Prevalence of Skin Cancer and Related Skin Tumors in High-Risk Kidney and Liver Transplant Recipients in Queensland, Australia

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The increased skin cancer incidence in organ transplant recipients is well-known, but the skin cancer burden at any one time is unknown. Our objective was to estimate the period prevalence of untreated skin malignancy and actinic keratoses in high-risk kidney and liver transplant recipients and to assess associated factors. Organ transplant recipients underwent full skin examinations by dermatologically trained physicians. The proportion of examined organ transplant recipients with histopathologically confirmed skin cancer in the 3-month baseline period was estimated. Prevalence ratios with 95% confidence intervals indicated significant associations. Of 495 high-risk organ transplant recipients (average age = 54 years, time immunosuppressed = 8.9 years), 135 (27%) had basal cell carcinoma, squamous cell carcinoma or Bowen's disease (intraepidermal carcinoma) present and confirmed in the baseline period, with respective prevalence proportions of 10%, 11%, and 18% in kidney transplant recipients and 10%, 9%, and 13% in liver transplant recipients. Over 80% had actinic keratosis present, with approximately 30% having 5 or more actinic keratoses. Organ transplant recipients with the highest skin cancer burden were Australian born, were fair skinned (prevalence ratio = 1.61, 95% confidence interval = [1.07, 2.43]), reported past skin cancer (prevalence ratio =3.39, 95% confidence interval = [1.93, 5.95]), and were receiving the most frequent skin checks (prevalence ratio = 1.76, 95% confidence interval = [1.15, 2.70]). In conclusion, high-risk organ transplant recipients carry a substantial measurable skin cancer burden at any given time and require frequent review through easily accessible, specialized services.

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INTRODUCTION

Long-term immunosuppressive therapy greatly increases the incidence of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin among organ transplant recipients (OTRs) (Euvrard et al., 2003; Mackenzie et al., 2010; Zavos et al., 2011). As OTRs' long-term survival rates rise with advances in surgery and improved immunosuppressive drug regimens, so too does the burden of these keratinocyte cancers (Berg and Otley, 2002; Euvrard et al., 2003) and the associated health-care costs (Fransen et al., 2012; Ruegg et al., 2012).

To date, the cumulative incidence rates of skin cancer after organ transplantation have mostly been used to indicate OTRs' long-term skin cancer burden (Fortina et al., 2000; Haagsma et al., 2001; Martin et al., 2013; Ramsay et al., 2002). Period prevalence, the proportion of a population who have a disease present in a given time window, provides a measure of the net effects of incidence and treatment. To our knowledge, no prevalence estimates of skin cancer in OTRs are currently available, yet the outlay of necessary clinical services should be guided by this knowledge. We therefore assessed the period prevalence of skin cancers in a tightly defined window, as well as actinic keratosis (AK) baseline prevalence, in kidney and liver transplant recipients in Queensland, Australia. We assessed those at high risk of keratinocyte cancer because these are the OTRs who carry most of the skin cancer burden in a community. We also assessed risk factors associated with having keratinocyte cancer present on the skin in this period.

RESULTS

Of 735 kidney and 394 liver transplant patients at Princess Alexandra Hospital, 749 (kidney, n = 464; liver, n = 285) met

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Abbreviations: AK, actinic keratosis; BCC, basal cell carcinoma; OTR, organ transplant recipient; SCC, squamous cell carcinoma

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Table 1. Characteristics of 495 organ transplant recipients

Characteristics[1]	Kidney (n = 287)	Liver (n = 208)	*P*-value[2]
Age in years			
Overall, mean (SD)	54 (11)	55 (13)	
<40, n (%)	30 (10)	27 (13)	
40–49, n (%)	66 (23)	21 (10)	
50–59, n (%)	79 (28)	74 (36)	
60–69, n (%)	95 (33)	71 (34)	
70+, n (%)	17 (6)	15 (7)	0.001
Sex, n (%)			
Female	105 (37)	75 (36)	
Male	182 (63)	133 (64)	0.900
Born in Australia, n (%)			
No	55 (21)	47 (25)	
Yes	208 (79)	143 (75)	0.340
Natural complexion, n (%)			
Olive/medium	102 (36)	88 (44)	
Fair	182 (64)	113 (56)	0.080
Skin reaction to acute sun, n (%)			
Only tan	59 (23)	51 (27)	
Burn then tan	132 (50)	103 (54)	
Always burn	72 (27)	35 (19)	0.080
Presence of elastosis of neck, n (%)			
None	28 (10)	22 (11)	
Little	134 (47)	85 (43)	
Moderate	112 (39)	81 (40)	
High	11 (4)	13 (6)	0.500
Past skin cancers in last 2 years,[3] n (%)			
No	111 (42)	103 (54)	
Yes	152 (58)	87 (46)	0.010
Frequency of skin checks in last 5 years, n (%)			
Less than once a year	116 (44)	114 (60)	
Once a year	40 (15)	26 (14)	
More than once a year	107 (41)	50 (26)	0.002
Number of protection measures used for sun exposure, n (%)			
<2	120 (46)	97 (51)	
2+	143 (54)	93 (49)	0.250
Time (years) since first transplant[4]			
Overall, mean (SD)	11 (9)	9 (7)	
1–5, n (%)	90 (31)	71 (34)	
>5–10, n (%)	65 (23)	53 (25)	
>10–20, n (%)	88 (31)	68 (33)	
>20, n (%)	44 (15)	16 (8)	0.080
Immunosuppressive therapy regimens, n (%)			
Antimetabolites[5]	0 (0)	2 (1)	
Antimetabolites and calcineurin inhibitors	14 (5)	15 (7)	
Antimetabolites and corticosteroid	7 (2)	9 (4)	
Calcineurin inhibitors[6]	4 (1)	107 (51)	
Calcineurin inhibitors and corticosteroid	19 (7)	46 (22)	
Triple therapy[7]	240 (84)	25 (12)	
mTOR therapy[8]	0 (0)	2 (1)	
mTOR inhibitors and corsticosteroid	2 (1)	2 (1)	
Corticosteroid and anti-CD20 antibody[9]	1 (1)	0 (0)	

Abbreviation: mTOR, mechanistic target of rapamycin.
[1]Percentages do not add to 100% because of missing values.
[2]Chi-square *P*-value.
[3]Other than melanoma.
[4]Time in years since first transplantation was calculated based on date of first transplantation.
[5]Co-treatment for posttransplantation lymphoproliferative disorder.
[6]Includes azathioprine, mycophenolate sodium, and mycophenolate mofetil.
[7]Includes calcineurin inhibitor, antiproliferative agent, and corticosteroid.
[8]Includes cyclosporin A and tacrolimus.
[9]Includes sirolimus and everolimus.

the eligibility criteria, and 509 (kidney, n = 295; liver, n = 214) agreed to participate (see Supplementary Figure S1 online). Main reasons for refusal were prior time commitments, living remotely, or already seeing a private dermatologist. Most (60%) ineligible patients were excluded because of dark skin color (not of European ancestry); the remainder had serious comorbidity. There were no differences by age, sex, and numbers of years of immunosuppression between consenting and nonconsenting patients. The current analysis was based on 495 (97%) participants who had undergone the baseline skin examination. Of these, 42 did not complete the self-administered questionnaire and so were not included in the multivariable analyses. Skin cancer prevalence was no different in those who completed the questionnaire and those who did not.

The average ages of kidney and liver transplant recipients were very similar despite differences in their age distributions (Table 1). More kidney than liver transplant recipients were fair skinned, had skin cancer treated in the past 2 years, underwent full skin checks more than once a year, and received transplants longer than 20 years ago. Most kidney transplant recipients (84%) were receiving triple immunosuppressive therapy, whereas most liver transplant recipients (73%) were receiving a calcineurin inhibitor, with or without corticosteroids.

In total,135 kidney and liver transplant recipients had 168 histopathologically confirmed skin cancers (50 BCCs, 41 SCCs, 77 Bowen's disease) in the baseline 3 months (Table 2), giving a 27% period prevalence. Multivariable analyses conducted separately for BCC and SCC and by organ transplant type showed no statistically significant differences in the magnitude of the effect estimates or the characteristics independently associated with each skin cancer type. Therefore, adjusted prevalence ratios (PRs) are presented for the combined outcomes of BCC or SCC in both kidney and liver transplant patients. Self-reported history of skin cancer in the previous 2 years was the factor most strongly associated with prevalence of BCC or SCC (prevalence ratio = 3.39, 95% confidence interval = [1.93, 5.95]), followed by frequent whole-body skin checks (more than annually), fair complexion, and being born in Australia (Table 3).