

Dermatological Complications after Organ Transplantation

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Syed Mohammad Husain Rizvi from the Department of Dermatology, Oslo University Hospital defended his doctoral thesis titled *Long-term dermatological complications after organ transplantation* at the University of Oslo on December 14, 2020. His supervisors were Petter Gjersvik and Jan-Øivind Holm. Stefano Piaserico from the University of Padova and John Paoli from the University of Gothenburg were first and second opponents Available from: <https://www.duo.uio.no/bitstream/handle/10852/81800/1/PhD-Rizvi.pdf>.

Organ transplant recipients have a high risk of developing premalignant actinic keratoses and skin cancer, particularly squamous cell carcinoma. The increased risk of such sun-induced skin lesions is linked to the use of immunosuppressive drugs. Avoiding sun exposure, however, may lead to vitamin D deficiency.

We set out to study the risk of skin cancer in organ transplant recipients in Norway with a special emphasis on possible time trends. Also, we have studied the effect of ablative fractional CO₂-laser-assisted daylight photodynamic therapy in post-transplantation actinic keratoses and vitamin D levels in organ transplant recipients living in south-east Norway.

In a population-based study with all patients who received a kidney, heart, lung or liver transplant in Norway in the period 1968–2012 ($n=8,026$), cumulative hazard for squamous cell carcinoma increased sharply in patients transplanted in 1983–1992, reaching 61% in heart transplant recipients and 23% in kidney transplant recipients after 15 years, and then declining in patients transplanted in 1992–2002 and 2003–2012 (1). Overall standardized incidence ratio (SIR) for squamous cell carcinoma was 51.9 (95% CI 48.4–55.5), for melanoma 2.4 (1.9–3.9) and for Kaposi sarcoma 54.9 (27.4–98.2). Unadjusted SIR for squamous cell carcinoma was 102.7 (85.8–122.1) in patients transplanted in 1983–1987, declining to 21.6 (16.8–27.0) in those transplanted in 2003–2007. Adjusting for different follow-up time and other relevant factors in a multivariable Poisson regression analysis of SIR ratio, SIR peaked in patients transplanted in 1983–1987 and later declined significantly with relative SIR being 0.42 (95% CI 0.32–0.55), 0.31 (0.22–0.42) and 0.44 (0.30–0.66) in those transplanted in 1998–2002, 2003–2007 and 2008–2012.

Using a within-subject randomized controlled study design, we found that ablative fractional CO₂-laser treatment followed by daylight photodynamic therapy was more effective than daylight photodynamic therapy alone in treating thick actinic



Syed Mohammad Husain Rizvi (doctoral candidate) and Petter Gjersvik (main supervisor).

keratoses of the scalp and forehead in 12 organ transplant recipients, with an odds ratio for complete clinical response of 19.42 (95% CI 6.94–54.34) (2).

In an observational study with 94 organ transplant recipients living in south-east Norway, vitamin D deficiency, defined as 25-hydroxyvitamin D < 50 nmol/l, was found in 28 patients (29.8%) during winter and in 23 patients (24.5%) during summer (3).

In conclusion, we document a dramatic decline in the risk of cutaneous squamous cell carcinoma after organ transplantation in recent decades, although the risk remains much higher than in the general population. The decline may be explained by the use of less aggressive, less carcinogenic and more individualized immunosuppressive treatment. Better dermatological follow-up and improved sun exposure habits may also play a role. Ablative fractional CO₂ laser-assisted daylight photodynamic treatment could be considered in organ transplant recipients with thick actinic keratosis. Organ transplant recipients should be monitored for vitamin D defi-

ciency. These studies have implications for our understanding of the relationship between immunosuppressive drugs and skin cancer and for the management of sun exposure-related complications in organ transplant recipients.

LIST OF PUBLICATIONS

- I. Rizvi SMH, Aagnes B, Holdaas H, Gude E, Boberg KM, Bjørtuft Ø, et al. Long-term change in the risk of skin cancer after organ transplantation: a population-based nationwide cohort study. *JAMA Dermatol* 2017; 153: 1270–1277.
- II. Rizvi SM, Veierød MB, Mørk G, Helsing P, Gjersvik P. Ablative fractional laser-assisted daylight photodynamic therapy for actinic keratoses of the scalp and forehead in organ transplant recipients: a pilot study. *Acta Derm Venereol* 2019; 99: 1047–1048.
- III. Rizvi SM, Veierød MB, Thorsby PM, Helsing P. Vitamin D in Norwegian renal transplant recipients: A longitudinal study with repeated measurements in winter and summer. *Eur J Dermatol* 2015; 25: 234–239.