CHEST Online Supplement

Therapeutic Bronchoscopy for Malignant Central Airway Obstruction

Success Rates and Impact on Dyspnea and Quality of Life

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e-Appendix 1.

Methods and Results:

Anatomic and Therapeutic Variable Definitions

Patients could have multiple sites of airway obstruction and multiple types of interventions could be used either at the same site or at different sites. So for example a patient might have extrinsic compression of the distal trachea with endobronchial obstruction of the left mainstem bronchus. Each anatomic location was classified in regards to the type of obstruction as either intrinsic (i.e. endobronchial), extrinsic, or mixed. For a given anatomic location these three categories are mutually exclusive and completely exhaustive. Since the analysis is on a per patient basis, the type of obstruction is listed as any intrinsic, any extrinsic, or any mixed disease, since a patient might have more than one site of obstruction. Thus, in the case of a patient with extrinsic compression of the distal trachea and endobronchial occlusion of the left mainstem, they were classified as extrinsic compression (value=1) and intrinsic obstruction (value=1) and no mixed disease (value=0). Note that the variable "any mixed" is still 0 for this patient, since mixed disease has a specific meaning distinct from intrinsic and extrinsic disease. Of the 1,115 patients, 725 (65%) had obstruction at one location only, 227 (20%) had two locations, 119 (11%) had three locations, 35 (3%) had four locations, and 8 (1%) had obstruction at five locations. In terms of the type(s) of obstruction present, 1,041 (93%) patients had only one type of obstruction, 68 (6%) had two types of obstruction, and 6 (1%) had all three types of obstruction present. The same system applied to interventions. A patient could have more than one type of stent placed, either in the

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same location or other locations, so ablative therapies and stent strategies are listed as "any" use of that type of technology.

Stent Classification

Stent use was classified on a per patient basis. Because patients could have more than one type of stent, the variables listed under stent type are not mutually exclusive. The domains for classifying a particular stent were material (silicone vs. metal) and shape (Y –shaped vs. simple tube). Some patients had metal Y-shaped stents that are not commercially available in the U.S., so Y-shaped is not necessarily synonymous with silicone material. For a particular patient, if they had more than one stent placed, they could end up with multiple variables being checked as a yes. For example, if a patient had only a Dumon Y-stent placed, this would be considered a silicone stent and a Y-stent. If a patient had only an Aero expandable metal stent placed this would be considered a metal stent and a tube stent. If a patient had both a Dumon Y-stent and an Aero stent placed then they would have a Y-stent, a tube stent, a silicone stent, and a metal stent.

Analysis

Regression to the Mean

Regression to the mean occurs when there is random error associated with observed values and repeated measurements are made on the same unit of study.[1] The effect of regression to the mean is more pronounced with increasing measurement error and when follow-up measurements are only examined for a selected subset depending upon their baseline measurements. In this study the decision to take follow-up measurements was not based upon baseline measurements so the latter consideration does not apply. However, measurement error is still present so regression to the mean remains a concern. Note that regression to the mean does not impact the observation that both dyspnea and utility improved following intervention. However, it is relevant when estimating the effects of other covariates on the outcomes of change in dyspnea (ΔBorg) and change in utility (Δutility).

Different methods have been proposed to estimate the size of the effect of regression to the mean and to adjust for this effect.[1-3] One method is to use analysis of covariance and adjust each subject's follow-up measurement according to their baseline measurement.[1] For ΔBorg, we included the baseline Borg score in the multivariate model to adjust for regression to the mean.

In the predictive analysis for Δutility we chose to construct multivariable models without using baseline utility as a covariate since we were most interested in the relationship between measures that are clinically available and subsequent changes in HRQOL. Physicians can easily assess baseline dyspnea but

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utility is not a measure usually available. In addition, baseline dyspnea and baseline utility were highly correlated ($\rho = 0.59$, $p<0.0001$) so including both would be problematic. We subsequently performed an additional analysis using backward selection with baseline utility as a candidate variable. When we included baseline utility in the multivariate predictive model for Δutility, the model only retained baseline utility (e-table 3). These findings suggest that while there was a significant improvement in utility associated with therapeutic bronchoscopy, the relationship between specific covariates and Δutility in the predictive model may be confounded by regression to the mean to some degree. This is complicated by the fact that dyspnea and utility are highly correlated, making interpretation difficult for the predictive model.

For the explanatory model of Δutility, we used ΔBorg rather than baseline Borg as a covariate, since we believe it is improvements in dyspnea that are likely to drive subsequent improvement in utility. We found absence of tracheal involvement, absence of bronchus intermedius involvement, and greater improvements in dyspnea were associated with greater improvements in utility (e-table 3). When we included baseline utility there was little change in the model, suggesting that even after accounting for regression to the mean these variables were associated with Δutility.

Discussion

Limitations of Generic HRQOL Instruments

HRQOL can be measured with either disease specific instruments, such as the FACT-L, or with generic instruments, such as the SF36. Each instrument has its own strengths and weaknesses. Disease specific instruments are more sensitive and are suitable for assessing impact of treatment, but they are not suitable if different treatment alternatives involve different types of risks and trade-offs (e.g. risk of bleeding vs. photosensitivity). Similarly, disease specific HRQOL instruments are not useful for comparing the benefits of treatment with the risks of complications if the nature of the outcomes being compared is different (i.e. dyspnea relief vs. death).[4] As such they are less useful when it comes to making clinical decisions that require trade-offs between HRQOL and complications.

Generic HRQOL instruments, while less sensitive, can be used for diverse groups of diseases and can be classified as either profile or single index measures. Single index measures, such as the SF-6D,[5] generate measures of utility and range from 0 to 1, with zero being death and 1 being perfect health. They are necessary for calculating QALYs and as such are essential for cost-effectiveness analysis. Quality adjusted survival can be thought of as the area under the curve with utility plotted on the vertical axis and time plotted on the horizontal axis. During recent years, the QALY has been recognized as the most important indicator of the effectiveness of health care interventions, as reflected by the position

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statements and guidelines of the National Institute of Health and Clinical Excellence (NICE)[6], the Agency for Health Care Research and Quality, and the U.S. Public Health Service.[7-9] Measuring utility pre and post procedure allows physicians to more realistically judge the trade-offs involved when assessing interventions, particularly when those interventions are palliative in nature, because it facilitates comparisons between improvements in HRQOL and the potential downside risk of shorter duration of life (see the online supplement for additional information on generic instruments).

The limitation of using generic instruments is that they can be insensitive. As such, using utility (or QALYs) as the sole outcome is not advisable when investigating a clinical problem. However, utility should be one of several metrics used to assess outcomes, depending on what the question is. If you are asking did the intervention achieve the objective (i.e. clinical efficacy study), you probably want to measure multiple dimensions, one of which might be QALYs, but the primary outcome would be more specific to the intervention – e.g. something like technical success defined as reestablishing luminal patency or dyspnea relief. Then you can infer whether the treatment "works" for that problem. When we look at utility, the question being asked is different. It says, in this particular population of patients, with the given clinical context, how much impact did relief of airway obstruction and the resultant change in dyspnea have on HRQOL? We are also in a better position to answer the question, given the risk of death involved, is this worth it. The answer is conditional on many other factors that impact HRQOL. This relates to the difference between clinical efficacy and clinical effectiveness and comparative effectiveness. In some cases you might totally eliminate a real problem (clinical efficacy) and yet have no or little impact on overall utility. Using utility as one of several outcome measures allows us to gain insights into clinical effectiveness because it helps identify factors that do not impact technical success of the procedure but do impact the global health of the patient and thereby modify the effect of the intervention on utility. This is particularly relevant for palliative interventions.

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e-Table 1. Comparison of Dyspnea Subset vs Other Patients at the Same Centers

	Dyspnea Subset (n=187)	Patients at the same centers not in dyspnea subset (n=291)	p-value vs. Dyspnea Subset
Age, years (mean ± std)	63.9 ± 13.2	62.3 ± 14.4	0.25†
Race White, n (%)			
Nonwhite	36 (19)	51 (18)	
White	151 (81)	240 (82)	0.63
Inpatient, n (%)			
No	143(76)	165 (57)	
Yes	44 (24)	126 (43)	<0.001
Urgency of the procedure, n (%)			
Elective	153 (82)	210 (72)	
Emergent	3 (2)	21 (7)	
Urgent	31 (17)	60 (21)	0.006
Zubrod score, mean (std)			
≤ 1	85 (45)	112 (38)	
>1	102 (55)	179 (62)	0.15
ASA score, n (%)			
≤ 3	148 (79)	212 (73)	
>3	39 (21)	79 (27)	0.13
Therapeutic bronchoscopy, n (%)			
First therapeutic bronchoscopy	126 (67)	211 (73)	
Redo bronchoscopy (2nd or later)	61 (33)	80 (27)	0.26
Comorbidities			
Asthma, n (%)			
No	177 (95)	281 (97)	
Yes	10 (5)	10 (3)	0.35
COPD, n (%)			
No	136 (73)	200 (69)	
Yes	51 (27)	91 (31)	0.36
Cardiac vascular disease, n (%)			
No	100 (53)	172 (59)	
Yes	87 (47)	119 (41)	0.26
Diabetes, n (%)			
No	166 (89)	259 (89)	

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Yes	21 (11)	32 (11)	1.0
GERD, n (%)			
No	182 (97)	285 (98)	
Yes	5 (3)	6 (2)	0.76
Hematologic malignancy, n (%)			
No	184 (98)	290 (99.7)	
Yes	3 (2)	1 (0.3)	0.31
Second primary solid tumor, n (%)			
No	183 (98)	288 (99)	
Yes	4 (2)	3 (1)	0.44
Renal failure creatinine >2 or HD, n (%)			
No	183 (98)	287 (99)	
Yes	4 (2)	4 (1)	0.72
Bleeding risk high meds, n (%)			
No	186 (99)	281 (97)	
Yes	1 (1)	10 (3)	0.06
Tobacco Use			
Never user	50 (27)	75 (26)	
Current or prior use	137 (73)	216 (74)	0.83
Cancer Related			
Time from cancer diagnosis			
≤ 75 days	59 (32)	108 (37)	
>75 days	128 (68)	183 (63)	0.24
Primary lung cancer, n (%)			
No	76 (41)	105 (36)	
Yes	111 (59)	186 (64)	0.34
Location of Disease			
Trachea, n (%)			
No	154 (82)	215 (74)	
Yes	33 (18)	76 (26)	0.03
Left main, n (%)			
No	114(61)	180 (62)	
Yes	73 (39)	111 (38)	0.85
Right main, n (%)			
No	126 (67)	192 (66)	
Yes	61 (33)	99 (34)	0.77
Bronchus intermedius, n (%)			
No	118 (63)	169 (58)	
Yes	69 (37)	122 (42)	0.29
Lobar, n (%)			
No	116 (62)	194 (67)	
Yes	71 (38)	97 (33)	0.33

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Any tracheoesophageal fistula, n (%)			
No	187 (100)	286 (98)	
Yes	0 (0)	5 (2)	0.16
Type of Obstruction			
Any intrinsic, n (%)			
No	58 (31)	110 (38)	
Yes	129 (69)	181 (62)	0.14
Any extrinsic, n (%)			
No	166 (89)	241 (83)	
Yes	21 (11)	50 (17)	0.09
Any mixed, n (%)			
No	137 (73)	205 (70)	
Yes	50 (27)	86 (30)	0.53
Procedural Variables			
Anesthesia, n (%)			
Moderate sedation	45 (24)	69 (24)	
Deep or general	142 (76)	222 (76)	1.0
Paralysis, n (%)			
No	76 (41)	110 (38)	
Yes	111 (59)	181 (62)	0.57
Type of ventilation, n (%)			
Volume cycled	58 (31)	79 (27)	
Jet	80 (43)	135 (46)	
Spontaneous	49 (26)	77 (26)	0.63
Type of bronchoscopy			
Flexible	66 (35)	153 (53)	
Rigid	121 (65)	138 (47)	<0.001
Any laser used			
No	149 (80)	261 (90)	
Yes	38 (20)	30 (10)	0.003
Any electrocautery used			
No	143 (76)	238 (82)	
Yes	44 (24)	53 (18)	0.16
Any APC used			
No	102 (55)	169 (58)	
Yes	85 (45)	122 (42)	0.45
Any cryotherapy used			
No	151 (81)	250 (86)	
Yes	36 (19)	14 (14)	0.16
Any dilation done			
No	150 (80)	232 (80)	
Yes	37 (20)	59 (20)	1.0
Stent			
Stent placed			

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No	128 (68)	184 (63)	
Yes	59 (32)	107 (37)	0.28
Metal stent			
No	143 (76)	203 (70)	
Yes	44 (24)	88 (30)	0.12
Silicone stent			
No	178 (95)	282 (97)	
Yes	9 (5)	9 (3)	0.34
Tube stent			
No	134 (72)	195 (67)	
Yes	53 (28)	96 (33)	0.31
Y stent			
No	180 (96)	278 (96)	
Yes	7 (4)	13 (4)	0.82

† Two-sample t-test; Fisher's exact test for all other categorical comparisons.

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e-Table 2. Patient and Clinic Characteristics by Improved Borg Score, Responder Analysis

	Borg not improved (Post – Pre > -1) (N=97)	Borg Improved (Post – Pre ≤ -1) (N=90)	P-value	Multivariate Odds Ratio (95% CI)‡	P-value
Baseline Borg (mean ± std)	2.1 ± 1.6	4.7 ± 2.1	<0.0001δ	2.40 (1.83-3.14)	<0.0001
Age, years (mean)	64.6	62.9	0.39†		
Race, n (%)					
Nonwhite	21(58.3)	15(41.7)			
White	76(50.3)	75(49.7)	0.39		
Inpatient, n (%)					
No	78(54.5)	65(45.5)			
Yes	19(43.2)	25(56.8)	0.19		
Urgency of the procedure, n (%)					
Elective	84(54.9)	69(45.1)			
Emergent	.(0)	3(100)			
Urgent	13(41.9)	18(58.1)	0.09		
Zubrod score, n (%)					
≤ 1	48(56.5)	37(43.5)			
>1	49(48)	53(52)	0.25		
ASA score, n (%)					
≤ 3	79(53.4)	69(46.6)			
>3	18(46.2)	21(53.8)	0.42		
Therapeutic bronchoscopy, n (%)					
First therapeutic bronchoscopy	58(46.0)	68(54.0)			
Redo bronchoscopy (2nd or later)	39(63.9)	22(36.1)	0.03		
Comorbidities					
Asthma, n (%)					
No	94(53.1)	83(46.9)			
Yes	3(30)	7(70)	0.20*		
COPD, n (%)					
No	72(52.9)	64(47.1)			
Yes	25(49)	26(51)	0.63		
Cardiac vascular disease, n (%)					
No	51(51)	49(49)			
Yes	46(52.9)	41(47.1)	0.80		
Diabetes, n (%)					
No	87(52.4)	79(47.6)			
Yes	10(47.6)	11(52.4)	0.68		
GERD, n (%)					

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No	96(52.7)	86(47.3)			
Yes	1(20)	4(80)	0.20*		
Hematologic malignancy, n (%)					
No	96(52.2)	88(47.8)			
Yes	1(33.3)	2(66.7)	0.60*		
Second primary solid tumor, n (%)					
No	95(51.9)	88(48.1)			
Yes	2(50)	2(50)	1.0*		
Renal failure creatinine >2 or HD, n (%)					
No	94(51.4)	89(48.6)			
Yes	3(75)	1(25)	0.62*		
Bleeding risk high meds, n (%)					
No	96(51.6)	90(48.4)			
Yes	1(100)	0(0)	1.0*		
Tobacco Use					
Never user	22(44)	28(56)		(reference)	
Current or prior use	75(54.7)	62(45.3)	0.19	0.38 (0.16-0.91)	0.03
Cancer Related					
Time from cancer diagnosis					
≤ 75 days	26(44.1)	33(55.9)			
>75 days	71(55.5)	57(44.5)	0.15		
Primary lung cancer, n (%)					
No	45(59.2)	31(40.8)			
Yes	52(46.8)	59(53.2)	0.10		
Location of Disease					
Trachea, n (%)					
No	82(53.2)	72(46.8)			
Yes	15(45.5)	18(54.5)	0.42		
Left main, n (%)					
No	67(58.8)	47(41.2)			
Yes	30(41.1)	43(58.9)	0.02		
Right main, n (%)					
No	69(54.8)	57(45.2)			
Yes	28(45.9)	33(54.1)	0.25		
Bronchus intermedius, n (%)					
No	56(47.5)	62(52.5)			
Yes	41(59.4)	28(40.6)	0.11		
Lobar, n (%)					
No	58(50)	58(50)			
Yes	39(54.9)	32(45.1)	0.51		
Any tracheoesophageal fistula, n (%)					

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No	97(51.9)	90(48.1)	
Yes	0(0)	0(0)	NA
Type of Obstruction			
Any intrinsic, n (%)			
No	30(51.7)	28(48.3)	
Yes	67(51.9)	62(48.1)	0.98
Any extrinsic, n (%)			
No	84(50.6)	82(49.4)	
Yes	13(61.9)	8(38.1)	0.33
Any mixed, n (%)			
No	74(54)	63(46)	
Yes	23(46)	27(54)	0.33
Anesthesia, n (%)			
Moderate sedation	22(48.9)	23(51.1)	
General anesthesia	75(52.8)	67(47.2)	0.65
Paralysis, n (%)			
No	36(47.4)	40(52.6)	
Yes	61(55)	50(45)	0.31
Type of ventilation, n (%)			
Volume cycled	30(51.7)	28(48.3)	
Jet	43(53.8)	37(46.3)	
Spontaneous	24(49)	25(51)	0.87
Type of bronchoscopy			
Flexible	32(48.5)	34(51.5)	
Rigid	65(53.7)	56(46.3)	0.49
Any laser used			
No	79(53)	70(47)	
Yes	18(47.4)	20(52.6)	0.53
Any electrocautery used			
No	72(50.3)	71(49.7)	
Yes	25(56.8)	19(43.2)	0.45
Any APC used			
No	49(48)	53(52)	
Yes	48(56.5)	37(43.5)	0.25
Any cryotherapy used			
No	79(52.3)	72(47.7)	
Yes	18(50)	18(50)	0.80
Any dilation done			
No	82(54.7)	68(45.3)	
Yes	15(40.5)	22(59.5)	0.12
Stent			
Stent placed			
No	69(53.9)	59(46.1)	
Yes	28(47.5)	31(52.5)	0.41

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Metal stent			
No	73(51)	70(49)	
Yes	24(54.5)	20(45.5)	0.68
Silicone stent			
No	94(52.8)	84(47.2)	
Yes	3(33.3)	6(66.7)	0.31*
Tube stent			
No	70(52.2)	64(47.8)	
Yes	27(50.9)	26(49.1)	0.87
Y stent			
No	95(52.8)	85(47.2)	
Yes	2(28.6)	5(71.4)	0.21

HD: Hemodialysis; APC: argon plasma coagulation; CI: Confidence interval; † Two-sample t-test. *Fisher's exact test. ‡ Firth's Penalized Likelihood Approach utilized for rare events. δ Wilcoxon-Mann-Whitney two-sample test.

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e-Table 3. Multivariate models for Difference in Utility (Post – Pre):

	Coefficient estimate (Error)	P-value
Predictive Model Not Including Baseline Utility		
Baseline Borg	0.010 (0.003)	0.005
Lobar obstruction yes vs. no	-0.036 (0.016)	0.02
Predictive Model Including Baseline Utility		
Baseline utility	-0.30 (0.058)	<0.001
Explanatory Model Not Using Baseline Utility		
Δ Borg Score	-0.024 (0.003)	<0.001
Tracheal involvement yes vs. no	-0.050 (0.019)	0.01
Bronchus intermedius obstruction yes vs. no	-0.032 (0.015)	0.03
Explanatory Model Including Baseline Utility		
Δ Borg Score	-0.020 (0.003)	<0.001
Tracheal obstruction yes vs. no	-0.041 (0.019)	.03
Bronchus intermedius obstruction yes vs. no	-0.030 (0.015)	0.04
Baseline utility	-0.18 (0.058)	0.002

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e-Table 4. Patient and Clinic Characteristics by Improved Utility, Responder Analysis

	Non-Responders (Post – Pre Utility < 0.033)	Responders (Post – Pre Utility ≥ 0.033)	P-value	Multivariate Odds Ratio (95% CI)‡	P-value
Baseline Borg (mean ± std)	3.1 ± 2.1	3.6 ± 2.5	0.15†		
Post - Pre Borg difference (mean ± std)	-0.5 ± 1.9	-1.7 ± 2.1	0.0002†		
Age, years (mean ± std)	62.6 ± 12.8	63.1 ± 14.7	0.80†		
Race White, n (%)					
Nonwhite	21(65.6)	11(34.4)			
White	86(57)	65(43)	0.36		
Inpatient, n (%)					
No	87(61.3)	55(38.7)			
Yes	20(48.8)	21(51.2)	0.15		
Urgency of the procedure, n (%)					
Elective	91(60.7)	59(39.3)			
Emergent	1(33.3)	2(66.7)			
Urgent	15(50)	15(50)	0.37		
Zubrod score, mean (std)					
≤ 1	59(67)	29(33)		(reference)	
>1	48(50.5)	47(49.5)	0.023	2.62 (1.35-5.06)	0.004
ASA score, n (%)					
≤ 3	91(61.5)	57(38.5)			
>3	16(45.7)	19(54.3)	0.09		
Therapeutic bronchoscopy, n (%)					
First therapeutic bronchoscopy	76(60.8)	49(39.2)			
Redo bronchoscopy (2nd or later)	31(53.4)	27(46.6)	0.35		
Comorbidities					
Asthma, n (%)					
No	103(59.2)	71(40.8)			
Yes	4(44.4)	5(55.6)	0.49*		
COPD, n (%)					
No	82(62.6)	49(37.4)			
Yes	25(48.1)	27(51.9)	0.07		
Cardiac vascular disease, n (%)					
No	56(57.1)	42(42.9)			
Yes	51(60)	34(40)	0.69		
Diabetes, n (%)					

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No	91(55.8)	72(44.2)	
Yes	16(80)	4(20)	0.05*
GERD, n (%)			
No	103(57.9)	75(42.1)	
Yes	4(80)	1(20)	0.40*
Hematologic malignancy, n (%)			
No	106(58.6)	75(41.4)	
Yes	1(50)	1(50)	1.0*
Second primary solid tumor, n (%)			
No	104(57.8)	76(42.2)	
Yes	3(100)	0(0)	0.27*
Renal failure creatinine >2 or HD, n (%)			
No	106(59.2)	73(40.8)	
Yes	1(25)	3(75)	0.31*
Bleeding risk high meds, n (%)			
No	107(58.5)	76(41.5)	
Yes	0(0)	0(0)	NA
Tobacco Use			
Never user	31(59.6)	21(40.4)	
Current or prior use	76(58)	55(42)	0.84
Cancer Related			
Time from cancer diagnosis			
≤ 75 days	34(58.6)	24(41.4)	
>75 days	73(58.4)	52(41.6)	0.98
Primary lung cancer, n (%)			
No	43(59.7)	29(40.3)	
Yes	64(57.7)	47(42.3)	0.78
Location of Disease			
Trachea, n (%)			
No	85(56.3)	66(43.7)	
Yes	22(68.8)	10(31.3)	0.19
Left main, n (%)			
No	73(63.5)	42(36.5)	
Yes	34(50)	34(50)	0.07
Right main, n (%)			
No	71(56.8)	54(43.2)	
Yes	36(62.1)	22(37.9)	0.50
Bronchus intermedius, n (%)			
No	68(58.6)	48(41.4)	
Yes	39(58.2)	28(41.8)	0.96
Lobar, n (%)			
No	60(53.1)	53(46.9)	

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Yes	47(67.1)	23(32.9)	0.06		
Any tracheoesophageal fistula, n (%)					
No	107(58.5)	76(41.5)			
Yes	0(0)	0(0)	NA		
Type of Obstruction					
Any intrinsic, n (%)					
No	30(57.7)	22(42.3)			
Yes	77(58.8)	54(41.2)	0.89		
Any extrinsic, n (%)					
No	93(56.4)	72(43.6)		(reference)	
Yes	14(77.8)	4(22.2)	0.13*	0.29 (0.09-0.97)	0.045
Any mixed, n (%)					
No	82(59.9)	55(40.1)			
Yes	25(54.3)	21(45.7)	0.51		
Procedural Variables					
Anesthesia, n (%)					
Moderate sedation	24(51.1)	23(48.9)			
Deep or general	83(61)	53(39)	0.23		
Paralysis, n (%)					
No	39(50)	39(50)			
Yes	68(64.8)	37(35.2)	0.05		
Type of ventilation, n (%)					
Volume cycled	38(63.3)	22(36.7)			
Jet	44(60.3)	29(39.7)			
Spontaneous	25(50)	25(50)	0.34		
Type of bronchoscopy					
Flexible	36(51.4)	34(48.6)		(reference)	
Rigid	71(62.8)	42(37.2)	0.13	0.44 (0.22-0.86)	0.016
Any laser used					
No	86(59.3)	59(40.7)			
Yes	21(55.3)	17(44.7)	0.65		
Any electrocautery used					
No	81(56.6)	62(43.4)			
Yes	26(65)	14(35)	0.34		
Any APC used					
No	58(58)	42(42)			
Yes	49(59)	34(41)	0.89		
Any cryotherapy used					
No	88(60.3)	58(39.7)			
Yes	19(51.4)	18(48.6)	0.33		
Any dilation done					
No	90(60)	60(40)			
Yes	17(51.5)	16(48.5)	0.37		

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Stent			
Stent placed			
No	75(58.6)	53(41.4)	
Yes	32(58.2)	23(41.8)	0.96
Metal stent			
No	87(60.8)	56(39.2)	
Yes	20(50)	20(50)	0.22
Silicone stent			
No	100(57.5)	74(42.5)	
Yes	7(77.8)	2(22.2)	0.31*
Tube stent			
No	80(59.7)	54(40.3)	
Yes	27(55.1)	22(44.9)	0.58
Y stent			
No	102(57.6)	75(42.4)	
Yes	5(83.3)	1(16.7)	0.40*

† Two-sample t-test; * Fisher's exact test.

Acknowledgements:

Institutional review board (IRB) approval was obtained by the primary site requesting the data (PI D.O. - MD Anderson Cancer Center). There was no personal health information (PHI) recorded in the database and all data was de-identified. All ages were given in years at the time of the procedure and unique identifiers for the registry were created that were separate from the patient's medical record number. Each institution maintained a separate secure file that listed medical record numbers and linked them to the registry unique identifier in case there were questions. However these files were never sent to the ACCP or AQuIRE hence this was de-identified data without any method of re-identifying patients.

Most institutional IRB's viewed this as de-identified data with the analysts not having access to the patient identifiers. If the people actually doing the research analysis on the data in the existing quality assurance database have no access to the patient identifiers, then they are doing research on de-identified data, and research on de-identified data is not human subjects research, therefore not reviewable by an IRB. Publication alone does not make a project human subjects research. They cited the following FAQ document regarding quality assurance (QA) vs research data: http://www.hhs.gov/ohrp/qualityfaq.html for the collection of the data at these sites. Their ruling was that the primary site requesting the data for publication would need IRB approval. We verified with our own IRB at MD Anderson that this is indeed true. Primary IRB approval was obtained by the MD Anderson site,

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which was the primary data request site. This was done under The University of Texas MD Anderson IRB committee 4, Protocol DR09-0101. This is similar to other registry data agreements like SEER, where the individual sites collecting the de-identified data do not provide IRB approval but the primary site(s) analyzing the data are required to do so.

However, each institution was asked to determine whether their local IRB required approval despite the de-identified QA data. A few institutions chose to have IRB approval even though the data was de-identified to facilitate collection and for their own research purposes. Here are the details for each site, their IRB ruling, and details of the IRB protocol numbers:

1. The University of Texas MD Anderson: IRB committee 4, Protocol DR09-0101. This was the primary site for the data request from AQuIRE.
2. Chicago Chest Center: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
3. Cleveland Clinic: IRB 09 – 315 PI: Gildea, Thomas Registry: AQuIRE-Bronchoscopy Registry-Quality Improvement Registry, Evaluation and Education (AQuIRE).
4. Duke University: Duke IRB Protocol 00027511 AQuIRE Project.
5. Foothills Medical Centre: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
6. Henry Ford Hospital: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
7. Johns Hopkins: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
8. Lyndon B. Johnson – The University of Texas Health Science Center Houston: Only one committee, Protocol HSC-MD-11-0377
9. Debakey Veteran Affairs Medical Center Baylor College of Medicine: Baylor College of Medicine IRB 2, H-26105.
10. Milton S. Hershey Medical Center: QA initiative, Pennsylvania State IRB approval number 00000823
11. Munroe Regional Medical Center: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
12. Papworth Hospital: Papworth Research Ethics Committee, Study approval number S01976
13. St. Elizabeth's Medical Center: QA initiative, IRB waiver for de-identified data collection, requiring primary site IRB approval.
14. University Hospital of Cincinnati Veteran Affairs Medical Center: IRB protocol 2013-0262. There is only one committee.
15. Yale-New Haven Hospital:

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