Skin carcinomas in organ-transplant recipients: from early oncogenic events to therapy

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CHAPTER 7

The occurrence of residual or recurrent squamous-cell carcinomas in organ-transplant recipients after curettage and electrodessication

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The occurrence of residual or recurrent squamous cell carcinomas in organ transplant recipients after curettage and electrodesiccation

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Conflicts of interest
None declared.

Summary

Background Organ transplant recipients frequently develop multiple squamous cell carcinomas (SCCs). Surgical excision and Mohs micrographic surgery are frequently used treatments for these carcinomas; however, curettage and electrodesiccation are a useful alternative in these patients.

Objectives To evaluate the efficacy of curettage and electrodesiccation for the treatment of appropriately selected low-risk SCCs in organ transplant recipients at different sites.

Methods Between April 1989 and December 2004, 211 SCCs in 48 organ transplant recipients were treated by curettage and electrodesiccation. Only histologically confirmed SCCs were considered in this study. The charts of these patients were retrospectively reviewed and checked for the rate of residual or recurrent SCCs. The occurrence of residual or recurrent SCCs at different locations after treatment of SCCs with curettage and electrodesiccation was estimated with Kaplan–Meier survival analysis.

Results The mean follow-up time after curettage and electrodesiccation of the individual SCCs was 50 months (median 41; range 3–186). In total, 13 residual or recurrent SCCs were observed in 10 patients. The overall rate of residual or recurrent SCCs was 6%, with 7% for SCCs on the dorsum of the hands or fingers, 11% for SCCs on the head and neck, 0% for the forearms, and 5% for the remaining nonsun-exposed areas (shoulder, legs). No major clinical or cosmetic adverse events were registered after treatment.

Conclusions In organ transplant recipients with many SCCs curettage and electrodesiccation can be a safe therapy for appropriately selected low-risk SCCs, with an acceptable cure rate.

Organ transplant recipients are at an increased risk of developing nonmelanoma skin cancer, of which cutaneous squamous cell carcinomas (SCCs) are the most prevalent tumours.[1,2] In these immunocompromised patients SCCs appear to be more aggressive than SCCs in immunocompetent patients, and multiple tumours frequently develop in short periods of time.[3]

SCCs in organ transplant recipients are often treated by surgical excision with histological examination.[4] Moh's micrographic surgery can be performed in high-risk tumours.[1] Recently, two international groups of mainly dermatologists published guidelines about treatment and prevention of SCC in the transplant population and recommended that these lesions should be managed by destructive or excisional modalities.[5,6]

Curettage and electrodesiccation is a treatment option in selected tumours, for example nonulcerated SCCs with well-defined margins, smaller than 2 cm and localized on low-risk locations such as the trunk and extremities.[6] Successful outcome is associated with the physician's experience.[6,7]

Large case series in immunocompetent patients are available that report on the efficacy of curettage and electrodesiccation for the treatment of skin cancer.[8] However, there are few data published on the specific outcome after curettage and electrodesiccation of different clinical types of SCCs and larger tumours.[9] A study in which 981 SCCs were treated with curettage and electrodesiccation reported recurrence rates of 1·3–3·7%.[10] Three larger series of 947, 894 and 104 cases, respectively, of both SCCs and basal cell carcinomas that were treated with curettage and electrodesiccation, reported excellent 5-year cure rates ranging from 96% to 100%.[11–13]

As far as we know there are no studies examining curettage and electrodesiccation as a treatment of SCCs in organ

transplant recipients. In the literature, there is only one case of multiple SCCs in an organ transplant recipient that were successfully treated by curettage.[14] Although not substantiated by the literature, curettage and electrodesiccation have been widely used in organ transplant recipients, usually for superficial or early skin cancers.[15] The purpose of this retrospective follow-up study was to evaluate the cure and recurrence rate of SCCs after treatment with curettage and electrodesiccation in organ transplant recipients and to compare the cure and recurrence rates at different skin locations.

Patients and methods

Since 1966, roughly 2000 patients received a kidney or kidney–pancreas transplant at the Leiden University Medical Centre (LUMC), Leiden, the Netherlands. Approximately 200 organ transplant recipients with skin problems were regularly seen at the Department of Dermatology at the LUMC. Liver and heart transplant recipients were also seen occasionally; these had received their organs at other centres. Initially, all SCCs were treated by surgical excision. In April 1989 we started to treat some SCCs with curettage and electrodesiccation. Gradually this treatment became a more common scenario in our clinic in appropriately selected low-risk SCCs.

Low-risk SCCs were selected based on clinical grounds only: we used curettage and electrodesiccation in tumours which were less than 2 cm in size, which had developed within less than 3 months, and which did not clinically appear to infiltrate into the deeper tissues. After local anaesthesia most of the tumour mass was removed with a scalpel and this material was always sent for histological examination. The remaining tumour mass was removed with a curette and the bottom and the margins of the tumour were subjected to electrodesiccation. The procedure of curettage and coagulation was repeated several times.

Only SCCs confirmed by histological examination and treated with curettage and electrodesiccation between April 1989 and December 2004 were included in the study. All patients in the study were routinely seen in the outpatient dermatology clinic of the LUMC at 3-monthly intervals or more frequently when indicated. Their medical records were reviewed. Data were collected on localization of the tumour; possible residual or recurrent SCC, and time period to this occurrence; length of follow-up; and complications of treatment.

Using curettage and electrodesiccation, the difference between noncured or residual tumours and *de novo* or recurrent tumours cannot be made clearly based on clinical or histological grounds. An SCC was considered not to be cured or to recur if a histologically confirmed SCC occurred at the same location as the primary tumour during the follow-up period. Most of the time the locations of new SCCs were clearly different compared with the initial SCC. If there was any doubt about the location, the new SCC was considered to be a residual or recurrent SCC. Sun-exposed skin was defined as skin on the dorsum of the hands and fingers, forearms, and the head and neck region; nonsun-exposed skin was defined as all remaining locations.

Data were analysed using SPSS version 12·0 for Windows (SPSS, Chicago, IL, U.S.A). The rate of residual or recurrent SCCs after treatment of SCC by curettage and electrodesiccation was calculated with a Kaplan–Meier survival analysis. The date of the curettage and electrodesiccation was used as the opening date for this calculation. As the closing dates we used the date of the histological diagnosis of the residual or recurrent SCC, the patient's death, or the last visit of the patient in our outpatient clinic. Survival functions for the different locations of the SCCs were compared using the log rank test.

Results

Altogether, 211 SCCs occurring in 48 organ transplant recipients were treated with curettage and electrodesiccation in our Medical Centre between 1989 and the end of 2004. All the lesions with a few exceptions were treated by one experienced dermatologist (J.N.B.B.) or under the direct supervision of this dermatologist.

The main characteristics of the patients with and without residual or recurrent SCCs are depicted in Table 1. The 48 patients were followed for a mean ± SD period of 73 ± 48 months (median 70, range 3–186) as the first SCC was treated with curettage and electrodesiccation.

The mean follow-up period of the individual 211 SCCs was 50 months (median 41, range 3–186). Residual or recurrent SCCs were observed in 10 of 48 patients. Patients with residual or recurrent SCCs tended to be younger, were more often female and had more SCCs in their medical history (Table 1). These differences did not reach statistical significance with the exception of the total number of SCCs treated with curettage and electrodesiccation, which was much higher in the patients with recurrent SCCs (Table 1).

Most of the SCCs treated with curettage and electrodesiccation were located on sun-exposed skin (n = 129, 61%), and predominantly on the dorsum of the hands and fingers (n = 81, 38%). The tumour characteristics for the different skin localizations are displayed in Table 2.

Residual or recurrent SCCs were clinically and histologically documented in 13 (6%) of the 211 treated SCCs occurring in 10 of the 48 patients (Table 3). The mean ± SD time to recurrence was 10 ± 10 weeks (median 8, range 2–40). All residual or recurrent skin cancers were treated by surgical excision and we did not observe any additional recurrences after this excision during the follow-up period of between 8 and 128 months (Table 3). Four patients died from non-SCC-related causes during the follow-up period. One of these patients had a residual or recurrent SCC on the left temple, 11 years before his death.

The rate of residual or recurrent SCC after treatment with curettage and electrodesiccation of the SCCs for the different locations is shown in Figure 1. The differences were not statistically significant (P = 0·44). The majority of the residual or recurrent SCCs, 11 of 13, developed within 12 weeks of

Table 1 Characteristics of the patients

	Without residual or recurrent SCCs	With residual or recurrent SCCs
Total number of patients	38	10
Sex: M/F	22/16	3/7
Type of transplantation		
Kidney	33	9
Kidney-pancreas	3	1
Liver	1	0
Heart	1	0
Time period after transplantation at last outpatient visit (years), mean ± SD (range)	24 ± 8 (7–38)	27 ± 7 (12–37)
Age at last outpatient visit (years), mean ± SD (range)	62 ± 9 (43–79)	56 ± 10 (44–72)
Age at time of first SCC (years), mean ± SD (range)	52 ± 10 (36–77)	47 ± 8 (37–62)
No. of SCCs per patient (total), mean ± SD (range)	8 ± 8 (1–38)	18 ± 11 (6–39)
No. of SCCs per patient treated with curettage and electrodesiccation, mean ± SD (range)[a]	3 ± 3 (1–18)	10 ± 7 (3–19)
Follow-up time since first SCC treated with curettage and electrodesiccation (months), mean ± SD (range)	70 ± 50 (3–186)	84 ± 39 (26–145)

SCC, squamous cell carcinoma. [a]The differences between the two groups were not statistically significant with the exception of number of SCCs per patient treated with curettage and electrodesiccation ($P = 0{\cdot}01$).

Table 2 Tumour characteristics

Location of SCCs	No. of primary SCCs (%)	No. of residual or recurrent SCCs	Time to residual or recurrent SCCs (weeks)
Dorsum of the hand and fingers	81 (38%)	6 (7%)	2, 6, 8, 9, 16, 40
Head and neck	28 (13%)	3 (11%)	5, 8, 8
Forearms	20 (10%)	0	
Remaining locations	82 (39%)	4 (5%)	3, 6, 10, 11
Total	211 (100%)	13 (6%)	

SCC, squamous cell carcinoma.

Table 3 Characteristics of patients with residual or recurrent SCCs after curettage and electrodesiccation

Patient no.	Sex	Age (years)	Localization of SCC and histological type	Time to residual or recurrent SCCs (weeks)	FU after excision residual or recurrent SCC (months)
1	M	42	Finger web (I-II) right hand[a]	2	25
2	M	55	Dorsum left hand[a]	8	33
		57	Left shoulder[a]	3	8
3[c]	M	50	Left temple[b]	5	128
4	F	45	Dorsum left hand[a]	6	85
5	F	49	Ventral part right upper leg[a]	6	26
		50	Right shoulder[a]	11	16
6	F	55	Frontal part of the scalp[a]	8	82
		55	Anterior part of the scalp[b]	8	82
7	F	39	Dorsum left hand[a]	9	53
8	F	66	Right lower leg[a]	10	81
9	F	67	Third finger right hand[a]	16	65
10	F	39	Third finger right hand[a]	40	83

SCC, squamous cell carcinoma; FU, follow-up. [a]Well-differentiated SCC; [b]poorly differentiated SCC; [c]patient died at age 61 years from other cause.

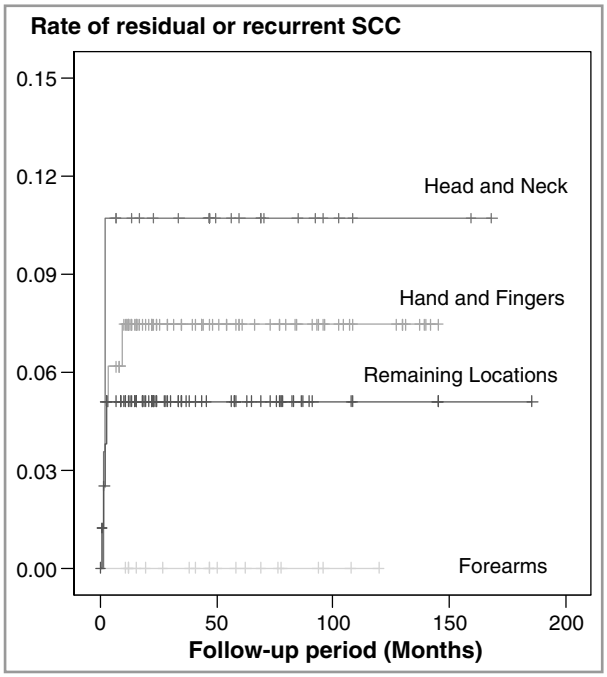

Fig 1. Kaplan–Meier survival analyses showing residual or recurrent SCCs on different locations of the body. The censored values are indicated.

follow-up; two developed within 40 weeks of follow-up. After this time period no additional residual or recurrent SCCs were observed (Fig. 1). No major clinical or cosmetic adverse events were registered after treatment.

Discussion

Our data show that curettage and electrodesiccation performed by a person with experience in this procedure is an effective treatment for SCCs in organ transplant recipients with multiple appropriately selected low-risk SCCs, with a low rate of residual or recurrent SCC of 6%. This rate is slightly higher than the rate of 1·3–3·7% in earlier case series with immunocompetent patients.[10–13]

Although we treated a limited number of SCCs in the head and neck region without encountering significant problems, these high-risk SCCs are usually not recommended for treatment with curettage and electrodesiccation, because of the more aggressive nature of these SCCs and a higher risk of metastases. Therefore, this procedure should be discouraged for the head and neck region until the safety of curettage and electrodesiccation in these locations has been proved.

Curettage and electrodesiccation have many advantages. It should be emphasized, however, that curettage and electrodesiccation should only be performed by somebody with experience in this procedure. The cosmetic result is generally good or excellent and it is a relatively easy procedure. Clinical diagnosis, biopsy and definitive treatment can be completed in one visit. Therefore, it is possible to treat more lesions at the same time. Furthermore, no sutures have to be removed afterwards. All this makes curettage and electrodesiccation convenient for the patient who usually has more than one SCC.

SCCs on the dorsum of the hands and fingers may require reconstructive surgery or the use of a skin graft. This may necessitate a short stay in the hospital and sometimes complete anaesthesia. Most of the appropriately selected low-risk SCCs on the dorsum of the hands and fingers can be treated effectively with curettage and electrodesiccation, which is a much simpler procedure. In case of a residual or recurrent SCC reconstructive surgery is still a good option.

The main disadvantage of curettage and electrodesiccation is the lack of histopathological evaluation of the tumour margins. If a patient is examined regularly, this should not form a major problem. Other disadvantages of curettage and electrodesiccation are slow healing, the possibility of impaired wound healing, the increased risk of superficial infections and the risk of hypopigmentation and more prominent scars as a result of the procedure.

Remarkably, nearly all recurrences were observed within the first 12 weeks after treatment. This suggests that most 'recurrences' can be regarded as residual tumour. We did not observe any residual or recurrent SCCs later than 10 months after treatment, suggesting that in the case of tumour cells remaining, regrowth will occur rapidly, usually within weeks or at the most within several months after the procedure. We can conclude that the most critical period for evaluation is the first year after treatment, but patients should continue to be monitored regularly.

This is the first study that reports on the efficacy of curettage and electrodesiccation for SCCs in organ transplant recipients. A substantially long follow-up time was completed. Prospective randomized controlled trials are the best way to compare two treatment modalities, but this retrospective noncomparative study also provides valuable information. A randomized controlled trial with sufficient power to distinguish between a rate of residual or recurrent SCC of 2% and 6% after surgical excision and curettage and electrodesiccation, respectively, would require 424 SCCs in each treatment arm (power calculation with $\alpha = 0{\cdot}05$ and $\beta = 0{\cdot}8$), which is practically impossible to perform in one centre. In addition, the question can be asked whether a rate of residual or recurrent SCC of 2% instead of 6% would be clinically relevant, if excision offers the patient a second chance for complete cure, anyway.

In conclusion, based on the low rate of residual or recurrent SCC and the absence of significant clinical or cosmetic adverse events, we recommend curettage and electrodesiccation for organ transplant recipients who develop multiple appropriately selected low-risk SCCs, provided that the procedure is performed by an experienced person.

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