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Free Tissue Transfer for Head and Neck Reconstruction in Solid Organ Transplant Patients

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Abstract

Background—Patients with head and neck malignancies who have had solid organ transplant and require free tissue transfer are a unique population. This study was performed to evaluate the effect of immunosuppression on the rate of perioperative complications and the success of free tissue transfer in the head and neck.

Methods—Complications in solid organ transplant patients undergoing free tissue transfer for reconstruction of head and neck malignancies from 1998–2010 were evaluated.

Results—A total of 22 flaps in 17 patients were performed. Eight patients (11/22 flaps) had complications. The median hospital stay was 6 days (range, 4–26 days). The median length of follow-up was 13.5 months (range, 3.5–49.9 months).

Conclusions—Solid organ transplant patients are at an increased risk of *de novo* malignancies due to chronic immunosuppression. This study demonstrates that free tissue transfer is a viable option in transplant patients with morbidity similar to nontransplant patients.

Keywords

Free flap; free tissue transfer; head and neck reconstruction; organ transplant; immunosuppression

Introduction

Solid organ transplant patients with head and neck malignancies requiring free tissue transfer are a unique population. The number of solid organ transplants in the U.S. increased by 29% from 1998–2007 (SRTR).¹ Patient 5-year graft survival rates following single solid organ transplantation range from 36.3–80.7% (SRTR) and continue to increase. The use of immunosuppressive agents increases the risk of *de novo* malignancy, including cutaneous malignancies.^{2–5} There is a cumulative risk of cutaneous malignancy reported at 5% per year.⁶ The increasing number of organ transplants and rates of graft survival will likely lead to greater rates of *de novo* malignancies. Organ transplant patients with head and neck malignancies occasionally require free tissue transfer for reconstruction of large defects.

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The presence of comorbidities potentially affecting wound healing is an important consideration in the preoperative work-up.⁷ Potential factors that may compromise wound healing include smoking, diabetes, malnutrition, previous irradiation, and immunosuppression.^{8–10} Initiation of the inflammatory cascade is an essential step in wound healing. Immunosuppression has been shown to affect wound healing through inhibition of necessary inflammatory mediators.¹¹ A recent study of free tissue transfer in solid organ transplant patients was performed, but the majority of the reconstruction sites were in distal extremities (11/19) with relatively few head and neck patients (5/19).¹² This study was performed to evaluate the effect of immunosuppression on the rate of perioperative complications and success of free tissue transfer in the head and neck.

Methods

We performed a retrospective review of all solid organ transplant patients undergoing elective free tissue transfer for head and neck malignancies between 1998–2010 at Oregon Health and Science University (OHSU) and the University of Alabama at Birmingham (UAB). Institutional review board approval was obtained at the respective institutions. Seventeen patients were identified and included in the study. Eleven patients were identified at OHSU and six patients at UAB. Patient age at the time of surgery, gender, primary malignancy, tumor stage, type of free flap reconstruction, transplanted organ(s), immunosuppression regimen, length of hospital stay, postoperative complications, and length of postoperative follow-up were evaluated. Complication outcomes included: flap failure, partial flap necrosis, wound infection, donor site or recipient site complications, hematoma, and seroma. Major complications were categorized as those requiring operative intervention or contributing to a prolonged hospital course.

Results

Seventeen patients had free tissue transfer following resection of head and neck malignancies. The median age of patients at the time of surgery was 62 years (range, 18–78 years) and a majority of patients were male (71%). Solid organ transplantation varied, with renal transplants comprising the majority of patients (65%) [Table I]. Patients had oral cavity SCC (29%), cutaneous SCC (47%), malignant fibrous histiocytoma (12%), basal cell carcinoma (6%), and spindle cell carcinoma (6%). The majority of flaps (59%) were performed following ablation of advanced T classification tumors, T3 or T4 [Table II]. Among the oral cavity SCC group, two patients were TNM stage II and three patients were stage III/IVa. The cutaneous SCC group had two patients with stage II, seven with stage III, and one patient with stage IV disease. In addition, 27% of flaps were performed for recurrent lesions. A total of 22 flaps were performed, with three patients receiving two flaps, and one patient receiving three flaps. A representative case is provided in Figure 1, with anterolateral thigh free flap reconstruction of a x by x cm defect following WLE. The majority of flaps used for reconstruction were radial forearm (36%) and anterolateral thigh flaps (32%) [Table III]. Most patients (59%) had extensive tumor resections, with wide local excision in addition to concurrent ablative surgery [Table IV]. The types of immunosuppressive medications used are listed in Table V. Only one patient was not on an immunosuppressive regimen at the time of free tissue transfer. There were postoperative complications in eight patients and 11/22 (50%) flaps [Table VI]. Of these complications, 45% were considered major and occurred in 24% of patients. Previous irradiation to the recipient site was present in 36% of all patients, and in 45% of flaps experiencing complications. The median hospital stay was 6 days (range, 4–26 days). There was not a significant difference between the mean hospital stay in the patient group experiencing flap complications (7.9 – 6.2 days) when compared to those not experiencing complications (6.1 – 1.2, $p = 0.35$). The median length of follow-up was 13.5 months (range, 3.5–49.9 months).

Survival was 29.4% at the time of last follow-up, with the deceased cohort surviving a median of 14.4 months (range, 3.2–49.9 months).

Discussion

Solid organ transplant patients are at an increased risk of *de novo* malignancies due to chronic immunosuppression.^{2–6} These patients will occasionally require free tissue transfer for coverage of large defects.¹³ Overall published free tissue transfer failure rates are 1–9%,¹⁴ but there are limited reports on failure rates in patients on immunosuppressive regimens. The flap failure rate in the current study is 4.5%.

Though there is a low rate of overall flap failure, a higher rate of complications exists. The impact of flap failure in the current series is demonstrated by Patient 1, who suffered multiple complications and hospitalizations. She had complications associated with all three free flap reconstructions. The last two free flaps were performed in an irradiated surgical field. In addition, she had a failed pedicled latissimus flap and wound dehiscence following a pedicled pectoralis flap. This resulted in a mean hospital stay of 13 days compared to the overall average hospital stay of 7 days.

Postoperative complications are common in the overall free tissue transfer population, with a recently reported rate of 29–33.5% in reconstruction of head and neck patients.^{10;15} A recent multicenter case series evaluating free tissue transfer in the solid organ transplant population had a complication rate of 42%, though the majority of flaps were performed on extremities in patients with peripheral vascular disease and diabetes.¹² This group of patients also had an average hospital stay of 10.5 days compared to 7.0 days in our cohort. This may indicate a population with greater comorbidities, including peripheral vascular disease and diabetes. The reason for free tissue transfer was not fully described. Some patients received free tissue transfer following malignancy extirpation, while others received flaps for treatment of chronic wounds. The mean follow-up was 6.8 years compared to 17.2 months in our cohort. The patients included in the current study represent a different patient population with respect to comorbidities. Another study by Moran et al. analyzed the contribution of renal failure and uremia-induced immunosuppression on free tissue transfer complications and survival.¹⁶ They had a 6% rate of primary free flap failure, with several other patients subsequently losing flaps to complications of progressive lower extremity ischemia. They noted immediate postoperative complications in 44% of their patients. They also had a high rate of diabetes (88%) and peripheral vascular disease (84%), compared to a diabetes rate of 24% in our cohort. Our study has a similar complication rate in head and neck patients treated with immunosuppressive medications.

Patient selection for free flap reconstruction includes assessment of comorbidities that may affect wound healing, including the immunosuppression regimen of solid organ transplant patients. Postoperative wound complications are reported to be increased with the use of rapamycin (sirolimus) compared to mycophenolate mofetil, tacrolimus and cyclosporine-based regimens.^{17–18} The increase of wound complications and lymphocele formation in patients on sirolimus is in exchange for decreased acute graft rejection and potential decreased risk of *de novo* malignancy. Only 10.8% of kidney transplant patients from 2006 had sirolimus included in their immunosuppressive regimen at one-year follow-up.¹ Though only two patients in the current cohort were on sirolimus, both experienced postoperative flap complications, including one seroma.

Other factors that may affect the rate of complications in our cohort include the presence of previous irradiation, compromising the vascularity of the recipient site. Yu et al. examined the outcomes of 1266 patients and reported a rate of radiation prior to free tissue transfer in

44% of patients.¹⁹ They found no significant difference in the rates of free flap failure between the non-irradiated and irradiated groups. The rate of other complications, such as wound infection, wound dehiscence, hematoma, and seroma was not specifically addressed. There is a reported significant increase in postoperative complications in patients having prior irradiation to the free tissue recipient site.⁹ Cohn et al. found a major complication rate of 66% in 35 patients who had a second round of radiation therapy prior to reconstruction.²⁰ The overall flap success rate was 94%.

Conclusion

Though there was a 50% postoperative flap complication rate, there was only a 4.5% flap failure rate. Of the complications experienced, 45% were considered major and occurred in 24% of patients. The majority of our patients presented with aggressive disease, resulting in significant ablative defects and poor survival. Free tissue transfer for reconstruction of complex head and neck defects is a viable option in transplant patients with failure rates similar to nontransplant patients.

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Figure 1.

A representative patient case is demonstrated. (A) A cutaneous squamous cell carcinoma is shown. Evidence of previous left ear surgery and malpositioning is seen. (B) A large soft-tissue defect is present following wide local excision. (C) Early post-operative follow-up with bulky soft tissue present prior to atrophy.

Table I

Type of Organ Transplant

Organ Transplanted	No. of Patients	%
Kidney	11	65
Liver	4	24
Heart	2	12
Lung	1	6

Table II

T Classification of Tumors

T Classification	No. of Patients	%
Tx	1	5
T1	0	0
T2	3	14
T3	3	14
T4	10	45

* Not included are three patients that had flaps for Malignant Fibrous Histiocytoma (no TNM staging system exists) and one patient that had two flaps due to osteoradionecrosis

Table III

Type of Flap

Flap	No. of Patients	%
Radial forearm	8	36
Anterolateral thigh	7	32
Latissimus dorsi	3	14
Fibula	2	9
Rectus abdominus	1	5
Lateral arm	1	5

Table IV

Ablative Procedures In Addition To WLE

Flap	No. of Patients	%
Parotidectomy	5	23
Segmental Mandibulectomy	5	23
Temporal bone resection	3	14
Total auriculectomy	2	9
Orbital exenteration	1	
Maxillectomy	1	5

WLE; wide local excision

Table V

Immunosuppressive Medications

Type of Immunosuppression	No. of Patients	%
Prednisone	15	88
Cyclosporine	7	41
Tacrolimus	6	35
Mycophenolate mofetil	4	24
Azathioprine	3	18
Sirolimus	2	12

Table VI

Postoperative Complications

Patient	Age	Type of Flap	Primary Disease	Complication	Immunosuppression
1	51	ALT	Oral SCC	Wound infection	Siro, Prednisone
	51	Fibula		Flap failure	
	53	Radial forearm		Donor site tendon exposure	
2	51	Lateral arm	Oral SCC	Donor site dehiscence	None
3	53	Latissimus dorsi	MFH	Donor site seroma	Siro, Prednisone
4	78	ALT	Cutaneous SCC	Partial flap necrosis	CyA, Prednisone
5	61	Radial forearm	Cutaneous SCC	Hematoma	Tac, AZA, Prednisone
	62	ALT		Wound infection	
6	66	Radial forearm	Cutaneous SCC	Hematoma	Tac, Prednisone
7	69	ALT	Spindle cell carcinoma	Hematoma	MMF, Tac, Prednisone
8	67	Radial forearm	MFH	Wound infection	MMF, Tac, Prednisone