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Pretransplant malignancy among lung transplant recipients in the modern era

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ABSTRACT

Background: Malignancy is a relative contraindication in transplant candidates, given the increased neoplastic risk accompanying posttransplant immunosuppression. However, the number of patients receiving a lung transplant despite pretransplant malignancy is rising, and their outcomes remain unclear. Our purpose was to examine the outcomes of lung transplant recipients with pretransplant malignancy in the modern era.
Methods: We evaluated the United Network for Organ Sharing registry for adult lung transplants that were completed between June 2005 and September 2016. Transplant recipients were stratified by pretransplant malignancy, with subgroup analysis by sex and active malignancy. The primary outcome was 5-year survival and the secondary outcome was cause of death. Kaplan–Meier estimates illustrated 5-year survival and multivariable Cox proportional hazards regressions controlled for demographics and comorbidities.
Results: Of 18,032 transplant patients, 1,321 transplant recipients (7.3%) possessed a pretransplant malignancy. Patients with pretransplant malignancy faced significantly greater mortality within 5 years (36.0% vs 32.8%, $P = .017$), an effect greatest in men with pretransplant malignancy (39.2% vs 33.7%, $P = .002$). Patients with pretransplant malignancy also faced greater risk of death from posttransplant malignancy (15.6% vs 9.4%, $P < .001$), particularly for those with active malignancy at transplant (34.8% vs 9.8%, $P < .001$). Pretransplant malignancy remained a significant predictor of 5-year mortality in adjusted Cox regressions (hazard ratio: 1.16 [1.05–1.27], $P = .003$).
Conclusion: Patients with pretransplant malignancy, and particularly men with pretransplant malignancy and those with active malignancy at transplant, are at an increased risk of 5-year mortality and posttransplant death from malignancy. Balancing individual risk of posttransplant malignancy with immunosuppressive care is necessary to optimize outcomes for pretransplant malignancy patients.
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Introduction

The need for immunosuppression after solid organ transplantation has long limited or excluded patients with pretransplant malignancies (PTM) from consideration for transplant.[1] The use of immunosuppressive therapies to prevent allograft rejection and subsequent failure puts patients with PTMs at potentially increased risk for cancer recurrence.[2] Furthermore, immunosuppressive therapy contributes a known and documented increased risk of de novo malignancies among transplanted patients.[2,3] As reported elsewhere, skin, lung, and prostate cancers may be especially prevalent in lung transplant candidates.[4]

Despite this concern, there are conflicting data to support the conclusion that lung transplant patients with PTM are at an increased risk of posttransplant malignancy. In an analysis of adult lung transplant recipients in the United States between 2000 and 2011, Beaty et al[5] concluded that PTMs were not associated with increased mortality in lung transplant patients at 5 years posttransplant.[5] However, given new listing practices and the increasing trend in recent years toward transplantation for patients

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Table I
Demographics of recipients with and without pretransplant malignancy

Demographics	No pretransplant malignancy ($N = 16{,}711$)	Pretransplant malignancy ($N = 1{,}321$)	P
Age (years)	55.2 ± 12.8	60.9 ± 10.4	.001
Female	6,804 (40.7%)	512 (38.8%)	.163
BMI (kg/m^2)	25.3 ± 4.6	25.4 ± 4.15	.720
Race			**< .001**
White	13,775 (82.4%)	1,227 (92.9%)	
Black	1,533 (9.2%)	48 (3.6%)	
Hispanic	1,019 (6.1%)	30 (2.3%)	
Asian	260 (1.6%)	13 (1.0%)	
Other	124 (0.7%)	3 (0.2%)	
Comorbidities			
Smoking history	10,156 (60.8%)	919 (69.6%)	**< .001**
Preoperative dialysis	53 (0.3%)	8 (0.6%)	.082
Diabetes mellitus	3,107 (18.6%)	191 (14.5%)	**< .001**
Previous cardiac surgery	736 (4.4%)	73 (5.5%)	.058
CMV positive	9,016 (54.0%)	685 (51.9%)	.141
Diagnosis			**< .001**
Obstructive/COPD	4,986 (29.8%)	419 (31.7%)	
PPH	347 (2.1%)	14 (1.1%)	
Cystic fibrosis	2,071 (12.4%)	25 (1.9%)	
Restrictive/IPF	6,280 (40.8%)	646 (48.9%)	
Other	2,487 (14.9%)	217 (16.4%)	
Pulmonary function			
FEV1 (%)	38.6 ± 20.8	40.7 ± 21.6	**< .001**
FVC (%)	48.5 ± 17.5	49.9 ± 18	**.002**
Preoperative mechanical ventilation	1,007 (6.1%)	89 (6.8%)	.313
Preoperative ECMO	451 (2.7%)	27 (2.1%)	.148
Mean PAP (mmHg)	27.8 ± 11	25.7 ± 9.4	**< .001**
Mean PCW (mmHg)	10.8 ± 5.5	10.4 ± 5.3	**.011**
Mean CO (L/min)	5.3 ± 1.4	5.3 ± 1.3	.805
Transplant year			**< .001**
2005–2008	4358 (94.3%)	263 (5.7%)	
2009–2012	5780 (92.4%)	477 (7.6%)	
2013–2016	6573 (91.9%)	581 (8.1%)	
Lung allocation score	46.7 ± 17.2	46.6 ± 16.9	.869
Mean wait time (days)	205 ± 385	143 ± 257	**< .001**
Preoperative creatinine (mg/dL)	0.85 ± 0.4	0.88 ± 0.53	**.015**
Double lung transplant	11,236 (68.1%)	796 (60.8%)	**< .001**
Ischemic time (hours)	5.15 ± 1.72	5.14 ± 1.83	.685
Donor age (years)	34.4 ± 14.2	35.4 ± 14.4	**.012**
Donor BMI (kg/m^2)	25.9 ± 5.3	26.1 ± 5.3	.156
Donor COD			.750
Anoxia	2,752 (16.7%)	225 (17.2%)	
Cerebrovascular	5,611 (34.0%)	464 (35.5%)	
Head trauma	7,615 (46.2%)	580 (44.3%)	
CNS tumor	108 (0.7%)	9 (0.7%)	
Other	412 (2.5%)	31 (2.4%)	
Donor/recipient sex match	11,348 (68.8%)	891 (68.1%)	.592
Donor/recipient CMV match	8,671 (52.7%)	696 (53.3%)	.676

BMI, body mass index; *CMV*, cytomegalovirus; *CNS*, central nervous system; *CO*, cardiac output; *COD*, cause of death; *COPD*, chronic obstructive pulmonary disease; *ECMO*, extracorporeal membrane oxygenation; *FEV1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *IPF*, interstitial pulmonary fibrosis; *PAP*, pulmonary arterial pressure; *PCW*, pulmonary capillary wedge pressure; *PPH*, primary pulmonary hypertension.

with PTM, outcomes may differ for patients with PTM since the adoption of the lung allocation score (LAS).[5] Furthermore, the effects of specific types of malignancies, including sex-specific cancers such as breast and prostate cancers, present a unique challenge.[2,5] Current guidelines suggest that each candidate be considered on an individual basis, although patients with active malignancies (other than basal cell skin cancers) within 2 years are discouraged from transplant, and 5-year waiting periods are advocated.[6]

Because the number of patients receiving a lung transplant (despite a pretransplant malignancy) is rising, continuing assessment of outcomes after transplantation is critical.[5] Furthermore, characterization of outcomes by sex and malignancy status at the time of transplant are critical to determining whether specific groups are at a greater risk for posttransplant malignancy and subsequently higher malignancy-related mortality. A better

Table II
Malignancy type in patients with pretransplant malignancy

Pretransplant malignancy	Recipients ($N = 18{,}032$)
None	16,711 (92.7%)
Any pretransplant malignancy	1,321 (7.3%)
Type	
Skin	468 (35.4%)
Genitourinary	142 (10.7%)
Breast	152 (11.5%)
Thyroid	22 (1.7%)
Tongue/throat/laryngeal	19 (1.4%)
Lung	42 (3.2%)
Leukemia	120 (9.1%)
Other	282 (21.3%)
Multiple	74 (5.6%)
Active malignancy at transplant	58 (0.3%)

Table III
Outcomes by pretransplant malignancy status

Outcomes	No pretransplant malignancy (*N* = 16,711)	Pretransplant malignancy (*N* = 1,321)	*P*
Acute rejection within 1 year	1,379 (8.4%)	115 (8.8%)	.594
5-year mortality	5,473 (32.8%)	475 (36.0%)	**.017**
Cause of death			**< .001**
Malignancy	611 (9.4%)	86 (15.6%)	
Cardiovascular	452 (6.9%)	44 (8.0%)	
Respiratory/BOS/rejection	1,888 (28.9%)	142 (25.7%)	
Other	3,582 (54.8%)	281 (50.8%)	

BOS, bronchiolitis obliterans syndrome.

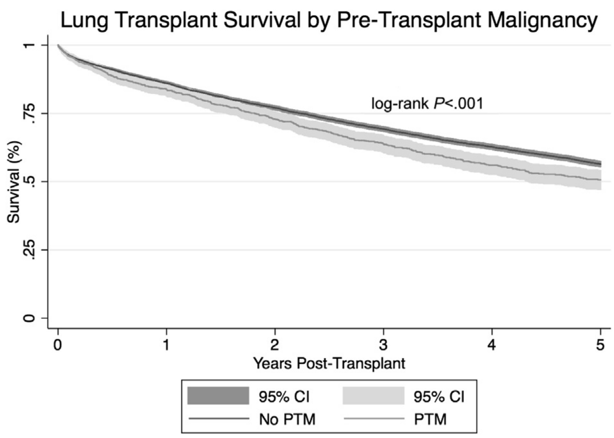

Fig 1. Kaplan-Meier survival estimate by presence of any pretransplant malignancy. Lung transplant recipients with a pretransplant malignancy faced greater mortality over 5 years than their counterparts without a pretransplant malignancy (log-rank *P* < .001).

understanding of the impact of PTMs in lung transplant candidates will inform clinical decision-making for transplant feasibility and appropriate posttransplant immunosuppressive care that balances rejection and malignancy risks. We hypothesized that patients with a PTM face increased mortality within 5 years, particularly from posttransplant malignancy. Thus, the purpose of this study was to examine the effects of PTM on mortality since the adoption of the LAS, with a particular focus on the differential impact of sex.

Methods

This was a retrospective study of all adult (>18 years of age) patients in the United Network for Organ Sharing (UNOS) registry undergoing lung transplantation from June 2005 to September 2016. We excluded patients who had experienced transplants and multiorgan transplants and those who were removed from the waitlist. Primary stratification was on the basis of any PTM. Secondary stratification included sex, active malignancy at transplant, and subtype of PTM, including skin, genitourinary, breast, thyroid, tongue/throat/laryngeal, lung, leukemia, other, and multiple cancers. The primary outcome was 5-year survival, and secondary outcomes included incidence of acute rejection within 1 year and cause of death.

Lung diseases were divided into 5 categories: obstructive disease, primary pulmonary hypertension, cystic fibrosis, restrictive or interstitial pulmonary fibrosis (IPF), and other diagnoses. Causes of death were defined as cardiovascular; malignancy; acute rejection, bronchiolitis obliterans syndrome (BOS), or respiratory; and other (including graft failure, multiple organ failure, and infection). Patients were categorized as either alive or dead posttransplant, with censoring at 5 years.

Demographic and comorbid factors for both transplant recipients and corresponding donors were analyzed for differences between PTM and non-PTM patients. Continuous variables were compared using the Kruskal-Wallis test and categorical variables were compared using χ^2 analyses. Kaplan-Meier curves were generated to estimate survival for transplant recipients differentiated by PTM. Cox proportional hazards regression models were utilized to evaluate the impact of any PTM on patient survival through the first 5 years after lung transplantation. Reported models included an unadjusted model and a standard model, controlling for age, sex, race, lung disease diagnosis, LAS) at transplant, organ ischemic time, transplant procedure (single versus double), and transplant year. All statistical analyses were performed using STATA 14.2 (StataCorp LLC, College Station, TX).

Results

Demographics

Of the 18,032 lung transplant recipients included for analysis, 1,321 (7.3%) were reported to have a PTM (Table I). Skin cancers constituted 35.4%, genitourinary cancers 10.7%, breast cancers 11.5%, and other cancers 21.3% of cases (Table II). Patients with PTM were on average older (60.9 vs 55.2 years of age, $P = .001$) and more likely to be Caucasian (92.9% vs 82.4%, $P < .001$). PTM patients were also more likely to have a history of smoking (69.6% vs 60.8%, $P < .001$), less likely to have diabetes (14.5% vs 18.6%, $P < .001$), more likely to be listed for restrictive lung disease/IPF (48.9% vs 40.8%, $P < .001$), and less likely to be listed for cystic fibrosis (1.9% vs 12.4%, $P < .001$).

The proportion of patients with PTM has increased through the years because patients with PTM accounted for 8.1% of transplants in 2013 to 2016 but only 7.6% of transplants in 2009 to 2012 and 5.7% of transplants in 2005 to 2008 ($P < .001$). Of interest, PTM patients spent significantly fewer days on the waiting list (143 vs 205 days, $P < .001$) and were less likely to receive a double lung transplant (60.8% vs 68.1%, $P < .001$). Differences in pulmonary function tests between the 2 groups were statistically significant but unlikely of clinical consequence, as presented in Table I. We observed no differences in pretransplant use of life support, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) between the 2 groups. No clinically significant differences in LAS, donor age, body mass index (BMI), cause of death, sex mismatch, or cytomegalovirus (CMV) matching were found between PTM and non-PTM cohorts.

Outcomes by pretransplant malignancy status

Although we observed no difference in the risk of acute rejection between patients with and without PTM (8.8% vs 8.4%, $P = .594$); patients with PTM were at an increased risk of mortality within 5 years posttransplant (36.0% vs 32.8%, $P = .017$ [Table III]).

Table IV
Analysis of active malignancy at time of transplant

Cause of death	No transplant malignancy ($N = 17{,}974$)	Transplant malignancy ($N = 58$)	Total	Odds ratio	P
Malignancy	689 (9.8%)	8 (34.8%)	697 (9.8%)	4.01 (1.90–8.50)	< .001
Cardiovascular	493 (7.0%)	3 (13.0%)	496 (7.0%)	1.93 (0.60–6.20)	.267
Respiratory/BOS/rejection	2,026 (28.7%)	4 (17.4%)	2,030 (28.7%)	0.31 (0.04–2.21)	.240
Other	3,855 (54.6%)	8 (34.8%)	3,863 (54.5%)	0.62 (0.32–1.20)	.159

BOS, bronchiolitis obliterans syndrome.

Table V
Cox hazards regression of malignancy on 5-year mortality

Factor	Hazard ratio	P	95% CI
Unadjusted PTM	1.20	**< .001**	1.09–1.32
Multivariable model			
PTM	1.16	**.003**	1.05–1.27
Age (years)	1.01	**< .001**	1.01–1.01
Male	1.10	**.001**	1.04–1.16
Race			
Caucasian	Ref		Ref
Black	1.06	.266	0.96–1.16
Hispanic	0.96	.522	0.85–1.08
Asian	0.92	.443	0.73–1.15
Other	0.86	.391	0.62–1.21
Lung allocation score	1.01	**< .001**	1.01–1.01
Ischemic time	1.02	**.050**	1.00–1.03
Diagnosis			
COPD	Ref		Ref
Primary pulmonary hypertension	1.41	**< .001**	1.17–1.70
Cystic fibrosis	1.18	**.010**	1.04–1.34
Restrictive/IPF	0.97	.464	0.91–1.05
Other	1.01	.826	0.92–1.11
Single lung transplant	1.22	**< .001**	1.15–1.30
Transplant year	0.98	**< .001**	0.97–0.99

COPD, chronic obstructive pulmonary disease; *IPF*, interstitial pulmonary fibrosis; *PTM*, pretransplant malignancy.

This difference in mortality can be visualized with the 5-year survival curves presented in Figure 1. Furthermore, PTM patients were more likely to die of a posttransplant malignancy compared with those without PTM (15.6% vs 9.4%, $P < .001$). Those with active malignancy at the time of the transplant were at even greater risk of dying of posttransplant malignancy than those with no PTM (34.8% vs 9.8%, $P < .001$ [Table IV]).

On unadjusted Cox regression analysis, the presence of any PTM significantly predicted death within 5 years (Table V; hazard ratio [HR]: 1.20 [1.09–1.32], $P < .001$). After multivariable adjustment for demographics and comorbidities, malignancy remained a significant predictor of mortality within 5 years (HR: 1.16 [1.05–1.27], $P = .003$).

The risks of overall and PTM-related mortality stratified by sex are presented in Table VI. Male patients with PTM experienced significantly higher rates of mortality within 5 years than men without PTM (39.2% vs 33.7%, $P = .002$). After excluding genitourinary cancers from analysis to account for prostate cancer, this difference in mortality persisted (38.4% vs 33.7%, $P = .009$). Female patients with PTM, however, were not at increased risk of mortality within 5 years relative to women without PTM (30.9% vs 31.3%, $P = .818$). Women with PTM faced the same risk of 5-year mortality as women without PTM, even after breast cancer was withheld from the analysis (31.3% vs 31.4%, $P = .567$). These differences in sex and mortality are presented in Figure 2.

Despite the finding of comparable mortality rates in women with and without PTM, women with PTM were more likely to die of posttransplant malignancy than women without PTM (odds ratio [OR] = 2.26 [1.48–3.45], $P < .001$). Men with PTM were also significantly more likely to die of posttransplant malignancy (OR = 1.57 [1.16–2.11], $P = .003$). These differences persisted even after excluding breast cancer in women and genitourinary cancers in men. Women (OR = 2.22 [1.33–3.69], $P = .002$) and men with PTM (OR = 1.65 [1.20–2.27], $P = .002$) were both more likely to die of posttransplant malignancies compared to their counterparts without PTM.

Discussion

Lung transplantation has been historically limited for candidates with an earlier malignancy because of the cancer recurrence risk with posttransplant immunosuppression. However, a growing number of patients with PTM have received lung transplants since the adoption of the LAS in 2005, with unclear impacts on mortality rates and causes of death. The current study analyzed 18,032 adult lung transplants since the adoption of the LAS, of which 1,321 (7.3%) possessed any PTM. Patients with any PTM were at significantly increased risk of death within 5 years and were more likely to die of posttransplant malignancy (15.6% vs 9.4%, $P < .001$) than patients without PTM. Although men and women with PTM both faced significantly greater mortality from posttransplant malignancy, only men with PTM faced significantly greater mortality within 5 years of transplant relative to men without PTM.

The International Guidelines for the Selection of Lung Transplant Candidates have historically suggested a waiting period of a minimum of 5 years for specific nonskin malignancies but acknowledge that the risk of recurrence for some patients may be too high for transplantation.[6] However, the association of PTM with posttransplant mortality has recently been questioned, with Beaty et al[5] finding no increased mortality in a smaller cohort of lung transplant recipients with less PTM (5.4%) across both pre-LAS and post-LAS epochs.[5] Our study, the first in the LAS era, supports keeping PTM as a relative contraindication for lung transplant, given the increased adjusted risk of mortality, particularly from posttransplant malignancy. Furthermore, our focus on the LAS epoch suggests a shift in outcomes with recent allocation practices, with an increased proportion of patients reporting a history of malignancy and greater risk-adjusted mortality for patients with PTM. However, our analysis also indicates that lung transplantation is still feasible, particularly for women with PTM. Lung transplantation for patients with PTM may necessitate a careful balance in the appropriate level of immunosuppression, with particular attention to the malignancy timeline and sex, to minimize the risks of rejection and posttransplant malignancy.

The comparative health of patients with and without PTM remains ambiguous. The finding that patients with PTM were on average 5 years older, more likely to have a diagnosis of restrictive lung disease or IPF, and more likely to receive a less-invasive single-lung procedure may support an overall greater frailty in PTM patients, which has been associated with poorer outcomes.[7,8] However, we observed no clinically significant differences in lung function tests or LAS at transplant between the 2 cohorts, and the adjusted regression accounting for baseline differences demonstrates that PTM remains a significant, independent predictor of 5-year mortality. Although patients with PTM experienced

Table VI
Analysis of sex and cancer

Pretransplant malignancy	5-year mortality	Cause of death: Malignancy	Cause of death: Malignancy OR (95% CI)
Women			
No PTM	2,133 (30.9%)	188 (7.3%)	Ref
PTM (all cancers)	158 (31.3%)	29 (15.1%)	2.26 (1.48–3.45)
	$P = .818$	$\mathbf{P < .001}$	
No PTM	2,133 (31.4%)	188 (7.3%)	Ref
PTM (excluding breast cancer)	108 (31.3%)	19 (14.8%)	2.22 (1.33–3.69)
	$P = .567$	$\mathbf{P = .002}$	
Men			
No PTM	3,340 (33.7%)	423 (10.7%)	Ref
PTM (all cancers)	317 (39.2%)	57 (15.8%)	1.57 (1.16–2.11)
	$\mathbf{P = .002}$	$\mathbf{P = .003}$	
No PTM	3,340 (33.7%)	423 (10.7%)	Ref
PTM (excluding GU cancer)	267 (38.4%)	50 (16.5%)	1.65 (1.20–2.27)
	$\mathbf{P = .009}$	$\mathbf{P = .002}$	

GU, genitourinary; *OR*, odds ratio; *Ref*, reference.

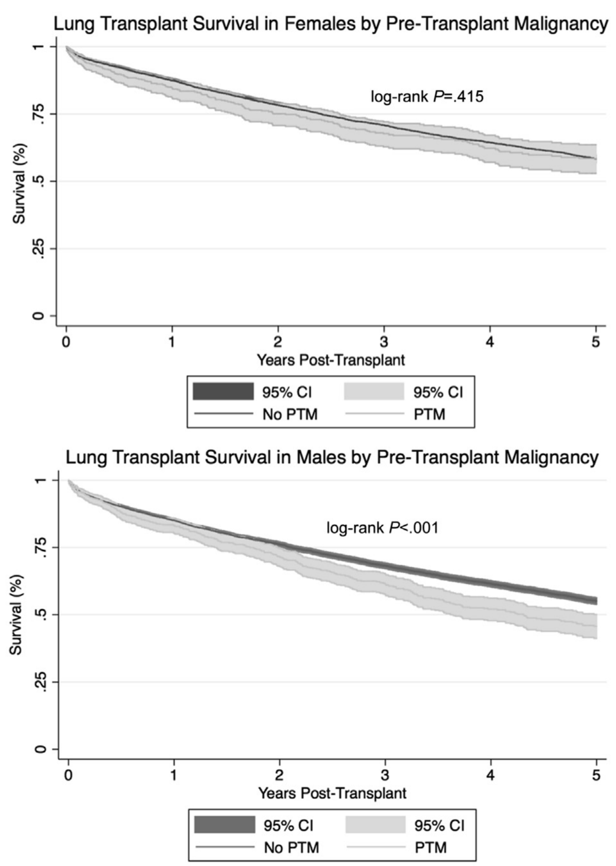

Fig 2. Kaplan-Meier survival estimate by presence of any pretransplant malignancy by sex. The 5-year mortality of women with pretransplant malignancy is not significantly different from women without PTM (log-rank $P = .415$). However, men with PTM have higher 5-year mortality than men without PTM (log-rank $P < .001$).

significantly shorter transplant waiting times, this difference may simply be reflective of increased single-lung transplantation, which reduces wait time on average by 100 days.[9] Furthermore, similar donor demographics and comorbidities suggest that PTM and non-PTM transplant patients received lungs of similar quality, reducing the likelihood that differences in transplanted organ quality are responsible for increased mortality in PTM patients.

As may be expected, those with an active malignancy at transplant were significantly more likely to die from a posttransplant malignancy relative to those without malignancy (34.8% vs 9.8%, $P < .001$). The literature confirms that recent malignancies are more likely to experience posttransplant recurrence, but our study is the first to confirm that lung transplant patients with active malignancy at transplant experience greater mortality from posttransplant malignancy.[1] Although it is unclear whether posttransplant death from malignancy indicates death from recurrence or a de novo cancer, the literature has extensively documented the elevated cancer risk for all lung transplant recipients, with risk ratios ranging 2.1–4.3 relative to the general population.[2,10–12] In vitro studies have demonstrated the ability of immunosuppressive drugs to promote tumor growth and metastasis,[13–16] and in vivo experiences with acute rejection—for which patients are treated with pulses of increased immunosuppression—exhibit a subsequent increase in the risk of malignancy.[11] Given that malignancy has emerged as one of the three leading causes of death for transplant patients and posttransplant malignancy survival remains poorer relative to the general population, our analysis indicates the importance of preemptively identifying and attenuating risk for patients with PTM.[17–21]

Perhaps most interesting, our study is the first to show that differences in survival within 5 years varied significantly by sex. Only men with PTM were significantly more likely to die within 5 years compared with those without PTM. Although the superior survival for female lung recipients is well-recognized, this analysis is the first to show disparate outcomes by sex for the population with PTM.[19,22] Considering the possible impact of sex-specific cancers, such as breast cancer for women and prostate cancer in men, the analyses were repeated with the exclusion of such malignancies and yielded similar results. Therefore, the differential outcomes by sex must be attributed to factors beyond sex-specific cancers.

Evidence underlying the difference in outcomes by sex remains uncertain and conflicted. Female recipients tend to receive lower doses of cyclosporine and other steroids, perhaps reducing the risk of adverse outcomes from immunosuppression without sacrificing graft survival.[23] Animal models have further shown a possible protective effect on estradiol on chronic rejection, potentially influencing outcomes for female patients.[23,24] Another possible explanation for the higher mortality in male patients, particularly from posttransplant malignancy, is the anabolic nature of testosterone, which has been shown in vitro to stimulate the growth of lung and colon cancer cells.[25] Among the general population, increased levels of testosterone in both men and women were associated with a significantly increased risk of early mortality from malignancy.[26] The relationship of testosterone and malignancy remains highly contested and merits further study because it could possibly underlie the differences observed in lung transplant outcomes by sex in patients both with and without PTM.[27]

This study has a number of limitations. UNOS does not provide access to relevant data regarding the nature of PTMs, including age at diagnosis, stage of malignancy, disease course and length of treatment, or the precise malignancy-free survival before transplantation. Furthermore, malignant cause of death was selected as a secondary end point because the database records only malignancy-related mortality, and not incidence of posttransplant malignancy, among recipients. We also cannot differentiate whether posttransplant death from malignancy is the result of de novo cancer or reoccurrence of a PTM. The UNOS database also does not include details of immunosuppressive regimens, so we are unable to correlate immunosuppression with outcomes. Despite the increasing number of transplants for patients with PTM and the broad range of years analyzed in this study, some cancer types remain rarely represented in lung transplants, limiting an analysis by cancer subtype. As with all databases, UNOS depends on accurate coding, and we are limited by the accuracy of the data and potential coding errors. Future research should explore more granular, institutional data on PTM characteristics and the nature of posttransplant malignancies developed.

In conclusion, the proportion of lung transplant recipients with a PTM is increasing. Patients with PTM face significantly higher mortality within 5 years, particularly from posttransplant malignancy, than patients without PTM. Our study is the first known to show that sex differences in mortality outcomes are present because women with PTM are not at increased risk of mortality, but men with PTM face significantly greater 5-year mortality relative to men without PTM. However, both men and women with PTM are significantly more likely to die of a posttransplant malignancy. These differences do not appear intrinsic to sex-specific cancers and thus warrant greater investigation. Ultimately, PTM patients necessitate increased surveillance and investigation into the role that immunosuppression may play in the development of posttransplant malignancies. Although transplantation appears feasible for PTM candidates, appropriate immunosuppression after a transplant may necessitate a careful weighing of the risks of rejection with the risks of posttransplant malignancy and death.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this manuscript.

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