

Impact of UV Modifying Factors on the Incidence of Keratinocyte Carcinomas in Solid Organ Transplant Recipients: A Systematic Review

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ABSTRACT Introduction: Solid organ transplant recipients (SOTR) are at an increased risk for developing keratinocyte carcinomas (KC). Four ultraviolet (UV) modifying factors have been identified that impact the incidence of KC: Fitzpatrick Skin Type (FST), race, sun exposure, and sun-protective factors. **Objectives:** We conducted a systematic review to summarize the association between UV modifying factors and the incidence of KC in SOTR. Methods: We systematically searched PubMed, Scopus, and Web of Science databases, and after screening for inclusion and exclusion criteria, we included 13 studies with 6,910 solid organ transplant recipients in our analysis. Results: Our review found that lower FST (I-II), white and Latinx populations, lack of regulated sunscreen application, and occupational and residential sun exposure are individual risk factors among solid organ transplant recipients for KC incidence. Although previous studies showed an increased SCC:BCC ratio, some studies found a contradictory increased BCC:SCC ratio. Limitations include few research studies that analyze these UV modifying factors and a lack of incorporating both varying immunosuppressant factors and transplantation follow-up times. Conclusions: These findings support the need for dermatological advice in increased risk patient demographic populations, lower FST and white and Latinx populations, and subsequently moderating sun exposure and protective factors.

Introduction

Keratinocyte carcinomas (KC) are non-melanoma skin cancers (NMSC) consisting of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) [1]. KCs are the most prevalent cancer worldwide with 20-25% of KCs being SCC [2,3]. Solid organ transplant recipients (SOTR) have an increased risk of developing KC and these patients are at a 65-250 increased risk for cutaneous SCC than the general population [4-6]. Specifically, a recent Delphi consensus survey found that male thoracic organ recipients aged 50 or older at the time of transplant are at the highest risk for developing skin cancer [7]. There are several UV modifying factors that can impact KC incidence in SOTR, however, the 4 major variables are: Fitzpatrick skin type (FST), race, sunscreen use, and sun exposure.

The FST classifies 6 skin complexions and reactions to sun exposure ranging from very light skin, burns easily, and never tans (FST I) to very dark skin, never burns, and tans profusely (FST VI) [8]. Although there are overlapping factors in FST and race, several other factors should be accounted for such as: environmental, geographic, and socioeconomic factors. All of these factors impact the association between race and KC incidence.

Aside from FST, sun exposure and sun protective actions are major contributors to skin cancer incidence [9]. Sun exposure and sunburn can be used indirectly as tools to assess skin cancer risk as it accounts for UV exposure amount and skin sensitivity [10]. Although some studies show that continuously high sun exposure is more closely associated with an increase in SCC incidence, other studies have also reported a positive association between sunburn history and KC incidence [11-15].

Sunscreen is a primary photoprotective factor against UV radiation that absorbs environmental UV rays to protect the skin [16]. A trial conducted in Queensland, Australia found that daily morning use of broad-spectrum sun protection factor (SPF)-16 sunscreen on the head, neck, arms, and hands of healthy individuals decreased both the number of individuals with SCCs and the incidence of SCC tumors up to 8 years post-cessation of intervention [17]. However, this same protective factor for regular use of sunscreen was not significant in reducing BCC incidence.

Objectives

To the author best knowledge, there is a lack of systematic reviews that assess the impact of UV modifying factors on skin cancer incidence in the adult SOTR population. Although there is substantial evidence suggesting immunosuppression increases the risk of SOTR developing KC, this systematic review will synthesize the evidence from retrospective cohort, prospective cohort, case-control, and observational studies to summarize the association between UV modifying factors and the incidence of KC in SOTR. The results of this study will help clinicians better assess what pertinent, significant risk factors to be aware of when treating adult SOTR and monitoring for the development of KC. Results of this study will allow us to lead a discussion regarding skin phenotype, race, and UV protection/exposure and better guide physicians treating SOTR adults.

Methods

Study Identification

A systematic literature search using PubMed and Scopus databases was performed. This search included all years through April 2022 and consisted of the search terms: "organ transplantation" OR "organ graft" OR "organ transplant recipients" AND "skin cancer" OR "squamous cell carcinomas" OR "basal cell carcinomas" OR "cutaneous squamous cell carcinoma" OR "nonmelanoma skin cancer" OR "keratinocyte carcinoma" AND "skin tone" OR "skin color" OR "Fitzpatrick skin type" OR "sunscreen" or "sun protective factors". Additionally, we searched the reference lists of selected studies. The search was conducted adhering to the updated 2020 standards of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [18].

Eligibility Criteria

Two reviewers (SR and FA) selected studies that met the following inclusion criteria: i) the population of interest adult solid organ transplant recipients, including FST or skin tone identification, race, sunscreen behaviors, or sun exposure; ii) the outcomes of interest - cutaneous squamous cell carcinomas, basal cell carcinomas, or non-melanoma skin cancers; and iii) observational or interventional study designs (cross-sectional studies, cohort studies, case studies, cases series, or randomized controlled trials). Studies were excluded if there was no record of UV modifying risk factors. Any disagreement was resolved by a third reviewer (AA).

Data Extraction

A total of 480 studies were screened and 13 were included. Information was collected on study design, data source, number of participants, selection criteria, and outcomes of interest including SCC, BCC, KC, and overall NMSC incidence based on our 4 UV modifying risk factors. FST and race data collected and analyzed is presented in Table 1. Sun exposure and sunscreen data collected and analyzed is presented in Table 2.

Table 1. Studies examining keratinocyte carcinoma risk variables, Fitzpatrick skin type, and race in solid organ transplant recipients.	Risk Type/Data	SCC HR (95% CI) 3.47 (1.46-8.28) 2.63 (1.16-5.92) 2.79 (1.24-6.30) 2.07 (0.91-4.70) 1.58 (0.66-3.81)	SCC BCC 52.3% 54.5% 25.0% 27.3% 18.2% 18.2% 4.5% 0%	Carcinoma type - HR (95% CI) NMSC - 0.60 (0.35-1.02) SCC - 0.57 (0.33-1.00) BCC - 0.55 (0.29-1.02) NMSC - 1* SCC - 1* BCC - 1*	Carcinoma type - accrual (SD) NMSC - 2.37 (± 3.25) SCC - 1.76 (± 2.70) BCC - 0.61 (± 1.66) NMSC - 3.05 (± 8.88) SCC - 2.41 (± 7.48) BCC - 0.64 (± 1.60) NMSC - 0.80 (± 1.57) SCC - 0.60 (± 1.40) BCC - 0.20 (± 0.49) NMSC - 0.45 (± 2.85) SCC - 0.40 (± 1.75) BCC - 0.05 (± 0.16)
tce in solid organ	UV Modifying Risk Variables Reported	FST S I II 2 III 2 III 2 IV 2 V 1	FST % S S S S S S S S S S S S S S S S S S	FST III-VI S S S F-II F F F F F F F F S F S F S F S F S F S	FST II IV II II II II II II II II II II II
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es, Fitzpatrick	KC Reported	317 cSCC	44 SCC and 22 BCC	1	253 cSCC and 88 BC
na risk variabl	Number of Subjects in Study	556	270	94	142
tinocyte carcinon	Data Collection Location (Year Ranges)	USA - CA 2004-2008	Ireland (2000-2001)	Australia	Australia (2004-2009)
examining kera	Study Design	Retrospective Cohort	Observational cohort	Retrospective Cohort	Prospective cohort
able 1. Studies	Study Author(S) And Year Published	Gogia et al 2013	Moloney et al 2005	De Rosa et al 2019	Ng et al 2014
Тĉ	KC Risk Variable Studied	FST			

Table1 continues

KC Risk Variable Studied	Study Author(S) And Year Published	Study Design	Data Collection Location (Year Ranges)	Number of Subjects in Study	KC Reported	Type of Transplant(S)	UV Modifying Risk Variables Reported	Risk Type/Data
	Garcia et al 2013	Prospective + Retrospective cohort	Mediterranean Region (1996-2010)	289	41 cSCC and 91 BCC	Kidney	FST LI-I ≥III	Relative NMSC HR (95% CI) 1* 0.5 (0.27-0.92)
	Ducroux et al 2014	Retrospective cohort	1996-2008 (France)	371	50 KC (cSCC and/or BCC)	Lung	FST I-III IV-VI	NMSC OR (95% CI) 10.91 (1.45-81.77) 1*
	Caforio et al 2000	Prospective Cohort	Italy	300	53 SCC and 37 BCC	Heart	FST II III-IV	NMSC HR (95% CI) 2.6 (± 1-7) 1*
Race	Dusendang et al 2022	Case-control	USA - CA (2009-19)	3308 OTR vs 65,883 no OTR		Heart, kidney, liver, lung, and pancreas	Race White AA Asian American Latinx Other	cSCC HR (95% CI) 1.00* 0.04 (0.02-0.07) 0.07 (0.05-0.09) 0.23 (0.18-0.29) 0.52 (0.41-0.65)

Table 1. Studies examining keratinocyte carcinoma risk variables, Fitzpatrick skin type, and race in solid organ transplant recipients. (continued)

AA = African American; BCC = basal cell carcinoma; CI = confidence interval; cSCC = cutaneous squamous cell carcinoma; FST = Fitzpatrick skin type; HR = Hazard Ratio; KC = keratinocyte carcinoma; NMSC = non-melanoma skin cancer; OR = Odds Ratio; SCC = squamous cell carcinoma; SD = standard deviation; * = hazard or odds ratio in reference to this value.

Published Study Design Kalgeoried Transplant(S) Reported Savoia et al 2011 Retrospective Italy (1977-2010) 282 99 Shin eancers Kidney S5 Use Savoia et al 2011 Retrospective Italy (1977-2010) 282 99 Shin eancers Kidney S5 Use Savoia et al 2010 Cohort Berlin, Germany 120 19 NMSC (BCC Heart, kidney, S5 Use significant link Ulrich et al 2009 Case-control Berlin, Germany 120 19 NMSC (BCC Heart, kidney, S5 Use significant link 2010 Cohort USA - Pittsburgh, S43 543 17 SCC Lung Risk factor: 2010 Prospective Italy 2003-2008) 330 53 SCC and 37 Heart Risk factor: Residence in Cohort (2003-2008) 330 53 SCC and 37 Heart Risk factor: Residence in Residence in Residence in region with high sun exposure sun exposure 2010 Prospective Italy 300 53 SCC and	KC Risk Variable	Study Author(S) and Year	-	Data Collection Location (Year	Number of Subjects In		Type of	UV Modifying Risk Variables	
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				(2012-2014)		77 Bowen)		Australia	

Table 2. Studies examining keratinocyte carcinoma risk variables, sunscreen, and sun exposure in solid organ transplant recipients.

HR = Hazard Ratio; KC = keratinocyte carcinoma; NMSC = non-melanoma skin cancer; OR = Odds Ratio; PR = Prevalence Ratio; SS = Sunscreen.

Results

Thirteen studies were selected for review after assessing a total of 480 full-text studies. Overall, the 13 studies included 6910 patients with solid organ transplantations in patients older than age 18 and collected one of the four UV modifying factors. These studies included solid organ transplants of the: kidney, heart, lung, liver, and pancreas. Dates for incorporated studies ranged from 2000 to 2022 (Figure 1).

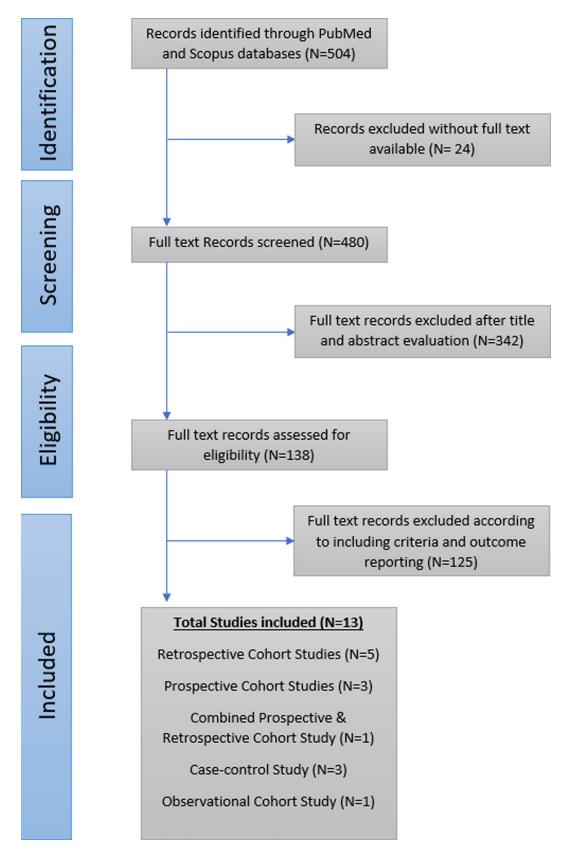


Figure 1. Flowchart of the identification of eligible studies.

All 13 studies provide adequate data supporting increased risk for KC associated with one of the four UV modifying risk factors. Seven studies explored FST impact and found that SOTR with lower FST (FST I and II) have an increased incidence of KC. One study identified the impact race has on KC incidence; the results indicated that white SOTR patients had a higher KC incidence than non-white SOTR. Within the non-white population, Latinx SOTR had the highest KC incidence. Two studies examined the impact of sunscreen application and suggested that controlled application of sunscreen can significantly reduce KC incidence in SOTR. Lastly, four studies explored sun exposure as a UV modifying factor and found that both occupational sun exposure and residence sun exposure are major contributors to KC incidence in SOTR.

The Impact of FST on KC in SOTRs

This systematic review explores the incidence of KC in adult solid organ transplant recipients of UV modifying risk factors, including FST. Seven studies supported an increased risk in KC for lighter skin FSTs (FST I-II).

A major cohort study by Gogia et. al examined 556 organ transplant recipients with skin cancer history between 2004 and 2008 and recorded patient demographics, transplant type, and FST [19]. SCC incidence and FST displayed an inverse relationship ie the risk of SCC increased with each incremental decrease in FST. FST I patients had a 1.67fold increased risk in developing SCC compared to FST IV patients, but a FST I patients had an even higher, 3.47-fold risk increase when compared to FST VI patients [19]. This trend continued over a 15-year period where SCC incidence of FST I participants was 68% compared to 27% in FST VI participants. However, the 15-year SCC incidence rates for FST II and FST III participants were 66% and 63%, respectively, indicating that fair skin types were more likely to have to develop SCC than the overall population. This trend was observed in an earlier study examining skin cancer development in renal transplant recipients. Out of the 44 subjects that developed squamous cell carcinomas, 52.3% were of FST I while 25.0% were of FST II [20]. The remaining 22.7% were of FST III and FST IV. The results of this study were also suggestive that SCC were more probable to develop in lighter skin type individuals. Furthermore, an Australian retrospective cohort study that traced 94 heart and/or lung transplant patients reported results that also supported this trend. Compared to FSTs I-II, FSTs III-VI had a 0.57-fold decreased risk of developing SCC [21]. Although these studies reiterated similar trends, some of the variability in SCC incidence can likely be attributed to the variability in worldwide sun exposure levels and various UV modifying factors.

FST also impacts BCC incidence in SOTR. A 60-month prospective Australian study examined FST impact on

NMSC incidence and found that higher tumor accrual rates in both FST I (1.76 SCC/patient per year, 0.61 BCC/patient per year) and FST II (2.41 SCC/patient per year, 0.64 BCC/ patient per year) compared to FSTs III, IV, and V [22]. A similar association was reported in an Italian cohort study where FST II was found to be a significant risk factor (HR=2.60) in NMSC incidence in heart SOTR compared to FSTs III, IV, and V [23]. Although the Australian study noted both SCC and BCC, it is vital to point out the increased SCC:BCC ratio (2.86:1), an association comparable with previous studies [24,25]. Additionally, FST I patients specifically had a much higher SCC:BCC ratio compared to other FSTs. It is imperative for clinicians to keep this increased SCC:BCC ratio in mind when treating SOTR patients as this impacts the regularity of skin screenings and requires more patient-centered treatment plans.

A retrospective and prospective follow-up study examined the risk factors for NMSC in renal transplant patients. Lighter FSTs (I and II) were associated with a significantly greater risk of NMSC compared to FST \geq III (HR 0.50 +/-0.27-0.92, P = 0.026) [26]. Interestingly, Garcia et al found an increased BCC:SCC ratio (2.21:1) which conflicts with the studies previously mentioned. This inverse relationship between lower FST and higher risk of NMSC in renal transplant patients was also supported by Savoia et al (BCC:SCC ratio 2.1:1) [27].

Lower FST has been shown in numerous studies to be a significant risk factor for incidence of NMSC, and more specifically, KC, in SOTR. Although previous studies have shown an overall increased SCC:BCC ratio, some studies have found a surprisingly increased BCC:SCC ratio. There is a need for additional well-designed prospective studies to be included in the literature to further distinguish the factors which affect varying SCC and BCC ratios.

The Impact of Race on KC in SOTR

Although race is associated with FST, many environmental, socioeconomic, genetic, and patient outcome factors contribute to race as a distinct identifier. Along with FST, race also contributes to SCC incidence in SOTR. A retrospective cohort study examining the incidence of SCC in SOTR from 2009 to 2019 found that the annual incidence rate of SCC in white SOTR was 4.70% compared to 0.38% in non-white SOTR (African American, Asian American, Latinx, Multiple/ Other, or Unknown) [28]. Additionally, white SOTR were more likely to have a history of skin cancers than non-white SOTR. This trend was consistent with Kang et al and could be the result of earlier diagnoses or a greater chance to get a diagnosis [28,29]. Latinx SOTR also had an increased SCC incidence compared to other non-white groups [28]. Our search was limited to one study that examined race association with KC incidence in SOTR.

Overall, white SOTR had a significantly higher incidence rate of SCC than non-white SOTR while the Latinx population had an increased SCC incidence when compared to the remaining non-white group.

The Impact of Sun Protective Factors on KC in SOTR

Sun protective factors, such as sunscreen, are major contributors to SCC incidence in SOTR. In a 24-month prospective case-control study of 120 patients, treatment groups were divided into a sunscreen group and a control group to explore the impact of regular application of >60 SPF sunscreen on SCC incidence in SOTR. The study included heart, kidney, and liver organ transplant recipients (OTR). After the 24-month phase, no new invasive SCC occurred in the sunscreen group while control patients developed 8 new invasive SCC (P < 0.01) (5 heart OTR, 3 kidney OTR, and 0 liver OTR) [30]. This trend was also supported by an Australian study of 1383 immunocompromised non-SOTR patients, demonstrating a similar trend found in both SOTR and non-SOTR populations [30,31]. Although the initial SOTR case-control study supported the potential protective benefits of sunscreen in decreasing the incidence of SCC, it is imperative to note that a 24-month period is too narrow to determine the full development of NMSC.

Lastly, in a single-center retrospective study in Italy, Savoia et al examined risk factors for skin cancers in kidney OTR. They found that the two exogenous risk factors that were significantly associated with skin cancers were the lack of sunscreen use (P = 0.0252) and outdoor occupation (P = 0.0413) [27]. Although this controlled trial suggested that sunscreen is a protective factor against SCC in SOTR, a retrospective study examining NMSC incidence in kidney OTR found that self-reported sunscreen was not a significant protective factor in NMSC incidence [32]. This comparison highlights the importance of educating SOTR patients on daily appropriate usage of sunscreen and emphasizing the use of higher sunscreen strength to best achieve the potential reduced risks of the development of SCC.

Overall, sunscreen may be an effective protective factor to reduce the incidence of NMSC in SOTR. However, due to the limited number of supporting studies, we cannot draw conclusions regarding sunscreen potential protective benefits. Further studies are required to understand the association between sunscreen and NMSC development. Additionally, although SPF was not a controlled variable, further research is required to determine the effect of varying SPF intensities in reducing NMSC incidence in SOTR. Future, prospective studies interested in this relationship should also explore determining an adequate cut-off point for SPF strength that is associated with a significantly decreased risk for NMSC.

The Impact of Sun Exposure on KC in SOTR

In addition to sun protective factors, sun exposure has been shown to be a major contributor to SCC in SOTR. For example, Queensland, Australia is known for its excessive sunlight exposure [33]. One study of SOTRs found that Australia SOTRs had a 10-year NMSC incidence of 70%, compared to SOTRs in Italy (10%) and Northern Europe (20%) [34]. Additionally, this study also found that cumulative amounts of sun exposure strongly predicted the risk of NMSC in both the Italian and Australian cohorts [34]. Moreover, the geographic impact of Australia sun exposure on NMSC was supported by Iannacone et al. The authors reported that patients born in Australia had a 2.38 prevalence ratio for NMSC compared to those born outside of Australia [35].

A separate retrospective case-cohort study (1:3 case-tocontrol ratio) in Pittsburgh examined the impact of highlevel sun exposure on SCC incidence in single and double lung OTR (N = 543). High-level sun exposure was defined as residence south of 35° latitude with high to very high UV indexes. The authors found that residing in high-level sun exposure areas was an independent risk factor for SCC in lung OTR (P = 0.0001) [36]. Additionally, 94% of the patients who developed SCC presented on sun-exposed parts of the body and this finding may be explained by the impact sun exposure has on the increased risk for SCC.

In addition to residential sun exposure, Savoia et al retrospective study reported that outdoor occupation was one of two exogenous risk factors significantly associated with skin cancer incidence [27]. Additional studies have also reported similar conclusions regarding the association between increased outdoor labor and increased risk of skin cancer. A case-control study in Mexico displayed that greater than 20 hours per week of occupational sun exposure was a significant risk factor associated with increased NMSC incidence (P < 0.01) [37]. Another study examined the risk factors for skin cancers in heart transplant recipients and found that cumulative increased sun exposure during work was independently associated with an increased risk of SCC (P = 0.0003) [23].

Limitations

This systematic review has several limitations. The first limitation is the high disparity in quantifiable variables to validly measure the effect of UV modifying factors reported in studies. Seven studies supported FST as a risk factor for skin cancer, but only one study supported race as a risk factor for cancer, even though both race and FST are factors determined by skin phenotype. Therefore, we require more standardized protocols for SOTR studies that monitor KC to collect demographics such as race to further support its impact on increased KC incidence. Additionally, we were unable to account for the effect of time from SOTR status to KC presentation, and how this would be related to various UV modification habits in SOTR patients. Lastly, although we analyzed the influence of exogenous factors on the development of NMSC, our review did not account for the impact of immunosuppression. Pharmacological immunosuppression is necessary for post-operative SOTR and is deemed the biggest risk factor contributing to NMSC incidence in SOTR [38]. NMSC incidence rates are proportional to the type of organ transplant, immunosuppressant type, dosage, and duration of the drug [39]. A single-center Norwegian study found a 3-fold higher risk of developing SCC in heart SOTR in comparison to kidney SOTR [39]. Gjersvik et al further confirmed this finding by displaying a 2.8-fold higher risk [40]. The increased risk can be explained by the elevated immunosuppressive dosage by heart SOTR compared to kidney SOTR [39]. Additionally, numerous studies have concluded that NMSC incidence increases in proportion to immunosuppressive duration [26,33,41,42]. We presented immunosuppressive drugs, percent distribution of drug types, and median time of immunosuppression for all included patients in Table 3.

Study	Type of Immunosuppressant	% of SOTR	Median time
Gogia et al 2013	NR	NR	NR
Moloney et al 2005	Cyclosporine, Azathioprine, and Prednisolone	NR	NR
De Rosa et al 2019	NR	NR	8.4 years (range: 0.4-27 years)
Dusendang et al 2022	Mycophenolate mofetil and Tacrolimus	93%	15 months
	Other Mycophenolate	53%	4 months
	Other Tacrolimus	44%	4 months
Savoia et al 2011	Tacrolimus	58.9%	7.2 years
	Cyclosporine	36.2%	_
	Azathioprine, Mycophenolate, and Sodium mofetil	NR	_
Ng et al 2014	Calcineurin inhibitors (Cyclosporine or Tacrolimus), Mycophenolate mofetil, and Prednisolone	53%	11.6 years (+/- 8.2 years)
	Azathioprine, Mycophenolate mofetil, and Prednisolone	27%	_
Garcia et al 2013	Mycophenolate, mTOR-Sirolimus, and/or Everolimus inhibitors	6.2%	NR
	Tacrolimus and Mycophenolate	66.4%	
	Cyclosporine and Mycophenolate	25.6%	
	Older regimens and Azathioprine	1.7%	
Ducroux et al 2014	Cyclosporine	19.5%	8.2 years
	Tacrolimus	95.7%	
	Sirolimus	20.8%	
Caforio et al 2000	Cyclosporin A and Azathioprine	79.3%	NR
	Cyclosporin A, Azathioprine, and prednisone	20.7%	
Ulrich et al 2009	Cyclosporine, Prednisolone, and Mycophenolate or Azathioprine	33.3%	24 months
	Tacrolimus, Mycophenolate, and Prednisolone	33.3%	
	Tacrolimus	33.3%	
Vadnerkar et al 2010	Calcineurin inhibitor, Mycophenolate, and Prednisolone	88.2%	NR
	Voriconazole	23.5%	6 months
	Voriconazole	76.5%	> 6 months
Rodriguez-Acosta et al 2015	Cyclosporine, Azathioprine, and Prednisolone	NR	NR
Iannacone et al 2016	Calcineurin inhibitor, Antiproliferative agent, and Corticosteroid	53.5%	8.9 years
	Calcineurin inhibitor with or without Corticosteroid	35.5%	

 Table 3. Immunosuppressive drugs, percent distribution of drug types, and median time of immunosuppression from studies included in retrospective analysis.

NR = not reported ; SOTR = solid organ transplant recipients.

Conclusions

Overall, our systematic review of 13 retrospective cohort, prospective cohort, case-control, and observational studies suggests a significant association between UV modifying factors and the risk of KC among individuals who have undergone solid organ transplantation. The four UV modifying factors were FST, race, sunscreen use, and sun exposure. This study identifies SOTR patient cohorts at increased risk for the development of KC by FST and race and identifies moderating factors that can contribute to the development of KC that providers can utilize in counseling patients. Geographic and occupational sun exposure are 2 noted UV modifying risk factors that increase the incidence of KC in SOTR. To the author's knowledge, there is a dearth of data in the literature which can adequately assess the relationship between SOTR patient status and the development of KC. Therefore, there is a need for more high-quality, well-powered, prospective studies to give clinicians a better understanding of optimal risk-reducing, patient-centered treatment plans when caring for SOTR patients.

References

- Sánchez G, Nova J, Rodriguez-Hernandez AE, et al. Sun protection for preventing basal cell and squamous cell skin cancers. *Cochrane Database Syst Rev.* 2016;7(7):CD011161. DOI:10.1002/14651858.CD011161.pub2. PMID: 27455163. PMCID: PMC6457780.
- Alam M, Ratner D. Cutaneous squamous-cell carcinoma. *N Engl J Med.* 2001;344(13):975-983. DOI:10.1056 /NEJM200103293441306 PMID: 11274625.
- Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. Lancet. 2010;375(9715):673-685. DOI:10.1016/S0140 -6736(09)61196-X. PMID: 20171403.
- Zamoiski RD, Yanik E, Gibson TM, et al. Risk of Second Malignancies in Solid Organ Transplant Recipients Who Develop Keratinocyte Cancers. *Cancer Res.* 2017;77(15):4196-4203. DOI:10.1158/0008-5472.CAN-16-3291. PMID: 28615224. PMCID: PMC5540772.
- Greenberg JN, Zwald FO. Management of Skin Cancer in Solid-organ Transplant Recipients: A Multidisciplinary Approach. *Dermatol Clin.* 2011;29(2):231-241, ix. DOI:10.1016/j .det.2011.02.004. PMID: 21421148.
- Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet*. 2007;370(9581):59-67. DOI:10.1016/S0140-6736(07)61050-2. PMID: 17617273.
- Crow LD, Jambusaria-Pahlajani A, Chung CL, et al. Initial skin cancer screening for solid organ transplant recipients in the United States: Delphi method development of expert consensus guidelines. *Transpl Int*. 2019;32(12):1268-1276. DOI:10.1111 /tri.13520. PMID: 31502728.
- Sachdeva S. Fitzpatrick skin typing: applications in dermatology. *Indian J Dermatol Venereol Leprol.* 2009;75(1):93-96. DOI:10.4103/0378-6323.45238. PMID: 19172048.

- Brenner M, Hearing VJ. The Protective Role of Melanin Against UV Damage in Human Skin†. *Photochem Photobiol*. 2008;84(3):539-549. DOI: 10.1111/j.1751-1097.2007.00226.x. PMID: 18435612. PMCID: PMC2671032.
- Watson M, Holman DM, Maguire-Eisen M. Ultraviolet Radiation Exposure and Its Impact on Skin Cancer Risk. *Semin Oncol Nurs.* 2016;32(3):241-254. DOI: 10.1016/j.soncn.2016.05.005. PMID: 27539279. PMCID: PMC5036351.
- Wu S, Han J, Vleugels RA, et al. Cumulative ultraviolet radiation flux in adulthood and risk of incident skin cancers in women. *Br J Cancer.* 2014;110(7):1855-1861. DOI:10.1038/bjc.2014.43. PMID: 24595003. PMCID: PMC3974077.
- Xiang F, Lucas R, Hales S, Neale R. Incidence of nonmelanoma skin cancer in relation to ambient UV radiation in white populations, 1978-2012: empirical relationships. *JAMA Dermatol.* 2014; 150(10):1063-1071. DOI:10.1001/jamadermatol.2014.762. PMID: 25103031.
- English DR, Armstrong BK, Kricker A, Winter MG, Heenan PJ, Randell PL. Case-control study of sun exposure and squamous cell carcinoma of the skin. *Int J Cancer*. 1998;77(3):347-353. DOI:10.1002/(sici)1097-0215(19980729) 77:3<347::aid-ijc7>3.0.co;2-o. PMID: 9663594.
- Iannacone MR, Wang W, Stockwell HG, et al. Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin--a case-control study. *BMC Cancer*. 2012;12:417. DOI:10.1186/1471-2407-12-417. PMID: 22994655. PMCID: PMC3517361.
- Zanetti R, Rosso S, Martinez C, et al. The multicentre south European study "Helios". I: Skin characteristics and sunburns in basal cell and squamous cell carcinomas of the skin. *Br J Cancer*. 1996;73(11):1440-1446. DOI:10.1038/bjc.1996.274. PMID: 8645595. PMCID: PMC2074488.
- Gabros S, Nessel T, Zito P. Sunscreens And Photoprotection. StatPearls. Published online November 15, 2021. Available from https://www.ncbi.nlm.nih.gov/books/NBK537164/Accessed April 2, 2022.
- van der Pols JC, Williams GM, Pandeya N, Logan V, Green AC. Prolonged Prevention of Squamous Cell Carcinoma of the Skin by Regular Sunscreen Use. *Cancer Epidemiol Biomarkers Prev.* 2006;15(12):2546-2548.DOI:10.1158/1055-9965.EPI-06-0352. PMID: 17132769.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. DOI:10.1136/bmj.n71. PMID: 33782057. PMCID: PMC8005924.
- Gogia R, Binstock M, Hirose R, Boscardin WJ, Chren MM, Arron ST. Fitzpatrick skin phototype is an independent predictor of squamous cell carcinoma risk after solid organ transplantation. J Am Acad Dermatol. 2013;68(4):585-591. DOI:10.1016/j .jaad.2012.09.030. PMID: 23107311. PMCID: PMC3562416.
- Moloney FJ, Almarzouqi E, O'Kelly P, Conlon P, Murphy GM. Sunscreen use before and after transplantation and assessment of risk factors associated with skin cancer development in renal transplant recipients. *Arch Dermatol.* 2005;141(8):978-982. DOI:10.1001/archderm.141.8.978. PMID: 16103326.
- DeRosa N,Paddon VL,Liu Z,Glanville AR,Parsi K.Nonmelanoma Skin Cancer Frequency and Risk Factors in Australian Heart and Lung Transplant Recipients. *JAMA Dermatol.* 2019;155(6):716. DOI:10.1001/jamadermatol.2018.4789. PMID: 30865218. PMCID: PMC6563540.

- 22. Ng JC, Cumming S, Leung V, Chong AH. Accrual of non-melanoma skin cancer in renal-transplant recipients: Experience of a Victorian tertiary referral institution: NMSC accrual in OTR. *Australas J Dermatol.* 2014;55(1):43-48. DOI: 10.1111 /ajd.12072. PMID: 23808627.
- Caforio ALP, Fortina AB, Piaserico S, et al. Skin Cancer in Heart Transplant Recipients: Risk Factor Analysis and Relevance of Immunosuppressive Therapy. *Circulation*. 2000;102(suppl_3). DOI:10.1161/circ.102.suppl_3.III-222. PMID: 11082391.
- Ramsay HM, Fryer AA, Hawley CM, Smith AG, Harden PN. Non-melanoma skin cancer risk in the Queensland renal transplant population. *Br J Dermatol.* 2002;147(5):950-956. DOI:10.1046/j.1365-2133.2002.04976.x. PMID: 12410706.
- 25. Carroll RP, Ramsay HM, Fryer AA, Hawley CM, Nicol DL, Harden PN. Incidence and prediction of nonmelanoma skin cancer post-renal transplantation: a prospective study in Queensland, Australia. *Am J Kidney Dis.* 2003;41(3):676-683. DOI:10.1053/ajkd.2003.50130. PMID: 12612993.
- 26. García J, Suárez-Varela M, Vilata J, Marquina A, Pallardó L, Crespo J. Risk Factors for Non-melanoma Skin Cancer in Kidney Transplant Patients in a Spanish Population in the Mediterranean Region. *Acta Derm Venerol.* 2013;93(4):422-427. DOI:10.2340/00015555-1525. PMID: 23303600.
- Savoia P, Stroppiana E, Cavaliere G, et al. Skin cancers and other cutaneous diseases in renal transplant recipients: a single Italian center observational study. *Eur J Dermatol.* 2011;21(2): 242-247. DOI: 10.1684/ejd.2011.1272. PMID: 21382788.
- Dusendang JR, Carlson E, Lee DS, et al. Cohort and nested case-control study of cutaneous squamous cell carcinoma in solid organ transplant recipients, by medication. *J Am Acad Dermatol.* 2022;86(3):598-606. DOI: 10.1016/j.jaad.2021.07.065. PMID: 34384835.
- Kang W, Sampaio MS, Huang E, Bunnapradist S. Association of Pretransplant Skin Cancer With Posttransplant Malignancy, Graft Failure and Death in Kidney Transplant Recipients. *Transplantation*. 2017;101(6):1303-1309. DOI:10.1097 /TP.000000000001286. PMID: 27336396.
- Ulrich C, Jürgensen JS, Degen A, et al. Prevention of non-melanoma skin cancer in organ transplant patients by regular use of a sunscreen: a 24 months, prospective, case-control study. Br J Dermatol. 2009;161 Suppl 3:78-84. DOI:10.1111/j .1365-2133.2009.09453.x. PMID: 19775361.
- Green A, Williams G, Neale R, et al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet*. 1999;354(9180):723-729. DOI:10.1016 /S0140-6736(98)12168-2. PMID: 10475183.
- 32. Zavattaro E, Fava P, Veronese F, et al. Identification of Risk Factors for Multiple Non-Melanoma Skin Cancers in Italian Kidney

Transplant Recipients. *Medicina (Kaunas)*. 2019;55(6):E279. DOI:10.3390/medicina55060279. PMID: 31208110. PMCID: PMC6631054.

- Bouwes Bavinck JN, Hardie DR, Green A, et al. The risk of skin cancer in renal transplant recipients in Queensland, Australia. A follow-up study. *Transplantation*. 1996;61(5):715-721. DOI:10.1097/00007890-199603150-00008. PMID: 8607173.
- 34. Tessari G, Girolomoni G. Nonmelanoma skin cancer in solid organ transplant recipients: update on epidemiology, risk factors, and management. *Dermatol Surg.* 2012;38(10):1622-1630. DOI:10.1111/j.1524-4725.2012.02520.x. PMID: 22805312.
- 35. Iannacone MR, Sinnya S, Pandeya N, et al. Prevalence of Skin Cancer and Related Skin Tumors in High-Risk Kidney and Liver Transplant Recipients in Queensland, Australia. J Invest Dermatol. 2016;136(7):1382-1386. DOI: 10.1016/j.jid.2016 .02.804. PMID: 26968258.
- 36. Vadnerkar A, Nguyen MH, Mitsani D, et al. Voriconazole exposure and geographic location are independent risk factors for squamous cell carcinoma of the skin among lung transplant recipients. J Heart Lung Transplant. 2010;29(11):1240-1244. DOI: 10.1016/j.healun.2010.05.022. PMID: 20591690.
- Rodríguez-Acosta ED, Calva-Mercado JJ, Alberú-Gómez J, Vilatoba-Chapa M, Domínguez-Cherit J. [Patients with solid organ transplantation and skin cancer: determination of risk factors with emphasis in photoexposure and immunosuppressive regimen. Experience in a third level hospital]. *Gac Med Mex.* 2015;151(1):19-24.
- Penn I, Starzl TE. Malignant tumors arising de novo in immunosuppressed organ transplant recipients. Transplantation. 1972;14(4):407-417. DOI:10.1097/00007890-197210000 -00001. PMID: 4345337. PMCID: PMC3006181.
- Jensen P, Hansen S, Møller B, et al. Skin cancer in kidney and heart transplant recipients and different long-term immunosuppressive therapy regimens. J Am Acad Dermatol. 1999;40(2):177-186. DOI:10.1016/S0190-9622(99)70185-4. PMID: 10025742.
- Gjersvik P, Hansen S, Møller B, et al. Are heart transplant recipients more likely to develop skin cancer than kidney transplant recipients? Transpl Int. 2000;13(7):S380-S381. DOI:10.1007 /s001470050366. PMID: 11112037.
- 41. Otley C, Pittelkow M. Skin cancer in liver transplant recipients. Liver Transpl. 2000;6(3):253-262. DOI:10.1016/S1527 -6465(05)80001-2. PMID: 10827224.
- 42. Ulrich C, Kanitakis J, Stockfleth E, Euvrard S. Skin Cancer in Organ Transplant Recipients-Where Do We Stand Today? *Am J Transplant.* 2008;8(11):2192-2198. DOI: 10.1111/j.1600 -6143.2008.02386.x. PMID: 18782290.