Lung Cancer and Lung Transplantation

A Review

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Abstract: With the increase in the number of lung transplants, it is expected that there will be a corresponding increase in the number of lung cancers reported in these patients. Longevity of the transplant recipients, lung transplantation for chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis, a history of smoking, and the increasing age of the lung donors make lung cancer more likely. Nodules and masses seen in chest imaging in lung transplant patients call for work up until a final diagnosis is achieved because there is a high likelihood of a serious infection or malignancy. The presence of a native lung is a major risk factor for lung cancer occurring in the transplant setting. Lung cancer of donor origin is rare. Bronchioloalveolar carcinoma confined to one lung can potentially be treated by transplanting the affected lung. Treatment for patients with lung cancer in the lung transplant setting has to be individualized because of the complexity of their medical problems and multiple medications. Attention needs to be focused on detecting lung cancer early in these patients to achieve a favorable outcome.

Key Words: Lung transplantation, NSCLC, Bronchioloalveolar cancer.

Lung transplantsations are being done in much larger numbers since the first successful procedure in 1983.1 In the year 2005 alone, 1530 lung transplants were performed in North America. The major indications for transplantation are emphysema or chronic obstructive pulmonary disease (COPD) in 29% of patients receiving a transplanted lung, and idiopathic pulmonary fibrosis (IPF) in 24.4%. The 3-year survival after transplantation in 29% of patients receiving a transplanted lung, and idiopathic pulmonary fibrosis (IPF) in 24.4%. The 3-year survival after lung transplantation is now approximately 65%.2 Immunosuppression after solid organ transplant may increase the overall risk for malignancy because of decreased immune surveillance. Data from the Cincinnati transplant registry show a 3- to 4-fold increase in cancer in immunosuppressed organ allograft recipients. The statistics display a strikingly increased incidence of skin cancers, cancers of the lip, cervical intraepithelial neoplasia, vulval and vaginal carcinomas, Kaposi sarcoma, renal cell carcinomas, hepatocellular carcinomas, and non-Hodgkin’s lymphomas. However, the incidence of common malignancies, such as carcinomas of lung, breast, or colon, was not particularly increased.3 This scenario is likely to change with the changing profiles of both recipients and organ donors. COPD and IPF as major indications for transplantation lead to the presence of a pool of recipients with a higher baseline risk of developing lung carcinoma. The association of lung cancer and IPF has been reviewed in several excellent reviews.4–6 While there is some controversy about the pathogenesis and causation of lung cancer in patients with IPF. The lowest reported prevalence rates were in studies based on review of death certificates with the attendant risks of under–reporting.7,8 This risk is not completely eliminated with lung transplantation, especially in those patients who receive a single lung transplant and have a native lung in situ. The increasing demand for donor organs implies that there are donors who are older and have a history of smoking again increasing the risk of developing bronchogenic carcinoma after lung transplantation. This review will outline the risks, epidemiology, and prognosis of lung cancer associated with lung transplantation.

SEARCH STRATEGY

Search terms used were “Lung Cancer” and “Lung Transplantation” as key words in Ovid medline with no date limits. Search terms in Pubmed were “Lung Cancer AND Lung Transplantation.” Case series of lung cancers in lung transplant patients were manually identified from the search results.

Bronchogenic Carcinoma in the Native Lung after Single Lung Transplantation

There seems to be a gradual increase in the number of patients with lung transplant reported to have bronchogenic carcinoma more than the last two decades. In a single institutional review of 219 patients treated from 1987 to 1997, a single squamous cell carcinoma of the lung was reported from a total of 13 malignancies in 9 of the 219 lung transplant patients (0.46%).9 In a similar manner, another retrospective study reviewing heart and lung transplant patients at an institution from 1968 to 1997 found only a single squamous cell lung cancer in the native lung of a patient with IPF out of 99 patients who survived the first month after transplantation.10 Another report showed a slightly increased incidence...
of lung cancer in a series of patients transplanted from 1991 to 2000. Six of the 251 (2.4%) patients who received lung transplants developed lung cancer. Another retrospective review of 396 patients who received lung transplants between 1985 and 2001 found one lung cancer (0.25%); genotyping of the tumor revealed it to be of donor origin. In a larger analysis of 2168 patients from seven centers, 24 lung cancers (1%) were recorded, all in the native lung. This study reviewed patients who underwent single lung, bilateral lung, or heart lung transplants from 1981 to 2001 and survived beyond 1 month. The frequency of bronchogenic carcinoma in patients who had unilateral lung transplantation was 2%. Finally, Dickson et al. compared 131 consecutive single lung transplant recipients to 131 matched bilateral lung transplant recipients who were transplanted between 1992 and 2005. Of the single lung transplant recipients, 6.9% developed primary lung cancer, whereas none of the bilateral lung transplant recipients developed lung cancer. In the current decade, there seems to be a gradual increase in the rate of lung cancer in patients after lung transplantation (Table 1).

This subtle upward trend in the reported incidence of lung cancer in single center and multicenter studies is likely related to a variety of factors including some of the following.

- Longer survival of transplant recipients:

  The average death rate in the first year after transplantation came down from 290 per 1000 patient years at risk to 169 per 1000 patient years at risk in 2004. The Lung Allocation Score (LAS) system was introduced in May 2005 and an increase in death rates to 200 per 1000 patient years was noticed in 2005 likely because of sicker patients being given priority in the new system rather than the time on the transplant list. The latest ISHLT transplant registry data report a 1-year survival of 82.3% reflecting a continuing improvement in survival. Improvements in survival noted in the most recent years have been concentrated in the first 3 months after transplantation. This likely reflects improvements in surgical techniques and early complications rather than improvements in management of late complications like chronic rejection.

- Effect of immunosuppressive therapies:

  The influence of immunosuppression as an etiological factor for the development of malignancy is discussed later in the article.

- Proportion of patients receiving transplants for COPD and IPF:

  There has been an increase in the proportion of lung transplantations performed for pulmonary fibrosis and a concomitant decrease in the proportion of patients with COPD who received lung transplants with the institution of the LAS system. However, these two diagnoses still account for the majority of transplants performed.

- Increasing age of the donor pool:

  With the increasing demand for organs for lung transplantation, international recommendations now allow the use of donors who are older than 60. Incidence of smoking in both donors and recipients. Incidence of smoking in both donors and recipients.

TABLE 1. Retrospective Studies of Lung Transplant Patients with Lung Cancer in the Native Lung

<table>
<thead>
<tr>
<th>Author</th>
<th>Institution</th>
<th>No. of Patients</th>
<th>No of Patients with Lung Cancer in the Native Lung</th>
<th>%</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiekerkoetter et al. 9</td>
<td>Hannover Medical School, Germany</td>
<td>219</td>
<td>1</td>
<td>0.46</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Choi et al. 10</td>
<td>Stanford University</td>
<td>99</td>
<td>1</td>
<td>1.1</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Arcasoy et al. 11</td>
<td>University of Pennsylvania</td>
<td>251</td>
<td>6</td>
<td>2.4</td>
<td>2 Squamous cell cancers</td>
</tr>
<tr>
<td>Collins et al. 13</td>
<td>7 North American lung transplantation centers</td>
<td>2168</td>
<td>24</td>
<td>1</td>
<td>8 Squamous cell carcinomas</td>
</tr>
<tr>
<td>de Perrot et al. 12</td>
<td>Toronto General hospital</td>
<td>396</td>
<td>1</td>
<td>0.25</td>
<td>7 Adenocarcinomas</td>
</tr>
<tr>
<td>Dickson et al. 14</td>
<td>Duke University</td>
<td>131 Single lung transplant patients</td>
<td>9</td>
<td>6.9</td>
<td>Poorly differentiated NSCLC</td>
</tr>
</tbody>
</table>

All of the studies summarized in Table 1 report cancer occurring in the native lung. In fact, the presence of the native lung was the strongest risk factor for developing lung cancer after transplantation identified by Dickson et al. The data from the single institution and multiinstitution studies argue strongly for smoking as a risk factor for developing lung cancer after lung transplantation. Not surprisingly, it has been reported that smoking more than 60 pack-years is a marked risk factor. The widely varying time to detection in these studies likely reflects the length of follow-up in each study rather than any identifiable significance in pathogenesis (Table 2). Another potential risk factor for lung cancer after lung...
transplantation is the presence of posttransplant immunosuppression. The most often used immunosuppressive regimen was cyclosporine, azathioprine, and corticosteroids.\textsuperscript{9,11–13} The use of increasingly long-term immunosuppression may lead to higher incidences of cancer in these patients, although no data are available on the lung cancer risk after different immunosuppressive regimens for lung transplantation.

**Bronchogenic Carcinoma in the Recipient’s Explanted Lung**

Lung cancer in the native lung after lung transplantation may gradually be on the rise (Table 1). However, the presence of lung cancer in the explanted lung either known or surreptitiously found at surgery presents an intriguing clinical problem as well. Svendsen et al. reported two patients who underwent single lung transplantation whose explanted lungs revealed well-differentiated adenocarcinomas less than a centimeter in size. Both these patients did well with the lung transplantation effectively functioning as a lung resection.\textsuperscript{20} A retrospective review of 214 consecutive lung transplants from 1991 to 2004 from the Cleveland Clinic reported four instances (2%) where lung cancers were found in the explanted lung. There were three adenocarcinomas and one squamous cell carcinoma. The primary indication for transplant was emphysema in three of the patients and IPF in the other. The patient with IPF had a stage 4 adenocarcinoma and died 1 week after the transplant. The other three had stage 1 disease and survived for a minimum of a year.\textsuperscript{21} The Toronto lung transplant group reported six patients with bronchogenic carcinoma in the explanted lung. Three of the six patients died within 35 months after transplant, whereas one patient with lymphangitic carcinomatosis died of bronchiolitis obliterans 10 months after surgery with no evidence of recurrence.\textsuperscript{22} However, the staging of these patients was incomplete.

An international survey involving 67 centers reported 43 patients with primary bronchogenic cancer found in the explanted lungs on transplantation for emphysema and pulmonary fibrosis. Not surprisingly, the 5-year and 10-year survival of patients with stage 1 disease was much better than patients with stage 2 or stage 3 disease. Sixty-four percent of patients with stage 1 disease were alive after a median follow-up of 30 months posttransplantation, whereas 64% of stage 2 and 3 patients were dead from recurrence after 8 months.\textsuperscript{23}

From these reports, although small in number, it is clear that patients who are found to have stage 1 non-small cell lung cancer (NSCLC) in the explanted lung have a much better chance of recurrence-free survival compared with those that have stage 2 or 3 disease. The practice of doing computed tomography (CT) scans of the chest in some centers before the transplant procedure is likely to bring the number of such cases down but will not totally eliminate them.\textsuperscript{24} Even during the actual surgery, the lung tumor may not be evident on examination of the gross specimen, precluding mediastinal node sampling for full staging. In multiple instances in the series mentioned earlier, the tumor was noted on pathologic study postoperatively. As patients wait for lung transplantation attention and follow-up to changes in periodic imaging studies would be prudent. At present, there are no data regarding adjuvant therapy in these patients. Adjuvant chemotherapy should be administered as appropriate after a full staging work up as would be done for nontransplanted patients.

**Bronchogenic Carcinoma of Donor Origin**

In contrast to the many reports of lung cancer in native lungs of transplant patients, reports of primary lung cancer in donor lungs are scarce. A 25-year-old patient with cystic fibrosis who received a bilateral lung transplant from a 50-year-old former smoker presented with metastatic small cell lung cancer 13 months after transplant. He was treated with standard chemotherapy with no clinical response and died a month later. Molecular genetic analysis confirmed the donor origin of the malignancy.\textsuperscript{25} Likewise, a 54-year-old woman with end-stage COPD and a 100-pack-year smoking history who underwent a bilateral lung transplant from a 55-year-old woman with a 45-pack-year smoking history developed a stage 2A moderately differentiated adenocarcinoma of the lung 28 months after the transplant. Cytogenetic analysis confirmed the donor origin of the cancer. The patient did well after surgical resection.\textsuperscript{26} In addition to these two patients, a 25-year-old woman, nonsmoker with cystic fibrosis who received sequential bilateral lung transplants from a male donor, was reported to have limited stage small cell lung cancer in the transplanted lung. The origin of the cancer from the recipient was confirmed by fluorescence in situ hybridization for chromosomes X and Y.\textsuperscript{27} The very rare occurrence of primary lung cancers in the transplanted lung is probably because of the younger age and nonsmoker status of the donors in the early lung transplant program. With the acceptance of donors who are older and with a history of smoking, together with the longer survival of recipients primary lung cancers of donor origin may increase with time.
Bronchioalveolar Carcinoma and Lung Transplantation

Bronchioalveolar carcinoma (BAC) with intrapulmonary metastasis has been treated in some centers with lung transplantation. In general, these patients are younger and many have a limited smoking history. In addition, the tendency of BAC not to spread as rapidly outside the lungs but rather presenting with intrapulmonary metastasis has been thought to make it a suitable disease for attempts at cure by lung transplantation.28 Garver et al. reviewed seven patients who had disease confined to lungs and received single or bilateral lung transplants with the intent of achieving a curative resection. Four patients had recurrent disease after a prior resection and three had stage 4 disease. Four of the seven recurrences occurred within the donor lung within 10 to 48 months from transplantation. The presentation of recurrent disease in the donor lung so soon after transplantation raises a variety of interesting questions regarding pathogenesis including the intriguing possibility of an infectious etiology for cancer in these patients. All the recurrences were identified as of recipient origin by polymerase chain reaction of microsatellite DNA.29 This cohort of patients has a 52% 5-year survival that did not differ significantly from the survival rates in their total lung transplant population. It seems that lung transplantation may be of palliative value in selected patients in view of the prolongation of life and relief of symptoms.30 An international survey identified 26 patients who received lung transplants for BAC from 67 centers. The 5-year and 10-year survival was 39 and 31%, respectively. The recurrence-free survival at 5 years was 35% and the median time of recurrence was 12 months from transplantation. The site of recurrence was always pulmonary raising the possibility of resection with curative intent if detected early enough.23 Nevertheless, lung transplant for advanced BAC is currently performed only in a few centers.

Possible Etiology of Lung Cancer in the Transplant Setting

A malignancy occurring in an immunosuppressed patient raises the possibility of an infectious etiology. Recurrences of BAC have been reported in the healthy donor lung within just several years after implantation.29 Malignant transformation mediated by a viral oncogene is a tantalizing possibility when lung cancer occurs in the context of lung transplantation and immunosuppression. Oncogenic viruses have long been known.31 For example, HTLV-1 and HTLV-2 cause T-cell leukemia in humans.32 In thoracic cancers, the connection between cancer and infectious etiologies remains somewhat more tenuous. Jaagsiekte sheep retrovirus causes pulmonary adenocarcinoma in sheep resembling human adenocarcinoma of the lung.33 Simian virus 40-related DNA is expressed in HPV16-infected lung adenocarcinoma cell lines, reinforcing the idea that HPV infection could be a cofactor in lung cancer development.37 However, HPV infection has not yet been shown to cause malignant transformation in normal lung tissue. The frequency of HPV viral DNA detection in lung cancers from transplanted patients is unknown. A viral etiology for posttransplant lung cancer remains purely speculative.

Lung cancer occurring in the context of scarring was described several decades ago.38,39 The etiology of these “scar carcinomas” is usually connected to previous tubercular infection. A similar association with scarring because of histoplasmosis has been suggested by a pathologic study of T1 cancers.40 Case–control studies have shown an elevated odds ratio for lung cancer in patients with a history of previous pulmonary tuberculosis.41 An inflammatory response to recurring or chronic infections may be the key to the development of these lung cancers.42 Whether chronic infection and inflammation has a role in developing lung cancer in lung transplant recipients is not known but remains an intriguing possibility.

The obvious etiologic factor for the development of malignancies in patients after organ transplantation is immunosuppression. In the 1980s, the introduction of cyclosporine allowed increased numbers of successful lung transplants. The majority of the patients were maintained on a triple drug combination of a calcineurin inhibitor (cyclosporine), cell cycle inhibitor (azathioprine), and steroids.43 Tacrolimus, which was introduced in the 1990s, is being increasingly used in immunosuppression in lung transplant recipients because of a decreased incidence of acute rejection.44 There is little data in lung transplant patients comparing the incidence of lung cancer in the different immunosuppressive regimens. A group from Spain reported 10 patients among 129 lung transplant patients who developed different malignancies. They did not find a significant difference in the incidence of lung cancer in the different immunosuppressive regimens.45 Sirolimus has been shown to reduce the incidence of malignancy in renal transplant patients compared with other regimens in a transplant registry.47 Conversion to sirolimus-based immunosuppressive regimens have been noted raising the possibility of an association with HPV, a strong etiological factor for cervical cancer.36 Overall, about 20% of all lung cancers tested contain HPV DNA, mostly in squamous cell carcinomas. The most common serotypes found were HPV16 and 18, which are strongly associated with cervical cancer.35 The viral E6 protein has been shown to be expressed in HPV16-infected lung adenocarcinoma cell lines, reinforcing the idea that HPV infection could be a cofactor in lung cancer development.47 However, HPV infection has not yet been shown to cause malignant transformation in normal lung tissue. The frequency of HPV viral DNA detection in lung cancers from transplanted patients is unknown. A viral etiology for posttransplant lung cancer remains purely speculative.

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sion of the immunosuppressive regimen to one based on sirolimus in lung transplant patients diagnosed to have lung cancer is a strategy that may have positive effects in terms of inhibiting the growth of the tumor. We do note a case series of 29 patients with different malignancies after renal transplantation who had calcineurin inhibitors withdrawn and a sirolimus-based regimen initiated. Of the six enumerated lung cancer patients, at least two progressed to metastasis at the time of the report.52

The recipient origin of bronchioalveolar cancers in Garver et al. indicates that there is some amount of chimerism of the cells in the transplanted lung as discussed by the author. It is unclear at this point whether the migration of recipient’s cells into the transplanted lung is hematogenous from a source of stem cells like the bone marrow or a migration of cells along the airways.29 Myelosuppression has been shown to accentuate bleomycin-induced lung injury in mice. Bone marrow-derived mesenchymal stem cells transferred to the injured mouse was shown to migrate to the injured lung and be protective.53 Hematogenous spread of stem cells has important implications for the hope of preventing lung cancer by bilateral lung transplantation, because even after bilateral lung transplantation there is the possibility of cancer recurrence through implantation of circulating stem cells.

Most of the reported lung cancers after lung transplantation were in the recipient’s native lung that was left in situ. (Table 1). The study by Dickson et al. compared 131 consecutive single lung transplant patients with 131 consecutive bilateral lung transplant patients matched by native disease. There were nine single lung transplant patients who developed primary lung cancer in the recipient’s native lung, whereas none of the matched bilateral lung transplant patients developed lung cancer.14 This raises the question whether a bilateral lung transplant will be more beneficial to the patient. Whether bilateral lung transplantation is superior to single lung transplantation has been studied for many years. Significantly, better forced expiratory volume in the first second, single breath diffusing capacity, and arterial oxygen tension were noted in the bilateral transplantation group compared with the single lung transplantation group.44 Initial studies did not show a significant advantage of bilateral lung transplantation in terms of survival.55 Single lung transplants had an advantage because of the scarcity of donated organs. Meyer et al. reported on the long-term survival advantage for patients less than 60 years with COPD.56 The number of bilateral lung transplantations exceeded single lung transplantations by 2002 and accounted for 63% of the procedures performed in 2005. Survival after bilateral lung transplantation was significantly better compared with single lung transplantation in COPD and IPF.57 At present, there is insufficient data to predict how this shift to bilateral lung transplantation will impact the presentation of lung cancer in lung transplant patients. The impact of the increased proportion of bilateral lung transplantation is likely to be felt over the next few years.

**Diagnosis**

All lung transplant patients are followed with frequent chest radiographs immediately after transplant. Imaging becomes less frequent with time. The diagnosis of lung cancer was based on the radiologic finding of a new or enlarging nodule or mass in asymptomatic patients in the majority of cases reported.10 On the other hand, the majority of nodules and masses noted in transplant patients tend to be of infectious origin. Schuman et al. found 15 patients with new nodules or masses out of 159 patients who survived the first 3 months after transplant in a mean follow-up period of 32 months. Ten were of infectious origin; the other five consisted of two lymphomas, two lung cancers, and one lung infarct.58 After reviewing 234 lung transplants from 1990 to 2000, Lee et al. also concluded that the majority of the pulmonary nodules discovered after lung transplant were due to infectious causes or PTLD. They found solitary nodules to be due to lung cancer or PTLD, whereas multiple nodules were due to infectious causes.59

In retrospective reviews, it has been noted that the lesion that was finally biopsied to prove malignancy was actually present in previous radiographs in certain patients.59,60 This is particularly notable in patients who have single lung transplants for COPD and IPF. The scarring and nodularity in the native lung may conceal the radiologic changes that would raise the suspicion of lung cancer. Because of this, these tumors may present at a more advanced stage. End et al. noted that 8 of 64 patients developed pulmonary nodules in a median follow-up period of 5.8 months. They recommended surveillance CT scans as routine follow-up every 3 to 6 months because some lesions may be missed on chest radiograph.51 In 2002, the University of Texas Southwestern Medical Center in Dallas, Texas, instituted a protocol for annual screening chest CT protocol for all heart transplant patients with a smoking history greater than 10 pack-years. All four patients identified by CT scans were resectable compared with 6 of 16 patients with lung cancer identified by chest radiograph. The authors recommended “routine” chest CT scans for high-risk patients with significant smoking history.62 Similarly, a French group recommended twice yearly combined chest radiographs and chest CT scans to detect lung cancer early in heart transplant patients.63 It may be legitimate to extrapolate the experience with heart transplant patients to lung transplant patients and recommend once or twice yearly chest CT scans to detect lung cancer early at a resectable stage. A strong recommendation is to work up all nodules and masses seen in transplant patients until a definite histologic diagnosis is made. If suspicion for malignant pathology remains, periodic chest CT is advisable considering the seriousness of an infectious or malignant etiology.

PET scans and combined CT/PET scans are attractive as a mode to help in distinguishing whether nodules are likely to be malignant. However, it is difficult to conclude that PET scans give unequivocal proof of malignancy without a tissue diagnosis. PET scans have utility in distinguishing infections from rejection, but in addition there is a modest PET uptake that is noted even in asymptomatic lung transplant patients without infection or rejection.64 PET scans have been shown to be useful in the diagnosis of PTLD in solid organ transplant patients including lung.65,66 The reports however are
limited by the small number of patients and by not being prospective in nature. Although there is dearth of data addressing the utility of PET scans in lung transplant patients suspected of having lung cancer; it would be legitimate to conclude that PET scans, although likely to be helpful in diagnosis and staging, cannot be a substitute for obtaining a tissue biopsy. In any case, PET positivity of a nodule in the lung of a transplant patient merits further work up.

CT-guided transthoracic biopsy of the lung has been shown to have a high sensitivity and nearly 100% specificity. Transthoracic needle biopsy has been used to evaluate for rejection in lung transplant patient with acceptable sensitivity and specificity. Diagnostic accuracy increases with the number of biopsies taken from a nodule. Transthoracic needle biopsy can be associated with significant morbidity. In a report on eight patients with severe emphysema who had CT-guided transthoracic biopsy done to work up lung nodules before transplantation, six developed pneumothorax with four requiring chest tubes. Considering the already compromised lung function in lung transplant patients, transthoracic biopsies need to be approached with sufficient caution. Fiber optic bronchoscopy with multiple transbronchial biopsies have been used successfully in lung transplantation patients to evaluate for rejection and infection. This is another modality that can be used to obtain a tissue diagnosis where the imaging studies are suspicious for malignancy in lung transplant patients. If suspicion for malignancy remains after unsuccessful or inconclusive attempts at biopsy, periodic chest CT to monitor the progression of the nodule is advisable considering the seriousness of an infectious or malignant etiology.

**Treatment**

Individualizing treatment decisions for lung transplant patients are complicated by several contending factors. The functional capacity is rarely optimum, the respiratory reserve may already be low because of the underlying disease, and there maybe ongoing issues with renal insufficiency and infection. Chemotherapeutic agents may interact with the patient’s immunosuppressive agents. A retrospective review regarding the management of 17 lung cancer patients who were heart and lung transplant recipients reported a median overall survival of 12 months. No patient with stage 2, 3, or 4 disease survived more than a year after diagnosis. The 5-year survival of patients with stage 1 disease was 35%. Eleven patients had stage 1 or 2 disease; two patients with resectable disease were poor surgical candidates and were treated with radiation therapy. The majority of patients presented with incidental radiographic findings regardless of clinical stage. Considering the disappointing treatment results in advanced lung cancer in the transplant setting, attention should be focused on detecting the tumor at an early stage when it can be resected.

The number of lung cancers in solid organ transplant patients requiring adjuvant chemotherapy that have been reported are few, making it difficult to draw clear conclusions. It is instructive to note that 3 of 10 renal transplant patients with invasive breast cancer who were offered adjuvant chemotherapy elected not to have adjuvant chemotherapy because of concerns regarding the viability of the renal graft. Of the five individuals who underwent chemotherapy, the four who had functioning grafts did not develop transplant failure or renal insufficiency. Decision making for chemotherapy for lung cancer in lung transplant patients is likely to be more complicated, considering the different response of NSCLC to chemotherapy compared with breast cancer and the different chemotherapy regimens used for lung cancer, especially the platinum compounds which are more likely to cause renal insufficiency. Chemotherapy in lung transplant patients is also likely to be more risky in terms of opportunistic infections because the lungs are in constant contact with the external environment. A study on heart transplant patients who underwent surgery for lung cancer reported that 7 of the 25 patients had postoperative infectious complications and three patients died in the postoperative period.

A careful reduction in immunosuppression and a change of the immunosuppression to sirolimus are promising strategies that need to be specifically investigated in lung cancers in lung transplant patients. Prospective studies pooling patients from multiple centers internationally are required to obtain sufficient data to make cogent recommendations about treatment strategies in these patients.

**CONCLUSION**

Bronchogenic carcinoma in lung transplant patients is uncommon but likely to become more frequent with the changing demographics of lung transplantation. This is most likely to be a NSCLC of recipient origin in the native lung. A history of smoking, COPD, IPF, and advanced age of either recipient or donor seem to be risk factors for developing a posttransplant lung cancer. Screening prospective donors with a smoking history with a CT scan of the chest may reduce this risk. An early diagnosis is important because treatment outcome of advanced disease is disappointing.

**REFERENCES**


