Lung Cancer Surgery: Decisions Against Life Saving Care - The Intervention

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STATISTICAL ANALYSES

Outcome Measures

Primary Outcome. Whether or not patients undergo lung resection surgery represents the main study outcome. We will conform to the 4 month standard used in the SEER database. To ascertain the result, we will first call patients' physicians to determine whether surgery occurred within the designated time frame. Given the possibility that individual patients could seek other opinions and receive surgical care elsewhere, when appropriate, we will ask the patient, or a family member (if the patient is dead or unavailable), whether surgery was performed by someone other than the index physician. If surgery has not occurred, we will ask for reasons. Through appropriate consent, we will retain the option of confirmatory medical records review. For secondary analyses, we will record surgeries that occur beyond the 4 month threshold.

Secondary Outcomes.

1. One year, post-enrollment survival in surgical and non-surgical groups
2. Satisfaction of patients that received interventions compared to those who did not
3. Patients' perceptions of communication for those patients that received intervention compared to those who did not
4. SF-12 scores at baseline, 6 months post-enrollment and 12 months post enrollment

6. *Data Analysis:*

Our current plan includes:

Descriptive statistics (means, standard deviations, frequencies, proportions, correlations, and graphical displays) will be computed for all study variables at baseline and post-baseline. The distribution of all outcome variables will be assessed to determine if distributional assumptions are valid. Descriptive statistics will be obtained for all the variables overall and by race and site. Statistical methods for addressing each of the specific aims of the study are detailed in this section. Since several statistical tests are planned, there is the possibility of incurring spurious results if we do not correct for multiple comparisons. All tests are based on a 2-sided alpha of 0.05.

The main outcome of interest is whether patients undergo surgery is a dichotomous variable, either yes or no. We will compute proportions to estimate the probability of surgery for blacks and whites and compute 95% confidence intervals for the proportions. Since the main outcome is dichotomous, logistic regression for clustered data (clustered within sites) using multiple predictors will be used to assess the simultaneous effect of predictors on the outcome.

Specific Aim 1. To maximize surgical rates for all patients with stage I and II, non-small cell lung cancer who do not have absolute contraindications for lung resection surgery.

hypothesis 1a. a cancer communicator who utilizes active listening and teach-back methods during discussions about lung cancer surgery with newly diagnosed, early stage patients will increase the rate of surgery in Caucasian and African-American patients who do not suffer absolute contra-indications for lung cancer surgery compared to usual care

The primary outcome variable, surgery yes or no, will be compared in the control group randomized to usual care, to the intervention group randomized to the cancer communicator. Bivariate analyses will be performed using the surgical outcome as the dependent variable. Independent variables in these analyses will include important group, demographic variables such as age, race, marital status, household income, health insurance, gender, and education as well as measures of trust, patient satisfaction, functional status, self-reported health, comorbid illness, perceptions of communication, and the communication intervention. We will use bivariate analyses, including correlations and chi-square tests of association, to make preliminary assessments of the relationships between study variables, overall and by race.

The modeling approach will be to initially define as large a maximum model as possible using main effects only (initially no interactions). Preliminary analyses of similar data indicates that the sample size combined with a sufficient number of events (surgery yes) will allow upwards of 30-35 main effects to be included in the model with good reliability for estimation and inference. The generalized estimating equations (GEE) for binary outcomes will be used to fit logistic regression models for clustered data [102]. The primary outcome variable is binary, surgery yes or no, and outcomes of patients clustered within the same site (and/or MD) are expected to be correlated. GEE will allow fitting a logistic regression to the binary outcome while adjusting for the effect of clustering within the same site (and/or MD). As stated previously, independent variables in these analyses will include important demographic variables such as age, race, marital status, household income, health insurance, gender, and education as well as measures of trust, patient satisfaction, functional status, self-reported health, comorbid illness, perceptions of communication, and the communication intervention. The significance of each of the main effects while adjusting for all other effects from the maximum model will be assessed. A backwards elimination approach will, initially, remove effects with a p-value of greater than 0.10. This excludes selected predictors forced predictors into the model (forced predictors include group, comorbid illnesses and selected baseline scores). The reduced model will be refit. Variables have p-values greater than 0.05 will then be removed. The final reduced main effects model, including forced predictors will be refit. Selected interactions will be considered for inclusion into the final reduced main effects model. For the secondary outcomes, survival analysis techniques will be used to assess the one year, post-enrollment survival in surgical and non-surgical groups. Kaplan-Meier curves will be generated. Linear regression models for repeated measures (discrete) outcomes using GEE will be used to assess patient satisfaction of patients that received interventions compared to those who did not, for patients' perceptions of communication for those patients that received intervention compared to those who did not, and for SF12 scores at 6 months post-enrollment and 12 months post enrollment. Covariates will include baseline, group, and other covariates listed above.

<u>hypothesis 1b.</u> the communication intervention will be more effective in patients who score lower in measures of health literacy

Using the logistic regression analyses for clustered data as noted above, the interaction effects of health literacy, S-TOFHLA scores, and intervention group will be tested in all models. . S-TOFHLA scores will be tested as a continuous variable and also, separately, as a dichotomous variable comparing those categorized as inadequate or marginal literacy with those categorized as adequate literacy [103]. Cumulative pre-intervention surgical rates will be compared at all sites with post-intervention rates using Pearson's chi-square test. Post-intervention rates will be compared using test of proportions and changes in proportions from baseline will be compared between surgical and nonsurgical groups using appropriate methods. To determine if the post-intervention rate approaches maximal surgical rates, we will identify patients with high risk co-morbidities, above the age of 80, and need for pneumonectomy or multiple lobectomy in the "no surgery group", subtract this sum from the denominator then re-calculate the surgical rate. We will analyze the secondary specific aim, To measure the effect of the intervention on patients' perceptions of communication and satisfaction with care, by dichotomizing these variables and replacing surgery as the dependent variable in chi-square and logistic regression models as described under the specific aim above.

Specific Aim 2. To reduce the documented difference in lung resection surgery and mortality between African-American and White patients with early stage, non-small cell lung cancer.

hypothesis 2a. giving physicians who make lung cancer surgery decisions data relating co-morbidity to surgical outcomes will reduce racial differences in surgery

hypothesis 2b. using a real time lung cancer registry to provide physicians race-specific feedback about their surgical treatment of early stage lung cancer patients will reduce racial differences in surgery

We will analyze patient level cross-sectional dichotomous outcome data using logistic regression growth models. We will both limit analyses to the cancer communicator control group and do an all enrollee analysis by adding a communicator intervention / no communicator intervention predictor variable to the models. First, we will fit a saturated growth model to estimate annual proportions of these outcomes, before and after the registry/feedback intervention, to assess the effects of the intervention on these outcomes by contrasting the proportions before and after the interventions. We will test the null hypothesis that the proportions before and after the intervention are the same. We will repeat this analysis by including “race” and “race x time” interaction in this model to examine changes in these outcomes between the two races and also if there are any differential changes over time. We will test the null hypothesis that the proportions before and after the intervention are the same for each race

Data interpretation: If our data feedback / registry intervention is found to produce an effect in less than the 4 Cancer Centers, it will prompt further examination of the factors that moderate or mediate the relationship between the intervention and completion of cancer treatment. Thus, by conducting an embedded randomized cohort-control study of the Cancer Communicator intervention component, we may be better able to provide more information about the dimensions along which these interventions can or cannot be generalized.

hypothesis 2c. a cancer communicator who utilizes active listening and teach-back methods during discussions about lung cancer surgery with newly diagnosed, early stage patients will increase the rate of surgery in African-American patients more than Caucasian patients compared to usual care.

We will compare post intervention, unadjusted, surgical rates between African-American and White lung cancer patients using chi-square analysis as discussed under Aim 1. We will also perform the maximum rate analysis stratified by race. The regression models described above under Aim 1. We will also apply these analyses to patients in the communicator group alone selecting patients on an intention to treat basis.

Specific Aim 3. To measure the effect of all elements of a multi-modal intervention that includes a cancer communication educator, data feedback, and a co-morbidity checklist on overall lung cancer surgery rates and rates for African-Americans.

To address specific Aim 3 we will first examine unadjusted relationships between race and clinical characteristics using chi-square analyses to obtain preliminary assessment of clinical characteristics that may be similar. A logistic regression model with binary outcome “undergo surgery or not undergo surgery” will be used to assess the effect of baseline scores, multiple clinical characteristics and patient race. Whether the effect of race remains constant across levels of clinical characteristics will be assessed in the logistic regression model using selected interaction terms of race x clinical characteristic. We will examine the direction and size of the interaction effects to help judge whether African-American patients undergo lung cancer surgery less often than Caucasian patients with similar clinical characteristics. We will repeat these analyses stratified by race to further examine predictors of differential effect. GEE with exchangeable correlation structure and generalized linear mixed models will be used to account for correlation within-physician. To measure the effect of the intervention, we’ll examine before and after lung cancer surgery rates and control for the variables as noted in Specific Aim 1. To help control for the varying lengths of time before and after lung cancer surgery, we will include a length of time measure in our models as both a main effect and with selected interactions.

Specific Aim 4. To follow patients' functional status over time and explore the relationship of surgery, race, and co-morbid conditions on functional status.

hypothesis 4a. Individuals who under go lung cancer surgery will experience better physical functioning at six months and 12 months than those who don't

hypothesis 4b. Individuals who under go lung cancer surgery will experience better mental functioning at six months and 12 months than those who don't

The SF-12 physical and mental component scores will be converted to 0 – 100 scales and utilized as the dependent variable. Baseline scores will be compared first to 6 month scores then 12 month scores using paired t-tests. Generalized linear mixed models for repeated measures data will be constructed in a similar manner as the logistic regression models described above; however, surgical status, race, and comorbid conditions will be forced predictors in these model.

Note that interim analyses regarding specific aims 1 and 2 will be performed at the end of study year 2 then annually. If statistically significant benefits in care are documented on surgical rates and reduction in disparities, the study will be terminated and workshops and individual training sessions of the communication methodologies will be initiated for the care teams at all the study sites.

7. *Sample Size*

Power computations are computed for post-intervention comparison of proportions. The project anticipates enrolling 496 patients into the study due to constraints on budget, patient availability, and study duration. Thus, we compute the minimal effect size we can detect with statistical power of 80% for our primary aim, AIM 1, using the specified sample size. In computing the effect size, we specify our main outcome as the probability of undergoing surgery for all patients post-baseline as compared to the probability for all patients in the previous study because all groups will receive the data registry and feedback interventions.

Let p_1 be the proportion all patients who undergo surgery in the present study and p_0 =0.63 be the proportion of patients who underwent surgery in the previous study. Using a one-sample test of proportion with 496 subjects overall and significance level of 0.05, we have 80% power to detect a minimally import difference (increase) in surgical rate of p_0 =0.63 to p_1 =0.69. With a sample size of 159 for blacks, we have 80% power to detect an overall increase from p_0 =0.55 (as measured in the previous study) to p_1 =0.66 with significance level of 0.05. With a sample size of 337 for whites, we have 80% power to detect an overall increase from p_0 =0.66 (as measured in the previous study) to p_1 =0.73 with significance level of 0.05.

From the analysis of our previous study, we found that practically negligible correlation existed between subjects for the primary outcome, surgery yes or no. The correlations seen ranged from -0.002 to 0.01 when using GEE for clustered observations in the previous study. In other words, clustering had a neglible effect on the results in the previous study. As such, we can expect the same in the proposed study. Therefore, we feel there is little or no need for power and sample size computation based on clustered observations However, we will still adjust for patients clustering within site and/or physicians in the logistic regression models using GEE described in the Data Analysis section.