Risk Prediction Model for Basal Cell Carcinoma in Cardiac Allograft Recipients

Nandini Nair[a*], Zhiyong Hu[b], Dongping Du[b], and Enrique Gongora[c]

[a]Division of Cardiology, Department of Internal Medicine, Texas Tech Health Sciences Center, Lubbock, Texas; [b]Department of Industrial, Manufacturing and Systems Engineering, Texas Tech University, Lubbock, Texas; and [c]Department of Cardiothoracic Surgery, University of Alabama at Birmingham, Birmingham, Alabama

ABSTRACT

Background. Basal cell carcinoma (BCC) is the second most common skin cancers in posttransplant patients. Long-term immunosuppression predisposes the patients to higher risk. This study was undertaken to develop a risk prediction model using the United Network for Organ Sharing (UNOS) database.

Materials and methods. Heart transplant recipients (2000~2015) from the UNOS database were analyzed. The Cox proportional hazards model was applied to screen the predictors associated with the development of BCC. Stepwise forward selection with Akaike information criterion was done to obtain the multivariate model. Area under the curve was derived from the receiver operating characteristics curve to assess the quality of the prediction model. A risk scoring system was developed to stratify patients into different risk groups, and the occurrence rates of posttransplant BCC among different groups were compared.

Results. There were 24,374 patients who received heart transplantation within this study period, and 1211 recipients have been reported with BCC. The multivariate model provides area under the curves at 5, 8, and 10 years posttransplant of 0.77, 0.76, and 0.76, respectively, in the derivation set and 0.75, 0.74, and 0.74, respectively, in the validation set. The predicted and observed probabilities of developing BCC in 5 years agree well across different risk groups. Kaplan-Meier survival curves were generated, which demonstrate significant differences between subjects in different risk groups.

Conclusion. A risk prediction model has been generated for the first time for BCC with a c-statistic of $\geq$0.74 in both derivation and validation sets, making it a good tool for risk stratification.

ONE of the major causes of morbidity and mortality for patients receiving heart transplantation is the development of posttransplant malignancies owing to the extended survival under chronic immunosuppression [1,2]. Nonmelanoma skin cancer (NMSC) has been reported as the most prevalent cancer after heart transplantation [1,3-6]. Many studies have been conducted to analyze the potential risk factors of posttransplant skin cancers; male sex, older age, white race, and greater sunshine exposure have consistently been identified as important factors associated with NMSC [6-9].

A better understanding of the risk factors associated with posttransplant skin cancers is important for accurate risk stratification of heart transplant recipients. Although many risk predictors have been identified for skin cancer, few risk-stratification models have been developed to guide posttransplant skin cancer screening. In addition, available risk stratification models are developed either for all types of solid organ transplant recipients [10,11] or for organs such as liver [12] or kidney [13]

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*Address correspondence to Nandini Nair, 3601 4th Street, Lubbock, TX 79430. Tel: 6108641687. E-mail: Nandini.nair@gmail.com

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other than the heart. Furthermore, NMSC is often studied by pooling the data from both squamous cell carcinoma and basal cell carcinoma (BCC) patient groups [10,11]. Limited studies have focused on the risk assessment and cancer screening for BCC after heart transplantation.

This study developed a robust risk prediction model for the BCC after heart transplantation using the United Network for Organ Sharing (UNOS) database. The risk stratification tool presented here can guide physicians in conducting early BCC screening to increase skin cancer awareness and prevention. This can potentially reduce the burden of skin cancer morbidity and mortality among heart transplant population and improve posttransplant survival and health care management.

MATERIAL AND METHODS

Data Source and Study Population

The UNOS registry of thoracic organ transplantation database was purchased and used in this analysis on local institutional review board approval. The database was queried to include adult patients (≥18 years) who underwent heart transplantation between 2000 and 2015. Patients listed for and received multiorgan transplantation were excluded.

Outcome and Risk Factors

Baseline patient characteristics were assessed, which include demographic data (i.e., age, sex, race, and residential zip code at the time of transplantation) and primary diagnosis. Zip code information was converted into latitude coordinates per the suggestion of previous studies to investigate the effect of sunshine exposure [8]. Important pretransplant data such as patient status at transplant, patients' malignancy status at listing and transplant were collected. Donor-related risk factors including skin and other types of cancer history, recipient, and donor human leukocyte antigen (HLA)−mismatch level were considered. Recipients' most recent tests for panel reactive antibody (PRA) against class I and class II antigens were also included in the analysis. In addition, to study the effect of immunosuppression drugs, induction with different types of drugs including thymoglobulin, antithymocyte globulins, orthoclone anti-T cell antibody directed to CD3 (OKT3), daclizumab, basiliximab, and alemtuzumab were also included in the analysis. Whether and when a patient developed skin BCC after transplant was determined based on the posttransplant follow-up of malignancy status. Days between transplantation and the time of diagnosis of BCC or the last follow-up were determined as the time to event data. The time to event for patients who did not develop BCC by the last follow-up were considered as censored data.

Statistical Analysis

Patients derived from the UNOS database were divided into derivation (80%) and validation (20%) groups. Patient characteristics were compared between the derivation and validation groups as well as between the cancer and noncancer groups. Continuous variables were reported as mean (standard deviation), and categorical variables were summarized by percentages. A χ^2 test was done for comparison of categorical variables, and the Wilcoxon rank-sum test was used for comparison of continuous variables.

The Cox proportional hazards model was developed to study the association of different risk factors with the posttransplant BCC event. Univariate analysis was performed, and variables with a P value less than .1 were selected as inputs to the multivariate analysis. Stepwise forward selection was done to assess the impact of each variable on the Akaike information criterion. The multivariate model was used to predict the probability of developing posttransplant BCC at 5, 8, and 10 years. Receiver operating characteristic curves were plotted, and area under the curves were calculated to assess the accuracy of the prediction model. From the multivariate model, a score is determined for each variable according to the hazard ratio. Patients were stratified into different groups based on their total risk scores, and the predicted and observed probability of developing BCC in 5 years for each group were compared. In addition, Kaplan-Meier survival curves were generated to show the occurrence rates of BCC among different groups, and the log-rank test was applied to compare the intergroup differences. All the analysis was performed using MATLB software from MathWorks, Inc (Natick, Massachusetts). This project was carried out in accordance with the rules of the institutional review board.

RESULTS

Patient Characteristics

There were 27,995 patients aged ≥18 years who received a heart transplantation during the study period. By excluding patients with unknown status at transplant and/or unknown posttransplant BCC, the final study cohort contains 24,374 recipients for heart transplantation. The characteristics of the whole population, as well as the derivation and validation cohorts, are shown in Table 1. Continuous variables were expressed as mean (standard deviation), and categorical variables were summarized by percentages. No significant differences were observed between the derivation and validation groups for all candidate risk factors. Within the study population, 1211 recipients (4.97%) developed BCC, whereas 23,163 recipients (95.03%) were not reported with the event. The patients in the cancer group were older, had a higher percentage of male and white race, had a lower level of recipient and donor HLA mismatch level, and had a lower level of PRA against class I and class II. Patients with coronary artery disease at listing and with malignancy at listing and at transplant were more likely to develop BCC. In addition, patients in the cancer group were less likely to be in status 1A and more likely in status 1B or status 2 than patients in the noncancer group. Furthermore, patients who had induction therapy with OKT3 or daclizumab were more likely to develop posttransplant BCC.

Effect of Era of Transplantation on Skin BCC Incidence

It has been reported that the incidence rate of skin cancer has demonstrated significant difference among patients transplanted at different years [8]. To show the consistency of the dataset, BCC-free survival curves after heart transplantation were compared between recipients transplanted during 1987 to 1999 and during 2000 to 2015. Figure 1 provides the 10-year survival curves for these 2 patient cohorts, which shows patients transplanted in the more recent years (i.e., 2000 to 2015) had a significantly higher risk of developing skin BCC (P value < .001). We postulated that the difference might be owing to more aggressive posttransplant immunosuppression in the more

Table 1. Patient Characteristics

	Total (n = 24,374)	Derivation Group (n = 19,499)	Validation Group (n = 4875)	*P* Value for Derivation vs Validation	Cancer (n = 1211)	No Cancer (n = 23,163)	*P* Value for Cancer vs No Cancer
Age, y	52.1 (12.6)*	52.2 (12.6)*	52 (12.7)*	.449	58.5 (7.87)*	51.8 (12.7)*	< .001
Female	24.6	24.8	23.6	.0818	11.5	25.3	< .001
HLA mismatch level	4.67 (1.01)*	4.67 (1.01)*	4.68 (1.01)*	.514	4.56 (1.1)*	4.68 (1.01)*	.001
Latitude	37.4 (5.31)*	37.4 (5.31)*	37.3 (5.28)*	.496	37.1 (5.52)*	37.4 (5.30)*	.200
PRA							
Class I antigens	5.39 (16.4)*	5.41 (16.5)*	5.31 (16.0)*	.894	3.43 (12.5)*	5.5 (16.5)*	< .001
Class II antigens	3.99 (14.5)*	4.03 (14.6)*	3.85 (14.1)*	.694	2.64 (11.2)*	4.06 (14.6)*	.001
Race							
White	71.6	71.9	70.6	.068	97.5	70.3	< .001
Black	17.5	17.4	17.9	.406	0.165	18.4	< .001
Hispanic	7.22	7.09	7.71	.133	1.73	7.50	< .001
Other	3.64	3.61	3.8	.525	0.578	3.80	< .001
Diagnosis at listing							
Dilated myopathy	81.9	82	81.3	.21	82.1	81.9	.857
Restrictive myopathy	2.21	2.13	2.52	.0929	2.56	2.19	.392
Heart retransplant	2.66	2.68	2.59	.722	1.65	2.71	.0254
Coronary artery disease	4.61	4.52	4.97	.183	5.95	4.54	.0227
Hypertrophic myopathy	1.95	1.93	2.03	.642	1.65	1.96	.443
Valvular heart disease	2.01	2.03	1.91	.585	2.81	1.96	.0413
Congenital heart defect	2.45	2.47	2.4	.789	1.40	2.51	.0154
Other	2.23	2.21	2.32	.647	1.90	2.25	.421
Donor cancer history							
No	98.1	98.1	98.2	.707	98.3	98.1	.563
Yes	1.6	1.63	1.48	.46	1.40	1.61	.584
Unknown	0.275	0.262	0.328	.426	0.248	0.276	.853
Malignancy at listing							
No	92.7	92.6	93.0	.332	89.5	92.9	< .001
Yes	5.79	5.86	5.52	.360	8.59	5.65	< .001
Unknown	1.51	1.52	1.46	.754	1.90	1.49	.249
Malignancy at transplant							
No	98.0	98.0	98.0	.874	97.4	98.0	.152
Yes	0.414	0.41	0.43	.841	1.16	0.376	< .001
Unknown	1.58	1.59	1.54	.779	1.40	1.59	.607
Donor skin cancer history							
No	97.3	97.4	97	.145	97.1	97.4	.601
Yes	0.139	0.144	0.123	.732	0.248	0.134	.301
Unknown	2.51	2.44	2.83	.115	2.64	2.51	.771
Patient status at transplant							
Status 1A	46.3	46.1	47.0	.238	37.2	46.7	< .001
Status 1B	37.7	37.8	37.2	.426	41.5	37.5	.005
Status 2	16.1	16.2	15.8	.581	21.4	15.8	< .001

(*continued on next page*)

Table 1 (*Continued*)

	Total (n = 24,374)	Derivation Group (n = 19,499)	Validation Group (n = 4875)	*P* Value for Derivation vs Validation	Cancer (n = 1211)	No Cancer (n = 23,163)	*P* Value for Cancer vs No Cancer
Induction with thymoglobulin	14.4	14.3	14.9	.230	15.0	14.4	0.520
Induction with ATGAM	4.96	4.87	5.33	.179	5.28	4.94	0.593
Induction with OKT3	2.53	2.52	2.59	.789	5.62	2.37	<0.001
Induction with daclizumab	8.23	8.25	8.15	.819	12.6	8	<0.001
Induction with basiliximab	17.2	17.2	17.5	.572	11.9	17.5	<0.001
Induction with alemtuzumab	1.52	1.59	1.23	.067	0.991	1.55	0.124

ATGAM, anti-thymocyte globulin; OKT3, orthoclone anti-T cell antibody directed to CD3; PRA, panel reactive antibody.

* Continuous variables are expressed as mean ± standard deviation shown in parentheses. The other values are categorical variables expressed as percentages.

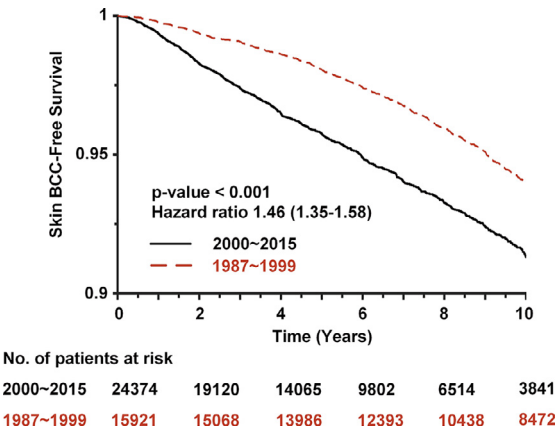


Fig 1. Skin BCC-free survival curves for patients transplanted during different time periods. BCC, basal cell carcinonma.

recent years. Considering the impired overall survival in the recent era because of newer immunosuppressive agents, risk model was developed using the data between 2000 and 2015.

Prediction of BCC

The univariate Cox regression analysis (Table 2) showed that age, sex, race, latitude, HLA mismatch level, PRA, malignancy at listing and at transplant, heart retransplant, patients' status at transplant, and induction therapy with OKT3 or daclizumab were significantly associated with posttransplant BCC ($P < .05$). Variables with a P value less than .1 were selected as inputs to the multivariate analysis. Furthermore, stepwise forward selection was performed to assess the impact of each variable on the estimator of model prediction error (i.e., Akaike information criterion). Six variables were included in the final multivariate model (Table 3), which include age, sex, race, latitude, malignancy at listing, and induction therapy with daclizumab. The receiver operating characteristics for 5, 8, and 10 years posttransplant BCC prediction showed area under the curves of 0.77, 0.76, and 0.76, respectively, in the derivation set and 0.75, 0.74, and 0.74, respectively, in the validation set (see Fig 2 A, B for the derivation and validation groups, respectively).

Risk Stratification

From the multivariate model, a risk score was developed to stratify patients into 4 risk groups by 5-year posttransplant incidence rate of BCC. The risk sore allocated points to age, sex, race, latitude, malignancy at listing, and induction with daclizumab. Points of 0, 1, and 2 were respectively assigned to patients younger than 40 years old, between 40 and 60 years old, and older than 60 years old; 0 and 1 were respectively assigned to female and male patients; patients with resident latitude $\leq 42^{o}$ got 1 point whereas patients with resident latitude $\geq 42^{o}$ got 0; white race patients and other race patients, respectively, had points of 3 and 0; patients with malignancy at listing got 1 point, otherwise 0 was assigned; patients who had induction

Table 2. Univariate Cox Regression Analysis

Covariates	Hazard Ratio			*P* Value
	Mean	95% CI		
Age	1.07	1.06	1.07	< .001
Female	0.380	0.311	0.464	< .001
HLA mismatch level	0.897	0.845	0.953	<.001
Latitude	0.979	0.968	0.990	< .001
PRA				
Class I antigens	0.995	0.99	1.00	.049
Class II antigens	0.995	0.99	1.00	.072
Race				
White	1			
Black	0.010	0.003	0.040	< .001
Hispanic	0.164	0.099	0.274	< .001
Other	0.120	0.050	0.288	< .001
Diagnosis at listing				
Dilated myopathy	1			
Restrictive myopathy	1.35	0.887	2.07	.161
Heart retransplant	0.568	0.335	0.964	.036
Coronary artery disease	1.15	0.873	1.50	.327
Hypertrophic myopathy	0.751	0.451	1.25	.273
Valvular heart disease	1.23	0.83	1.81	.307
Congenital heart defect	0.672	0.41	1.10	.115
Other	0.884	0.547	1.43	.615
Donor cancer history				
No	1			
Yes	0.936	0.562	1.56	.801
Unknown	1.01	0.252	4.04	.990
Malignancy at listing				
No	1			
Yes	1.89	1.51	2.36	< .001
Unknown	1.03	0.655	1.63	.890
Malignancy at transplant				
No	1			
Yes	2.74	1.42	5.29	.003
Unknown	0.58	0.336	1.00	.052
Donor skin cancer history				
No	1			
Yes	0.936	0.562	1.56	.801
Unknown	1.01	0.252	4.04	.99
Patient status at transplant				
Status 1A	1			
Status 1B	1.16	1.00	1.33	.043
Status 2	1.07	0.897	1.27	.463
Induction with thymoglobulin	1.13	0.943	1.34	.189
Induction with ATGAM	0.978	0.735	1.3	.876
Induction with OKT3	1.42	1.06	1.89	.018
Induction with daclizumab	1.21	1.00	1.47	.048
Induction with basiliximab	0.978	0.805	1.19	.824
Induction with alemtuzumab	0.759	0.407	1.42	.387

ATGAM, anti-thymocyte globulin; OKT3, orthoclone anti-T cell antibody directed to CD3; PRA, panel reactive antibody.

with daclizumab got 1 point, otherwise 0 was assigned. A total risk score ranging from 0 to 9 can be calculated for each patient by summing the point of each variable. The patients were stratified into 4 groups: very low-risk group (score $\leq$ 3, n = 5818), low-risk group (score = 4 or 5, n = 6650), moderate-risk group (score = 6 or 7, n = 11,315), and high-risk group (score $\geq$ 8, n = 591). The predicted and observed probabilities of developing BCC at the fifth year were computed and compared in Fig 3, which agree well with each other. The stratification showed the risk of developing BCC after transplant in the high-risk group increased sixfold compared to the low-risk group.

Table 3. Multivariate Cox Regression Analysis

Covariates	Hazard Ratio			*P* Value
	Mean	95% CI		
Age	1.051	1.043	1.059	< .001
Female	0.499	0.407	0.610	< .001
Latitude	0.967	0.955	0.978	< .001
Race				
White	1			
Black	0.013	0.003	0.054	< .001
Hispanic	0.171	0.102	0.287	< .001
Other	0.131	0.054	0.316	< .001
Malignancy at listing				
No	1			
Yes	1.705	1.361	2.135	< .001
Unknown	1.088	0.690	1.715	.728
Induction with Daclizumab				
No	1			1
Yes	1.359	1.122	1.647	.002

To further demonstrate the occurrence rate of BCC after transplantation, Kaplan-Meier survival curves and risk tables were generated for each group (Fig 4). As seen in Fig 4, the very low-risk group shows significantly lower probability of developing BCC than the high-risk group, and about 14% of the subjects in the high-risk group have BCC after 5 years. In addition, a log-rank test was performed to test the null hypothesis that there is no difference regarding the incidence rate among different groups. The result showed that the incidence rate of the high-risk group was 1.84-fold higher than that of the moderate-risk group, the incidence rate of moderate-risk group was 2.67-fold higher than that of the low-risk group, and the incidence rate of low-risk group was 8.77-fold higher than that of the very low-risk group. *P* values of the log-rank test were significantly small ($\leq$ 0.05), illustrating the differences between groups.

DISCUSSION

Risk Predictors

This paper summarizes a retrospective study of the posttransplant event of BCC using the UNOS database. The final study cohort includes 24,374 heart transplant recipients, among which 4.97% have been reported with BCC. Based on the Cox proportional hazards model, 6 different predictors were selected to predict the occurrence of BCC after transplantation. Older age, male sex, low latitude, white race, malignancy at listing, and induction therapy with daclizumab increased the risk of cutaneous BCC. Among all these predictors, older age, male sex, and white race are factors that have been consistently reported as risk factors for the development of skin cancer in both the general population and the solid organ transplantation recipients [6-9,14-16]. Malignancy history at listing is an indicator for the history of cancer, which has been recognized as risk factors for

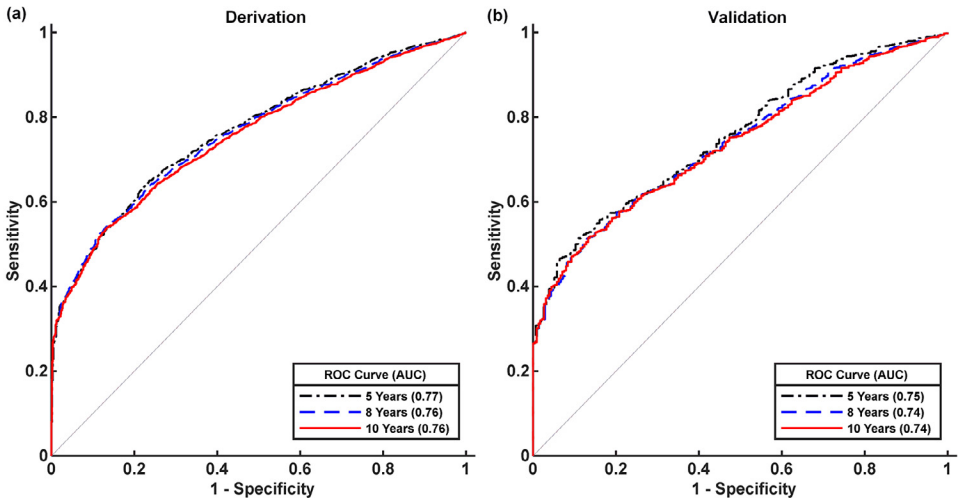


Fig 2. ROC curves of skin BCC prediction at 5, 8, and 10 years posttransplant. **(A)** Derivation set. **(B)** Validation set. BCC, basal cell carcinonma; ROC, receiver operating characteristics.

skin cancer development in various studies [9,10,17] and was also identified as a major risk factor for posttransplant BCC in our study. Latitude was also identified as a significant factor; the higher the latitude, the lower the risk of developing BCC. This is a reasonable result because latitude is used as proxy for the ultraviolet exposure level, and the latter is an established risk factor of skin cancer in the general population [8,13].

Incidence and Risk Score of BCC in Posttransplant Recipients

The risk scoring system stratifies patients into 4 risk tiers, and the average 5-year observed and predicted incidence rates of BCC are 0.003 and 0.001, 0.022 and 0.020, 0.069 and 0.066, and 0.135 and 0.134, respectively (Fig 3). Among all the predictors, latitude level is negatively correlated with the cancer event. A latitude level higher than 42° decreased the total risk score by one unit. The model highlighted white race as the most significant risk factor, and white race alone placed a recipient with a latitude level ≤42° in the 2nd risk tier (i.e., low-risk group) and caused a 5-year BCC risk of 1% (Fig 5). In addition, the risk factors of male, white race, and age over 40 years old placed a recipient with a latitude level ≤42° in the moderate-risk tier. Specifically, when the age was between 40 and 60 years old, the probability of developing BCC 5 years after transplant is 5%; age older than 60 years further elevated this risk to 9% (Fig 5). Furthermore, malignancy at listing and/or induction therapy with daclizumab brought a white and male recipient with a latitude level ≤42° from the moderate-risk tier to the high-risk tier. As shown in Fig 5, induction therapy with daclizumab elevated the risk of developing BCC 5 years after transplant from 9% to 13% among male, white recipients who were older than 60 years, and had a latitude level ≤ 42°.

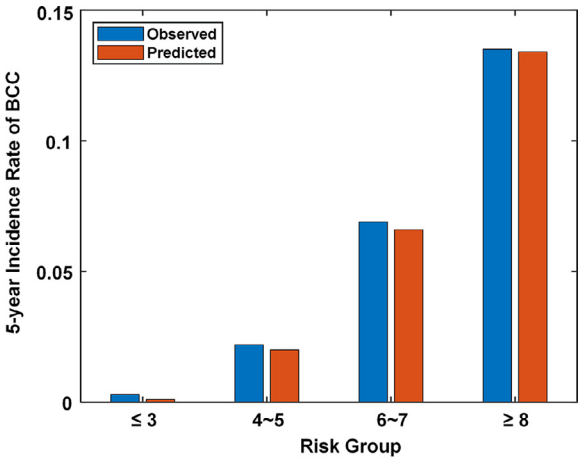
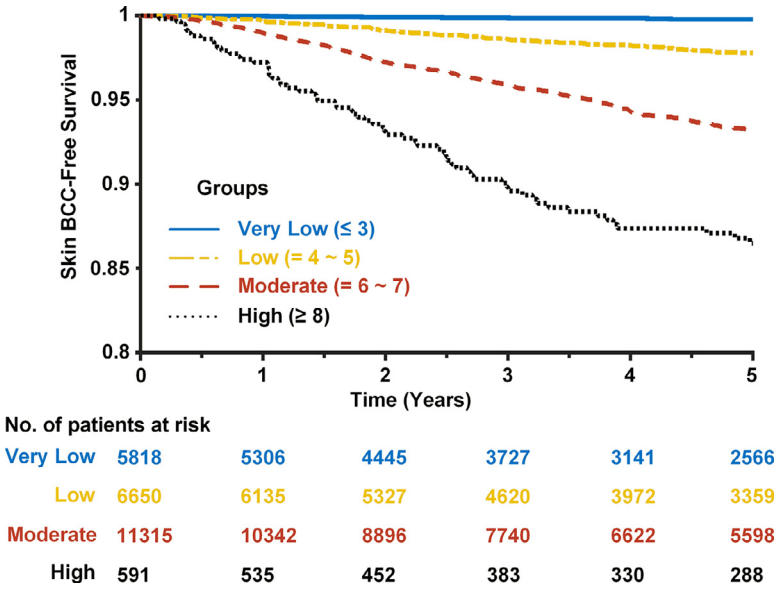


Fig 3. Predicted versus observed probability of BCC in 5 years.

Limitations

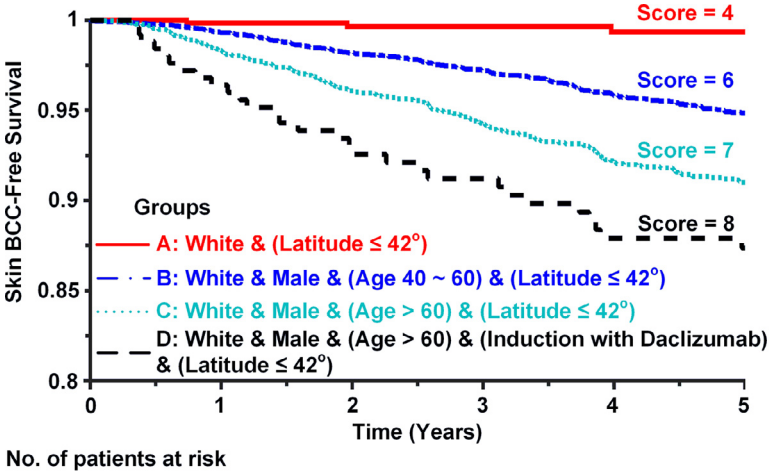
There are some limitations that should be noted in the current research. To study the effect of sunshine exposure, the latitude information was calculated as a surrogate based on patients' residential zip code at the time of transplantation. However, such surrogate is not accurate, and more reliable biomarkers of ultraviolet radiation should be developed [8]. In addition, because the UNOS database has limited posttransplant measurements, the risk prediction model in this study was developed using variables collected before and at transplantation; impacts of immunosuppressive medications were limited to the analysis of different types of induction drugs. However, the effect of different immunosuppressive medications is subject to their levels and durations [7,10,18]. Future analysis can be done to study the association of immunosuppressive medications with the posttransplant incidence of BCC. Some posttransplant malignancy forms



No. of patients at risk

Very Low	5818	5306	4445	3727	3141	2566
Low	6650	6135	5327	4620	3972	3359
Moderate	11315	10342	8896	7740	6622	5598
High	591	535	452	383	330	288

Fig 4. Skin BCC-free survival curves for very low-, low-, moderate-, and high-risk groups. BCC, basal cell carcinoma.



No. of patients at risk

A	649	610	514	440	358	298
B	5014	4640	4055	3572	3093	2629
C	3428	3042	2533	2127	1744	1436
D	264	241	216	202	183	168

Fig 5. Effect of risk factors on the skin BCC-free survival. BCC, basal cell carinoma.

submitted to the Organ Procurement Transplant Network registry have been reported to be incomplete [8,19]. Further studies are required to validate the usage of UNOS database for skin cancer analysis.

CONCLUSIONS

In conclusion, this study develops a risk stratification model to predict posttransplant BCC risk based on a group of regularly available characteristics of heart transplant recipients and provides a simple tool to guide dermatology referral for skin cancer screenings. The accurate determination of the occurrence rate of skin cancer for different risk groups can suggest timely screening and improve posttransplant care. The identification of high-risk patients can help raise cancer awareness and reduce mortality and morbidity of skin cancer, which will help improve the quality of life in the posttransplant population.

REFERENCES

[1] Van Keer J, Droogne W, Van Cleemput J, Vörös G, Rega F, Meyns B, et al. Cancer after heart transplantation: a 25-year single-center perspective. Transplant Proc 2016;48:2172–7.

[2] Mahr S, Paireder M, Aliabadi A, Seebacher G, Grimm M, Wolner E, et al. 74: incidence and outcome of de-novo malignancy after cardiac transplantation−20 years experience of a single center. J Heart Lung Transplant 2008;27:S86.

[3] Euvrard S, Kanitakis J, Claudy A. Skin cancers after organ transplantation. N Engl J Med 2003;348:1681–91.

[4] Jäämaa-Holmberg S, Salmela B, Lemström K, Pukkala E, Lommi J. Cancer incidence and mortality after heart transplantation−a population-based national cohort study. Acta Oncol 2019;58:859–63.

[5] Ertas NM, Uysal AC, Albayati A, Ozkan B, Haberal M. Nonmelanoma skin cancers in solid organ transplant recipients: a single center experience. Transplantation 2018;102:S645.

[6] Howard MD, Su JC, Chong AH. Skin cancer following solid organ transplantation: a review of risk factors and models of care. Am J Clin Dermatol 2018;19:585–97.

[7] Molina B, Leiro M, Pulpón L, Mirabet S, Yanez J, Bonet L, et al. Incidence and risk factors for nonmelanoma skin cancer after heart transplantation. Transplant Proc 2010;42:3001–5.

[8] Garrett GL, Blanc PD, Boscardin J, Lloyd AA, Ahmed RL, Anthony T, et al. Incidence of and risk factors for skin cancer in organ transplant recipients in the United States. JAMA Dermatol 2017;153:296–303.

[9] Alam M, Silber D, Mullen M, Brown R, Yancy C, Feldman D, et al. Cutaneous malignancies after cardiac transplantation-risk factors and effect on late survival. J Heart Lung Transplant 2005;24:S46.

[10] Jambusaria-Pahlajani A, Crow LD, Lowenstein S, Garrett GL, Melcher ML, Chan AW, et al. Predicting skin cancer in organ transplant recipients: development of the SUNTRAC screening tool using data from a multicenter cohort study. Transpl Int 2019;32:1259–67.

[11] Lowenstein S, Garrett G, Toland A, Jambusaria-Pahlajani A, Asgari M, Green A, et al. Risk prediction tools for keratinocyte carcinoma after solid organ transplantation: a review of the literature. Br J Dermatol 2017;177:1202–7.

[12] Tanaka T, Voigt MD. Decision tree analysis to stratify risk of de novo non-melanoma skin cancer following liver transplantation. J Cancer Res Clin Oncol 2018;144:607–15.

[13] Urwin HR, Jones PW, Harden PN, Ramsay HM, Hawley CM, Nicol DL, et al. Predicting risk of nonmelanoma skin cancer and premalignant skin lesions in renal transplant recipients. Transplantation 2009;87:1667–71.

[14] Rubin AI, Chen EH, Ratner D. Basal-cell carcinoma. N Engl J Med 2005;353:2262–9.

[15] Lear J, Tan B, Smith A, Bowers W, Jones P, Heagerty A, et al. Risk factors for basal cell carcinoma in the UK: case-control study in 806 patients. J R Soc Med 1997;90:371–4.

[16] España A, Redondo P, Fernández AL, Zabala M, Herreros J, Llorens R, et al. Skin cancer in heart transplant recipients. J Am Acad Dermatol 1995;32:458–65.

[17] Kransdorf E, Patel J, Kittleson M, Czer L, Chang D, Dimbil S, et al. Does a history of malignancy prior to heart-transplant increase posttransplant risk? J Heart Lung Transplant 2018;37:S421.

[18] Vos M, Plasmeijer EI, van Bemmel BC, van der Bij W, Klaver NS, Erasmus ME, et al. Azathioprine to mycophenolate mofetil transition and risk of squamous cell carcinoma after lung transplantation. J Heart Lung Transplant 2018;37:853–9.

[19] Garrett GL, Yuan JT, Shin TM, ST Arron, Colegio O, Curiel C, et al. Validity of skin cancer malignancy reporting to the Organ Procurement Transplant Network: a cohort study. J Am Acad Dermatol 2018;78:264–9.