*P* Value
Paralysis, No. (%)					
No	78	0.04 (0.11)	…	…	…
Yes	105	0.01 (0.11)	.036	…	…
Type of ventilation, No. (%)					
Volume cycled	60	0.02 (0.11)	…	…	…
Jet	73	0.01 (0.11)	…	…	…
Spontaneous	50	0.04 (0.1)	.35	…	…
Type of bronchoscopy					
Flexible	70	0.04 (0.11)	…	…	…
Rigid	113	0.01 (0.1)	.039	…	…
Any laser used					
No	145	0.02 (0.11)	…	…	…
Yes	38	0.02 (0.11)	.97	…	…
Any electrocautery used					
No	143	0.03 (0.1)	…	…	…
Yes	40	−0.01 (0.11)	.034	…	…
Any APC used					
No	100	0.03 (0.12)	…	…	…
Yes	83	0.01 (0.1)	.3	…	…
Any cryotherapy used					
No	146	0.02 (0.11)	…	…	…
Yes	37	0.03 (0.11)	.59	…	…
Any dilation done					
No	150	0.02 (0.1)	…	…	…
Yes	33	0.04 (0.12)	.31	…	…
Stent					
Stent placed					
No	128	0.02 (0.1)	…	…	…
Yes	55	0.04 (0.12)	.3	…	…
Metal stent					
No	143	0.02 (0.1)	…	…	…
Yes	40	0.05 (0.12)	.08	…	…
Silicone stent					
No	174	0.02 (0.11)	…	…	…
Yes	9	0.02 (0.09)	.86	…	…
Tube stent					
No	134	0.02 (0.1)	…	…	…
Yes	49	0.04 (0.12)	.12	…	…
Y stent					
No	177	0.03 (0.11)	…	…	…
Yes	6	−0.03 (0.12)	.22	…	…

Data are given as mean (SD) unless otherwise indicated. See Table 1 legend for expansion of abbreviations.
[a]Coefficient of linear regression with dependent variable being change in utility.
[b]*t* test.

improvement in dyspnea. This is consistent with prior studies of therapeutic bronchoscopy for malignant central airway obstruction, which also demonstrated improvements in dyspnea and HRQOL as measured by disease-specific instruments.[2,4,5,17-23] Although useful, these prior studies are not sufficient to fully inform clinical decision-making, because the trade-offs involve different units that cannot be easily compared. For example, what risk of death is acceptable to achieve success, when success is defined as relief of anatomic obstruction? What if we define success in terms of dyspnea? Since therapeutic bronchoscopy for malignant central airway obstruction is essentially palliative, we need to quantify the HRQOL gains in units that allow physicians to compare the benefits accrued to the risks incurred. This requires a specific type of HRQOL instrument—a generic single-index measure such as the SF-6D that can be used to calculate utilities (additional details on HRQOL instruments can be found in e-Appendix 1).

This is the first report, to our knowledge, of therapeutic bronchoscopy for malignant central airway obstruction from a multicenter registry that evaluates technical success and dyspnea relief and combines it with an analysis of utility. The MCID for the SF-6D has been estimated to be 0.033 (95% CI, 0.029-0.037).[15,25] This is similar to the MCID for other indirect utility measures, such as the Health Utilities Index Mark 2 (HU12), Health Utilities Index Mark 3 (HU13), and EQ-5D.[25,26] Our data suggest that when baseline dyspnea is higher, interventions have a greater impact on utility. We also found that patients with more severe functional impairment were more likely to benefit from intervention. Of note, with respect to the outcomes of dyspnea relief and utility, there was no single best method in terms of ablative techniques, and there was no single best type of stent.

This study provides a more accurate assessment of the relationship between baseline dyspnea, improvements in dyspnea, the resulting improvement in utility, and how physicians might use this to weigh the benefits of intervention vs the possibility of procedure-related complications. Specifically, although high ASA score and more severe functional impairment predict increased risk of complications and adverse events, the benefits of intervention are also higher and probably warrant careful consideration. Based on these findings, high levels of functional impairment and high surgical risk should not necessarily preclude bronchoscopic intervention, provided that there is significant dyspnea and that the dyspnea is contributing to the patient's poor performance status.

Although these findings are useful, it is important to recognize the limitations of the data. Although we did find that stenting was associated with higher technical success rates, this needs to be weighed against the risk of longer-term complications that may arise.[27-29] Similarly, although this is the first study to our knowledge to evaluate change in utility following therapeutic bronchoscopy, the outcomes measured are short term (ie, 30 days). Longer term studies that measure quality-adjusted survival beyond 30 days will be needed so that quality-adjusted life years can be determined. This has been done for malignant pleural effusions, and a similar method could be used for therapeutic bronchoscopy.[30] In addition, although we did not find evidence of a relationship between average number of cases per month and technical success rates, the number of patients enrolled from low-volume centers was small. Therefore, the findings on volume-outcome relationships should be considered as limited and preliminary. In addition, the data on dyspnea and HRQOL were available for only a subset of patients from select centers, and these patients differed from the rest of the cohort in some regards, so the generalizability of the findings needs to be verified. Finally, the indications for the procedures may have differed in subtle but significant ways. Physicians may choose to intervene "early" for lesions that are anatomically significant ($>$ 50% stenosis) even when patients do not have dyspnea, if the perception is that the disease is likely to progress. In such instances, improvements in dyspnea and even HRQOL are likely to be small. This does not necessarily mean that such early interventions are ineffective, since they presumably prevent future deterioration and may allow procedures to be done in an elective manner while patients are more stable. As such, predictors of impact on dyspnea and HRQOL may be subject to subtle confounding by indication, since the indication for some of these procedures may be to avoid future deterioration in dyspnea and HRQOL, whereas in other instances the indication is for immediate relief.

In conclusion, this report from the AQuIRE registry is the first multicenter registry study, to our knowledge, of therapeutic bronchoscopy for malignant central airway obstruction to evaluate patient and hospital predictors of technical success, impact on dyspnea, and changes in utility. Procedures were usually technically successful, with 93% of patients having their central airways reopened. No single ablative technology was superior in terms of achieving technical success, although stenting was associated with improved success

rates. Improvements in dyspnea and utility were greatest in patients who had more dyspnea at baseline. Therapeutic bronchoscopy should not be withheld from patients based solely on an assessment of the risks involved, since patients at the highest risk recognized the greatest benefits. The decision process therefore requires not only risk assessment but also consideration of the magnitude of the potential benefits. Future studies should explore the interactions between hospital-level and patient-level variables on outcomes. Longer term studies evaluating quality-adjusted survival following therapeutic bronchoscopy are needed as well.

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References

1. Ernst A, Simoff M, Ost D, Goldman Y, Herth FJ. Prospective risk-adjusted morbidity and mortality outcome analysis after therapeutic bronchoscopic procedures: results of a multi-institutional outcomes database. *Chest*. 2008;134(3):514-519.
2. Ernst A, Feller-Kopman D, Becker HD, Mehta AC. Central airway obstruction. *Am J Respir Crit Care Med*. 2004;169(12):1278-1297.
3. Casal RF, Iribarren J, Eapen G, et al. Safety and effectiveness of microdebrider bronchoscopy for the management of central airway obstruction. *Respirology*. 2013;18(6):1011-1015.
4. Chung FT, Chen HC, Chou CL, et al. An outcome analysis of self-expandable metallic stents in central airway obstruction: a cohort study. *J Cardiothorac Surg*. 2011;6:46.
5. Husain SA, Finch D, Ahmed M, Morgan A, Hetzel MR. Long-term follow-up of ultraflex metallic stents in benign and malignant central airway obstruction. *Ann Thorac Surg*. 2007;83(4):1251-1256.
6. Saad CP, Murthy S, Krizmanich G, Mehta AC. Self-expandable metallic airway stents and flexible bronchoscopy: long-term outcomes analysis. *Chest*. 2003;124(5):1993-1999.
7. Morice RC, Ece T, Ece F, Keus L. Endobronchial argon plasma coagulation for treatment of hemoptysis and neoplastic airway obstruction. *Chest*. 2001;119(3):781-787.
8. Ost DE, Ernst A, Lei X, et al; on behalf of the AQuIRE Bronchoscopy Registry. Diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration: results of the AQuIRE Bronchoscopy Registry. *Chest*. 2011;140(6):1557-1566.
9. Eapen GA, Shah AM, Lei X, et al; on behalf of the American College of Chest Physicians Quality Improvement Registry, Education. Complications, consequences, and practice patterns of endobronchial ultrasound-guided transbronchial needle aspiration: results of the AQuIRE registry. *Chest*. 2013;143(4):1044-1053.
10. ACCP Quality Improvement Registry Education and Evaluation (AQuIRE). AQuIRE video overview. CHEST website. http://chestnet.org/guidelines-and-resources/payment-practice-and-quality/practice-resources/AQuIRE. Updated July 24, 2009. Accessed April 30, 2013.
11. Yarmus LB, Akulian J, Lechtzin N, et al; on behalf of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation (AQuIRE) Participants. Comparison of 21-gauge and 22-gauge aspiration needle in endobronchial ultrasound-guided transbronchial needle aspiration: results of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation Registry. *Chest*. 2013;143(4):1036-1043.
12. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. 2002;21(2):271-292.
13. Dorman S, Jolley C, Abernethy A, et al. Researching breathlessness in palliative care: consensus statement of the National Cancer Research Institute Palliative Care Breathlessness Subgroup. *Palliat Med*. 2009;23(3):213-227.
14. Ries AL. Minimally clinically important difference for the UCSD Shortness of Breath Questionnaire, Borg Scale, and Visual Analog Scale. *COPD*. 2005;2(1):105-110.
15. Walters SJ, Brazier JE. What is the relationship between the minimally important difference and health state utility values? The case of the SF-6D. *Health Qual Life Outcomes*. 2003;1:4.
16. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol*. 2005;34(1):215-220.
17. Razi SS, Lebovics RS, Schwartz G, et al. Timely airway stenting improves survival in patients with malignant central airway obstruction. *Ann Thorac Surg*. 2010;90(4):1088-1093.
18. Oviatt PL, Stather DR, Michaud G, Maceachern P, Tremblay A. Exercise capacity, lung function, and quality of life after interventional bronchoscopy. *J Thorac Oncol*. 2011;6(1):38-42.
19. Furukawa K, Ishida J, Yamaguchi G, et al. The role of airway stent placement in the management of tracheobronchial stenosis caused by inoperable advanced lung cancer. *Surg Today*. 2010;40(4):315-320.
20. Amjadi K, Voduc N, Cruysberghs Y, et al. Impact of interventional bronchoscopy on quality of life in malignant airway obstruction. *Respiration*. 2008;76(4):421-428.
21. Bolliger CT, Sutedja TG, Strausz J, Freitag L. Therapeutic bronchoscopy with

immediate effect: laser, electrocautery, argon plasma coagulation and stents. *Eur Respir J*. 2006;27(6):1258-1271.

22. Bolliger CT, Breitenbuecher A, Brutsche M, Heitz M, Stanzel F. Use of studded Polyflex stents in patients with neoplastic obstructions of the central airways. *Respiration*. 2004;71(1):83-87.
23. Wood DE, Liu YH, Vallieres E, et al. Airway stenting for malignant and benign tracheobronchial stenosis. *Ann Thorac Surg*. 2003;76(1):167-172.
24. Simoff MJ, Lally B, Slade MG, et al. Symptom management in patients with lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5_suppl):e455S-497S.
25. Marra CA, Woolcott JC, Kopec JA, et al. A comparison of generic, indirect utility measures (the HUI2, HUI3, SF-6D, and the EQ-5D) and disease-specific instruments (the RAQoL and the HAQ) in rheumatoid arthritis. *Soc Sci Med*. 2005;60(7):1571-1582.
26. Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI): concepts, measurement properties and applications. *Health Qual Life Outcomes*. 2003;1:54.
27. Agrafiotis M, Siempos II, Falagas ME. Infections related to airway stenting: a systematic review. *Respiration*. 2009;78(1):69-74.
28. Ost DE, Shah AM, Lei X, et al. Respiratory infections increase the risk of granulation tissue formation following airway stenting in patients with malignant airway obstruction. *Chest*. 2012;141(6):1473-1481.
29. Grosu HB, Eapen GA, Morice RC, et al. Stents are associated with increased risk of respiratory infections in patients undergoing airway interventions for malignant airways disease. *Chest*. 2013;144(2):441-449.
30. Ost DE, Jimenez CA, Lei X, et al. Quality-adjusted survival following treatment of malignant pleural effusions with indwelling pleural catheters. *Chest*. 2014;145(6):1347-1356.