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Targeting NF-κB signaling in B cells as a potential new treatment modality for ANCA-associated vasculitis

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RESEARCH LETTER

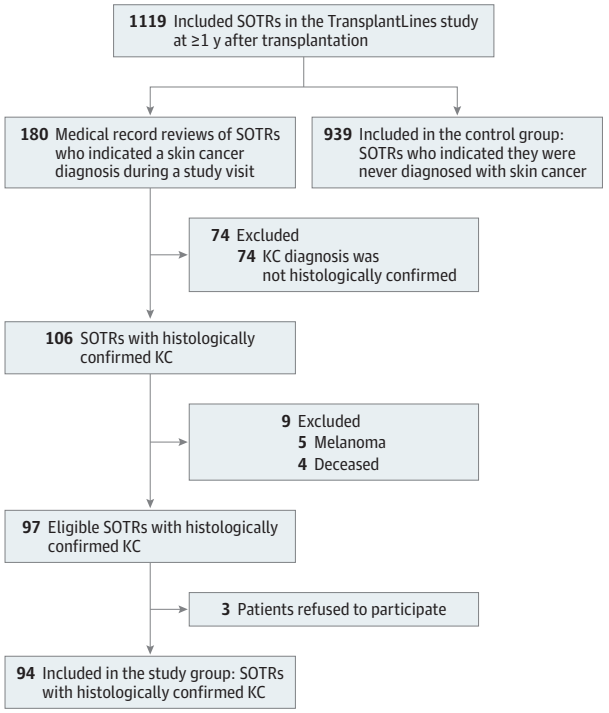
Health-Related Quality of Life in Solid Organ Transplant Recipients With vs Without Keratinocyte Carcinoma

Keratinocyte carcinoma (KC) is the most common malignant disease in solid organ transplant recipients, but we know little about its association with overall (generic) health-related quality of life (HRQoL) and KC-specific HRQoL in solid organ transplant recipients.[1,2] Although previous research showed that sun-protective behavior increases after KC treatment,[3] this topic is not addressed by KC-specific HRQoL questionnaires.[4] The recently developed Basal and Squamous Cell Carcinoma Quality of Life (BaSQoL) questionnaire does assess the association of behavior changes with HRQoL.[5] In this study, we compared generic HRQoL between solid organ transplant recipients with and without KC and explored variables associated with KC-specific HRQoL in solid organ transplant recipients using the BaSQoL.

Supplemental content

Methods | In this cross-sectional study, data of the TransplantLines study was used (NCT03272841).[6] Overall, 1119 solid organ transplant recipients included between June 2015 and February 2019, at 1 year or more after transplantation, were considered potentially eligible (**Figure**). Of those, there were 180 participants who indicated prior skin cancer, and medical record review identified 106 cases with histologically confirmed KC; 74 solid organ transplant recipients without histologically confirmed KC diagnosis were excluded. Of the 106 solid organ transplant recipients with histologically confirmed KC, 9 were excluded (n = 5 melanoma; n = 4 deceased) from further filling out the BaSQoL questionnaire. The 939 solid organ transplant recipients who indicated they were never diagnosed with skin cancer served as controls. The study was approved by the University Medical Center Groningen institutional review board and all participants provided written informed consent. Generic HRQoL was measured using the Physical and Mental Component Scale (PCS, MCS) of the Short Form 36 (SF-36) Health Survey (Supplement), where higher scores indicate better perceived HRQoL. Disease-specific HRQoL was measured using the BaSQoL, a 16-item KC-specific HRQoL instrument comprising 5 subscales.[5] Higher BaSQoL subscale scores indicate worse perceived KC-specific HRQoL. Mann-Whitney *U* tests were used to compare SF-36 scores between solid organ transplant recipients with and without KC. Log transformation was applied to the number of KCs before statistical analyses. The effect of age, sex, type of transplantation, number of KCs and time after transplantation on BaSQoL subscale scores was examined by multivariable linear regression analyses. No mathematical correction of multiple comparisons has been performed. Statistical analyses were performed using SPSS statistical software (version 23.0, IBM) and *P* value was set at <.05, 2 sided.

Figure. Study Flowchart



SOTR indicates solid organ transplant recipient; KC, keratinocyte carcinoma.

Data analyses were performed between April 11, 2019, and June 29, 2019.

Results | All included solid organ transplant recipients (94 with prior KC, 939 without KC) filled out the SF-36 questionnaire and all solid organ transplant recipients with prior KC also filled out the BaSQoL questionnaire; those solid organ transplant recipients with KC filled out the SF-36 questionnaire after KC diagnosis. Demographic data, clinical variables, and raw questionnaire scores are shown in the **Table**. The solid organ transplant recipients with KC were significantly older, had a longer time since transplantation, and were more often retired. There were no significant differences in generic HRQoL scores between solid organ transplant recipients with and without KC (Table). Multivariable analysis showed that having a higher number of KCs was independently associated with worse KC-specific HRQoL on the appearance (β, 0.64; 95% CI, 0.31-0.96; $P < .001$) and behavior (β, 0.60; 95% CI, 0.25-0.94; $P < .001$) subscales. Being female showed an independent association with worse KC-specific HRQoL on the appearance subscale (β, 0.29; 95% CI, 0.04-0.54; $P = .03$).

Discussion | Solid organ transplant recipients with and without KC did not differ in their generic HRQoL. However, when

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Table. Cohort Characteristics and Raw Questionnaire Scores

Variable	Study Group SOTRs With Prior KC (n = 94)	Control Group SOTRs Without KC (n = 939)	*P* Value
Age, mean (SD), y	67.0 (7.4)	54.5 (13.6)	<.001[a]
Sex, No. (%)			
Male	49 (52.1)	530 (56.4)	.45[b]
Solid organ transplant type, No. (%)			
Kidney	53 (56.4)	523 (55.7)	
Liver	23 (24.5)	238 (25.3)	.99[c]
Heart/lung	18 (19.1)	178 (19.0)	
Time after OT, median (IQR), y	15.9 (9.3-23.2)	6.2 (2.4-13.0)	<.001[d]
Employment status, No. (%)			
Employed	11 (11.7)	338 (36.0)	
Retired	55 (58.5)	230 (24.5)	
Incapacitated	11 (11.7)	240 (25.6)	<.001[c]
Other[e]	9 (9.6)	122 (13.0)	
Unknown	8 (8.5)	9 (1.0)	
Type and No. of KC per patient, No. (%)			
Basal cell carcinoma			
Yes	60 (63.8)	NA	
Single	25 (26.6)	NA	
Multiple	35 (37.2)	NA	
Range	1-53	NA	
Squamous cell carcinoma			
Yes	55 (58.5)	NA	
Single	24 (25.5)	NA	
Multiple	31 (33.0)	NA	
Range	1-61	NA	
Total KC lesions per patient, median (IQR), range	2 (1-5), 1-62	NA	
Questionnaire			
SF-36, median (IQR)			
PCS	71.9 (49.8-83.4)	75.7 (58.7-86.3)	.07[d]
MCS	80.0 (65.3-88.0)	81.6 (67.7-89.8)	.29[d]
BaSQoL[f] median (IQR)			
BH (range 0-3)	.75 (.25-1.50)	NA	
DT (range 0-3)	.67 (.33-1.08)	NA	
WS (range 0-3)	.75 (.25-1.06)	NA	
AP (range 0-3)	.33 (0-1.00)	NA	
OP (range 0-3)	.50 (0-1.00)	NA	

Abbreviations; AP, appearance; BaSQoL, Basal and Squamous Cell Carcinoma Quality of Life; BH, behavior; DT, diagnosis and treatment; IQR, interquartile range; KC, keratinocyte carcinoma; MCS, mental component scale; NA, not applicable; OP, other people; OT, organ transplantation; PCS, Physical Component Scale; SF-36, Short Form 36; SOTRs, solid organ transplant recipients; WS, worries.

[a] Student *t* test.

[b] χ^2 test.

[c] Fisher-Freeman-Halton test.

[d] Mann-Whitney *U* test.

[e] Student, housekeeping, or unemployed.

[f] Cronbach α values were 0.86, 0.80, 0.83, 0.86, and 0.76, respectively.

assessed with a KC-specific HRQoL instrument (BaSQoL), differences were noted. Among solid organ transplant recipients with a prior KC, more KCs were associated with reductions in HRQoL related to sun-protective behavior and appearance, and women had worse HRQoL related to appearance than men. Use of KC-specific HRQoL instruments in solid organ transplant recipients may identify changes that are not apparent with instruments designed to assess overall HRQoL and may allow targeted counseling for those at higher risk of impaired HRQoL.

Misclassification regarding KC status of our control group may have occurred unintentionally due to recall bias. However, we believe that it is unlikely that KC significantly impairs HRQoL in those who reported they were never diagnosed with KC.

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Study concept and design: Frie, Annema, Bakker, Ranchor, Racz.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Frie, Annema, Knijff, Ranchor, Eisenga, Racz.
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