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

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STUDY PROTOCOL

A. Overview: We propose a multiple site, imbedded randomized clinical trial. Overall lung surgery rates and black / white disparities have not improved during a decade of documentation [38]. We will establish baseline rates of surgery at each site accounting for race and co-morbid illness using a 2-year retrospective chart review. All patients with Stage I or II non-small cell lung cancer who enroll in the study will be entered into real time registries at every site and patients' progress through the registries including follow-up provider visits, diagnostic tests, and procedures will be transparent to lung cancer providers. The randomized trial will compare patients who receive usual care to those who receive visits and calls from a trained cancer communicator who is well versed in issues specific to lung cancer and trained in active listening and communication that accounts for patients' limitations in health literacy.

B. Description of the Study Areas: The proposed study area is comprised of 3 North Carolina sites (Chapel Hill, Greensboro, and Greenville), in addition to Columbia, South Carolina (Appendix G). One is purely staffed as an academic medical center (AMC) for which the hospital has no community staff members, two have a mix of academic-based and community practices, and one consists entirely of community practices. In addition to the mix of practice settings, both urban and rural geographic settings with large African-American populations will be included. We have successfully recruited at all 4 sites in our recent prospective study. The selection of these sites was motivated by 4 considerations: (i) the university hospitals have large referral bases that concentrate many lung cancer patients in a few focused areas. ECU and the MCHS are partners in the community engagement core of the UNC CTSA. We will take advantage of CTSA infra-structure to execute a multi-modal intervention that will translate into improved lung cancer care. We will also involve the education core of the CTSA to help train students and fellows interested in cancer-related translational research.

C. Early Stage, Non-Small Cell, Lung Cancer Cases: The table below includes number of patients from 2007 with stage I and II, non-small cell lung cancer entered in each local cancer registry. These data only include patients with tissue proven diagnoses and not those who had CT lesions with extremely high cancer probability and refused surgery or dropped out of follow-up (we did include these patients in our prospective study). Therefore, eligible patients are underestimated while "percent surgery" rates are overestimated when factoring in all patients with early stage, non-small cell disease.

Site	Number of Cases	African-Americans	Percent Surgery
ECU	63	11	70
MCHS	141	24	69
UNC	57	14	74
USC	66	17	75

From our prospective study, we anticipate an average recruitment rate of 70% across sites. Only 11% of all patients approached during the post-diagnosis – pre-treatment recruiting interval refused participation and there was no difference by race.

D. Retrospective Chart Review: Our recently completed study demonstrated that co-morbid

conditions differentially affected black patients' care. Given these data, during the first six months of the intervention trial we will perform a retrospective chart review for the 2008 and 2009 calendar years. We will review all patients diagnosed with stage I or II, non-small cell cancer to serve as a baseline for surgical rates and to examine outcomes of patients treated with and without surgery using a very specific analysis of co-morbid conditions and severity. These data will be checked against Strand's report [45] to assess compatibility and level of detail. The results will be used by our expert panel of co-investigators and site investigators to create an educational checklist to remind lung cancer providers that surgical contra-indications are often relative and subjective. We anticipate the availability of approximately 100-150 charts per site in the 2-year pre-study window. Charts will be selected using appropriate ICD-9 billing codes. Data will be collected in an aggregate manner and no linkage files or specific patient identifiers will be maintained.

E. Prospective Study: All sites will begin recruiting patients by the beginning of study Month 13. As most cancer programs have at least rudimentary patient tracking and navigation, this degree of usual care will serve as the control. All providers will receive the co-morbid illness educational checklist at all sites and will receive monthly data concerning surgical rates by comorbid condition and race. Patients will be randomized to either usual care or a more intense communication intervention delivered by a trained cancer communication educator as described below. Since we are building on the methods of our prior cohort study, pretesting of recruitment methods and study instruments can proceed quickly before randomization. Lung cancer surgery rates in the control groups will be compared to historical controls at the individual sites to account for a passive effect of the registry and educational checklist. As care registries and data compilation by race is a mandate of the HITECH portion of the American Recovery and Reinvestment Act, we don't believe that it's ethical to deny any group access to the registry. Given the flat rate of lung cancer surgery and persisting racial gap documented for over a decade in datasets of national scope [7, 36, 38], historical controls for this portion of the study are justified.

1. *Inclusion and Exclusion Criteria for Patients*

We will enroll patients who meet these criteria: (1) age 21 years or greater; (2) a probability of 60% or higher of a lung lesion being malignant as calculated by Bayesian analysis derived from clinical and radiographic criteria or, alternatively, biopsy proven disease; and (3) the patient has received a clinical classification of stage I or II disease. By "clinically classified", we mean using all studies including CT scans, PET scans, bone scans, mediastinoscopy, and / or any study or procedure performed short of thoracotomy.

We will exclude patients from this study for 3 reasons:(1) incarceration / ward of the state status, (2) severe cognitive impairment, (3) absolute contraindications by pulmonary function testing, or (4) Non-English speaking. Hispanic patients represent less than 4 percent of lung cancer patients in North Carolina restricting our ability to document an intervention effect.

Note that we do not propose enrolling patients based on tissue diagnosis alone. Any patient diagnosed with non-small cell lung cancer by bronchoscopy or needle biopsy who has been staged with I or II disease will automatically be included. Obtaining tissue prior to open surgery is not always possible. To assess these patients, several reports have reliably demonstrated the use of Bayesian logic to calculate the probability that a lung lesion is malignant [89-92] has published the most comprehensive compendium of likelihood ratios for clinical and radiographic findings; this study will serve as the basis for our preoperative analysis. Because of the difficulty of obtaining a diagnosis in small peripheral lung lesions with less invasive approaches, many patients proceed to surgery with only an estimation of "odds" for cancer. When these individuals decide to have surgery, they generally agree to 1 operation with a 2-step approach: (1) thoracoscopic biopsy and then (2) if frozen sectioning of the biopsy reveals cancer, the appropriate resection procedure. Some individuals, particularly those who suffer from advanced chronic obstructive lung disease, will refuse surgery if the preoperative diagnosis is not certain.

For the patients who agree to this 1-surgery, 2-step approach, there is no time between tissue diagnosis and definitive surgery. Therefore, these patients need to be enrolled based on their preoperative probabilities.

2. *Patient Recruitment*

Patient flow from the time of initial diagnostic studies, to actual diagnosis and to treatment differs at every site. We are experienced with these patterns and can incorporate recruitment strategies into the clinical flow of care. The UNC patients are all processed through a central site, the Multi-disciplinary Thoracic Oncology Program (MTOP). Note that a patient list is available the Friday prior to MTOP clinic. This list includes patients' names, the description of his or her lung lesion, diagnosis, cancer stage (if determined), and whether the appointment is an initial appointment or follow-up visit. The RA and site PI will identify patients, in advance, who are most likely to be study candidates. The appropriate clinicians will be approached at the beginning of MTOP to confirm the patient's study eligibility and to obtain permission to approach the patient. As MTOP only meets one day a week and in a single location, a research assistant will spend every Tuesday at the MTOP site and work with staff to identify specific patients that meet inclusion criteria, obtain informed consent, and arrange a time for completion of the patient questionnaire. The RA will administer all questionnaires orally, and all participating patients will be paid $30 at completion. Patients will also receive $10 for each completed follow-up interview (6 months then 12 months after enrollment). At ECU, the format is identical except about one-fifth of lung cancer patients enter the system through a standard pulmonary clinic. The review of the patient list, the confirmation of eligibility, and enrollment process at ECU will proceed exactly as per the description at UNC. Lung cancer care in Greensboro has been decentralized in the past. However, the regional cancer center has recruited a lung cancer navigator and established a formal MTOP structure. All lung cancer providers (thoracic surgeons, pulmonologists, oncologists, and radiation oncologists) have agreed to refer potential and diagnosed lung cancer patients for case discussion to the program clinic prior to surgical or other treatment decisions and will utilize a multidisciplinary and multi-specialty decision-making format. Patients will now be accessible at a common site before treatment decisions are finalized. The MTOP clinic roster will be available to the RA and site PI 48 hours in advance and the patient identification and enrollment process will proceed as described at ECU and UNC.

USC also has an MTOP conference but about one-third of patients are discussed after therapy has been determined by the referring physician. However, the pulmonary division has established a solitary pulmonary nodule clinic specifically designed to identify patients with early stage lung cancer who then rapidly progress to diagnostic evaluation and treatment recommendations. There are 2 clinic sessions per month and 15 patients evaluated in each clinic. The USC site investigator and RA will have access to the nodule clinic schedule and determine potential patient eligibility prior to clinic. As with the MTOP clinics above, the RA will attend the nodule clinic, the appropriate clinicians will be approached to confirm patient's study eligibility and to obtain permission to approach the patient. We will also intensify recruitment at thoracic surgery offices in an effort to capture the patients treated prior to MTOP and not seen in solitary nodule clinic. Note that none of the participating sites use formal communication protocols that define minimum information delivery or ascertainment of patient comprehension.

All 4 study sites are referral centers for lung cancer treatment with large catchment areas. We surveyed the lung cancer physicians and coordinators at all 4 centers regarding a potential diffusion effect between study patients and controls. Because of widespread geographic distribution of patients and MTOP scheduling sequences during visits the possibility of intervention and control patients meeting and discussing variations in communication is remote. To further ensure against a diffusion effect, we will alternate control and intervention recruitment dates as part of the randomization scheme.

In our cohort study, 80% of the patients enrolled identified a pulmonologist, thoracic surgeon, or oncologist as the individual who told them the most about lung cancer. These specialists

almost uniformly will refer their patients to an MTOP. However, the remaining 20% whose CT scans are suggestive of early stage lung cancer did not encounter a lung cancer related specialist within the timeframe of our study. Therefore, it remains paramount that we identify patients who have probable, early stage non-small cell lung cancer, and ensure that they enter the progression of care most likely to lead to appropriate treatment. This group may be particularly resistant to surgery either because of a provider's advice against surgery, because of perceptions of co-morbid illness or because the patient avoids referral due to personal health perceptions, disbelief of diagnosis, or attitudes toward cancer or life. Since nearly all individuals with lung masses receive chest computerized tomography scans (chest CT), data derived from these tests serve as a common identifier of patients who do not engage the appropriate system of care for early stage lung cancer just as laboratory blood glucose measurements identify diabetics. The CT protocol is described in our recent report [13]. We feel that the modification utilized in our initial multi-site study meets the intent and spirit of the common rule governing human subject's protection and actually resulted in a net benefit because we ushered lung cancer patients into care who otherwise would not have had this opportunity. This methodology allowed us to broaden recruitment and overcome referral bias. All study enrollees, whether identified by standard recruitment or the CT strategy will be entered into the lung cancer registry and receive intervention as per their randomization.

Given the continued late stage of lung cancer presentation, particularly among African-Americans [3], we will continue our multi-pronged recruitment approach to find as many patients with early stage, non-small cell cancer as we possibly can. In addition to the electronic CT search, we will continue to engage specialists who see those patients with lung cancer that are indeed referred. Pulmonologists and thoracic surgeons care for the largest concentration of non-small cell lung cancer patients. We'll focus our physician office recruiting efforts on these specialties. As we did with our first prospective study, we will give participating physicians and their office liaisons a project summary sheet that will include the telephone number and beeper number of the PI and research assistant (RA). We will ask that all patients who have the probable diagnosis of resectable lung cancer be referred. We will advise practices that we are responsible for confirming inclusion criteria and obtaining informed consent. In addition, we will provide participating offices information sheets to give to potential enrollees. These documents will describe the study and contain clear statements emphasizing that patient care would not be compromised should individuals decide against participating. For patients who express interest, the office liaison will record the patient's name and telephone number. We will contact each office on at least a weekly basis to remind the staff of the study and to obtain the information on potential enrollees. We will telephone patients to further explain the study and arrange a meeting to obtain informed consent and proceed with the interview.

Patients with lung cancer represent an extremely small proportion of primary care and resident physician practice panels. However, we will not eliminate these practices from consideration. We will attend primary care staff meetings and residency morning reports on a regular basis to remind these physicians of the study. Traditionally, oncologists have been consulted for patients who have advanced disease. With the growing emphasis on adjuvant chemotherapy for early stage lung cancer, these specialists are much more likely to encounter potential study patients. We will therefore regularly attend thoracic oncology conferences and remind oncology physicians, including radiation oncologists of our study.

Given the ratio of catchment area patients that receive their lung cancer care at each study site and a conservative, estimated an overall recruitment rate of 50%, we will be able to recruit 165 stage I and II patients per year combining all study sites. We anticipate 3 yrs of patient recruitment with the accrual of 496 patients. We will oversample black patients, as we did in our prospective study, to attain an enrollment goal of 30%.

3. *The Interview and Survey Instruments*

Patient Interview. We will administer the surveys as face-to-face interviews, conducted by

thoroughly trained RAs at each site. We will attempt to arrange interviews at the convenience of the patient. Before the project begins we will give all RAs a script and provide rigorous training in its use so that interview technique and content will be consistent at all sites; we will also develop and provide training manuals. We will interview patient-participants in private settings. For onsite interviews, we will identify rooms in the same building or adjacent buildings that are apart from clinic. Offsite interview venues will include the investigator's institution, the patients' homes, or other mutually agreeable locations. All interview sites will be private and secure. If patients require more than one sitting to complete the survey because of fatigue or time constraints, we will accommodate such needs.

Patient Questionnaire. The proposed instrument builds on our preliminary work (Appendix E) by formally measuring health literacy. Low literacy likely identifies patients for whom the communication intervention might be more needed and effective. The questionnaire also covers the following constructs and relies on reliable and validated items or batteries drawn from previous instruments. Specifically areas included will be:

1. *Demographic Information*: age, sex (recorded only by interviewers, not asked), marital status, race, educational attainment, estimated household income, type of health insurance, access to a regular source of care, and affiliation with any church or denomination.
2. *Health Status*: Physicians may use poor physical or emotional function as a contraindication for cancer surgery; patients may opt against surgery because of poor health-related quality of life. We will use the SF-12 [23], to assess this domain. (Appendix C)
3. *Health Literacy*: Test of Functional Health Literacy in Adults-short form [61] (Appendix C)
4. *Communication Variables:* The attitudes coupled with Likert-type scales that identified perceptions of communication associated with surgical decisions from the initial study.
5. *Trust*: The Medical Mistrust Index [93]

6-month Telephone Interview

1. Health Status: repeat SF-12
2. Communication Variables as above
3. Patient satisfaction cancer care including the choice of treatment

12-month Telephone Interview. Will repeat 6 month items. To fully assess the importance of lung resection surgery within 4 months of diagnosis, we will determine whether each patient, surgical and nonsurgical, remains alive one year. We will re-administer the SF-12 survey and satisfaction measures by telephone to survivors. We will find patients by maintaining a linkage file that includes best telephone number file, stored separately from original survey information. If the patient is not located at the original number, we will seek current information from the office of their physician or through local phone listings. If a patient surrogate answers the phone, we will seek the patient's availability and clinical status in the conversation with the surrogate.

4. *Interventions – Each site will identify a physician leader to serve as a liason to the CCE.*

A. Cancer Communication – Because of the gaps between documented outcomes of lung cancer surgery and patient communication barriers identified in our recent work, our communication intervention will focus on improving presentation of risk information and confirmation of understanding [13]. Given good post operative outcomes [45, 94] in most patients with significant comorbidities, and the doubling of one-year mortality in our prospective "no surgery" group, patients' perceptions of worse one-year prognosis with surgery are either misinterpreted or poorly explained. In lung cancer only one-half of patients comprehend proposed treatment within 3 days of their clinical visit and only 40% expressed satisfaction with communication [60]. Moreover, effective communication skills, such as active listening and the teach-back method, which can assist education and confirm understanding are used infrequently in clinical care. For example, Schillinger demonstrated that only 12% of new concepts had confirmation (teach back) by the clinician in encounters for diabetes [59]. Several studies have documented difficulty understanding numbers and calculations, particularly the idea of risk [95].

Presenting risk clearly, with specific formats, and talking through the issues can help to improve patient understanding. Health literacy related oral communication techniques, such as the teach-back method, can help the educator confirm understanding and enhance clinical outcomes [59]. Because of difficulty in communicating risk, and the infrequency of optimal communication strategies in usual care, our experienced investigator team will carefully construct content and nuances of risk communication and training and protocols for educators to use best practices, such as active listening and the teach-back. Our team includes experts in health literacy (Dr. Dewalt) and disparities communication (Drs. Corbie-Smith, Cykert, and Dilworth-Anderson) and we have extensive experience developing successful, culturally sensitive risk communication [96-100, 13]. We will ensure that short term consequences and cure rates are well understood and one year mortality information is clearly described with and without surgery. The communicator will "close the loop" at **multiple points over time** to ensure patient comprehension. If surgical decisions don't fit prognosis, we will use alternative methods to convey information such as narratives or story telling [101]. As a key component of intervention development, we will test comprehension of our message and acceptability of communication techniques using individual patient interviews prior to the randomization phase. We will use the interviews iteratively to develop the intervention techniques and include people with low health literacy and low numeracy. These interviews will be taped (with consent) for fidelity of factual information and delivery techniques, and the CCE will be given feedback based on the tapes. After the final tools are developed, the CCE will use the lung cancer algorithms and teach-back confirmation with all participants *who are randomized to the CCE intervention. The CCE will have a face to face sessions at initial diagnosis and one 10 to 14 days after diagnosis*. More visits will be scheduled if the CCE cannot confirm patient understanding of risk and prognosis. *The CCE will* re-engage any individual *who is randomized to the patient intervention and* who drops out of care *as defined by a lack of follow-up appointment within a month of the index visit, failure to schedule surgery when recommended, or a missed appointment for follow-up or procedures*. *The CCE will inform the designated site physician champion about direct recommendations against surgery if no absolute contra-indications are defined in the record. The physician champion will arrange clinical evaluations as noted below. Patients in the intervention group will be encouraged to initiate contact with the CCE when questions or concerns occur.*

B. Data Feedback – Results of the retrospective chart review will be distributed to and reviewed with all lung cancer care providers at their participating institutions. Particular emphasis will be placed on the role of co-morbid conditions and outcomes according to race (VII). Since small clusters of physicians perform nearly all lung cancer care in each health system, cross-contamination for any physician-specific intervention is very likely. Therefore, prospective physician feedback will be delivered at all institutional sites. Cumulative data feedback that includes race, co-morbidity variables and surgical rates will be presented to lung cancer providers *by an identified physician champion at each clinical* site quarterly. "Drop outs" and negative provider recommendations will be flagged in real time. The clinic champion will arrange intensive clinical review if the barrier stems from clinical recommendations while the CCE will re-examine patient related barriers. Current IT systems at cancer care organizations do not often factor in patient race, track "real time" clinical performance, generate regular provider reports or suggest options for improvement (V). Although routine quality improvement has not always been effective in addressing disparities [28], we will create a race-specific registry for our study patients similar to the effective registry that Bickell et al. [16] employed for adjuvant breast cancer therapies. We will follow the effect of the registry function via historical controls.

C. Registry development – note that Dr. Cykert and Mr. Jonnson have past experience designing a diabetes registry with care flags and point of care reminders that is utilized for paper-based practices in a statewide quality improvement project (formally IPIP, now the North Carolina Healthcare Quality Alliance). The same electronic backbone will be used to track appointments, procedures, adherence and recommendations related to care for early stage, non-small cell, lung cancer.

D. Co-morbidity educational checklist – The co-morbidity check list will be designed to address the seeming over interpretation of co-morbid states in decisions against surgery by African-American patients or their physicians (II and VII). Derived from the retrospective chart review, this checklist will be used to help inform physicians' decisions in patients who do not have absolute contra-indications for surgery. Overall results of the retrospective chart review will be delivered at the beginning of designated MTOP conferences at each study site or at a mutually agreeable meeting that includes the whole lung cancer care team. For African-American study patients randomized to intervention who are identified as having dropped out of care per the definition in section 1, the most recent physician in the specific patient's chain of care, will be given that patient's co-morbidity list via the CCE. This list will serve as a reminder that decisions for African-American patients have been different and will be designed to attenuate the subjective use of co-morbid states to justify decisions against lung resection surgery.

5. *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