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# Factors Affecting Cancer Recurrence after Microvascular Flap Reconstruction of the Head and Neck

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***Objective:*** **Our objective was to determine which factors are associated with cancer recurrence after microvascular reconstruction of the head and neck for squamous cell carcinoma (SCC).** ***Study Design:*** **A cohort of patients who fit the inclusion/exclusion criteria were identified retrospectively.** ***Methods:*** **A group of 184 patients who underwent successful surgical resection and simultaneous microvascular reconstruction of the head and neck for treatment of SCC were identified. The mean age was 60 (range 23–90) years, there were 115 males and 69 females, and mean follow-up was 26.2 (range 1–99) months. Various factors were analyzed to determine whether they were associated with cancer recurrence, including those pertaining to 1) recipient vessel choice, 2) prior cancer treatment, and 3) cancer staging criteria. Statistical analysis was performed using SPSS statistical software.** ***Results:*** **Overall cancer stage ($P = .005$), T stage ($P = .0001$), history of previous cancer treatment ($P = .004$), and history of previous chemotherapy ($P = .044$) were found to be statistically significant predictors of cancer recurrence on univariate analysis. However, on multivariate analysis, only T stage ($P = .005$) and history of previous cancer treatment ($P = .008$) remained as statistically significant predictors of cancer recurrence. Recipient vessel selection was not statistically associated with cancer recurrence.** ***Conclusions:*** **In our study, only T stage and a history of previous cancer treatment were associated with increased cancer recurrence. Neither the recipient vessel chosen nor its location impacted cancer recurrence. This suggests that recipient vessel selection and preparation for microvascular reconstruction do not jeopardize the adequacy of oncologic resection and are therefore oncologically sound.** ***Key Words:*** **Microvascular reconstruction, head and neck cancer, neck dissection, cancer recurrence, vessel selection.**
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## INTRODUCTION

Surgical resection of head and neck cancer enables removal of the disease and gives hope for cure; however, it also leads to defects that may cause major dysfunction and disfigurement. Reconstruction of defects created by tumor ablation attempts to minimize loss in form and function and has thereby enabled the oncologic surgeon to perform procedures that could not have been undertaken in the past.[1] Over the past few decades, the major contribution to head and neck reconstruction has been microvascular free tissue transfer.[2] This technique has gained acceptance as a reliable and versatile means of one-stage reconstruction in patients with head and neck cancer.[3–5]

Although progress in reconstructive surgery by way of microvascular free flaps has enabled more aggressive primary tumor resection, its use has at the same time required a more conservative approach to neck dissection. This is because of the necessary preservation of a recipient artery and a recipient vein to serve as the vascular supply to the free flap. These recipient vessels may lie in close proximity to the primary tumor or lymph nodes that contain metastatic disease, and, in this light, recipient blood vessel preservation may compromise the adequacy of resection. This modification to standard neck dissections, although necessary for free tissue transfer, can theoretically increase the risk for cancer recurrence.

To our knowledge, no previous study has investigated the impact of recipient vessel selection on cancer recurrence in patients who have undergone microvascular reconstruction for carcinoma of the head and neck. The aim of this study was to analyze multiple variables, including those pertaining to 1) recipient vessel choice, 2) prior cancer treatment, and 3) cancer stage, to determine which factors are associated with cancer recurrence after microvascular reconstruction of the head and neck for squamous cell carcinoma (SCC). We identified the factors that are associated with recurrence of SCC by an-

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TABLE I.
Cancer Stage of Patients.

| | Stage | T Stage | N Stage |
|---|---|---|---|
| 0 | Ø | 2 | 97 |
| 1 | 4 | 11 | 18 |
| 2 | 37 | 60 | 68 |
| 3 | 28 | 42 | 1 |
| 4 | 115 | 69 | Ø |

TABLE III.
Recipient Arteries.

| Artery | Quantity |
|---|---|
| Facial | 110 |
| Lingual | 18 |
| Superior thyroid | 28 |
| Occipital | 1 |
| Superficial temporal | 3 |
| External carotid | 12 |
| Transverse cervical | 12 |

alyzing a series of 184 patients who underwent free flap reconstruction.

## PATIENTS AND METHODS

This series comprised 184 patients who underwent complete surgical resection and simultaneous microvascular flap reconstruction for the treatment of SCC of the head and neck between 1995 and 2004 at the UCLA Medical Center. Complete surgical resection was defined as histologically uninvolved resection margins on pathologic analysis of the resection specimen. There were 115 men and 69 women ranging in age from 23 years to 90 (mean 60) years at the time of treatment. Primary tumors were located in the oral cavity/oropharynx in 166 cases, in the larynx or hypopharynx in 10 cases, and in the midface/skull base in 8 cases. The follow-up period varied from 1 month to 99 months, with the average length of follow-up being 26.2 months.

The main outcome measure was cancer recurrence. In recognition that most cases of cancer recurrence occur within 2 years of treatment in patients with SCC of the head and neck, a minimum follow-up period of 24 months was required for patients who were classified as being free from cancer recurrence. Patients with less than 24 months of follow-up included only those with cancer recurrence within 2 years of surgical resection. The length of follow-up in those patients who were classified as being free of disease at the end of follow-up ranged from 24 months to 99 months, with a mean follow-up period of 44.3 months in these patients.

A variety of factors were analyzed to determine whether they were associated with the incidence of cancer recurrence. These factors included the recipient artery used for free flap perfusion, the recipient vein used for free flap perfusion, the location of the recipient vessels in the side of the neck that was ipsilateral or contralateral to the primary tumor site, the overall cancer stage, the tumor T stage, the tumor N stage, history of any prior head and neck cancer treatment, history of prior radiation therapy, history of prior head and neck cancer surgery, and history of prior chemotherapy. For midline primary tumors and for tumors with significant bilateral involvement, the recipient vessels were classified as being ipsilateral to the tumor location. Additional analyses were performed to see whether the above factors influenced the pattern of cancer recurrence, with cancer recurrence being subclassified as either local cancer recurrence, regional cancer recurrence, or distant metastasis cancer recurrence.

The methods used for statistical analysis were selected after consultation with the Department of Biostatistics at the David Geffen School of Medicine at University of California Los Angeles. Statistical analysis was performed using SPSS statistical software (SPSS for Windows Version 11.0.1, SPSS Inc., Chicago, IL). Univariate statistical analysis was performed using the chi-square method. Multivariate analysis using logistical regression was then undertaken with those factors showing statistical significance on univariate analysis. Statistical significance was set at a level of $P < .05$.

## RESULTS

The cancer stage of patients included in this series is summarized in Table I. Most patients were treated for advanced cancer, with 78% of patients classified as either stage 3 or stage 4. The history of previous cancer treatments is summarized in Table II. The majority of patients (58%) were undergoing salvage surgery for cancers previously treated using surgery, radiation therapy, or chemotherapy. Table III summarizes the recipient arteries used for free flap perfusion, whereas Table IV summarizes the recipient veins used for free flap perfusion. Recipient vessels were located ipsilateral to the primary tumor site in 148 cases and contralateral to the primary tumor site in 36 cases. Table V summarizes the donor sites used for free flap reconstruction of the defects created by tumor resection. The radial forearm and fibular flaps represented the vast majority in our series.

Cancer recurrence was noted in 107 patients during the follow-up period, whereas 77 patients remained free of disease during the follow-up period. The pattern of cancer recurrence is summarized in Table VI. Second primary cancers that were anatomically remote from the initial primary cancer site were diagnosed in nine patients during the follow-up period. These were not classified as cancer recurrence.

TABLE II.
History of Previous Cancer Treatments.

| | Recurrent CA? | Previous XR | Previous H&N Surgery | Previous Chemo |
|---|---|---|---|---|
| Yes | 107 | 76 | 68 | 13 |
| No | 77 | 108 | 116 | 171 |

CA = cancer; XR = radiation therapy; H&N = head and neck.

TABLE IV.
Recipient Veins.

| Vein | Quantity |
|---|---|
| Internal jugular | 85 |
| External jugular | 83 |
| Both | 16 |

TABLE VI.
Cancer Recurrence.

| | Yes | No |
|---|---|---|
| Cancer recurrence | 107 | 77 |
| Tumor recurrence | 58 | 126 |
| Nodal recurrence | 50 | 134 |
| Metastatic recurrence | 19 | 165 |

The results of the univariate statistical analysis of factors that might influence the incidence of cancer recurrence and the pattern of cancer recurrence are listed in Tables VII to X. In summary, overall cancer stage ($P$ = .005), T stage ($P$ = .0001), history of previous cancer treatment ($P$ = .004), and history of previous chemotherapy ($P$ = .044) were found to be statistically significant predictors of cancer recurrence on univariate analysis. On multivariate analysis, only T stage ($P$ = .005) and history of previous cancer treatment ($P$ = .008) remained as statistically significant predictors of cancer recurrence. Local cancer recurrence was only significantly associated with T stage ($P$ = .049). Regional cancer recurrence was only significantly associated with history of previous cancer treatment ($P$ = .028). None of the analyzed factors was found to be a statistically significant predictor of distant metastasis.

The recipient artery selection and recipient vein selection were not statistically associated with the incidence or pattern of cancer recurrence. There was no difference in the incidence or pattern of cancer recurrence when using recipient vessels that were located ipsilateral versus contralateral to the primary tumor site.

## DISCUSSION

Microvascular flap reconstruction in patients with SCC of the head and neck requires modification of the standard procedures commonly used for neck dissection to preserve a length of a recipient artery and a recipient vein to provide for free flap perfusion. In most instances, a branch of the external carotid artery or thyrocervical trunk is preserved to provide arterial inflow, whereas during a routine neck dissection, these vessels are usually ligated close to their point of origin. Some of the commonly used recipient arteries may lie in close proximity to primary tumor sites in the head and neck. For instance, the facial artery and the lingual artery may lie in close proximity to primary tumors involving the mandible, oral cavity, or oropharynx, whereas the superior thyroid artery and thyrocervical trunk may lie in close proximity to primary tumors involving the larynx, hypopharynx, or cervical esophagus. In other cases, recipient arteries may lie in close proximity to lymph nodes that contain metastatic cancer. Dissection and preservation of a length of an artery lying in close proximity to a primary tumor or metastatic lymph node may compromise the adequacy of resection and potentially increase the risk for cancer recurrence.

In addition, a length of either the internal or external jugular vein is preserved to provide venous drainage for patients undergoing microvascular head and neck reconstruction. In a standard neck dissection, the external or internal jugular veins are frequently resected, especially when located in close proximity to lymph nodes that are suspected to contain metastatic disease. Preservation of a length of a vein that potentially lies in close proximity to metastatic lymph nodes could theoretically increase the risk for future cancer relapse in the neck.

Recent series have established that free flaps provide for a reliable method of head and neck reconstruction and are associated with an acceptable incidence of postoperative complications.[5,6] However, no previous series has examined the oncologic soundness of the procedure, specifically with respect to the potential adverse impact that modifications in the technique used for neck dissection might have on cancer recurrence.

In this study, we found no demonstrable impact of recipient artery or recipient vein selection on the incidence or pattern of subsequent cancer recurrence. Recipient artery and vein selection was not associated with cancer recurrence, local cancer recurrence, regional cancer recurrence, or

TABLE V.
Donor Site Flap.

| Flap Type | Quantity |
|---|---|
| Forearm | 83 |
| Fibula | 75 |
| Rectus abdominis | 14 |
| Latissimus dorsi | 11 |
| Iliac crest | 1 |

TABLE VII.
Versus Cancer Recurrence.

| | Chi-Square | *P* Value |
|---|---|---|
| Tumor stage | 12.653 | .005 |
| T stage | 23.231 | .000 |
| N stage | 2.085 | .555 |
| Previous Tx | 2.085 | .004 |
| XRT | 7.412 | .060 |
| Chem | 4.025 | .045 |
| Surgery | 1.145 | .285 |
| Artery | 2.692 | .846 |
| Vein | 0.556 | .757 |
| Ipsi/Cont neck | 0.925 | .336 |

Tx = transplantation; XRT = radiation therapy; Chem = chemotherapy; Ipsi/cont = ipsilateral/contralateral.

TABLE VIII.
Versus T Recurrence.

| | Chi-Square | *P* Value |
|---|---|---|
| Tumor stage | 2.664 | .446 |
| T stage | 9.489 | .050 |
| N stage | 9.489 | .152 |
| Previous Tx | 0.644 | .422 |
| XRT | 2.946 | .400 |
| Chem | 0.004 | .952 |
| Surgery | 0.265 | .607 |
| Artery | 3.531 | .740 |
| Vein | 2.284 | .319 |
| Ipsi/Cont neck | 0.531 | .466 |

Tx = transplantation; XRT = radiation therapy; Chem = chemotherapy; Ipsi/cont = ipsilateral/contralateral.

distant metastasis. In addition, use of recipient blood vessels in the contralateral neck did not result in a reduction in the rate of cancer recurrence, even though these blood vessels are remote from the primary tumor site and often outside the field of primary lymphatic drainage.

On multivariate statistical analysis of this series, only T stage and history of previous cancer treatment were found to be significant predictors of cancer recurrence. Local cancer recurrence was associated with T stage, and regional cancer recurrence was associated with history of previous cancer treatment. This analysis therefore suggests that modifications in the technique used for neck dissection to preserve recipient blood vessels are not associated with increased risk of cancer recurrence. One potential limitation of our analysis, beside the fact that it was conducted retrospectively, was the disproportionate study groups in terms of primary tumor location. The oral cavity represented the vast majority in this series, whereas other primary tumor locations of the head and neck were limited in quantity. This uneven distribution, however, does not effect our conclusion but rather weakens its implications toward head and neck cancers other than those of the oral cavity.

TABLE IX.
Versus N Recurrence.

| | Chi-Square | *P* Value |
|---|---|---|
| Tumor stage | 7.050 | .070 |
| T stage | 7.707 | .103 |
| N stage | 3.733 | .292 |
| Previous Tx | 4.782 | .029 |
| XRT | 5.773 | .123 |
| Chem | 0.901 | .343 |
| Surgery | 0.032 | .858 |
| Artery | 0.816 | .992 |
| Vein | 3.149 | .207 |
| Ipsi/Cont neck | 0.446 | .504 |

Tx = transplantation; XRT = radiation therapy; Chem = chemotherapy; Ipsi/cont = ipsilateral/contralateral.

TABLE X.
Versus M Recurrence.

| | Chi-Square | *P* Value |
|---|---|---|
| Tumor stage | 3.704 | .295 |
| T stage | 5.422 | .247 |
| N stage | 1.501 | .682 |
| Previous Tx | 0.425 | .515 |
| XRT | 2.085 | .555 |
| Chem | 0.387 | .534 |
| Surgery | 1.030 | .310 |
| Artery | 2.747 | .840 |
| Vein | 0.487 | .784 |
| Ipsi/Cont neck | 0.052 | .819 |

Tx = transplantation; XRT = radiation therapy; Chem = chemotherapy; Ipsi/cont = ipsilateral/contralateral.

## CONCLUSIONS

Microvascular reconstruction of head and neck cancer requires modification to standard neck dissections in that it is necessary to preserve a length of recipient artery and vein. However, on the basis of the present series, recipient vessel selection is not associated with the risk of local cancer recurrence, regional cancer recurrence, or distant metastasis. Moreover, even the use of recipient blood vessels contralateral to the primary cancer site did not result in a reduction in the rate of cancer recurrence. On the basis of our analysis, current techniques used in microvascular reconstruction for recipient vessel selection and preparation are oncologically sound and do not put the patient at higher risk for cancer recurrence. In this study, factors that were associated with increased cancer recurrence included only T stage and a history of previous cancer treatment. More specifically, local cancer recurrence was associated with T stage, and regional cancer recurrence was associated with history of previous cancer treatment. Necessary modifications to standard neck dissections made for microvascular reconstruction, namely selection and preservation of recipient vessels, do not increase the risk of cancer recurrence.

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