Brief report

Evaluating additional risk factors with the Skin and UV Neoplasia Transplant Risk Assessment Calculator in Canadian heart and lung transplant recipients

Key Message: *Smoking history and pre-transplant actinic keratoses were independently associated with skin cancer risk in thoracic transplant recipients and may improve risk stratification beyond SUNTRAC alone.*

Solid organ transplant recipients are at increased risk of skin cancer from chronic immunosuppression, with squamous cell carcinoma (SCC) the most common and most aggressive.[1,2] Thoracic recipients are at particularly high risk.[1] The Skin and Ultraviolet Neoplasia Transplant Risk Assessment Calculator (SUNTRAC) was developed to guide screening, incorporating age, sex, race, transplant type, and pre-transplant history of skin cancer.[3] However, it does not account for treatment exposures or markers of ultraviolet damage. This study evaluated additional predictors of skin cancer in a Canadian thoracic transplant cohort, building on the SUNTRAC tool.

This retrospective study included 296 recipients seen at the University Dermatology Centre (Edmonton, Alberta) in 2023. Data included demographics, Fitzpatrick type, smoking, pre-transplant actinic keratoses (AKs) or skin cancer, and azathioprine or voriconazole exposure. The primary outcome was post-transplant skin cancer. Independent predictors were identified using a multivariable Fine and Gray model incorporating SUNTRAC score and additional factors, accounting for death as a competing risk. To assess whether inclusion of additional covariates improved risk stratification beyond SUNTRAC alone, predicted risk from Fine−Gray models was used to stratify patients into tertiles, and cumulative incidence functions were compared across risk groups. Ethics approval was obtained (Pro00145738).

Of 296 recipients, 70.9% were male and the median age was 56 years; most had Fitzpatrick types I-III (90.9%) (Table I). AKs were present in 201 (67.9%). Ninety-three patients (31.4%) developed skin cancer, including 57 with SCC (19.3%), 36 with basal cell carcinoma (12.2%), 2 melanomas, and 1 eccrine carcinoma.

Multivariable analysis showed that age ≥50 years (SHR 2.42, 95% CI 1.23-4.75, $P = .01$), Caucasian race (SHR 2.87, 95% CI 1.00-8.26, $P = .049$), smoking (SHR 2.56, 95% CI 1.34-5.25, $P = .005$), and pre-transplant AKs (SHR 3.51, 95% CI 1.91-6.43, $P < .001$) were independently associated with post-transplant skin cancer risk (Table II). Pre-transplant history of skin cancer was not significant (SHR 1.76, $P = .32$).

In additional analyses, azathioprine use was associated with skin cancer (31.8% vs 15.2% without, $P = .026$). Voriconazole was not significant. Among Fitzpatrick types III-VI, azathioprine remained associated (25.0% vs 0%, $P = .0033$), although subgroup numbers were small and not part of the multivariable model.

In comparative competing-risk analyses, SUNTRAC alone demonstrated significant separation of cumulative incidence curves ($P = .0002$). When pre-transplant actinic keratoses and smoking history were added, risk stratification was further refined, with substantially stronger separation between risk groups ($P < .0001$). In the highest-risk tertile, cumulative incidence increased from 1.0% at 1 year, 28.4% at 5 years, and 42.3% at 10 years using SUNTRAC alone to 2.1%, 33.5%, and 58.4%, respectively, with the augmented model. Conversely, the lowest-risk tertile demonstrated lower cumulative incidence at 5 and 10 years (2.4% and 7.5%) compared with SUNTRAC alone (6.1% and 15.2%).

In this Canadian thoracic cohort, we identified risk factors consistent with SUNTRAC (age, race) and additional predictors not captured in that tool (smoking, azathioprine, AKs). Azathioprine further increased risk, including in darker skin types. AKs may serve as precursors and as markers of cumulative ultraviolet exposure, smoking as a carcinogenic exposure relevant even after cessation, and azathioprine as a post-transplant immunosuppressant that may affect screening timing. These routinely available factors may enhance risk stratification by informing referral timing and surveillance intervals.

In secondary competing-risk analyses, incorporation of smoking history and pre-transplant AKs also resulted in clearer separation of cumulative incidence across risk strata, with earlier divergence of the highest-risk group and lower long-term incidence among those classified as low risk. This suggests that these factors may refine clinical risk stratification beyond SUNTRAC alone, rather than simply adding statistical associations.

Table I. Demographic and clinical characteristics of thoracic transplant recipients

Characteristic	SUNTRAC score; patients (*N* = 296), no (%)				
	Low risk (*N* = 33)	Medium risk (*N* = 103)	High risk (*N* = 155)	Very high risk (*N* = 5)	Total (*N* = 296)
Sex					
Male	17 (51.5)	77 (74.8)	112 (72.2)	4 (80.0)	210 (70.9)
Age at transplantation					
Median (Q1-Q3)	53 (28-59)	54 (42-62)	56 (43-61)	65 (53-66)	56 (42-61)
<50 y	15 (45.5)	38 (36.9)	56 (36.1)	1 (20.0)	110 (37.2)
≥50 y	18 (54.5)	65 (63.1)	99 (63.9)	4 (80.0)	186 (62.8)
Years post transplantation (time since transplant at assessment)					
Median (Q1-Q3)	5 (2-9)	8 (4-15)	6 (3-10)	3 (2-6)	6 (3-11)
Caucasian*					
Yes	0 (0.0)	80 (77.7)	155 (100.0)	5 (100.0)	240 (81.1)
Phototype					
I	0 (0.0)	21 (20.4)	23 (14.8)	1 (20.0)	45 (15.2)
II	2 (6.1)	59 (57.3)	128 (82.6)	4 (80.0)	193 (65.2)
III	14 (42.4)	15 (14.6)	2 (1.3)	0 (0.0)	31 (10.5)
IV	11 (33.3)	6 (5.8)	2 (1.3)	0 (0.0)	19 (6.4)
V	2 (6.1)	2 (1.9)	0 (0.0)	0 (0.0)	4 (1.4)
VI	4 (12.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.4)
Type of first transplant					
Lungs	15 (45.5)	46 (44.7)	100 (64.5)	4 (80.0)	165 (55.7)
Lungs and kidney	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.3)
Heart	17 (51.5)	54 (52.4)	54 (34.8)	1 (20.0)	126 (42.6)
Heart and lungs	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (0.3)
Heart and kidney	1 (3.0)	2 (1.9)	0 (0.0)	0 (0.0)	3 (1.0)
History of pre-transplant skin cancer					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	5 (100.0)	5 (1.7)
Post-transplant skin cancer					
No	33 (100.0)	84 (81.6)	101 (65.2)	1 (20.0)	219 (74.0)
Yes	0 (0.0)	16 (15.5)	48 (31.0)	4 (80.0)	68 (23.0)
Death	0 (0.0)	3 (2.9)	6 (3.8)	0 (0.0)	9 (3.0)
History of actinic keratoses					
Yes	0 (0.0)	2 (1.9)	23 (14.8)	3 (60.0)	28 (9.5)
History of smoking					
Yes	7 (21.2)	48 (46.6)	116 (74.8)	3 (60.0)	174 (58.8)

*Race was classified according to the original SUNTRAC study[3] and analyzed separately from Fitzpatrick phototype.

Unlike prior attempts to add variables such as body mass index or human leukocyte antigen mismatch, which offered minimal gains,[4,5] our findings suggest that simple, routinely collected factors may provide greater clinical utility and refine transplant-specific risk tools.

Limitations include retrospective design, single center setting, and small subgroup sizes. Male sex and pre-transplant history of skin cancer were not significant, likely reflecting limited power. Only 5 patients had such a history, which may explain the lack of significance after adjustment; collinearity with AKs may also have contributed. Larger multicenter cohorts are needed to confirm these associations.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI was used in the writing of this manuscript.

Adam C. Yu, MSc, MD,[a] Julie Shatto, BSc, MD,[a] Pamela Mathura, PhD,[a,b] Julie Zhang, MSc,[b] and Eunice Y. Chow, MD[c]

From the University of Alberta, Faculty of Medicine and Dentistry, Edmonton, Alberta, Canada[a]; Alberta Health Services, Edmonton, Alberta, Canada[b]; and Division of Dermatology, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada.[c]

Table II. Subdistribution hazard ratios for skin cancer risk factors among thoracic transplant recipients

Risk factor	SHR (expanded model)	95% CI	*P*-value
Male sex	1.53	0.81, 2.89	.19
Age ≥ 50 y at transplantation	2.42	1.23, 4.75	.01*
Caucasian	2.87	1.00, 8.26	.049*
Pre-transplant history of skin cancer	1.76	0.58, 5.38	.32
Pre-transplant history of actinic keratoses	3.51	1.91, 6.43	<.0001*
Smoking history	2.56	1.34, 5.25	.005*

CI, Confidence interval; *SHR*, subhazard ratio.
*Statistically significant ($P < .05$).

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Correspondence to: Dr Eunice Y. Chow, MD, Division of Dermatology, Department of Medicine, University of Alberta, 8-112 Clinical Sciences Building 11304 83 Ave NW, Edmonton, Alberta T6G 2G3, Canada

E-mail: eunicew@ualberta.ca

Conflicts of interest

None disclosed.

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