Cutaneous Squamous Cell Carcinoma in Organ Transplant Recipients

A Study of the Swedish Cohort With Regard to Tumor Site

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Objective: To establish the anatomical site distribution of cutaneous squamous cell carcinoma (SCC) in organ transplant recipients (OTRs) with regard to age and sex.

Design: Retrospective population-based cohort study of OTRs.


Patients: From the cohort of 5931 OTRs, we could include 179 patients with 475 cutaneous SCCs. Information on the sites was received from the cancer registry and from the histopathological reports.

Results: The site of each SCC was registered in a computer program displaying the results on a 3-dimensional human figure. The head and neck were the predominant sites in male patients, and the trunk was the predominant site in female patients. The most common site in younger patients (born in 1940 or after) was the chest; and in older patients, the face. The ear was a common site in male patients, but, in contrast, no tumors were located there in female patients. Overall, the OTRs were younger compared with the overall Swedish population with cutaneous SCC.

Conclusions: There are differences in the anatomical site distribution of cutaneous SCCs in OTRs with regard to sex and age, and with regard to the general distribution in Swedish patients. The level of sun exposure is considered the most important factor in explaining those differences, and highlights the importance of sun avoidance in this group of patients.

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During the past several decades, organ transplantations have been performed with increasing success and the number of recipients and years of life extended are steadily growing. However, the dark side of this success story is the complications of the lifelong immunosuppressive therapy the patients experience to prevent rejection of the new organ. There is a well-known increased risk of cancer in organ transplant recipients (OTRs), and skin cancer is the most common malignancy. For cutaneous squamous cell carcinoma (SCC), there is a 100-fold increased risk. There is also a general agreement that skin cancer in OTRs is caused by the interaction of multiple factors. These include the direct effect of immunosuppression, exposure to UV radiation (UVR), and local infection with oncogenic human papillomavirus.

The importance of UVR is indicated by the occurrence of tumors predominantly on sun-exposed sites, particularly in fair-skinned individuals who have had a high level of UVR exposure. Poor tanning ability, rather than the amount of sun exposure, seems to be the most important factor.

See also pages 467 and 507

In this study, we performed a detailed analysis of the distribution of SCCs on different body sites by a newly developed computer program containing a movable 3-dimensional human figure. The purpose was to establish whether there are differences in the localization of SCC in OTRs with regard to sex and age. The base of this study was the Swedish organ transplant cohort.
The 475 tumors consisted of 387 SCCs and 88 SCCs in situ. Of the patients, 49.2% had 1 SCC, 47.4% had 2 to 10 SCCs, and 3.4% had 11 to 26 SCCs. The anatomical site distribution of the SCCs is shown for both sexes in the Table. As expected, the predominant sites were located on sun-exposed areas. The head and neck were the predominant sites in male patients, while SCCs on the trunk, especially on the chest and extremities, were more frequently observed in female patients. No SCCs were located on the ears of the female patients, in contrast to the male patients, who had many SCCs at that site (Figure 1).

The site distribution of SCC by age (Figure 2) shows that older (born before 1940) patients’ SCCs are located predominantly on the head, while younger patients have their SCCs predominantly on the trunk and extremities.

We also compared the age distribution of the SCCs (n=475) in OTRs (Figure 3a) with the general age distribution of the SCCs (n=2562) in the Swedish Cancer Registry, 1997 (Figure 3b). The SCCs in OTRs are much more common in younger persons than in the general population in the Swedish Cancer Registry, reflecting the increased risk of cancer after transplantation.

The main finding of our study was that the anatomical site distribution of SCCs in OTRs differed depending on sex and age, and that SCCs in younger persons are more common than in the general population of Swedish SCC patients. The most common sites were the head and neck for males, and the trunk for females. These findings, together with the fact that several SCCs were located on the ears of males in contrast to females (who had no SCCs there), point out the importance of UVR. Because of differences between males and females with regard to hairdo fashions, the obvious explanation might be that females had protection from their hair. That younger patients had their SCCs predominantly on the trunk and extremities is a bit more difficult to explain in terms of UVR exposure. One probable explanation is that the protection of hair is important also in this group, and prevents the high incidence on the head and neck. As young males grow older, many of them lose their hair protection and become bald. Apart from the hair protection factor, the angle of incident UVR entering the skin at different body sites seems to be important. Obviously, this factor can explain the concentra-

### METHODS

### PATIENTS

From the Swedish organ transplant cohort composed of 5931 patients who underwent transplantation of their kidney (n=5139), liver (n=397), or other organ (heart, lung, and pancreas) (n=395) from January 1, 1970, through December 31, 1997, described in detail elsewhere, we selected all patients, living or dead, with cutaneous SCC who were registered in the national Swedish Cancer Registry.

We could identify 273 patients with a total of 656 SCCs. After approval from the Karolinska Institute Research Ethical Committee and with a written consent from all living patients, we sent a request to all 33 different histopathological laboratories that had reported the SCCs and asked for the original histopathological report. Twenty-four laboratories (73%) sent us the requested documents. With this method, 179 patients with 475 SCCs were available for the analysis of tumor site: 132 male patients had 329 SCCs and 47 female patients had 146 SCCs. The mean time from transplantation to first SCC was 7.2 years (range, 0-21 years) for male patients and 47 years (range, 11-71 years) for female patients. The mean age at transplantation was 51 years (range, 30-77 years) for male patients and 55 years (range, 30-77 years) for female patients; the mean age at first SCC was 58 years (range, 22-74 years) for male patients and 47 years (range, 11-71 years) for female patients. The main finding of our study was that the anatomical site distribution of the SCCs is shown for both sexes in the Table. As expected, the predominant sites were located on sun-exposed areas. The head and neck were the predominant sites in male patients, while SCCs on the trunk, especially on the chest and extremities, were more frequently observed in female patients. No SCCs were located on the ears of the female patients, in contrast to the male patients, who had many SCCs at that site (Figure 1).

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### RESULTS

The main finding of our study was that the anatomical site distribution of SCCs in OTRs differed depending on sex and age, and that SCCs in younger persons are more common than in the general population of Swedish SCC patients. The most common sites were the head and neck for males, and the trunk for females. These findings, together with the fact that several SCCs were located on the ears of males in contrast to females (who had no SCCs there), point out the importance of UVR. Because of differences between males and females with regard to hairdo fashions, the obvious explanation might be that females had protection from their hair. That younger patients had their SCCs predominantly on the trunk and extremities is a bit more difficult to explain in terms of UVR exposure. One probable explanation is that the protection of hair is important also in this group, and prevents the high incidence on the head and neck. As young males grow older, many of them lose their hair protection and become bald. Apart from the hair protection factor, the angle of incident UVR entering the skin at different body sites seems to be important. Obviously, this factor can explain the concentra-
tion of SCCs on the chest of females, and the fact that the arms are a more common site than the legs in OTRs. However, there are probably several other important risk factors that might differ in different age groups, including sun habits, the immunosuppressive regimen, and infection with human papillomavirus. Genetic factors and skin type are also important.

When the tumors were plotted, we mainly used data from the histopathological reports. In doing so, we were able to achieve a more precise anatomical location than the information already existing in the Swedish Cancer Registry (ie, body sites according to International Classification of Diseases, Seventh Revision [ICD-7] code). Despite the many studies reporting skin cancer in OTRs, only a few have reported the anatomical site distribution of the tumors. In a study of 138 SCCs in 39 patients from the Netherlands, SCCs in renal transplant recipients were far more often confined to sun-exposed areas than basal cell carcinomas. In a study of 580 kidney and 150 heart transplant recipients from France, most premalignant and malignant epithelial lesions were located on sun-exposed areas. These findings correspond with our research. In another study of 33 SCCs in 94 patients from Italy, the researchers concluded that the anatomical site distribution of the SCCs diagnosed in their OTRs roughly resembled the distribution in the general population. However, in that study, the figures used for the anatomical site distribution in the general population were not based on the population of Italy. The resemblance with the general population was also found in this study when including only first cancers, and adjusting for age differences between the OTRs and the general population. This implies that the transplantation and immunosuppression do not change the site distribution of first cancers. However, the site distribution for all cancers (Table) differs from the distribution of the general population. This difference comes from a different site distribution

Figure 1. Distribution of squamous cell carcinomas in the head and neck region of organ transplant recipients.
of nonfirst cancers. A few patients with many cancers affect the site distribution of cancers because some of their cancers are clustered on the same anatomical site. The influence of these extremes is most noticeable for female patients, because the number of patients was fewer compared with males (47 vs 132). As an example of the clustering, the patient with the most cancers had 26, 21 of which were located on the trunk.

Our findings again stress the importance of extensive education of OTRs about the risk of developing skin cancer and its association to sun exposure. They should be advised to wear protective clothing and use an effective UV-B/UV-A sunscreen with a sun protective factor of 15 or higher daily, and tanning bed use should be prohibited. Patients with Fitzpatrick skin type I or II must be even more strictly advised,11 and males should protect their ears from sun exposure. Despite the advice given to OTRs, their knowledge about the skin cancer risk and preventive measures is not good. In a British15 study, only 54% of the OTRs remembered receiving such advice, and in a recent study, only 42% of OTRs with SCC and 39% of control OTRs (without SCC) stated that they had received information about sun protection.11

In conclusion, there are differences in the anatomical site distribution of SCCs in OTRs with regard to sex, age, and the general distribution in Swedish patients. This must be considered to optimize the monitoring of this group of patients.

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REFERENCES


\[\text{Archives Web Quiz Winner}\]

Congratulations to the winner of our January quiz, Alfred F. Ammoury, MD, fourth-year resident in dermatology, Division of Dermatology, Faculty of Medicine, Lebanese University, Beirut, Lebanon. The correct answer to our January challenge was Sweet syndrome. For a complete discussion of this case, see the “Off-Center Fold” section in the February ARCHIVES (Guevara-Gutiérrez E, Tlacuilo-Parra A, Uribe-Jímenez E. Erythematous plaques with fever and leukocytosis. Arch Dermatol. 2005;141:263-268).

Be sure to visit the Archives of Dermatology Web site (http://www.archdermatol.com) to try your hand at the Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of The Art of JAMA II.