SKIN

BRIEF ARTICLE

Characterizing Skin Cancers Arising for the First Time Following Solid Organ Transplant with Subsequent Recurrence

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ABSTRACT

Introduction: There is an established relationship between solid organ transplantation (SOT) and increased incidence of skin cancers. There is a paucity of data characterizing skin cancers arising for the first-time post-transplant that subsequently recur.
Methods: We conducted a retrospective review to identify SOT recipients (SOTRs) at our institution with recurrence of skin cancer that initially developed post-transplant ("recurrence"). Patients with pre-transplant history of skin cancer were excluded. Data was analyzed using one-sample t-tests.
Results: Of 530 SOTRs identified, 33 had recurrence (mean 3.97 $\pm$ 6.97). SOTRs with recurrence were male (87.9%), white (97%), renal recipients (75.7%) with a mean age at transplant of 56.52 [$\pm$11.69] years (p-value$\leq$0.001 each). Recurrences arose from SCC (66.7%) on the face or scalp (57.5%), which were invasive at time of diagnosis (63.6%) (p-value$\leq$0.001 each).
Conclusion: In our cohort, white renal and cardiac transplants and a history of smoking appear to have a higher risk for recurrence of de novo post-transplant skin cancers. Our data supports that all SOTRs should have close and routine dermatologic follow-up due to risk for skin malignancy, which are disproportionately high-risk and invasive at the time of presentation.

INTRODUCTION

There is an established relationship between solid organ transplantation (SOT) and increased incidence of skin cancers.[1] Exposure to ultraviolet A (UVA, 280 – 315 nm) and ultraviolet B (UVB, 315 – 400 nm) radiation significantly increases risk of developing keratinocyte carcinoma (KC) and malignant melanoma (MM) by promoting DNA damage and stimulating inflammation.[2] In patients receiving immunosuppressive treatment necessary to prevent graft rejection following any transplant, natural immunosurveillance mechanisms are inhibited.[2] Thus, there is an observed association between chronic immunosuppression and increased carcinogenesis as well as persistence of oncogenic viral infections.[3] In patients diagnosed with either KC or MM prior to organ transplantation, there have been observed increases in both mortality and recurrence,[4] however, little is known regarding skin cancers which arise for the

first-time post-transplant and subsequently recur. We aimed to further characterize the incidence of such recurrences in SOT recipients (SOTRs).

METHODS

After IRB approval was received by the Medical University of South Carolina (IRB-I, Pro00120456), a retrospective review was conducted to identify SOTRs at our institution who were seen within a dermatology clinic. Patients who had a history of skin cancer prior to transplant were excluded. Demographic data and information regarding transplant and dermatologic course were collected. Patients were then stratified by presence of any skin cancer arising for the first-time post-transplant, and then further divided by subsequent recurrence of post-transplant skin cancers (hereafter referred to as recurrence). Data was analyzed using one-sample t-tests.

RESULTS

Between January 1, 2012, and June 1, 2022, 530 SOTRs were seen within a dermatology clinic. The majority were white (63.58%) and male (70.19%), with a mean age of 49.44 years at time of transplant. Among SOTRs, 203 patients (38.3%) developed 1,641 skin cancers for the first-time following transplant, which included KC, MM, Merkel cell carcinoma (MCC), and porocarcinoma. SOTRs with cancerous lesions were white (95.1%), male (72.9%), renal transplant recipients (64.0%) with a mean age of 54.33 [±11.52] years at transplant.

A total of 33 patients experienced at least 1 recurrence arising from a de novo post-transplant skin cancer (mean 3.97 ± 6.97). Patients with recurrence were most often male (87.9%, p-value≤0.001), white (97%, p-value≤0.001), renal transplant recipients (75.7%, p-value≤0.001) with a mean age at transplant of 56.52 [±11.69] years. Slightly over half of patients are currently living (57.6%). Patients were also likely to be current or former smokers (57.6%, (p-value≤0.001) (**Table 1**).

Significant comorbid conditions include hypertension (p-value≤0.001), type 2 diabetes (p-value=0.002), hyperlipidemia (p-value≤0.001), chronic kidney disease/end stage renal disease (p-value≤0.001), and cardiomyopathy or coronary artery disease (p-value≤0.001) (**Table 1**). Risk factors for recurrence include family history of skin cancer (p-value=0.006), heart transplant (p-value=0.006), and the use of post-transplant meds including tacrolimus (p-value≤0.001), cyclosporine (p-value=0.006), mycophenolate mofetil (MMF) (p-value≤0.001), and prednisone ((p-value≤0.001) (**Table 2**).

First skin cancers were most commonly SCC (66.7%, p-value≤0.001), and invasive at time of diagnosis (63.6%, p-value≤0.001), of which half were high risk (50%, p-value=0.006). Subsequent skin cancers were most often SCC (69.7%, p-value≤0.001). Skin cancers most frequently developed on the face or scalp (57.5%, p-value≤0.001) (**Table 2**).

DISCUSSION

Given improvements made in post-transplant mortality rates with standardized immunosuppressive therapies, patients are living longer and incidence of post-transplant morbidities such as cutaneous malignancies are increased.[1] Skin cancers account for approximately 40% of all post-transplant malignancies. In fact, it is estimated that as

Table 1. Patient demographics of organ transplant recipients with first skin cancer occurring post-transplant, with subsequent recurrence.

	All SOTRs (n=530)	SOTRs with Post-transplant Skin Cancer (n=203)	SOTRs with Recurrent Post-Transplant Skin Cancer (n=33)	p-value
Age at transplant (mean, SD)	49.44 [±16]	54.33 [±11.52]	56.52 [±11.69]	<0.001*
Race (n, %)				≤0.001*
African American	177 (33.4%)	7 (3.4%)	0 (0%)	
American Indian/Alaska Native	2 (0.4%)	1 (0.5%)	0 (0%)	
Asian	7 (1.3%)	0 (0%)	0 (0%)	
Caucasian	337 (63.6%)	193 (95.1%)	32 (97%)	
Hispanic or Latino	5 (0.9%)	1 (0.5%)	1 (3.0%)	
Pacific Islander	1 (0.2%)	0 (0%)	0 (0%)	
Other	1 (0.2%)	1 (0.5%)	0 (0%)	
Sex (n, %)				≤0.001*
Female	372 (70.2%)	148 (72.9%)	4 (12.1%)	
Male	203 (29.8%)	55 (27.1%)	29 (87.9%)	
Transplant type (n, %)[+]				≤0.001*
Renal	374 (70.6%)	130 (64.0%)	25 (75.7%)	
Liver	80 (15.1%)	37 (18.2%)	1 (3.0%)	
Heart	85 (16.0%)	45 (22.2%)	7 (21.2%)	
Lung	16 (3.0%)	10 (4.9%)	2 (6.1%)	
Pancreas	49 (9.2%)	21 (10.3%)	1 (3.0%)	
Smoking Status				≤0.001*
Never Smoker	270 (50.9%)	78 (38.4%)	14 (42.4%)	
Current Smoker	18 (3.4%)	7 (3.4%)	1 (3.0%)	
Former Smoker	242 (45.7%)	118 (58.1%)	18 (54.5%)	
Comorbid Conditions				
Hypertension	397 (74.9%)	146 (71.9%)	23 (69.7%)	≤0.001*
Type 2 Diabetes Mellitus	187 (35.3%)	59 (29.1%)	9 (27.3%)	0.002
Hyperlipidemia	198 (37.4%)	86 (42.4%)	14 (42.4%)	≤0.001*
CKD/ESRD	289 (54.5%)	100 (49.3%)	21 (63.6%)	≤0.001*
Cardiomyopathy/CAD	143 (27.0%)	55 (27.1%)	10 (30.3%)	≤0.001*

SOTR: Solid organ transplant recipient
CKD: Chronic kidney disease
ESRD: End-stage renal disease
*Indicates statistically significant result (p-value ≤0.05)
[+]Patients may have received more than one organ type

Table 2. Risk factors for skin cancer recurrence in organ transplant recipients with skin cancer arising for the first-time post-transplant.

	SOTRs with Recurrent Skin Cancer (n = 33)	p-value
Family History of skin cancer		0.006*
Post-transplant Medications (n, %)		
Tacrolimus	25 (75.8%)	≤0.001*
Cyclosporine	7 (21.2%)	0.006*
Mycophenolate mofetil	18 (54.5%)	≤0.001*
Prednisone	27 (81.8%)	≤0.001*
Type of First Skin Cancer (n, %)		
Squamous Cell Carcinoma	22 (66.7%)	≤0.001*
*SCCis**	7 (31.8%)	0.006*
Invasive⁺	14 (63.6%)	≤0.001*
Low risk	4 (28.6%)	
High risk	7 (50.0%)	
Very high risk	4 (28.6%)	
Basal Cell Carcinoma	11 (33.3%)	≤0.001*
Melanoma in situ	1 (3.0%)	0.325
Location of Skin Cancer (n, %)		≤0.001*
Scalp	8 (24.2%)	
Face	12 (36.4%)	
Neck	2 (6.1%)	
Chest or back	3 (9.1%)	
Upper Extremities	5 (15.2%)	
Lower Extremities	2 (6.1%)	
Unknown	1 (3.0%)	
Total Number of Skin Cancers (n)	**n = 412**	
Squamous Cell Carcinoma	269 (65.3%)	
Basal Cell Carcinoma	138 (33.5%)	
Malignant Melanoma	5 (1.2%)	

*SCCis: Squamous Cell Carcinoma in situ.
**Indicates statistically significant result (p-value ≤0.05)
⁺Low risk: trunk/extremities, <2 cm OR well/moderately differentiated, <6 mm deep. High risk: trunk/extremities, 2 -4 cm OR anywhere on head/neck. Very high risk: any site >4 cm OR poorly differentiated, >6 mm deep, or perineural/lymphatic involvement.

many as 70% of patients with lower Fitzpatrick phototypes (I or II) will be diagnosed with a skin cancer within 20 years following transplant.[5] Among our cohort, there was a correlation between white patients, who tend to have Fitzpatrick phototypes I or II, and a higher risk for recurrence of skin cancers that arose for the first time post-transplant, in the absence of a pre-transplant history of skin cancer. Other risks factors correlated with recurrence among our cohort included renal or cardiac transplant, smoking status, and family history of skin cancer. Common transplant medications such as tacrolimus, cyclosporine, MMF, and prednisone were also correlated with increased risk for skin cancer recurrence.

CONCLUSION

It is evident that regular practice of skin cancer prevention strategies is critical for immunosuppressed patients.[1] Transplant recipients should perform monthly cutaneous self-examinations. As SOTRs are high-risk for post-transplant skin cancer, which are disproportionately high-risk and invasive at the time of diagnosis, transplant recipients should have regular and close examinations performed by a dermatologist. Additionally, a potential modification of the immunosuppressive treatment regimen should be considered should skin cancer arise.[4]

Conflict of Interest Disclosures: None

Funding: None

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