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**CLINICAL REPORT**

# Warts in a Cohort of Danish Kidney Transplanted Patients: Impact on Quality of Life

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**There are no published clinical studies evaluating the impact of warts on quality of life after transplantation. The aim of this study was to determine the frequency of self-reported skin warts and skin cancer and their impact on quality of life in kidney transplanted patients, as measured with the Dermatology Life Quality Index (DLQI). Of 740 patients with a functioning renal allograft and were free of dialysis who were surveyed, 568 returned the questionnaires. Patients were asked about general health issues, with a focus on transplantation history, cutaneous warts and whether they had ever had cutaneous cancer. A total of 285 (52%) patients replied that they had warts, and these increased with time since last transplantation, with a *p*-value < 0.0001. A total of 101 patients (18%) reported that they had ever had skin cancer. The median DLQI was 0 for patients not having warts, 1 for patients with warts, and 2 for patients having warts and skin cancer. In conclusion, renal transplant recipients experience increasing numbers of warts and skin cancer over time, and having skin cancer impairs patients' quality of life to a greater degree than warts.** ***Key words: transplantation; warts; skin cancer; DLQI.***

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Cutaneous warts, verruca vulgaris, are common and often harmless, but troublesome for patients. Most warts resolve spontaneously within months or years due to natural immunity. However, warts may become more resistant to treatment over time, they can be painful depending on their location, and they are viewed as socially unacceptable when located on visible areas.

Immunocompromised patients, e.g. renal transplant recipients, may develop cutaneous warts, keratoses, and skin cancers that are very difficult to treat and that persist over years with a low rate of spontaneous regression. There is great variation in the reported percentage of transplanted patients who have warts. This figure has been reported to be as high as 85% at 5 years after transplantation (1), while others (2) have reported up to 50% of renal transplant recipients having cutaneous warts at one year and 77–95% having warts at 5 years after transplantation.

There are no clinical studies evaluating the impact of warts on quality of life after transplantation. The relative importance of having cutaneous warts is likely to vary from patient to patient, and for some may represent no more than an inconvenience and be seen as a small price to pay for the benefit of a well-functioning renal allograft. It is important to acknowledge that, although not important for skin-related quality of life, over time warts may have an impact on the transplanted patient's life-span due to their importance in skin cancer development.

The aim of this study was to determine the frequency of skin warts and skin cancer and their impact on quality of life in kidney transplanted patients.

## MATERIALS AND METHODS

### *Patients*

This is a questionnaire study of a cohort of kidney transplant patients attending the out-patient clinics at Rigshospitalet and Herlev Hospital, both university hospitals in Copenhagen, Denmark. All patients registered with a functioning renal allograft graft at the 2 clinics by 1 May 2007 were invited to participate in the study. The recruitment period ended on 1 October 2007. Approximately 500 patients with a functioning renal allograft and free of dialysis were identified at Rigshospitalet, and 240 patients at Herlev Hospital. Patients were reminded once to complete the questionnaire. The study was conducted in accordance with the requirements of the local ethics committee.

### *Questionnaire*

The patients were asked about general health issues, with a focus on transplantation history and current medication. Regarding cutaneous warts, the patients were asked about the presence, time of occurrence, localization and treatment. Furthermore, they were asked whether they had ever had cutaneous cancer, and a validated Danish version of the Dermatology Life Quality Index (DLQI) was distributed to the patients (3, 4). The questionnaire comprises 10 questions, each with a maximum score of 3. Thus, the maximum score for DLQI is 30, which describes the maximum influence on skin-related quality of life.

Quality of life assessment was completed only by those patients aged 18 years and above. Formal permission to use the DLQI questionnaire was obtained from Professor Andrew Y. Finlay.

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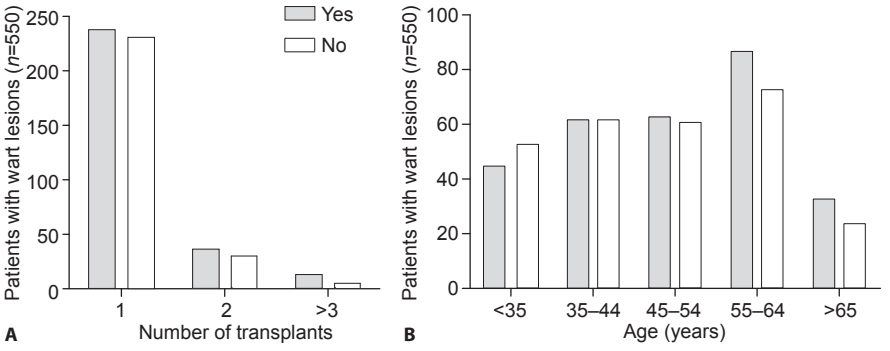


*Fig. 1.* (A) Wart lesions classified by number of transplants. (B) Wart lesions classified by age group.

*Statistical analysis*

The percentage of patients reporting having warts was analysed using logistic regression, with sex, hospital, number of transplants and age (categorized as < 35, 35–44, 45–54, 55–64 and ≥ 65 years) as factors, and time since last transplantation as an explanatory variable. Effects of skin conditions on DLQI scores were analysed using an over-dispersed generalized linear model with Poisson-distributed observations, where the effects on sex, age (categorized as above) and time since last transplantation (categorized as 0–5, 6–10, 11–15 and > 15 years) on DLQI scores were also assessed.

## RESULTS

A total of 700 questionnaires were distributed, 597 were returned and 568 (81.1%) could be analysed and were included in the study. Apart from the use of immunosuppressive drugs there was no statistical difference between the 2 transplantation centres at Rigshospitalet and Herlev Hospital.

Demographic data are summarized in Table I; 61% of the patients were males and the mean time since last transplantation was 8.0 years. Wart lesions classified by number of transplants and by age group are shown in Fig. 1.

A total of 553 patients answered the questions regarding cutaneous warts. Information on gender was not available for 6 patients. A total of 285 (52%) patients reported that they had warts. There was no statistical difference between gender and transplant centres. As shown in Fig. 2, the percentage of patients reporting having warts increased with time since last transplantation. This was found to be statistically significant ($p < 0.0001$) by logistic regression analysis.

A total of 557 patients answered the question about whether they had ever had skin cancer. Of these, 101 patients (18%), equally distributed between genders, answered positively.

Table I. *Demographic data*

| | Men *n* (%) | Women *n* (%) | Total *n* (%) |
|---|---|---|---|
| Gender ($n = 547$) | 335 (61) | 212 (39) | 547 (100) |
| Patients with warts ($n = 553$) | 166 (50) | 115(54) | 281 (51) |
| Patients with skin cancer ($n = 557$) | 59 (17) | 42 (19) | 101 (18) |

There were minor differences in the use of immunosuppressants between the 2 transplanting centres, as shown in Table II. There were no differences in the incidence of warts and skin cancer between the 2 transplanting centres.

Regarding quality of life, the DLQI questionnaire was answered by 508 patients and the scores were analysed using an over-dispersed Poisson model, with type of lesion, sex, age and time since last transplantation as explanatory variables. The DLQI was affected significantly by type of lesion (ratio of expected DLQI for warts and cancer to warts only: 1.75, 95% confidence interval (CI) (1.26, 2.42); for no warts to warts only: 0.55, 95% CI (0.41, 0.75); $p < 0.0001$ for no difference between the 3 lesion types). Similarly, sex affected the DLQI significantly (ratio of expected DLQI for females to males: 1.56, 95% CI (1.22, 2.00)), $p = 0.007$ for no difference between males and females. A summary of the DLQI answers is shown in Table III.

Age and time since last transplantation, as well as transplantation centre, did not influence DLQI ($p > 0.10$).

The patients were also asked about their self-perceived health. Sixty-nine percent judged their health to be very good or good, while only 3% judged their health to be poor or very poor. This was not influenced by the presence of warts.

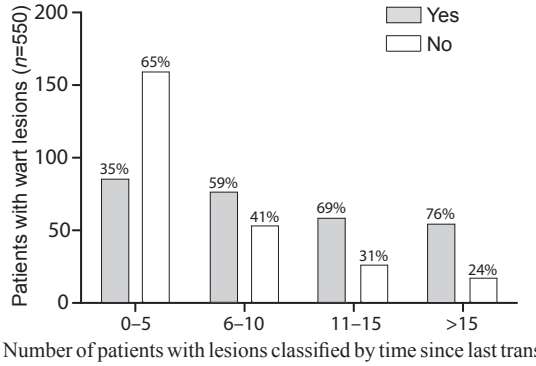


*Fig. 2.* Number of patients with lesions classified by time since last transplant (years). Effect of time since last transplantation: $p < 0.0001$ when analysed with logistic regression analysis.

Table II. *Immunosuppressive medication, classified by hospital*

| | Hospital | | |
|---|---|---|---|
| | Herlev *n* (%) | Rigshospitalet *n* (%) | Total *n* (%) |
| Glucocorticoid | 189 (98) | 368 (98) | 557 (98) |
| Cyclosporine | 160 (83) | 235 (63) | 395 (70) |
| Tacrolimus | 22 (11) | 92 (25) | 114 (20) |
| Azathioprine | 87 (45) | 100 (27) | 187 (33) |
| Mycophenolate mofetil | 75 (39) | 218 (58) | 293 (52) |
| Sirolimus | 4 (2) | 19 (5) | 23 (4) |
| Mycophenolic acid | 0 (0) | 16 (4) | 16 (3) |
| Total | 193 (100) | 374 (100) | 567 (100) |

Table III. *Dermatology Life Quality Index (DLQI)*

| | Wart lesion or skin cancer | | | |
|---|---|---|---|---|
| | Warts only | Warts and cancer | No warts | Total |
| Patients, *n* (median) | 199 (1.0) | 77 (2.0) | 232 (0.0) | 508 (1.0) |
| [q1;q3] | [0;3] | [1;5] | [0;1] | [0;2] |
| Min–Max | 0.0–23.0 | 0.0–21.0 | 0.0–28.0 | 0.0–28.0 |

Effect of skin conditions: $p<0.0001$.
Subjects who have not answered the DLQI are not included.
Min: minimum; Max: maximum.

## DISCUSSION

Over the last decades improvements in the handling of transplanted patients have brought increased graft survival after renal transplantation. With increased graft survival and duration of immunosuppressive treatment, increased comorbidity has been seen. Cutaneous side-effects are particularly common, especially warts and cutaneous cancers.

The results of this study confirm that a high percentage of kidney transplanted patients develop cutaneous warts with increasing time after transplantation. In 1984 Boyle et al. (5) reported that 31% of kidney transplanted patients had cutaneous warts, while 5% had cutaneous cancer. These patients had a mean time since transplantation of 4.2 years.

It is well established that the incidence of warts increases with increasing time of immunosuppression. This has been confirmed in our cohort, as the incidence of self-reported warts increased with increasing time since last transplantation.

In our study patients were asked whether they had warts, but it was not specified whether this meant common warts or warts in general, thus 52% is not a surprisingly high proportion of the patients in our cohort having warts. Common warts, which have a general preference for the hands and feet, were present in our cohort at 12% on the palms and 11% on the soles of the feet. The highest incidence of self-reported warts was mainly located at the sun-exposed parts of the skin, such as the back of the hands and face (Fig. 3). It should be taken into consideration that these lesions might have been actinic keratoses, seborrhoeic keratoses, or anything that patients believed to be warts, as there was no validation by physician assessment or histology.

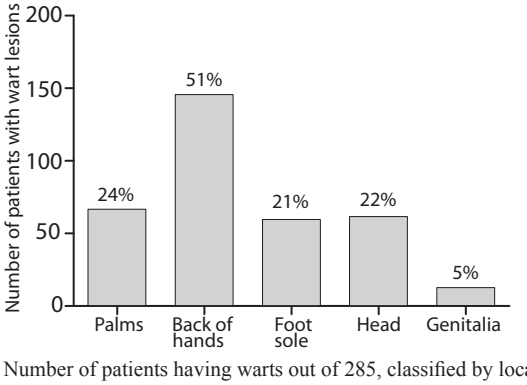


*Fig. 3.* Number of patients having warts out of 285, classified by location.

The cumulative risk of skin cancer in transplant recipients depends on geographical location and ethnicity and has been estimated as 10–15% after 10 years in a mainly Caucasian population in the northern part of Europe (5–7). In our study self-reported cumulative risk of skin cancer was 18%, with a mean of 7.8 years after transplantation.

It is widely accepted that quality of life is greatly increased when comparing patients on dialysis with successfully transplanted patients (8). It is also well known that many skin complications accompany the maintaining of a functional graft, with warts and cutaneous cancers being the most common. Cutaneous warts in immunosuppressed patients are very difficult to treat, and it has been reported previously that these problems have a significant impact on quality of life. Moloney et al. reported that 16% of the transplanted patients had a DLQI of above 6 (1). In our population 12.3% of the transplanted patients with warts reported a DLQI of above 6.

It was confirmed in our population that having warts has a significant impact on the patient´s quality of life, as the median DLQI was 0 for patients not having warts, 1 for patients with warts and 2 for patients having warts and skin cancer.

Although our data does not prove that the skin cancer impaired quality of life, it was shown that having skin cancer impaired quality of life related to the skin to a greater extent than having warts alone or none at all, and that females are more impaired than males.

However, it is clear that the DLQI value for the population with or without warts, as well as with or without cancer, is considerably smaller than is seen for dermatological out-patients at a dermatological department in Denmark, where the mean DLQI for a population of 200 outpatients was 6.9 and 12.9 for hospitalized dermatological patients (4). The maximum value that can be

obtained in the DLQI questionnaire is 30, and the DLQI measurement is used when judging disease severity of patients with psoriasis, where a value of 10 and above is considered sufficiently high for systemic treatment (9). The mean DLQI score in a population of 100 healthy controls was 0.4 (4). In the same study a subpopulation of dermatological outpatients with viral warts the mean DLQI was 4.4 (4). Transplantation patients with warts had a median DLQI of 1, while patients with warts as well as cancer had a median DLQI of 2. This suggests that having skin cancer impairs the patient's quality of life to a greater degree than having warts. However, overall these are surprisingly low values, and it seems that the burden of the patient's skin problems is experienced as very low compared with the benefit of having a functioning renal allograft. These observations confirmed the results obtained by Moloney et al., where dry skin, itch, hypertrichosis, sebaceous gland hyperplasia and acne were factors perceived to have significant impact on quality of life, in contrast to the presence of viral warts and a history of skin cancer (1). In our study this was further confirmed by measurement of the patients' self-perceived health, as 69% judged their health to be very good or good, and this figure was not influenced by whether the patients had warts.

*The authors declare no conflicts of interest.*

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