# Sublobar resection versus lobectomy for stage I non-small cell lung cancer: an appropriate choice in elderly patients?



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# SUBLOBAR RESECTIONS VERSUS LOBECTOMY FOR STAGE I NON-SMALL CELL LUNG CANCER (NSCLC): AN APPROPRIATE CHOICE IN ELDERLY PATIENTS ?

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**ASTRACT**

**PURPOSES:** To evaluate whether sublobar resections afforded recurrence and survival rates equivalent to lobectomy in high-risk elderly patients.

**METHODS:** This is a retrospective multicenter study including all consecutive patients aged > 75 years operated for Clinical Stage I Non Small Cell Lung Cancer. Clinico-pathological data, postoperative morbidity and mortality, recurrence rate and vital status were retrieved. Overall survival, cancer specific survival and disease-free survival were assessed.

**RESULTS:** 239 patients (median age: 78 years) were enrolled. Lobectomies were performed in 149 (62.3%) patients, sublobar resections in 90 (39 segmentectomies, 51 wedge resections). The recurrence rate following lobar versus sublobar resections showed no significant difference (19% versus 23% respectively, p=0.5), as well as overall survival (p=0.1), cancer specific survival (p=0.3) and disease-free survival (p=0.1). Even after adjusting for 1:1 propensity-matching score and matched pair analysis, results were unchanged. Tumor size > 2 cm and pN2 disease were independent negative prognostic factors in unmatched (p=0.01 and p=0.0003 respectively) and matched (p=0.02 and p=0.005 respectively) analysis.

**CONCLUSIONS:** High-risk elderly patients may benefit from sublobar resections which provide equivalent long-term survival, compared to lobectomy.

## INTRODUCTION

Surgical resection constitutes the most effective treatment for early-stage non-small cell lung cancer (NSCLC). In recent years, computed tomography screening has allowed diagnosing approximately 25-30% of NSCLCs at an early stage and it is expected that this incidence will increase in the future [1].

Despite some authors [2,3,4,5] supported the hypothesis that in selected patients with clinical Stage I T1aN0M0 NSCLC sublobar resection produces similar survival rates compared to greater resection, lobectomy remains the approach of choice as stated several years ago by the only existing randomized controlled trial from the Lung Cancer Study Group [6]. This observation was also recently confirmed by Whitson et al. [7] who evaluated 14.473 patients with clinical Stage I NSCLC from the Surveillance Epidemiology and End Results (SEER) register and found that lobectomy had conferred superior overall 5-year survival ($p<0.0001$) and 5-year cancer-specific survival ($p=0.0053$) rates over segmental resection. Two multicentre, prospective, randomized studies focused on this topic (lobectomy versus sublobar resection) are currently under way (Cancer and Leukemia Group B 140503; Japanese Clinical Oncology Group 0802/West Japan Oncology Group 4607L) but the data have not been published yet and will help define the role of sublobar resection in the treatment of NSCLC patients.

However, a considerable number of elderly patients with early-stage NSCLC are unfit for lobectomy due to poor cardiopulmonary reserve and multiple comorbidities. Thus, in such cases sublobar resection may be indicated as an alternative to lobectomy in order to reduce the perioperative morbidity and mortality, at the price of questionable oncologic validity.

The aim of the present study was to evaluate if sub-lobar resection (SLR) was a reasonable alternative to lobar resection (LR) in terms of survival in high-risk, elderly patients with Stage I NSCLC.

## MATERIAL AND METHODS

### Study Design

This is a retrospective multicenter study including all consecutive patients aged over 75 years-old, with Clinical Stage T1a,b-2aN0 (Stage I) NSCLC as determined by positron emission tomography/computed tomography (PET/CT) scan, and undergoing LR or SLR from January 2006 to December 2012. Patients with (i) a final histological diagnosis different from NSCLC (i.e. small cell lung cancer; carcinoid tumor etc…); (ii) neoadjuvant therapy; and (iii) radiologically non-solid tumor as pure ground glass opacity (GGO) or mixed GGO were excluded. SLR was considered as primary resection therapy for patients with peripheral lung cancer and significant cardiopulmonary impairment or important co-morbidity. In all other cases, a LR was performed.

The two study groups (SLR versus LR) were statistically compared to assess any differences in recurrence, overall survival (OS), cancer specific survival (CSS) and disease-free survival (DFS). To avoid difference bias due to the retrospective nature of the study, LR patients were then chosen with the highest concordance with SLR patients using propensity score matching analysis and the different outcome between the new two groups was re-analyzed.

The data and variables were collected retrospectively from structured lung cancer databases of each participating center. Chart review was used as necessary to complete data collection. A written signed consent was obtained by patients for entry into database according to the policy of each participating center and patients were aware that these data would be used for research purpose. Ethical Review Board of each participant center approved the study design.

**Study Population**

254 patients were eligible for the present study. All patients were clinically staged by PET/CT scan. In cases with a positive PET/CT scan (N2 or M1), additional diagnostic testing was carried out for confirmation purposes. If bone or brain were suspected to harbor metastases, magnetic resonance imaging (MRI) was considered as the standard reference. Pulmonary function was evaluated with spirometry and lung carbon monoxide diffusion testing (DLCO). Preoperative cardiac function evaluation was routinely performed by echocardiography with left ejection fraction (EF) and pulmonary artery pressure (PAP) estimate and treadmill stress test; occasionally, the quantitative V/Q scan and cardiopulmonary stress test were required for borderline patients to assess oxygen consumption and pulmonary function. The histological diagnosis of the tumor was obtained whenever possible preoperatively with transparietal CT guided-biopsy and/or bronchoscopy or on the resected specimen at on-site analysis at surgery.

The type of resection was categorized in two groups according to the extent of pulmonary resection. LR group included standard lobectomy while SLR counted segmentectomy and wedge resection. Patients were considered unfit for lobectomy and scheduled for sublobar resection in presence of major cardiovascular, respiratory and other heavy significant co-morbidity conditions. Hilar and mediastinal lymph nodes (LN) were sampled or systematically dissected during lobectomy or segmentectomy to evaluate for the possibility of occult lymph node involvement. On the other hand, only enlarged nodes were sampled in patients undergoing wedge resection.

Hospital and office records of each patient were reviewed for demographic, clinical and pathological data, including gender, smoking status, co-morbidities stratified according Charlson Co-Morbidity Index, clinical and pathological stage, according to the seventh edition of TNM. Operative mortality was defined as any death within 30 days of operation or prior to dismissal. Complications were classified as major (potentially life-threatening) including pneumonia, myocardial infarction, stroke, bleeding, adult respiratory failure, and need for re-intubation occurring within 30 days of surgery, or within 3 months in case of empyema or bronchopleural fistula; and as minor (non-life-threatening, requiring medical therapy and/or prolonged hospital stay.

**Survival**

End points of the analysis included recurrence pattern (locoregional or distant), OS, CSS, and DFS. Loco-regional recurrence was defined as any recurrence within the same lobe of the lung, or interlobar and hilar lymph nodes. All other relapses were classified as distant recurrence. OS was measured from the date of surgery until death. In addition, patients without event was censored at the time of last follow up. CSS was measured from the date of surgery to the date of death related to lung cancer. DFS was calculated from the date of surgery until any loco regional, or distant disease recurrence occurred, or until last follow-up.

**Statistical Analysis.**

The summary statistics of patient's characteristics were tabulated either as number of patients (N), mean ± standard deviation (SD), for continuous variables or as number of patients and percentages for categorical variables. Student's t-test and chi-square test were used to compare different variables, as appropriate. Survival was calculated by the Kaplan-Meier method and difference assessed by logrank test. A multivariable analysis for prognostic factors was performed using the Cox proportional-hazards regression model.

To control the differences in prognostic and stratification factors between the study groups, we created a propensity score matched pairs without replacement (1:1). The following covariates were used for propensity score matching analysis: ppoFEV1 % (≤40% or >40%); ppoDLCO % (≤40% or >40%); heart cardiac failure (yes or no); pT (≤20 mm or >20 mm); pN2 disease (yes or no); major post-operative complications (yes or no). Specifically, we sought to match each lobar patient to a sublobar patient who had a propensity score that was identical to 6 digits. If this match could not be found, the algorithm then proceeded sequentially to the next highest digit match (a 5-; 4-; 3- or 1- digit) on propensity score to make "next best" matches, in a hierarchical sequence until no more matches could be made. Once a match was made, previous matches were not reconsidered before making the next match.

A $p < 0.05$ was considered significant. MedCalc statistical software (Version 12.3, Broekstraat 52; 9030 Mariakerke; Belgium) and STATA version 11.0 (College Station, TX) were used for analysis.

## RESULTS

Among 254 eligible patients, 15/254 (6%) were excluded because of final histological diagnosis different from NSCLC (2 small cell lung cancers and 4 carcinoid tumors); neodjuvant therapy (n=1); and non-solid tumor (n=8). Thus, our study population included 239 patients (median age: 78 years). LR was performed in 149 (62.3%) patients while SLRs in 90 (39 segmentectomies, 51 wedge resections) cases. The flow chart of the study is shown in Figure 1.

The characteristics of the two study groups are reported in Table 1. There were no significant differences in age, gender, clinical and pathological tumor size, or histology when the SLR and LR cohorts were compared. On the other hand, compared to patients undergoing LR, patients undergoing SLR showed significantly worse preoperative and predicted postoperative pulmonary function, impaired cardiac status, and higher Charlson comorbidity index. In the SLR group, 11 wedge resections were performed using Video-Assisted Thoracic Surgery (VATS) while only one VATS procedure was carried out in the LR group (p=0.0003). Fewer mediastinal LN stations were sampled during sublobar resection compared with lobar resection (p=0.0001) as well as during wedge resection compared with segmentectomy (p=0.01). The pathological tumor size was similar in the study groups. Major (p=0.4) and minor (p=0.2) complications were not correlated with the extent of resection. One patient undergoing LR died within 30 days of operation due to respiratory failure.

**Recurrence**

The incidence and distribution of recurrences are summarized in Table 2. The recurrence rate following LR versus SLR showed no significant difference (19% versus 23%; respectively, p=0.5). However, patients who underwent SLR had a significantly higher local recurrence rate than patients undergoing LR (13% versus 2%; p=0.0005). In the SLR group, local recurrences were significantly fewer after segmentectomy compared to wedge resection (3% versus 21%; respectively, p=0.03) while no significant differences were found when considering overall (26% versus 19%; respectively, p=0.5) and distant recurrence rates (5% versus 16%; respectively, p=0.1). Following local recurrence, 3 out of 3 patients in the LR group and 10 out of 12 patients in the SLR group underwent radiation therapy while, following distant recurrence, only 14 (54%) out of 26 patients in the LR group and 2 (22%) out of 9 patients in the SLR group received chemotherapy.

**Survival**

In LR group, 50/149 (34%) patients died; 23/50 (46%) for cancer-related cause and 27/50 (54%) for not-cancer related causes including respiratory failure (n=9/27; 33%), heart failure (6/27; 22%); acute myocardial infarction (n=5/27; 19%); and cerebrovascular accident (n=7/27; 26%). The remaining 99/149 (66%) were alive with stable disease status (n=6/99; 6%) or no evidence of disease (93/99;94%).

In SLR group, 30/90 (33%) LR patients died; 11/30 (37%) for cancer-related cause and 19/30 (63%) for not-cancer related causes including respiratory failure (n=2/19; 11%), heart failure (7/19; 37%); acute myocardial infarction (n=4/19; 21%), cerebrovascular accident (n=5/19; 26%), and kidney failure (1/19; 5%). The remaining 60/90 (67%) were alive with stable disease status (n=10/60; 17%) or no evidence of disease (50/60;83%).

***Overall Survival.*** The unmatched 5-year OS (Figure 2/A) was 60.5% in LR group and 45% in SLR group. Despite LR group presented a better trend compared to SLR group, the difference was not significant (Hazard Ratio (HR): 0.7; 95% Confidence Interval (CI): 0.45-1.17; p=0.1). The matched 5-year OS of LR and SLR group was 58% and 41%, respectively (HR=0.7; 95% CI: 0.44-1.22; p=0.2; Figure 3/A). No significant difference in OS was found between different types of resection after unmatched (p=0.1, Figure 4/A) and matched analysis (p=0.4; Figure 5/A).

***Cancer Specific Survival.*** The unmatched 5-year CSS was 71% in LR group and 59% in SLR group. Despite SLR group presented a worse trend compared to LR group, the difference was not significant (HR: 0.7; 95% CI: 0.39-1.437; p=0.3; Figure 2/B). The matched 5-year CSS of LR and SLR group was 69% and 62%, respectively (HR: 0.6; 95% CI: 0.32-1.17; p=0.6, Figure 3/B). The comparison of different types of resection showed no significant difference in unmatched CSS (p=0.5, Figure 4/B) and matched CSS (p=0.1, Figure 5/B), respectively.

***Disease Free Survival.*** The unmatched 5-year DFS was 60% in SL group and 36% in SLR group (HR: 0.7; 95% CI: 0.44-1.16; p=0.1, Figure 2/C). The matched 5-year DFS was 59% in SL group and 38% in SLR group (HR=0.7; 95% CI: 0.43-1.22; p=0.2, Figure 3/C). Also the comparison of different types of resection showed no significant difference after unmatched (p=0.1, Figure 4/C) and matched (p=0.4, Figure 5/C) analysis.

**Cox regression analysis**

The results were summarized in Table 3. Tumor size > 2 cm (HR= 2.8; 95% CI: 0.65-3.48; p=0.01) and pN2 disease (HR= 3.4; 95% CI: 0.27-4.87; p=0.0003) were independent negative prognostic factors of overall survival in unmatched analysis and matched analysis (pT> 2cm: HR= 2.7; 95% CI: 0.47-1.58; p=0.02; pN2 disease: HR= 3.3; 95% CI: 0.78-2.33; p=0.005)

## DISCUSSION

The increasing age among the general population, improvements in imaging technology, and the use of CT scan in screening programs have produced larger numbers of elderly patients referring to their physicians with localized, early-stage NSCLC. LR is the standard of care for resection of NSCLC but it may not be so well defined for the elderly as it is for the younger counterpart.

When treating elderly patients, resection planning (LR or SLR) must carefully balance the risks of postsurgical morbidity and mortality against those affecting cancer recurrence and long-term survival. There are many elderly patients with poor preoperative functional reserve and increased comorbidity for whom LR is not recommended but that could benefit from a SLR that minimizes perioperative morbidity and mortality with a small decrement, if any, in long term-survival due to limited life expectancy. In fact, if left untreated, these patients die of their malignancy rather of age and/or comorbidities.

Having in mind such hypothesis, we evaluated in a multicenter retrospective study the impact of the extent of resection (LR versus SLR) on recurrence rate and pattern and as well as on long-term survival of elderly patients with Stage I NSCLC. The issue is still controversial due to the paucity of data in literature, most likely because older patients tend to be poorly represented in cancer treatment trials, and generally undergo fewer diagnostic and therapeutic procedures than younger patients [8].

The period following January 2006 was chosen for our analysis as during this time CT-PET scan was routinely performed in all participating centers for preoperative staging. Patients undergoing pneumonectomy were excluded since pneumonectomy is a well-known negative predictive factor of morbidity and mortality in elderly patients [9]. In addition, patients with a final histological diagnosis different from NSCLC (i.e. patients with small cell lung cancer or carcinoid tumor) and patients with radiologically non-solid nodules (i.e. GGO or mixed GGO) were excluded due to the different biologic behavior of these tumors.

Our study showed that LR did not confer a significant survival advantage over SLR. Similarly, Okami et al [10] in a retrospective review of 133 elderly (≥75 years) patients undergoing LR (n=79) and SLR (n=54) showed no substantial difference in the 5-year survival rate (67.6% and 74.3%; p=0.92). Mery et al. [11] using the SEER database found that among patients who were ≥ 75 years of age LR and SLR provided similar median survival (44 versus 42 months, respectively, p=0.47) but that there was a significant difference in survival in the younger subjects (both less than 65 and between 65 and 74 years of age). Dell'Amore [12] et al as well as Okami et al [13] confirmed that lobar vs. sublobar resection did not confer any survival benefit in octogenarian patients with c-Stage I NSCLC.

Despite the incidence of recurrence was similar for the two study groups, the pattern of recurrence was significantly different because locoregional recurrences were more frequent in SLR than in LR group. Similarly, Dell'Amore et al [12] found a 9% rate of local recurrence after LR and of 29% after SLR (p=0.001). Okami et al. [10] reported a higher incidence of local recurrence following sublobar rather than lobar resection in patients aged ≥ 75 years old. Since in all our cases SLRs had a radical intent with a 2 cm of normal lung margin, the suboptimal extent of pulmonary and mediastinal LN dissection might explain the higher incidence of locoregional recurrence seen in our SLR group compared to the LR group.

Guidelines from the National Comprehensive Cancer Network (NCCN) recommend that at least three different N2 stations should be sampled during lung cancer resection, but these goals were not routinely achieved, especially in the SLR group. In only 53% (48/90) of SLR patients three or more different N2 stations were sampled compared to 80% (119/149) in LR group. The less accurate mediastinal staging could also explain the significantly lower incidence of pN2 upstaging in SLR compared to LR group (3% versus 13%; p=0.01). Interestingly, segmentectomy compared to wedge resection had a higher incidence of LN stations sampled (62% versus 38%, respectively; p=0.01) and a loser incidence of local locoregional recurrence (3% versus 21%, respectively; p=0.03). Similarly, Landreneau et al [14] found that segmentectomy had a reduced risk of locoregional recurrence compared with wedge resection and that anatomic segmentectomy more closely approximated the oncologic results of lobectomy. Sienel et al [15] in a retrospective study of 87 patients with Stage I NSCLC unfit for lobectomy, found a lower rate of local recurrence (p=0.001) among patients who had segmentectomy, compared to patients undergoing wedge resection. Wolf et al [16] showed that patients undergoing SLR with LN sampled (n=45, 29%) had a local recurrence rate similar to that of patients undergoing LR, while SLR patients without LNs sampled (n=109, 71%) had a local recurrence rate more than double compared to LR patients (p=0.0594).

The multicenter and retrospective nature of this study reduces the possibility to evaluate the individual surgeon's decision and/or patient-related factors that may impact on the choice of performing or not an accurate mediastinal staging. The dissection along the segmental bronchus that is required for segmentectomy allows removal of adjacent hilar and mediastinal lymphatic drainage, which might explain the higher number of N2 lymph node stations resected during segmentectomy, compared to wedge resection. On the other hand, pre-operative clinical conditions may influence the decision to perform or not an accurate mediastinal LN resection. Most likely, patients undergoing complete LN staging were those with better medical condition and thus scheduled for lobectomy or an anatomic sublobar resection. Conversely, patients with poor clinical status were more likely to be scheduled for wedge resection and an accurate sampling or resection of mediastinal LNs was avoided in order to minimize perioperative morbidity and mortality.

However, these findings have been replicated in a number of large surgical series. El-Sherif et al [17] reported that more than half of lobectomy patients had an extensive nodes dissection, whereas only 20% of sublobar resection patients underwent adequate LN sampling ($p<0.0001$). Altorki et al. [18] in a recent multicenter study of the International Early Lung Cancer Action Program reported that 21% and 43% of patients undergoing LR and SLR, respectively, did not have any mediastinal LNs sampled. However, the 2 groups experienced similar long-term survival. Wolf et al. [15] found that, compared to patients who underwent lobectomy, patients undergoing sublobar resection were significantly less likely to have LN sampling at surgery (94% and 29%, respectively; $p<0.0001$). Finally, according to Kent et al. [19], 28% of patients having wedge resection had no LNs sampled.

The number of LNs and mediastinal LN stations sampled at the time of surgery improves the accuracy of pathologic staging, avoids misclassification of patients, and more adequately identifies which patients should be treated with adjuvant therapy. Indeed, our data confirm that pN2 was an independent negative predictor of survival. Although patients undergoing LR had more accurate mediastinal staging than patients undergoing SLR, long-term survival was not statistically different between the 2 groups. As a matter of fact, only 3 out of 12 pN2 patients in the LR group received adjuvant chemotherapy while the 9 remaining patients were deemed to be unfit for adjuvant treatment due to presence of comorbidity, the refusal of treatment by the family or the patient, or the subjective and sometimes unconscious perception of frailty by the physician or the family. On the other hand, 10 out of 12 (83%) SLR patients with local recurrence received radiotherapy following locoregional recurrence. This might explain why locoregional recurrence was not significantly associated with decreased survival.

Such finding was confirmed when comparing long-term survival between groups. The CSS curves of LR and SLR patients are much closer than those observed for OS, confirming the impression that most of the patients die for their pre-operative clinical conditions rather than for cancer. In addition, the life expectancy of 75 years old in Italy is about 87.8 years. The mean age of our SLR population is of $79.2 \pm 3.1$ and the 5-year OS after SLR was 45% and 41% in unmatched and matched groups, respectively. Despite the questionable oncological validity, sublobar resection seems to confer a survival advantage since more than 40% of our elderly population has a normal life expectancy.

In SLR group, 63% (57/90) of cancers were adenocarcinoma but only 1/57 (2%) had a lepidic pattern while the remaining 56/57 (98%) had a solid growth probably because we included in our analysis only patients with radiologically solid tumor but excluded GGO or mixed GGO lesions. Theoretically, additional survival advantage should be expected in elderly population having GGO lesions and undergoing sublobar resection. Evidences are accumulating that sublobar resections (segmentectomy or big wedge resection) are oncologically equivalent to standard lobectomy for small (≤2 cm) less invasive histology (Adenocarcinoma in situ or Minimal Invasive Adenocarcinoma) appearing as GGO on CT scan [20,21,22,23].

Nakayama et al. [24] studied sublobar resections (49 wedge resections, 14-segmentectomy) for 63 cT1N0M0 adenocarcinomas ≤2 cm in size. Overall survival was 95% for GGO and 69% for solid lesions, while recurrence-free survival was 100% in the former versus 57% in the latter.

Fang et al. [20] in a retrospective multicenter study including 173 segmentectomy patients and 181 patients with wedge resection found that OS, CSS, and local recurrence rates were similar between the two groups. Lung CSS rate at 10 years was significantly better in patients with GGO than in those with solid tumors (98.2% *vs.* 85.1%, P<0.0001). In multivariate Cox regression analysis, GGO was identified as an independent prognostic factor, while extent of resection had no impact on survival.

In agreement with other reports [25,26,27], tumor size was confirmed as independent prognostic factor in the multivariable analysis. Tumors smaller than 2 cm in diameter have a more favorable biology. Long-term survival was significantly worse for tumors larger than 3 cm. Port et al found that tumor size of ≤2 cm had a better 5-year overall survival than tumor size > 2cm (77.2% versus 60.3%; p=0.03) [20]. Similarly, Port et al [21] found that the 5-year survival rate in patients with tumors 2 cm or less in diameter was 77.2% as compared with 60.3% for those with larger tumors (p=0.03). Okada et al [22] in a retrospective study including 1.272 patients showed that a 10-mm increase in tumor size was significantly associated with reduced survival.

Finally, our data reveal that patients undergoing SLR had a significantly worse cardiorespiratory function and a higher Charlson comorbidity index, as compared with patients who underwent LR. However, there were no significant differences in postoperative morbidity and mortality between the 2 groups. Most likely, the limited resection and further preservation of lung volume contributed to limit postoperative complications and deaths.

### Study Limitations

Our study presents several limitations, as follows.

First, despite all patients had a standard pre-operative evaluation, surgical treatment and follow-up, there are differences among-participating centers about clinical, pathological information data and treatment strategy.

Second, due to the retrospective nature of the study, the patients were not randomly allocated to receive LR or SLR but this choice and surgical technique were influenced by the surgeons and each institution's preference and experience. Even though we used a propensity score method to balance the distribution of measured confounders, observational data do not provide the same level of evidence as a prospective trial. In addition, residual confounding due to unconsidered covariates may remain. In particular, despite all resection margins included at least 2 cm of normal lung and were negative for tumor (R0 resection), we have no data on the exact distance from tumor to resection margin or the ratio between tumor size and resection margin. In addition, no data on the total number of sampled LNs was available.

## CONCLUSIONS

Our data show that elderly patients, in poor general condition, with Stage I NSCLC may benefit from SLR, which is associated with similar rates of complications and perioperative mortality, when compared to LR. Furthermore, although the rate of locoregional recurrence was significantly higher in the patients who received SLR than in  LR cases, long-term survival was equivalent between the 2 groups. Further investigation is warranted to definitely elucidate the role of SLR in high-risk, elderly patients with Stage I NSCLC.

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**FIGURE LEGENDS**

**Figure 1.** Flow chart of study population

**Figure 2.** The comparison of between Lobar and Sublobar groups showed no significant differences in unmatched overall survival (p=0.1; Part A); cancer specific survival (p=0.3; Part B); and disease free survival (p=0.1; Part C).

**Figure 3.** The comparison of Lobectomy, Segmentectomy and Wedge resections showed no significant differences in matched overall survival (p=0.2; Part A); cancer specific survival (p=0.6; Part B); and disease free survival (p=0.2; Part C).

**Figure 4.** The comparison between different resections showed no significant differences in unmatched overall survival (p=0.1; Part A); cancer specific survival (p=0.5; Part B); and disease free survival (p=0.1; Part C).

**Figure 5.** The comparison of Lobectomy, Segmentectomy and Wedge resections showed no significant differences in matched overall survival (p=0.4; Part A); cancer specific survival (p=0.1; Part B); and disease free survival (p=0.4; Part C).