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Dermatologic management, sun avoidance and vitamin D status in organ transplant recipients (OTR)

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ABSTRACT

It is well known that skin cancer, especially cutaneous squamous cell carcinoma (SCC), in organ transplant recipients (OTRs) has higher incidence rates, behaves more aggressively and has higher rates of metastasis. OTRs who have been treated for many years with immunosuppressive medication are at the highest risk for developing malignant skin tumors. Protection against solar and artificial UV-radiation is crucial to prevent skin cancer in OTRs. However, investigations have revealed that solar UV-B-exposure and serum 25(OH)D levels positively correlate with decreased risk for various internal malignancies (e.g. breast, colon, prostate, and ovarian cancer) and other severe diseases. Therefore, it is important to detect and treat vitamin D deficiency in OTRs. This review discusses guidelines for the optimal management of these patients, that require communication between the transplant teams, the treating dermatologist and other clinicians.

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1. Introduction

There is a high need in developing guidelines of care for organ transplant recipients (OTR) for these patients represent an increasing and significant challenge to clinicians including dermatologists. During the last decades, the annual numbers of performed solid organ transplants have been continuously increasing world-wide. As the United Network for Organ Sharing reported, over 25,000 solid organ transplantations were performed in 2003 In the United States of America (US) alone (based on OPTN data as of January 1, 2004) [1]. OTR have an increased risk to develop malignancies, with skin cancer representing the most common malignancy [2]. Moreover, OTR in general develop a more aggressive form of these malignancies. In consequence, dermatologic surveillance is of high importance for OTR, and these patients represent an increasing and significant challenge to clinicians including dermatologists. In OTRs, patient and organ survival have increased remarkably over the past three decades as a result of better immunosuppressive regimens and better post-transplant care. However, it now has become evident that the more effective immunosuppression regimens have as severe and unintended consequence resulted in more frequent and aggressive skin cancers [3–6]. It is well known that solar and artificial UV-exposure both before and after organ transplantation increase the risk to develop skin cancer and that the incidence of skin cancer increases with survival time after transplantation [3]. The biological behaviour of these malignant skin tumors reveals a much more aggressive profile when compared to the non-immunosuppressed population, leading to considerable cutaneous morbidity, mortality and decrease in quality of life.

2. Solid organ transplant recipients: a high-risk group with increased incidence and prevalence of nonmelanoma skin cancer (NMSC)

Nonmelanoma skin cancer (NMSC), most importantly basal cell carcinomas (BCC) and cutaneous squamous cell carcinomas (SCC) is the single most commonly diagnosed malignancy in the Caucasian population. In the US alone, an estimated 1 million new cases are reported annually [7]. Cutaneous SCCs are in general easily managed in immunocompetent patients where they rarely grow aggressively or metastasize. However, when SCCs develop in individuals who have been immunosuppressed over long time periods (e.g. in solid OTRs), they grow aggressively and represent a difficult clinical management problem with substantial morbidity and mortality. The clinical characteristics of different types of skin cancer in solid organ transplant recipients are summarized in Table 1. We know today that NMSC accounts for appr. 90% of all skin cancers in transplant recipients [8–10]. SCC represents the most common skin cancer in transplant recipients, occurring up to 250 times as frequently as in the general population [10]. The incidence of BCC is increased by a factor of appr. 10 in solid OTRs [10]. It has been shown that following transplantation, the usual BCC/SCC ratio in the general population (4:1 in higher latitude, respectively

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Table 1
Clinical characteristics of different types of skin cancer in solid organ transplant recipients.

	Incidence	Growth pattern	Metastatic behaviour	Special considerations for therapy
Malignant melanoma (MM)	2–8-fold increased incidence as compared to the general population	More aggressive as compared to the general population	More aggressive as compared to the general population	Sentinel lymph node biopsy may be useful for MM that are more than 1 mm thick or that are ulcerated In patients with metastatic MM, reduction or discontinuation of immunosuppressive medication should be considered
Basal cell carcinoma (BCC)	Incidence increased appr. by a factor of 10 as compared to the general population	More aggressive as compared to the general population	None	BCC can be treated with various therapeutic modalities, including Electrodessication and curettage (ED&C), surgical excision, or Mohs' surgery depending on the size of the lesion, its location and whether it is recurrent. Topical imiquimod for superficial BCC has been reported in a limited number of cases, but preliminary results are encouraging.
Squamous cell carcinoma (SCC)	Incidence increased appr. by a factor of 250 as compared to the general population. Develop at younger ages, starting in general 3–5 years after transplantation.	More aggressive as compared to the general population. Can be divided in low and high risk SCCs. High frequency of local recurrence (13.4%) during the first 6 months after excision	More aggressive as compared to the general population. Remarkably high frequency of lymph node metastasis (7%) during the second year after excision. Metastatic SCCs are characterized by poor prognosis with a 3-years disease specific survival of 56%	Any lesion suspicious for SCC should be biopsied or excised. Electrodessication and curettage (ED&C) may be performed at the time of biopsy for those lesions that are clinically determined to be less aggressive. For lesions judged to be low risk, treatment options include: cryosurgery with curettage, ED&C, surgical excision, or Mohs' micrographic surgery. Aggressively growing SCC should be treated with excisional techniques, particularly Mohs' micrographic surgery, surgery with intraoperative frozen section evaluation, or excision with postoperative margin assessment. Margins should include the subcutaneous fat and 6–10 mm beyond any surrounding erythema. If there is evidence of perineural involvement, invasion of surrounding bones or glands, unclear margins, or if the lesion persists after excision, then further evaluation is necessary. Radiation therapy should be considered in cases where there is perineural involvement or where there is inability to achieve clear margins. Sentinel lymph node biopsy (SLNB) should be considered for patients with high risk SCC. The decision to decrease immunosuppressive therapy should be discussed with the patient's transplant team. Any patient with metastatic nodal spread should be evaluated for excision with therapeutic lymphadenectomy or primary radiation therapy (XRT). Patients with in-transit cutaneous metastasis who do not have lymph nodes that are positive for metastatic spread should have excision of the primary and satellite lesions. In these patients, Mohs' surgery is recommended. Chemotherapy, the use of systemic retinoids, and the reduction of immunosuppressive medication are additional options that should be considered in patients with nodal spread or satellite lesions

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