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Field Therapy in Solid Organ Transplant Recipients: Are We Initiating Early Enough?

Christina Topham BS, Dylan Haynes BS, R. Samuel Hopkins MD, Justin Leitenberger MD
Oregon Health & Science University, Portland, OR

ABSTRACT

Organ transplant recipients (OTRs) are at increased risk for more aggressive non-melanoma skin cancer (NMSC). Recent emphasis on field therapy has complimented the canonical surgical treatment paradigm. This retrospective analysis of survey responses by patients seen at Oregon Health and Science University from 2013-2018 offers insights into patient trends and practice gaps in caring for OTRs. All patients completed a 57-point questionnaire at their first clinic visit, which included questions regarding demographics, transplant history, dermatologic history, and use of field therapy. Of the 295 patients (mean age, 56 years; M/F: 193/102) who completed the questionnaire, field therapy was reported by 31 (11%) patients. Field therapy patients noted an overall higher AK and SCC burden, with a greater proportion of patients reporting >20 AKs and >10 SCCs. Field therapy use was sparse in the low AK/low SCC group (n=25) when compared to those reporting high AK/high SCC (n=11) burden (n=4 (16%) vs n=8 (73%), $P<0.01$). This data suggests that OTRs with several clinically evident AKs and/or a low number of SCCs are less likely to have been treated with field therapy modalities compared to OTRs who have developed >10 AKs or ≥6 SCCs. A delay in initiation of preventative measures or field therapy in this population, however, may be a missed opportunity for intervention. Early intervention with field therapy in particularly high-risk OTRs with a low skin cancer burden may mitigate future skin cancer development.

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INTRODUCTION

Organ transplant recipients (OTRs) are at increased risk for skin cancer, especially non-melanoma skin cancer (NMSC). In OTRs, NMSC tends to be more aggressive and result in higher rates of local recurrence and metastases.[1] Furthermore, areas of high (pre-)malignant burden, or "field cancerization," are common in this population.[1] Recent emphasis on "field therapy," or topical immunomodulatory regimens levied against field cancerization, has complimented the canonical surgical treatment paradigm.[2] We highlight survey data of a single-center specialty clinic noting a practice-gap in early initiation of field therapy in immunosuppressed patients.

METHODS

This retrospective cohort included all OTRs seen in a high-risk, post-transplant NMSC clinic in the Department of Dermatology at Oregon Health and Science University (OHSU) from 2013 to 2018. All patients completed a 57-point questionnaire at their first clinic visit, which included questions regarding demographics, transplant history, dermatologic history, and use of field therapy. Survey responses were entered into the Research Electronic Data Capture application. Data analysis was performed in the STATA statistical analysis program, version 15. Inferential statistics were performed using McNemar's and two-sample tests of proportion. The institutional review board at OHSU approved this study.

RESULTS

In total, 295 patients completed the questionnaire. Mean respondent age was 56 ± 15 years and 193 (65%) were men (Table 1). Field therapy was reported by 31 (11%) patients. Of those patients, 18 (58%) noted some improvement from the field therapy and four (13%) experienced an adverse effect as a result of field therapy. Actinic keratosis (AK) burden survey categories were defined as <5, 5-10, 11-20, >20, and unknown. Squamous cell carcinoma (SCC) burden survey categories were defined as 1, 2-5, 6-10, >10, and unknown. Field therapy patients noted an overall higher AK and SCC burden, with a greater proportion of patients reporting >20 AKs and >10 SCCs (Table 2).

Mid-range survey categories were used to define post-hoc cutoffs for low and high skin cancer burden for both AKs and SCCs. Low burden was defined as ≤10 AKs and <6 SCCs, whereas high skin cancer burden was defined as >10 AKs and ≥6 SCCs. Twenty-five patients reported a low AK/low SCC burden, and 11 reported a high AK/high SCC burden post-transplant. Field therapy use was sparse in the low AK/low SCC group when compared to those reporting high AK/high SCC burden (n=4 (16%) vs n=8 (73%); $P<0.01$) (Table 2).

TABLE 1.

Demographics and Field Therapy[a,b]	
Sex	0.7
Male	193 (65.4)
Female	102 (34.6)
Age in years	2.6-3.1
Mean (SD)	56.06 (15)
Transplant type	0.3
Kidney	141 (47.8)
Liver	59 (20)
Heart	63 (21.4)
Lung	14 (4.7)
Pancreas	11 (3.7)
Field therapy	31 (10.5)
5-FU	24 (8.1)
Imiquimod	6 (2)
Ingenol Mebutate	2 (0.7)
Diclofenac	2 (0.7)
Photodynamic therapy	5 (1.7)
Chemo-wrap	0
CO2 laser resurfacing	6 (2)

Abbreviations: 5-FU, 5-fluorouracil; CO2, carbon dioxide
[a]Unless otherwise indicated, data are given as number (percentage) of patients
[b]Totals failing to add to 100% indicate incomplete survey responses

TABLE 2.

Skin Cancer Burden Stratified by History of Field Therapy[a,b]		
Skin cancer burden, n (%)	Field therapy (n=31)	Non-field therapy (n=264)
Actinic keratosis	23 (74.1)	34 (12.8)
≤20	10 (32.3)	21 (8)
>20	8 (25.8)	4 (1.5)
Squamous cell carcinoma	21 (67.7)	38 (14.4)
≤10	6 (19.4)	26 (9.8)
>10	9 (29)	2 (0.7)
Nodal metastasis	1 (3.2)	1 (0.4)
Basal cell carcinoma	16 (51.6)	22 (8.3)
≤10	9 (29)	16 (6.1)
>10	5 (16.1)	0
Melanoma	2 (6.5)	4 (1.5)
1	1 (3.2)	2 (0.7)
≥2	1 (3.2)	1 (0.4)
Rare skin cancers	3 (9.7)	4 (1.5)
Low skin cancer burden[c] (n=25), n (%)	4 (16)	21 (84)
High skin cancer burden[d] (n=11), n (%)	8 (72.7)	3 (27.3)

[a]Unless otherwise indicated, data are given as number (percentage) of patients
[b]Totals failing to add to 100% indicate incomplete survey responses
[c]Low skin cancer burden was defined post-hoc as ≤10 actinic keratoses and <6 squamous cell carcinomas
[d]High skin cancer burden was defined post-hoc as >10 actinic keratoses and ≥6 squamous cell carcinomas

DISCUSSION

This data suggests that OTRs with several clinically evident AKs and/or a low number of SCCs are less likely to have been treated with field therapy modalities compared to OTRs who have developed >10 AKs or ≥6 SCCs. We hypothesize this practice is common in the general population of immunocompetent patients. Given that the risk factors for skin cancer in OTRs are known, however, a delay in initiation of preventative measures or field therapy in this population may be a missed opportunity for intervention.[3] Early intervention with field therapy in particularly high-risk OTRs with a low skin cancer burden may mitigate future skin cancer development.

In the general population, field therapies have demonstrated significant efficacy in treating AKs and early SCC lesions, and may reduce the risk of SCCs requiring surgery as well as the incidence of new SCC development.[4] Published data demonstrating a benefit to field therapy in reducing skin cancer risk in OTRs specifically, however, is limited.[5] Nonetheless, dermatologists who specialize in care for OTRs report 5-fluorouracil cream as the most commonly used prophylactic intervention.[6] Hopefully future studies can align 'common practice' with evidence based medicine to best define optimal timing of field therapy initiation and advance preventative care guidelines in this high-risk population.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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AUTHOR CORRESPONDENCE

Justin J. Leitenberger MD
E-mail:..... leitenbe@ohsu.edu