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Lung Cancer Prognosis in Elderly Solid Organ Transplant Recipients

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Abstract

Background—Treatment-related immunosuppression in organ transplant recipients has been linked to increased incidence and risk of progression for several malignancies. Using a population-based cancer cohort, we evaluated whether organ transplantation was associated with worse prognosis in elderly patients with non-small cell lung cancer (NSCLC).

Methods—Using the Surveillance, Epidemiology and End Results registry linked to Medicare claims we identified 597 patients age ≥ 65 with NSCLC who had received organ transplants (kidney, liver, heart or lung) prior to cancer diagnosis. These cases were compared to 114,410 untransplanted NSCLC patients. We compared overall survival (OS) by transplant status using Kaplan-Meier methods and Cox regression. To account for an increased risk of non-lung cancer death (competing risks) in transplant recipients, we used conditional probability function (CPF) analyses. Multiple CPF regression was used to evaluate lung cancer prognosis in organ transplant recipients while adjusting for confounders.

Results—Transplant recipients presented with earlier stage lung cancer ($p=0.002$) and were more likely to have squamous cell carcinoma ($p=0.02$). Cox regression analyses showed that having received a non-lung organ transplant was associated with poorer OS ($p<0.05$) while lung transplantation was associated with no difference in prognosis. After accounting for competing risks of death using CPF regression, no differences in cancer-specific survival were noted between non-lung transplant recipients and non-transplant patients.

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Disclosure

The authors declare no conflicts of interest.

Contribution of Authors

Keith Sigel and Juan Wisnivesky participated in the study design, data analysis, interpretation, and manuscript writing. Rajwanth Veluswamy participated in the data analysis, results interpretation, and manuscript writing. Grace Mhango participated in the data analysis and interpretation of results. Katherine Krauskopf, Anita Mehrotra, and Carlie Sigel participated in the results interpretation and manuscript writing.

Conclusions—Non-lung solid organ transplant recipients who developed NSCLC had worse OS than non-transplant recipients due to competing risks of death. Lung cancer-specific survival analyses suggest that NSCLC tumor behavior may be similar in these two groups.

Background

The number of Americans with solid organ transplants is increasing each year, with an estimated 197,593 transplant recipients alive in 2008(1). The average age of patients with solid organ transplants is also increasing due to the aging of the US population and improved long-term survival post transplantation(2). As a consequence, malignancies developing after organ transplantation are now a leading source of morbidity and mortality in this population(3).

Solid organ transplantation and its subsequent management with long-term immunosuppressive therapy has been associated with a greater risk of incident malignancies, including cancers of the head and neck, liver, and lung (4–6). Lung cancer, in particular, is emerging as the second most common malignancy in transplant recipients, after non-Hodgkin's lymphoma, excluding non-melanomatous skin cancer (7). Epidemiological studies have suggested that the risk of lung cancer development in transplant patients is more than double that of the general population(8).

Cancer outcomes data for several malignancy types, including colorectal cancers, breast cancers, and melanoma, have suggested that these cancers may behave more aggressively in transplant recipients (9–11). Limited data regarding lung cancer in organ transplant recipients have shown poorer overall survival (OS) compared to non-transplanted patients (11). It is unclear, however, if worse OS in transplant recipients with lung cancer is a result of more aggressive tumors, or other factors, such as an increased burden of comorbidities or a decreased tolerance of cancer therapies.

Clarifying the prognosis of lung cancer in solid organ transplant recipients has important therapeutic implications and may allow for a better understanding of potential differences in cancer biology and behavior in the setting of therapeutic immunosuppression. In this study, we used population-based data to compare the outcomes of older Medicare enrollees with lung cancer with and without prior solid organ transplant.

Methods

Study Population

Our study used data from the Surveillance, Epidemiology, and End Results (SEER) registry linked to Medicare claims. The SEER program has collected clinicopathologic data on incident cancer cases from population-based registries since 1973(12). From this data, we created a cohort initially including all incident cases of NSCLC diagnosed in patients ≥65 years old (the start of age-based Medicare eligibility). From this cohort, we identified all recipients of kidney, liver, heart and lung transplants prior to lung cancer diagnosis. We excluded all lung cancer patients enrolled in healthcare maintenance organizations or those without part B Medicare insurance (coverage for outpatient care) as we lacked some claims for these patients and could not ascertain comorbid conditions and use of chemotherapy. Our

final analytic sample included 114,879 patients, with 597 elderly transplant recipients (195 kidney, 103 liver, 111 heart, 109 lung, 19 heart/lung, 9 heart/liver/kidney, 27 liver/kidney, 19 heart/kidney, 5 heart/liver).

Study Variables

Main Exposure: Solid Organ Transplant—Solid organ transplants were identified with International Classification of Disease codes (ICD-9) or Diagnosis Related Group (DRG) codes designating solid organ transplants or complications associated with transplantation (ICD-9 996.81, V42.0, 55.6, 55.69 or DRG 302 for kidney transplant; ICD-9 996.83, V42.1, 37.51 or DRG 103 for heart transplant; ICD-9 996.82, V42.7, 50.59, 50.5, or DRG 480 for liver transplant and ICD-9 33.50, 33.51, 33.52, 996.84, V42.6 or DRG 480 for lung transplant) and CPT codes for organ transplant procedures (33945 for heart transplantation; 47135 or 47136 for liver transplantation; 50360 or 50365 for kidney transplantation; and 00580 or 32854 or 32853 or 32852 or 32851 or 33935 for lung transplantation). We collected data on the date of transplant surgeries (for subjects where these data were available) to determine the length of time from transplantation to lung cancer diagnosis. For most analyses we compared three groups: non-lung transplant recipients, lung transplant recipients, and untransplanted patients. We grouped lung transplant recipients separately because of several unique issues in this group, including cancers potentially developing in non-native organs (and therefore not reflecting the previous exposures of the recipient), and likely increased rates of increased chest imaging.

Covariates—We collected sociodemographic variables (age, sex, race/ethnicity, and marital status) and tumor characteristics (location, size, stage, and histology) from SEER. We used Medicare data to estimate patient income. Using Medicare claims, we applied a published algorithm to calculate modified Charlson comorbidity scores quantifying patients' burden of comorbid illnesses, an index that has been used previously in transplant patients (13–15). As a proxy for performance status, we searched for claims related to home medical services and nursing home use from 90 days before to 30 days following patients' lung cancer diagnosis (16).

Lung cancer surgery was identified using relevant SEER codes as well as Medicare claims. Administration of radiotherapy (RT) within four months of diagnosis was also established using both data sources. Treatment with chemotherapy was identified using a validated algorithm capturing Medicare claims for chemotherapeutic drugs (17).

Outcomes—Both SEER and Medicare provide survival time data, which were used as the primary outcome in study analyses. Survival analyses using SEER data were censored if no death was noted in SEER by December 31, 2009. Analyses using Medicare survival time were censored on December 15, 2011. Competing risk analyses used SEER data, as determination of the primary outcome relied on cause of death data (lung cancer versus non-lung cancer-related), obtained from SEER death certificate data. OS analyses used Medicare survival times.

Statistical Analysis—We first compared baseline characteristics of patients in three groups: those with a non-lung solid organ transplant, those with lung transplants, and those without solid organ transplants using ANOVA testing for our age comparison, and the chi-squared test for our binary and categorical comparisons. We then evaluated OS in patients with and without organ transplants. OS analyses show long-term outcomes resulting from all causes, including those driven by comorbidities (CV disease, DM, etc) and transplant-related complications as opposed to cancer-related complications. This is particularly true among patients with non-metastatic lung cancer. We estimated 5-year OS rates by transplant status using the Kaplan-Meier method. As organ transplant recipients tended to present with earlier stage lung cancer, we repeated these analyses stratifying the sample by stage (I–IIIA vs. IIIB–IV). To account for possible imbalances in lung cancer treatment among patients with and without prior transplant, we also performed additional survival analyses stratifying the cohort according to whether the patients received stage appropriate treatment (as defined by National Comprehensive Cancer Network criteria) or were untreated(18). To assess differences in OS after accounting for potential confounders, we fitted Cox models using solid organ transplantation as our primary exposure of interest, adjusting for age, race, sex, income, marital status, comorbidity score, cancer stage and histologic subtype, use of stage appropriate treatment, year of cancer diagnosis, nursing home residence, and use of home medical services. To assess the role of length of time from organ transplantation and complications of transplantation on survival, we also fitted unadjusted and adjusted Cox regression models with time to transplant as a primary exposure.

Organ transplant recipients are likely to have a reduced life expectancy due to the complications of transplantation and/or the medical conditions that led to the transplant(19, 20). These competing risks may not be fully accounted by OS analyses adjusting for comorbidities, as adjustment is unlikely to adequately represent the spectrum of severity of these conditions. Thus, we used conditional probability function (CPF) methods to compare the behavior of lung cancer in patients with and without prior transplantation. CPF methods isolate the risk of death from lung cancer given that patients have not died from competing causes of death. These methods are helpful in circumstances where Kaplan-Meier methods may be biased in the presence of competing risks(19, 20). We plotted CPF curves to determine the risk of death from lung cancer and tested for differences in survival by transplant status using the methods proposed by Pepe and Mori(21). As in the OS analyses, we then stratified this analysis by stage groups and use of stage appropriate treatment. To assess the association of organ transplantation and lung cancer prognosis adjusted for potential confounders, we fitted a multivariable conditional probability regression. This model estimated proportional odds of lung cancer death among patients with and without transplantation after controlling for competing risks and other confounders(20).

Based on the number of deaths and median survival observed among patients in the cohort, we estimated that the study had an 80% power to detect a 3% difference in median OS in organ transplant recipients (compared to non-transplanted patients) at a 0.05 significance level. All analyses were performed in SAS 9.2 (SAS Corporation, Cary, NC), STATA Version 10 (Stata Corporation, College Station, TX) and R Version 2.15.1 (R Development

Core Team). This study was reviewed by the Institutional Review Board of the Icahn School of Medicine at Mount Sinai and deemed exempt from review (#13-00016).

Results

The study included 469 (0.4%) patients with claims data indicating non-lung solid organ transplantation and 128 (0.1%) with evidence of lung transplants prior to lung cancer diagnosis. Solid organ transplant recipients were less likely to be female ($p<0.001$) and more likely to be married ($p=0.001$), and non-lung transplant recipients were more likely to be African-American, Hispanic or other non-white race ($p<0.001$) than patients without evidence of organ transplant (Table 1). In terms of histology, transplant patients were more likely to have squamous cell carcinomas and less likely to have adenocarcinomas than patients without transplants ($p=0.02$) and were also more likely to present with early stage cancers ($p=0.002$). Patients with a history of solid organ transplantation also had a greater burden of comorbid illness compared to patients without a history of organ transplantation ($p<0.001$).

Use of stage appropriate treatment was not different among patients with and without non-lung transplants for patients with stage I–IIIA NSCLC, but lung transplant recipients were more likely to receive surgical interventions than either non-lung transplant recipients or untransplanted patients ($p=0.02$). In NSCLC patients with advanced disease, transplanted patients were less likely to receive combined chemoradiotherapy and more likely to receive no treatment as compared to non-transplanted patients ($p<0.001$).

Overall Survival Comparisons

OS was similar among non-lung transplant patients compared to non-transplanted patients (Figure 1A; $p=0.05$) but was significantly better for lung transplant patients ($p=0.003$) compared to non-transplant patients. However, stratified analyses showed that non-lung transplant patients with stage I–IIIA NSCLC (Figure 1B; $p=0.01$) and stage IIIB–IV NSCLC (Figure 1C; $p=0.04$) had worse OS than untransplanted patients. Lung transplant patients, in contrast, had better OS than untransplanted patients with stage I–IIIA (Figure 1B; $p=0.02$) and stage IIIB–IV NSCLC (Figure 1C; $p=0.007$). Stage I–IIIA patients who received stage-appropriate lung cancer treatment had no difference in survival when compared by transplant status or lung versus non-lung transplant ($p>0.05$ for all comparisons), nor did patients with stage IIIB–IV NSCLC ($p>0.05$ for all comparisons). Untreated lung and non-lung transplant patients with stage I–IIIA NSCLC had worse OS compared to non-transplant patients (both $p=0.02$) but no significant differences in OS were found among untreated stage IIIB–IV patients (both $p>0.6$). OS also differed by transplant type among non-lung recipients, with heart transplant patients having worse survival when compared to patients who underwent liver or renal transplants (Figure 1F; $p=0.02$). Cox regression analyses showed that non-lung solid organ transplantation prior to cancer diagnosis was associated with worse OS (hazard ratio [HR]: 1.14; 95% CI: 1.03–1.26) after adjustment for potential confounders, but that lung transplantation was not associated with worse OS (HR: 1.11; 95% CI: 0.91–1.35). In unadjusted and adjusted analyses comparing OS among transplant

recipients we found no significant effect associated with length of time from transplant surgery to cancer diagnosis.

Conditional Probability Analysis

Conditional probability function curves showing the risk of lung cancer death conditional on no death from competing causes are shown in Figure 2. Non-lung organ transplant recipients had similar lung cancer survival compared to patients without transplants ($p=0.9$; Figure 2A). Similar findings were observed for patients with early ($p=0.5$; Figure 2B) or late ($p=0.3$; Figure 2C) stage disease, among those who received stage appropriate treatment ($p=0.07$; Figure 2D) or received no lung cancer treatment ($p=0.08$; Figure 2E). There were no differences in lung cancer survival by transplant type ($p=0.3$, not otherwise shown.)

Competing Risk Proportional Odds Regression

Multivariable competing risks analysis also showed that after accounting for non-lung cancer sources of mortality and controlling for potential confounders, there was no increase in the risk of lung cancer death associated with non-lung solid organ transplantation (Table 3; odds ratio [OR]: 1.17; 95% CI: 0.90–1.53) or lung transplantation (OR 1.11; 95% CI: 0.90–1.60).

Discussion

This population-based study of NSCLC outcomes in solid organ transplant recipients shows that although non-lung transplant patients have poorer OS, after accounting for competing risks of death in transplant recipients there is no difference in lung cancer-specific survival. We also found that lung transplant recipients had better survival than non-transplant patients in unadjusted analyses, but this was no longer observed after adjustment for potential confounders. The use of anti-rejection immunosuppressive medications has been shown to affect the overall risk of developing lung cancer. However, the tumors that may arise in the presence of these medications do not appear to act more aggressively. Moreover, transplant recipients who receive appropriate lung cancer treatment appear to have cancer-related outcomes similar to non-transplant patients. These results suggest that organ transplant recipients with lung cancer who are good candidates for lung cancer treatment should be managed with stage appropriate treatment.

The effect of chronic immunosuppression on lung tumor behavior is unclear. Immunosuppressive therapy inhibits the host-tumor immune response, impairing the ability of the lymphoreticular system to recognize and eliminate oncogenic cells(22). This mechanism is potentially responsible for the increased risk of NSCLC in transplant recipients. Some studies suggest that suppression of cell mediated immunologic processes, as with therapeutic immunosuppression to prevent transplant graft rejection, may also promote lung cancer progression(23). Studies evaluating prognosis of NSCLC in the setting of other chronic cell-mediated immunodeficiencies, such as HIV, have demonstrated mixed results. In a recent study, NSCLC patients with HIV had poorer prognosis after accounting for potential confounding factors and competing causes of death(24). Worse cancer-specific survival has been observed in other studies of lung cancer in the setting of HIV

infection(25). It is possible that these findings among HIV infected patients reflect cancer behavior in the setting of more severe immune suppression than with therapeutic immunosuppression, or alterations in different pathways of cell-mediated immune function, therefore explaining the lack of effect we have observed in transplant recipients.

Earlier studies of lung cancers among transplant recipients reported short time intervals between transplantation and cancer diagnosis, as well as more advanced initial stages of cancer, suggesting potentially more aggressive tumor behavior(11). However, these studies were limited by relatively small numbers of cancers(26, 27). The only previous population-based analysis compared outcomes of de novo lung cancer cases from a transplant registry to those of the general population as represented by SEER registry data, finding worse survival in transplant patients(11). However, this study was limited by a lack of adjustment for comorbid illness and competing risks of death, two important confounders of the association between transplantation and survival. The organ transplant patients in our study had a significantly greater burden of medical comorbidity than the non-transplanted patients. Conversely, in the present study we found that the differences in OS between lung cancer patients with and without non-lung solid organ transplants were due to competing risks of death, suggesting that lung cancers that develop in the setting of therapeutic immunosuppression do not exhibit more aggressive behavior. We also found that organ transplant recipients with de novo lung cancer diagnoses were more likely to present with early stage lung cancer than non-transplanted patients. This differs from previous studies of lung cancer in organ transplant recipients that reported higher rates of late stage lung cancers(11, 26, 28). Two of those studies did not have comparison groups, and all were much smaller than the current analysis, and not population-based. As transplant recipients receive more frequent medical care, it is possible that the increase in proportion of early stage cancers in this group is a result of increased surveillance, and not a difference in tumor biology. This hypothesis is further supported by the large proportion of early stage lung cancers found among lung transplant recipients, a group likely to have had frequent chest imaging.

The predilection for early stage lung cancers and lesser burden of comorbid illness in the lung transplant patients in our cohort likely contributed to the better OS we found in this group in unadjusted analyses. Unlike the non-lung transplant recipients, we did not find worse OS in lung transplant patients compared to untransplanted patients after adjustment for potential confounding factors. It is possible that either competing risks play less of a role in prognosis in this patient group, or its smaller size was underpowered to detect a difference. There is limited previous data on lung cancer prognosis in lung transplant patients, but our findings are consistent with a pooled analysis suggesting that these patients experience similar outcomes with appropriately treated early stage lung cancers as untransplanted patients(29).

Although chronic immunosuppression does not appear to lead to poorer prognosis in NSCLC patients that are transplant recipients, it may still be a factor in the pathogenesis of NSCLC in this patient population. We found higher rates of NSCLC with squamous cell histology in transplant recipients, a finding also reported in prior studies(26, 28). A possible explanation for the predominance of squamous cell cancers in patients who received

transplants is that chronic immunosuppression diminishes T-cell mediated control of viral infections. This can potentiate virally mediated carcinogenesis which is known to be associated with the development of squamous cell carcinomas in other organs(30, 31).

In our multivariable analyses (Table 3) we found that radiotherapy was associated with improved overall survival and worse lung cancer-specific survival. This is possibly explained by selection bias; if patients with good performance status but more aggressive tumors were offered treatment then radiotherapy could appear to improve overall survival but lung cancer-specific survival would be worse. Additionally, our overall survival analyses had two years longer follow-up than our cancer-specific survival analyses, and it is possible that the cancer-specific analysis was less influenced by the long-term benefits of radiotherapy and more reflected the short-term complications.

A major limitation of this study was the lack of data on immunosuppressive therapies used in the transplant recipients. Data regarding the optimal management of immunosuppressive therapies in transplant recipients with de novo malignancies is limited. Several studies have found anti-proliferative effects associated with the m-TOR inhibitor class of immunosuppressive agents, and these findings have been incorporated into existing recommendations for management of immunosuppressive therapy in cancers arising in transplanted patients(32). Clinical guidance has been published advocating conversion from calcineurin-based immunosuppression to proliferation signal inhibition-based regimens in eligible kidney and heart transplant patients with de novo cancers.(33, 34) Reduction of immunosuppression for kidney transplant recipients has also been suggested as a strategy for improving cancer outcomes.(34) In our study, it was unclear from SEER-Medicare whether transplant recipients were on immunosuppressive therapy at the time of cancer diagnosis, and if so, whether these medications were attenuated or discontinued following diagnosis.

This study has other strengths and limitations that should be noted. A major strength of using the SEER-Medicare registry is that it provides a large population-based sample, allowing us to report the lung cancer outcomes of the largest number of transplant recipients who have developed NSCLC to date. Information from Medicare claims allowed us to control for multiple confounders and more accurately evaluate the risk of lung cancer-specific death according to transplant status by using competing risks methods. We also expected imbalances in cancer characteristics, such as stage at diagnosis, between transplant recipients and non-recipients. The large number of patients in SEER-Medicare allowed us to account for these differences by stratifying the analyses by several patient and tumor characteristics. There are limitations to using SEER-Medicare data, particularly our inability to prospectively validate the transplant status of the patients we identified using claims data. However, the specificity of transplantation related claims has demonstrated high levels of accuracy when validated against clinical records.(35) We also lacked data on smoking status, so we were unable to control for the effect of smoking on survival. Additionally, we used modified Charlson comorbidity scores to quantify the burden of coexisting illness in this cohort. Modified Charlson comorbidity scores have not been validated in transplant patients, and therefore may not accurately represent the effect of comorbidity on outcomes in this group. To address this, we employed competing risk methods to further account for increased risks of death from comorbid illness. Finally, use of death certificate data to

determine cause of death has the potential to be inaccurate and could thus affect our competing risks analyses. However, death certificate validation studies suggest determination of lung cancer specific death is more accurate than death from other causes(36).

In this population-based study, non-lung solid organ transplant recipients with NSCLC experienced worse all-cause mortality than patients without transplants. This survival difference appears to stem from an increased burden of comorbidities and resultant competing, non-cancer causes of death in transplant recipients, rather than more aggressive cancer behavior. Physicians should thus continue to treat transplant recipients using stage appropriate guidelines.

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Abbreviations

NSCLC	Non-small cell lung cancer
SEER	Surveillance, Epidemiology and End Results Registry
OS	Overall Survival
CPF	Conditional probability function

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Figure 1.

Overall survival by transplant status (non-lung transplant recipients versus lung transplant recipients versus non-transplanted patients); (A) All patients; (B) Patients with stage I–IIIA NSCLC; (C) Patients with stage IIIB–IV NSCLC; (D) Patients who received stage appropriate NSCLC treatment; (E) Patients who did not receive NSCLC treatment; (F) Different non-lung transplant types compared versus non-transplanted patients.

Figure 2. Conditional probability function curves for lung cancer survival by transplant status. (A) All patients; (B) Patients with stage I–IIIA NSCLC; (C) Patients with stage IIIB–IV NSCLC; (D) Patients who received stage appropriate NSCLC treatment; (E) Patients who did not receive NSCLC treatment.

Table 1

Baseline Characteristics of Non-Small Cell Lung Cancer Patients by Transplant Status

Characteristic	Non – Lung Transplant N=469	Lung Transplant N=128	No Evidence of Transplant N=114,410	P-value
Age, years, mean	74	75	75	<0.001
Age at Transplant, mean	70	68	–	0.1
Female, No. (%)	174 (37)	56 (43)	52,093 (46)	<0.001
Race/Ethnicity, No. (%)				
White	362 (77)	108 (84)	95,334 (83)	<.001
African-American	43 (9)	<11 (<7)	9,684 (9)	
Hispanic	26 (6)	<11 (<7)	3,848 (3)	
Other	38 (8)	<11 (<7)	5,580 (5)	
Marital Status, No. (%)				
Married	272 (58)	87 (67)	60,447 (53)	0.001
Median Income in Area of Residence, No. (%)				
Lowest quartile	104 (22)	31 (24)	29,914 (26)	0.4
Second quartile	129 (28)	29 (23)	29,016 (25)	
Third quartile	123 (26)	38 (30)	27,720 (24)	
Highest quartile	112 (24)	31 (24)	27,647 (24)	
Modified Charlson Comorbidity Score, No. (%)				
<1	148 (32)	61 (47)	61,051 (53)	<0.001
1–2	76 (16)	33 (26)	29,185 (26)	
>2	245 (52)	35 (27)	24,174 (21)	
Histology, No. (%)				
Adenocarcinoma	218 (46)	64 (50)	56,540 (49)	0.02
Squamous cell carcinoma	183 (39)	48 (37)	37,894 (33)	
Large cell carcinoma	19 (4)	<11 (<4)	7,303 (6)	
Other	49 (11)	<11 (<4)	12,673 (11)	
Tumor Site				
Upper Lobe	242 (52)	64 (50)	57,383 (50)	0.07
Middle Lobe	22 (5)	<11 (<7)	4,592 (4)	
Lower Lobe	128 (28)	47 (36)	30,950 (27)	
Other Site	77 (16)	>11 (>7)	21,484 (19)	
Tumor Stage				
I	161 (34)	50 (39)	31,392 (27)	0.002
II	21 (5)	11 (9)	5,619 (5)	
IIIA	44 (9)	11 (9)	12,693 (11)	
IIIB	81 (17)	26 (20)	22,367 (17)	
IV	162 (35)	31 (24)	42,338 (37)	
Time from Transplant to Cancer Diagnosis, Years	3.3	3.0	–	0.5
Nursing Home Resident	72 (15)	12 (9)	13,945 (12)	0.03
Home Medical Services	110 (23)	25 (19)	23,257 (20)	0.09

Table 2

Frequency of Treatment Modalities by Transplant Status

Stage	Non-Lung Transplant <i>N</i> (%)	Lung Transplant <i>N</i> (%)	No Evidence of Transplant <i>N</i> (%)	P-value
Stage I–II				
Surgery	120 (66)	53 (87)	25,334 (68)	0.02
Lone Radiotherapy	40 (22)	<11 (<6)	7,605 (21)	
Other	<11 (<6)*	<11 (<6)	1,528 (4)	
No Treatment	>11 (>6)*	<11 (<6)	2,637 (7)	
Stage IIIA				
Surgery with Adjuvant Chemotherapy	<11 (14)*	*	1,884 (15)	0.9
Chemoradiotherapy	24 (55)	*	7,327 (58)	
Other	<11 (20)*	*	2,039 (16)	
No Treatment	<11 (11)*	*	1,440 (11)	
Stage IIIB–IV				
Radiation and Chemotherapy	45 (18)	11 (19)	17,222 (27)	<0.001
Lone Radiation or Lone Chemotherapy	109 (45)	25 (44)	31,330 (48)	
No Treatment	89 (37)	21 (37)	16,153 (25)	

* Exact numbers not reported to maintain patient confidentiality

Table 3

Adjusted Association Between Transplant and Lung Cancer Outcomes

Characteristic	Hazard Ratio for All-Cause Mortality	95% CI	Odds Ratio for Lung Cancer Mortality	95% CI
Non-Lung Solid Organ Transplant	1.14	1.03–1.26	1.17	0.90–1.53
Lung Transplant	1.11	0.91–1.35	1.11	0.90–1.60
Age (Per 10 Year Difference)	1.12	1.09–1.13	1.37	1.36–1.38
Female	0.81	0.79–0.82	0.70	0.68–0.72
Race/Ethnicity				
White	Ref		Ref	
African-American	0.96	0.94–0.98	0.95	0.89–1.01
Hispanic	0.97	0.93–1.00	0.91	0.83–1.00
Other	0.84	0.82–0.87	0.75	0.69–0.81
Married	0.96	0.95–0.98	0.87	0.84–0.90
Income in Zip Code of Residence Above Median	0.94	0.93–0.96	0.83	0.82–0.88
Nursing Home Resident	1.44	1.41–1.47	1.60	1.50–1.70
Home Medical Services	0.98	0.99–1.02	0.82	0.80–0.85
Modified Charlson Comorbidity Score				
<1	Ref		Ref	
1–2	1.06	1.04–1.07	1.12	1.08–1.17
>2	1.17	1.16–1.22	1.34	1.28–1.40
Tumor Stage				
I*	Ref		Ref	
II	1.66	1.60–1.72	2.84	2.64–3.05
IIIA	1.81	1.77–1.86	3.40	3.21–3.60
IIIB	2.21	2.16–2.26	5.03	4.76–5.32
IV	3.21	3.15–3.28	10.0	9.50–10.5
Tumor Histology				
Adenocarcinoma	Ref		Ref	
Squamous Cell Carcinoma	1.05	1.03–1.06	1.11	1.07–1.16
Large Cell Carcinoma	1.12	1.09–1.15	1.36	1.26–1.47
Other	1.07	1.04–1.09	1.25	1.17–1.33
Surgical Resection	0.36	0.35–0.37	0.16	0.14–0.16
Radiotherapy	0.90	0.89–0.91	1.17	1.13–1.21
Platinum-based Chemotherapy	0.64	0.63–0.91	0.60	0.57–0.62
Year of Cancer Diagnosis				
1992–1994	Ref		Ref	
1995–1997	0.99	0.96–1.01	0.98	0.91–1.05
1998–2000	0.95	0.93–0.98	0.85	0.80–0.90
2001–2003	0.94	0.91–0.96	0.68	0.64–0.72
2004–2006	0.84	0.82–0.86	0.38	0.35–0.41
2007–2009	0.78	0.76–0.80	0.07	0.06–s0.08

CI: Confidence Interval,

* Lung transplant cases not included in competing risk regression analysis.

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