Sunscreen Use Before and After Transplantation and Assessment of Risk Factors Associated With Skin Cancer Development in Renal Transplant Recipients

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Objective: To determine the degree of compliance with sunscreen use among renal transplant recipients before and after transplantation and to determine risk factors associated with skin carcinogenesis.

Design: Single-observer study with structured interview using a standardized questionnaire. Medical records and histology reports were examined for details of prior skin cancer. Cox proportional hazards regression was used for analysis of risk factors for developing skin cancer after transplantation.

Setting: Patients attending Beaumont Hospital, the national renal transplantation center in Dublin, Ireland.

Patients: The study population comprised 270 patients (182 male and 88 female).

Main Outcome Measures: Patients’ use of sunscreens before and after transplantation relative to known skin cancer risk factors and subsequent skin carcinogenesis.

Results: Prior to transplantation, 68.5% of patients never applied sunscreen on a sunny day compared with 25.9% after transplantation. Patients 50 years or younger were more likely to always apply sunscreen both before and after transplantation (P = .01), as were female patients prior to transplantation (P = .02). Those patients who participated in an outdoor recreation were more likely to subsequently develop nonmelanoma skin cancer (P = .04), as were those older than 50 years (P < .001) and those with a history of 2 or more painful sunburns (P = .03).

Conclusions: Transplant recipients are poorly compliant with the use of sunscreens both before and after transplantation. Compliance is poorest in those groups at higher risk of nonmelanoma skin cancer.

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RENAL TRANSPLANT RECIPIENTS develop neoplasms more commonly compared with the general population, especially squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) of the skin. The risk of skin cancer increases in proportion to the duration of immunosuppressive drug use. The past decade has seen an exponential increase in the numbers of skin cancers, paralleling the noticeable improvement in long-term graft survival. Cumulative sun exposure is also a major contributing risk factor. Of Irish renal transplant recipients, 40% will develop skin cancer after 20 years since transplantation. In contrast, over a similar period, 82% of transplant patients in Queensland, Australia, have developed a skin cancer. Historically, skin cancer prevention had low priority in the pretransplantation and early posttransplantation period. Seukeran et al have previously highlighted poor compliance among transplant recipients with advised sun protection measures. The present study aimed to establish patterns of sunscreen use in the pretransplantation and posttransplantation settings, identify factors associated with poor compliance with sun protection measures, and outline a set of guidelines for skin cancer education and prevention in renal transplant recipients.

Methods

A study of skin cancer prevalence was carried out from 2000 to 2001 in Beaumont Hospital, the national renal transplantation center in Dublin, Ireland. A total of 270 patients (182 male and 88 female) were interviewed in the setting of the renal and dermatology outpatient departments. The patients’ median age was 46.9 years (age range, 13.6-84.2 years), with a median duration since transplantation of 6.8 years.
There was no history of malignant melanoma in the 270 patients interviewed. Fifty-six patients developed 100 nonmelanoma skin cancers (76 SCCs and 24 BCCs). Ten patients had both SCC and BCC. The nonmelanoma skin cancers occurred predominantly on sun-exposed sites, in particular SCC with 93.5% situated on the arms or head and neck. The median time from transplantation to the development of first BCC (3.5 years) was slightly less than the median time to the development of first SCC (4 years); however, the median age at first tumor was older in the BCC group. There was no significant difference in pattern of sunburn history or skin type between those patients with SCC and those with BCC. There was, however, an overrepresentation of skin type I observed in those transplant recipients with skin cancer; 52.3% of transplant recipients who developed SCC and 54.5% of those who developed BCC had skin type I. The expected prevalence of skin type I in an Irish population is 26%.7

Prior to transplantation, 68.5% of the patients questioned admitted to having never applied sunscreen on a sunny day, with a further 25.9% applying occasionally. Only 5.6% had always applied sunscreen. After transplantation, the percentage that always applied sunscreen had increased to 36.7%; however, more than a quarter (25.9%) conceded that they would still never apply sunscreen on a sunny day.

Prior to transplantation, patients with the following characteristics were less likely to apply sunscreen on a sunny day: older than 50 years, male sex, outdoor occupation, outdoor hobbies, or a subsequent history of skin cancer (Table 2). Prior to transplantation, the median age of those who always applied sunscreen on a sunny day was 31.6 years (age range, 13.6–65.9 years) compared with a median age of 51.3 years (age range 18.4–
Finally, the 45.5% of patients who worked outdoors and the 54.2% who enjoyed outdoor hobbies were less likely to apply sunscreen prior to transplantation.

After transplantation, there was again better compliance with sun avoidance measures in the younger age groups. A median age of 45.5 years (age range, 13.6-84.2 years) for those who always applied sunscreen compared with 53.9 years (age range, 18.6-80.6 years) for those who never applied sunscreen. There was no significant difference identified in sun protection habits after transplantation, based on sex, duration since transplant, skin type, family history of skin cancer, or attendance at a dermatology clinic.

Table 2 indicates that pattern of sunscreen use before transplantation is a significant predictor of skin cancer after transplantation. This association was not significant using a univariate Cox regression model (Table 3); however, the hazard ratio (0.61), indicates a decreased risk associated with the pretransplantation use of sunscreen. Variables that predicted skin cancer included older age, history of bad sunburn, and outdoor recreational sun exposure. Male sex, while indicating an influence on outcome, did not achieve significance. When the chosen variables were placed in a multivariable model to test for independence of effect, only older age group remained significant at the 5% level (Table 4). This variable remained the dominant
UV radiation is the major environmental cause for melanoma and nonmelanoma skin cancer. Skin cancer risk is determined by both total amount and patterns of sun exposure. Increased cumulative lifetime sun exposure is associated with increased risk of SCC. Transplant recipients are at particularly high risk of SCC, with up to a 100-fold increase in the relative risk compared with the population without transplants. After transplantation, skin cancer occurs primarily on sun-exposed sites. Of the SCC in our patient group, 93.5% occurred on the head, neck, dorsa of the hands, and forearms, which are traditionally sun-exposed sites. The relative risk of BCC after transplantation is also increased but to a lesser extent than SCC. It is perceived that infrequent intense exposure to UV may have a greater influence on increasing the risk of BCC compared with total cumulative UV exposure. This was not reflected in the sunburn histories of our patient group; however, sample size may not have been large enough to detect a difference. The short mean latent period from transplantation to development of first skin cancer in this study supports recent findings of a study in Mediterranean renal transplant recipients.

Sunscreen use reduces the prevalence of actinic keratosis and recurrent SCCs in a nonimmunosuppressed population. For monitoring renal transplant recipients, sun avoidance and sunscreen application techniques are included in guidelines as part of a skin cancer reduction strategy. This study illustrated that female renal transplant recipients are much more likely to wear sunscreen than their male counterparts and also encouragingly showed that those transplant recipients who always applied sunscreen prior to transplantation were less likely to subsequently develop a skin cancer. Younger-aged renal transplant recipients were more likely to apply sunscreen both before and after transplantation, perhaps reflecting a poorer understanding in prior generations of the dangers of UV radiation. It is of concern that those with fairer skin types and high cumulative occupational and recreational sun exposure in our transplant population were no more likely to observe sun protective measures than were renal transplant recipients with lower skin cancer risk profiles. Kelly et al showed that skin types I and II are photoinmunosuppressed at lower levels of UV radiation exposure. The 2- to 3-fold greater sensitivity of skin types I and II for a given level of sunburn is linked to increased risk of skin cancer in later years. In this study, there was an overrepresentation of skin type I observed in those transplant recipients with skin cancer.

It is equally concerning that duration since transplantation, attendance at a dermatology clinic, or even a prior skin cancer seem to have little bearing on sunscreen use. Prior studies suggest that knowledge of skin cancer and the damaging effect of sunbathing do not seem to affect sunbathing habits or use of sun protection.

So why would more than a quarter of transplant recipients not wear sunscreen on a sunny day? The reasons given for not using sunscreens included the cost of sunscreens, lack of knowledge regarding the harmful effects of UV radiation, a belief that “my skin can take the sun,” simply forgetting to apply sunscreen, and finding sunscreens cosmetically unacceptable or impractical in a work environment. Cyclosporin induces sebaceous gland hyperplasia, folliculitis, acne, and hirsutism. Steroids also cause acne. Such factors are likely to have a significant effect on the cosmetic acceptability of a given sunscreen to transplant recipients. The physical or inorganic sunscreens, which are contained in most broad spectrum sunscreens recommended to transplant patients are greasy, comedogenic, and more difficult to rub in. Studies suggest that this cosmetic undesirability results in smaller amounts of sunscreen used, providing a sun protection factor of roughly half that achieved with chemical sunscreens. Newer sunscreens available in gel formulation are less greasy and likely to be more cosmetically acceptable.

Motivating people toward using immediate measures to prevent long-term problems has always proved a difficult prospect. This is particularly relevant in the transplant population. Previous studies have indicated that the transplant population complies poorly with sun avoidance measures, with only 57% applying a sunscreen and a minority wearing protective clothing when in the sun. This reflects sun protection patterns in the general population and points to the importance of public education campaigns about skin cancer protection. Other studies indicate that less than half of transplant recipients recalled receiving specific skin cancer education.

To address the increasing skin cancer incidence and lack of awareness among transplant recipients, we have instituted protocols aimed at targeting those patients with the highest risk and poorest compliance with sun avoidance. Patients are stratified prior to transplantation into low-, intermediate-, and high-risk skin cancer groups based on skin type, hair and eye color, cumulative sun exposure, and history of skin cancer or precancerous lesions. All patients are given a detailed patient information leaflet on skin care after transplantation. The appropriate application of a cream- or gel-based sunscreen that protects across the UV-B and UV-A spectrum is advised. Allowances are made for those who cannot afford to pay for sunscreens to reclaim the expense under the

### Table 4. Multifactorial Model of Risk Factors Pertaining to the Development of Skin Cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR ± SE (95% CI)</th>
<th>z Statistic</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;50 y</td>
<td>4.96 ± 1.77 (2.46-9.99)</td>
<td>4.48</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Outdoor recreation</td>
<td>1.50 ± 0.41 (0.88-2.55)</td>
<td>1.50</td>
<td>.14</td>
</tr>
<tr>
<td>≥2 Painful sunburns</td>
<td>1.64 ± 0.45 (0.96-2.80)</td>
<td>1.83</td>
<td>.07</td>
</tr>
<tr>
<td>Sunscreen not applied</td>
<td>0.87 ± 0.29 (0.46-1.66)</td>
<td>-0.43</td>
<td>.67</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio.
*Results significant at 5% level are in bold.
medical card scheme. Low-risk patients, with no risk factors, are seen routinely 1 year after transplantation. Intermediate-risk patients have a full skin examination every 6 months after transplantation, while those that fall into the high-risk category are seen in a dermatology clinic every 3 months after transplantation. Very-high-risk patients may require monthly assessment. Education and reinforcement of written information on skin care received at time of transplantation occurs at each of the follow-up visits.

The improvement in graft survival outcomes has resulted in a significant increase in immunosuppression-related skin cancers. Lack of appropriate sun protection among the past generation of renal transplant recipients has contributed to this increase. Allowing for recall bias when determining cumulative sun exposure, skin type, and sunscreen use, this study illustrates poor compliance with sun protection measures, particularly in the patient groups at the highest risk of skin cancer. Raising patient awareness, regular skin screening after transplantation, and instituting sun protection protocols with hats, clothing, and cosmetically acceptable broad spectrum sunscreens are the cornerstones to tackling the increasing incidence of skin cancer in renal transplant recipients.

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REFERENCES


Trial Registration Required

As a member of the International Committee of Medical Journal Editors (ICMJE), Archives of Dermatology will require, as a condition of consideration for publication, registration of all trials in a public trials registry (such as http://ClinicalTrials.gov). Trials must be registered at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment before this date, registration will be required by September 13, 2005, before considering the trial for publication. The trial registration number should be supplied at the time of submission.

For details about this new policy, and for information on how the ICMJE defines a clinical trial, see the editorial by DeAngelis et al in the January issue of Archives of Dermatology (2005;141:76-77). Also see the Instructions to Authors on our Web site: www.archdermatol.com.