Online Supplement:

Long-term Quality Adjusted Survival Following Therapeutic Bronchoscopy for Malignant Central Airway Obstruction

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Conflict of Interest:

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Methods:

Definitions of Covariates and Outcomes

Lesions were classified based on the location of the most proximal airway obstruction that was >50%. The number of segments that were obstructed was calculated based on the site(s) of obstruction and the airway distal to them. So if a patient had a LLL tumor located just distal to the superior segment, then 3 segments would be counted as obstructed (anteromedial, lateral, and posterior basilar). Conversely if the left mainstem was obstructed then this would count as 8 segments (LUL 4 + LLL 4).

Complications

Early complications used the AQuIRE registry definitions.[1] Late complications included stent migration, stent fracture, granulation tissue from stenting, and lower respiratory tract infections (see online supplement for details).

We used a previously published definition of lower respiratory tract infection developed in patients with malignant central airway obstruction (CAO).[2,3] Lower respiratory tract infection was defined as present on the basis of clinical findings of fever, purulent sputum, and worsening cough, with or without radiographic evidence of pneumonia. Documentation by the managing physician of a clinical diagnosis of lower respiratory tract infection and the antibiotics prescribed for it was also required. Bronchoscopic evidence of infection was not required. Lower respiratory tract infections

were classified as pneumonia if there was evidence of new areas of consolidation on either chest x-ray or CT scan. If there were no infiltrate or no imaging, then the infection was classified as acute bronchitis.

Restenosis by tumor overgrowth was determined by either bronchoscopy or CT scan. The severity of the obstruction was graded on the basis of a combination of bronchoscopic and CT scan findings.

Granulation tissue causing stent obstruction, mucus impaction requiring therapeutic interventions, stent migration, and stent fracture were recorded. Each of these adverse events required bronchoscopic verification. For mucus impaction to be considered a complication it had to be severe enough to require therapeutic bronchoscopic intervention.

Statistical Methods

For the analysis of the short term impact of therapeutic bronchoscopy on dyspnea and HRQOL, we performed two analyses for each outcome. The first analysis considered the outcome as a continuous variable. The second was a responder analysis.

For outcomes that were continuous variables, we used a generalized linear model to determine the association of variables with short-term improvements in dyspnea and HRQOL. The dependent outcome variable was the pairwise difference between day 7 post procedure scores and baseline values. For the outcome of dyspnea, we used change in Borg scores (ΔBorg-day-7) and for HRQOL we used utilities (Δutility-day-7).

For the responder analysis of dyspnea we used a ΔBorg-day-7 of ≤-1 to define what constituted a clinically significant improvement. This was based on the minimal clinically important difference (MCID) of the Borg score, which is a one unit change.[5,6] To control for regression to the mean when analyzing ΔBorg-day-7 we included baseline Borg in the multivariate models.[7] For the responder analysis of utility we used a Δutility-day-7 of +0.033 to define what constituted a clinically significant improvement. This was based on the MCID of the SF-6D.[8] We used logistic regression to determine the association of variables with the outcomes of dyspnea and HRQOL in the responder analysis.

We analyzed the impact of therapeutic bronchoscopy on long-term standard survival (i.e. without quality adjustment). For the outcome of standard survival following therapeutic bronchoscopy, we first used a standard Kaplan-Meier (K-M) product-limit method and a Cox model to identify risk factors for the outcome of time to death. Each patient has a survival time outcome measured in days along with a failure time status (alive at study finish = censored (0), lost to follow up = censored (0), or dead (1)). We used the K-M method to calculate median survival and univariate Cox and extended Cox models to identify risk factors and report hazard ratios (HR). We used extended Cox models with time varying covariates to represent variables that change for a given patient over the course of their lifetime (e.g. infections come and go, a stent could be placed and later removed, dyspnea changes over time as does utility). Lower respiratory tract infection was treated as a time-varying covariate. So infection was defined as 0 (absent) at baseline but could change to 1 (present) at the corresponding time points when they occurred. With resolution of infection this would change back to 0. For time to death, infection was considered to last for 2 weeks and then resolve. So

if a patient died within 2 weeks of a lower respiratory tract infection diagnosis, this would increase the hazard ratio (HR) associated with infection. If a patient died on day 15 or later after an infection without any subsequent infection being present, it would not be considered associated with infection, and would therefore not increase the HR associated with infection.[2,3]

Quality adjusted survival was the primary outcome of the study, and for this we used a previously described method to calculate QALDs for each patient as described in the main methods section.[9] Each patient had their quality adjusted survival determined by calculating the area under the curve, with utility on the vertical axis and time on the horizontal axis. Utility was determined by the SF-6D.[4] To determine the median quality adjusted survival, we again use the K-M method, but we use quality adjusted survival time rather than days alive. So a patient that survived 90 days and had a quality adjusted survival of 75 QALDs and died was listed as 75 QALDs for this analysis and the failure status would be 1. A patient who lived 150 days and 120 QALDs and was alive at study completion would be 120 with a failure status of 0 (censored). We use the K-M method to arrive at the median quality adjusted survival so that we could still use data from patients that were censored due to lost to follow-up. Note that time varying covariates were not used in the quality adjusted survival analysis.

For linear regression models we used plots of residuals versus fitted values to check for outliers and homoscedasticity and we used White's general test for heteroscedasticity. For survival analysis we checked the proportional hazards assumption using log (-log (time to event) versus log of time graph and Shoenfeld residuals.

Results:

Patient enrollment

Consecutive patients deemed eligible for enrollment were approached so long as therapeutic bronchoscopy for malignant CAO was planned. Patients that could not speak English or that were born and lived outside of the United States were not eligible, since our measurement of quality adjusted survival required use of the SF-6D and this has not been validated in all cultures and languages. Patients were not excluded based on medical severity, provided they or their family could provide informed consent (e.g. mechanical ventilation) and the patient subsequently agreed. Patients with chronically impaired cognition (e.g. severe Alzheimer's) were not eligible to participate since they could not fill out the SF-6D reliably. A log of all patients approached for enrollment was kept. There were 171 patients with 201 encounters, with 110/171 giving consent and 61/171 not being included or refusing. The reason encounters are greater than patients is that all patients scheduled for a procedure were screened and occasionally a patient came back for a 2nd procedure after either accepting or declining to participate previously but this would still generate an encounter. Of the 110 patients who initially consented, 8 patients were not included in the study. Reasons included withdrawal of consent prior to the procedure because the follow-up schedule was inconvenient, due to the patients personal preference, because upon doing the bronchoscopy no intervention was feasible (i.e. nothing was done, only a visual assessment) or because the lesion found on bronchoscopy turned out to be < 50% obstructing. The 61 patients who did not

give consent / were not enrolled generated 87 encounters. Reasons recorded for non-enrollment encounters included one patient that had their higher cognitive function being borderline (but not delirium) who would not be able to fill out the SF-6D reliably, 2 we missed because the coordinator was out, 22 met other exclusion criteria (e.g. insufficiently severe obstruction), and 62 refused or had other reasons to not participate (e.g. prior refusal).

Relief of Anatomic Obstruction and Technical Success

There was one site of obstruction in 51 patients. Successful reopening of the airway was achieved in 41 (80%) patients while 10 (20%) had significant residual stenosis. Two sites of obstruction were present in 26 patients. Both sites were reopened in 18 (69%) patients while one of the two sites were reopened in 8 (31%) patients. Of the remaining 25 patients that had three or more sites of obstruction, 9 (36%) had all sites reopened, 15 (60%) had one or more sites reopened but not all, and 1 had no sites reopened.

Imputation

Follow-up measurements for dyspnea (Borg) and utility (SF-6) were available for 83% of all time points. In 11% of all time points there was a single missing data point (i.e. the prior and next data points were complete) and in 6% of all time points the missing data point was adjacent to another missing data point. We used a last-one-carried forward (LOCF) for imputation in the primary analysis. In a secondary analysis, we used the subsequent measure after the missing value to impute the missing value.

The reason we chose this was that utilities are fairly stable. Studies of quality adjusted survival will measure them typically at three, six months, or even twelve month intervals.[10,11] Since we oversampled (i.e. measured monthly) our baseline assumption is that the missing value has to be somewhere between the prior value and the subsequent value. So if there are three values, A→ B → C and B is missing, then B must be between A and C inclusive. When we used the subsequent measure (measure C, i.e. carry backwards) there was no difference in the results.

Complications

Early complications occurred in 3 (3%) patients. One patient had a pneumothorax due to an airway injury from a Y-stent. One patient developed new onset atrial fibrillation. One patient came to the emergency room with dyspnea, was found to have malignant CAO, received rigid bronchoscopy, had extensive disease, was extubated following bronchoscopy, developed respiratory failure the following day, and had to be intubated. There was no short term mortality related to procedural complications and the overall number of early complications was too small for analysis.

Late complications were all related to stents. Of the 34 patients that received an airway stent, 6 (18%) eventually developed stent migration. Five of the six patients were admitted because of symptoms related to stent migration and required intervention which involved removal of the stent. In three of the 5 cases a new stent was inserted. In the other two cases stent migration was caused by response of tumor to treatment and no replacement stent was needed. Granulation tissue developed in 10 (29%) patients and nine of these required bronchoscopic intervention. Four of the 10 stents had to be

removed and replaced. All 4 of these patients had to be admitted to hospital – 3 to a general inpatient ward and one to ICU with respiratory failure. Three of the 10 patients with granulation tissue developed a second episode of granulation resulting in obstruction requiring another bronchoscopic intervention. Two of the three required admission to hospital. One of these three patients had a third episode of granulation tissue which required intervention and admission as well. Stent fracture occurred in 2 (6%) patients, both required stent removal and replacement.

A total of 28 additional bronchoscopies were performed after the initial study entry bronchoscopy. A bronchoscopy could have more than one indication (e.g. stent fracture and granulation tissue). Bronchoscopy was performed to address stent complications or tumor recurrence with restenosis or both. In addition to the late complications listed above, airway restenosis due to tumor requiring bronchoscopic intervention occurred in 20 patients. In 6 of these 20 patients stents had to be placed.

Therapeutic Bronchoscopy and Multimodality Treatment

Therapeutic bronchoscopy for malignant CAO is really part of a multimodality approach. As such, it is useful to consider the treatment context in which therapeutic bronchoscopy takes place. In this cohort, 32 patients undergoing therapeutic bronchoscopy had received no prior treatment (e-table 3). Of these 32 patients, 26 (72%) went on to receive subsequent chemotherapy, radiation therapy, or both. Conversely, 70 patients had received prior chemotherapy, radiation therapy, or both prior to therapeutic bronchoscopy. Of these 70 patients, 54 (77%) went on to receive subsequent chemotherapy or radiation therapy.

Discussion

Utility and Quality Adjusted Survival

Improving outcomes in patients with malignant CAO requires the ability to efficiently measure health-related quality of life (HRQOL) and link it to clinical data. 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 strengths and weaknesses.[12] Disease specific instruments are more sensitive and are suitable for assisting in clinical decision making. However, they are not suitable for comparing treatments if different alternatives involve different types of risks and trade-offs (e.g. risk of bleeding vs. risk of pneumothorax). In a like manner, disease specific instruments will not be useful when comparing the benefits of treatment to the risks of complications from that treatment when the nature of the outcomes are different (e.g. benefit is measured as dyspnea relief vs. risk of death from bleeding).[9] For example, in patients with malignant CAO, one of the disadvantages of stenting is increased risk of infection, stent migration, and granulation tissue.[2,3,13] How can we compare these risks to the benefits, when benefit is expressed as relief of anatomic obstruction or an improvement in dyspnea? Specific instruments can measure dyspnea (e.g. Borg score), but how do you trade off dyspnea measured using the Borg score vs. future infection risk? How much of a change in dyspnea would be equivalent to one additional lower respiratory tract infection? Disease specific instruments are not well suited to analyze these questions since they are designed to operationalize only one construct in one particular context (e.g. pain, dyspnea, anxiety). As such they cannot deal effectively with trade-offs between HRQOL and complications.

Generic 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,[4] generate measures of utility and range from 0 to 1. They are necessary for calculating quality adjusted life years (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 being plotted on the vertical axis and time being plotted on the horizontal axis. If time is expressed in years the result yields QALYs but other units of time, such as days or months, are also appropriate depending on the clinical context. The position statements and guidelines of the National Institute of Health and Clinical Excellence (NICE)[14], the Agency for Health Care Research and Quality, and the U.S. Public Health Service recognize the QALY as the most important indicator of the effectiveness of health care interventions.[15-17] However, most studies reporting on QALYs use economic modeling. Few studies report directly measured patient-derived utilities or QALYs. Indeed, a systematic review in 2006 identified only 70 studies that reported QALYs based on pre- and post-treatment measures.[18] Reasons for the paucity of studies include the high cost of longitudinal data collection and the fact that many clinicians are not familiar with the techniques.

One of the benefits of measuring utility pre and post procedure and following it over time to calculate QALYs is that it allows physicians to more realistically judge the trade-offs involved when assessing interventions, particularly interventions that are palliative in nature. This is because measuring QALYs facilitates comparisons between treatments that result in improved quality of life vs. the risks which result in a shorter duration of life.

Unfortunately, while generic instruments can be used to derive QALYs, they can be very insensitive to some interventions. As such, using QALYs as the sole outcome metric are probably not advisable when investigating a particular clinical problem. However, quality adjusted survival should be one of several metrics used to assess outcomes.[12] It really depends on what the question is. If you are asking how often does the intervention achieve the objective of the treatment (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. success rate as measured by reopening of an obstructed airway or relief of dyspnea in the case of malignant CAO. These disease specific outcomes allow physicians to answer the question of whether or not the treatment "works" for that clinical problem (i.e. how often did you succeed in reopening the airway?).

When we assess QALYs, the question being asked is subtly but importantly different. It says, in this particular population of patients, with the given clinical context, with all of the other disease processes and burdens being present, how much impact does anatomic reopening of the airways have on dyspnea? How does this in turn impact HRQOL? By expressing the impact in terms of QALYs, we are in a better position to answer the question, given the risk of death, is this intervention worth it. The answer is conditional on many other factors that impact on HRQOL. This relates to the difference between clinical efficacy trials and clinical effectiveness and comparative effectiveness trials. You could in some cases totally eliminate a real problem (clinical efficacy is high) and yet have no or little impact on overall utility (i.e. quality adjusted survival does not change much). In many patients with cancer this is exactly the problem.[9] This is not to say intervention is useless, merely that we have to be realistic about the impact of treatments on overall quality adjusted survival when there are multiple comorbidities and that our estimates of clinical effectiveness (as compared to clinical efficacy) need to be different because of the interaction of multiple systems on patient quality adjusted survival. Using utility as one of several outcomes allows us to gain insight into factors that do not impact technical success of the procedure but do impact the global health of the patient and thereby modify the magnitude of the effect of the intervention on utility. For palliative interventions, this is particularly critical.

Giving clinical context to utility measures

Comparing the impact of interventions between very different populations using QALYs is not always valid.[5,19-21] Using QALYs to determine the relative value of different services or interventions is difficult because of the "disability paradox".[22] Specifically, people with severe or even life threatening diseases may not rate their quality of life as significantly poorer than people with mild disease or people who are healthy. So care must be taken when choosing a comparator population and intervention. It would not be valid to compare the incremental benefit in HRQOL of an intervention for arthritis in otherwise healthy adults with the incremental benefit in HRQOL for a palliative intervention for dyspnea in patients with metastatic cancer.

Limitations of LOCF imputation

As with any long-term longitudinal study, imputation for missing data can be a problem. We pre-specified the LOCF method based on prior studies,[9] but the LOCF methodology can be prone to bias under certain conditions.[23,24] However, the intra-patient variation between months in utility was low, such that whether we used a LOCF or a carry-backwards imputation method, this did not change the results. So directional bias in estimates is unlikely given the relatively short interval in time from measurement to measurement and absence of difference between carry forward and carry backwards results. However, even when imputation is unbiased, imputation methods can lead to overestimates of the precision and reliability of a trial. This is because when data is missing, the sample size on which the estimates are based is actually lower, leading to a loss of power. However, in this study, we found a very strong association between dyspnea relief and subsequent improvement in HRQOL despite this loss of power.

While the true confidence intervals are probably slightly wider than reported, the association is very strong for dyspnea measures, such that it is unlikely that the missing data would have changed the results. For factors with more moderate measures of association (e.g. surgery as initial treatment type) this may be a consideration. These limitations do not apply to the short-term outcomes measured at day 7 which did not require any imputation.

e-Table 1. Patient and Clinical Characteristics Associated with Improved Borg Score, Responder Analysis*

	Univariate				Multivariate Predictive				Explanatory			
	Odds ratio	95% CI		P Value	Odds ratio	95% CI		P Value	Odds ratio	95% CI		P Value
Predictive Variables												
Age	0.97	(0.93	1.01)	0.19								
Male gender	0.58	(0.24	1.38)	0.22								
Zubrod 2-4 vs 0-1	1.11	(0.49	2.52)	0.80								
Baseline Utility	0.88	(0.04	20.39)	0.93								
Baseline Borg	1.63	(1.28	2.07)	<0.001	1.63	(1.28,	2.07)	<0.001	1.68	(1.31,	2.17)	<0.001
Urgent/emergent vs elective	0.67	(0.24	1.85)	0.44								
Time from diagnosis to procedure (weeks)	1.00	(1.00	1.00)	0.48								
Comorbidities												
COPD	2.43	(0.62	9.49)	0.20								
Cardiovascular	1.12	(0.43	2.91)	0.81								
Diabetes	0.81	(0.31	2.09)	0.66								
Second primary	0.62	(0.17	2.32)	0.48								
Cancer type												
Lung	0.87	(0.37	0.38)	0.75								
Other malignancies	<ref>											
Initial treatment type												
Surgery	2.07	(0.73	5.84)	0.17					4.39	(1.15	16.72)	0.03
Chemotherapy	2.83	(0.88	9.08)	0.08					3.99	(0.90	17.62)	0.07
Radiation therapy	12.94	(1.43	117.2)	0.02					22.30	(1.95	255.4)	0.01
No treatment	<ref>								<ref>			
Any prior therapeutic bronchoscopy	0.08	(0.01	0.66)	0.02								

Purpose of procedure												
Tracheoesophageal fistula												
Hemoptysis	0.35	(0.13	0.95)	0.04								
Number of bronchopulmonary segments obstructed	1.04	(0.96	1.13)	0.34								
Location of most proximal obstruction												
Trachea	2.17	(0.55	8.59)	0.27								
Bilateral mainstem	1.78	(0.28	11.12)	0.54								
RMS	2.67	(0.71	10.05)	0.15								
LMS	2.44	(0.57	10.45)	0.23								
RBI	2.00	(0.38	10.41)	0.41								
Lobar only	<ref>											
Obstruction type of most proximal location												
Endobronchial	<ref>											
Extrinsic	0.60	(0.23	1.53)	0.28								
Mixed	0.69	(0.17	2.83)	0.60								
Explanatory Variables												
Ventilation Type												
Jet ventilation	0.74	(0.17	3.17)	0.69								
Volume Cycled	1.35	(0.32	5.74)	0.69								
Bronchoscopy type												
Rigid and flexible	0.48	(0.09	2.52)	0.39								
Flexible only												

Treatment modalities												
Any laser	0.92	(0.32	2.68)	0.88								
Electrocautery	1.06	(0.44	2.54)	0.90								
Argon plasma	0.41	(0.17	1.00)	0.05								
Cryorecanalization	1.70	(0.59	4.89)	0.33								
Microdebrider	2.16	(0.80	5.79)	0.13					3.93	(1.11,	13.97)	0.03
Rigid "coring"	1.17	(0.32	4.29)	0.82								
Dilation	1.16	(0.41	3.26)	0.79								
Stent at first procedure	1.06	(0.44	2.54)	0.90								
Stent type placed												
Aero	0.73	(0.14	3.80)	0.71								
Y-Stent	1.38	(0.27	7.04)	0.70								
Technical success												
Complete or partial	0.86	(0.23	3.15)	0.82								
Failed	<ref>											
Post procedure treatment												
Surgery	0.64	(0.09	4.77)	0.67								
Chemotherapy	0.83	(0.36	1.92)	0.66								
Radiation therapy	0.33	(0.14	0.81)	0.02								

*Responder analysis is based on the MCID for the Borg score, which is a 1 unit improvement. So responders were defined as patients with an improvement in Borg score $\geq$ 1.

e-Table 2. Patient and Clinical Characteristics Associated with Improved Utility, Responder Analysis*

	Univariate				Multivariate Predictive				Explanatory			
	Odds ratio	95% CI		P Value	Odds ratio	95% CI		P Value	Odds ratio	95% CI		P Value
Predictive Variables												
Age	1.03	0.99	1.07	0.14					1.05	1.01	1.09	0.03
Male gender	0.78	0.35	1.74	0.54								
Zubrod 2-4 vs 0-1	0.85	0.39	1.86	0.69								
Baseline Utility	1.87	0.10	36.45	0.68								
Baseline Borg	1.07	0.91	1.25	0.42								
Urgent/emergent vs elective	0.70	0.26	1.83	0.46								
Time from diagnosis to procedure (weeks)	1.00	1.00	1.00	0.96								
Comorbidities												
COPD	0.35	0.10	1.20	0.09					0.22	0.06	0.87	0.03
Cardiovascular	1.23	0.50	3.00	0.65								
Diabetes	1.94	0.76	4.97	0.17								
Second primary	0.53	0.15	1.95	0.34								
Cancer type												
Lung	1.38	0.63	3.02	0.42								
Other malignancies	<ref>											
Initial treatment type												
Surgery	0.90	0.32	2.50	0.84								
Chemotherapy	1.08	0.36	3.24	0.90								
Radiation therapy	1.17	0.30	4.51	0.82								
No treatment	<ref>											
Any prior therapeutic bronchoscopy	0.31	0.06	1.60	0.16								

Purpose of procedure												
Tracheoesophageal fistula	0.33	0.03	3.25	0.34								
Hemoptysis	1.13	0.43	2.95	0.81								
Number of bronchopulmonary segments obstructed	0.92	0.85	1.00	0.05	0.92	0.85	1.00	0.05				
Location of most proximal obstruction												
Trachea	0.53	0.13	2.13	0.37								
Bilateral mainstem	1.13	0.18	6.93	0.90								
RMS	2.70	0.74	9.81	0.13								
LMS	3.00	0.72	12.46	0.13								
RBI	1.80	0.37	8.68	0.46								
Lobar only	<ref>											
Obstruction type of most proximal location												
Endobronchial	<ref>											
Extrinsic	0.75	0.30	1.86	0.54								
Mixed	1.13	0.31	4.07	0.86								
Explanatory Variables												
ΔBorg	0.78	0.63	0.97	0.02					0.72	0.56	0.92	0.01
Ventilation Type												
Jet ventilation	2.55	0.62	10.46	0.20								
Volume Cycled	<ref>											
Bronchoscopy type												
Rigid and flexible	3.27	0.63	17.02	0.16								

Flexible only	<ref>											
Treatment modalities												
Any laser	2.83	0.92	8.74	0.07								
Electrocautery	2.10	0.89	4.94	0.09								
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Cryorecanalization	2.38	0.87	6.51	0.09								
Microdebrider	1.00	0.41	2.44	1.00								
Rigid "coring"	5.25	1.07	25.66	0.04								
Dilation	0.47	0.17	1.28	0.14								
Stent at first procedure	0.59	0.25	1.35	0.21								
Stent type placed												
Aero	1.94	0.40	9.55	0.41								
Y-Stent	1.20	0.26	5.59	0.82								
Technical success												
Complete or partial	1.23	0.35	4.31	0.75								
Failed	<ref>											
Post procedure treatment												
Surgery	1.00	0.14	7.39	1.00								
Chemotherapy	1.63	0.74	3.61	0.23								
Radiation therapy	1.49	0.68	3.27	0.32								

*Responder analysis is based on the MCID for utility using the SF6D, which is a 0.036 utile change. So responders were defined as patients with an improvement in utility $\geq$ 0.036.

e-Table 3. Pre and Post Bronchoscopy Chemotherapy and Radiation

Pre Bronchoscopy Treatments	**Post Bronchoscopy Treatment**				
	Chemo no RT	RT no Chemo	Chemo + RT	Nothing	**Total**
Chemo no RT	14	2	11	2	**29**
RT no Chemo	1	1	1	0	**3**
Chemo + RT	8	9	7	14	**38**
Nothing	0	8	18	6	**32**
Total	**23**	**20**	**37**	**22**	**102**

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