

# Prospective Analysis of Outcomes and Complications of 300 Consecutive Microvascular Reconstructions

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**Objective:** To prospectively follow up patients requiring microvascular reconstruction of head and neck defects to determine preoperative factors predictive of surgical complications.

**Methods:** A prospectively collected database comprising 300 consecutive microvascular head and neck reconstructions performed by a single surgeon (D.S.A.) in a tertiary care hospital over a 6-year period was reviewed in a retrospective manner. Data collected included preoperative medical and surgical history (presence of documented cardiac disease, diabetes mellitus, and hypertension) and previous cancer treatment (surgery or radiation therapy). Postoperative data, including early or late complications, hematocrit during hospitalization, and functional status, were also collected. A multiple linear regression was used to identify predictors of surgical complications and secondarily crossed to determine the

strength of the prediction. Statistical significance was set at  $P = .05$ .

**Results:** Patients were stratified into 4 groups based on (1) previous radiation therapy, (2) previous surgery, (3) no previous radiation therapy or surgery, and (4) both previous radiation therapy and previous surgery, with an increased predictability of complications with both. Diabetes also added to the predictability of complications, with a smaller effect. Cardiac disease and hypertension were not predictive.

**Conclusions:** Previous radiation therapy and surgery are positive predictors for wound complications after microvascular reconstruction. Diabetes may add further risk in this setting.

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**M**ICROVASCULAR FREE tissue transfer has become the mainstay for head and neck reconstruction over the past 2 decades.<sup>1</sup> Initial concerns regarding the reliability of small-vessel anastomosis continue to dissolve. Recent large series have shown a greater than 98% flap survival rate.<sup>2-4</sup> The greatest challenge remaining in head and neck reconstruction is to avoid perioperative complications. In a series of 400 free flap reconstructions, Suh et al<sup>4</sup> demonstrated a perioperative complication rate of 36.1%. They found previous surgery, medical comorbidities, defects, and flap types to be predictive factors in the development of surgical complications.

There is controversy regarding the effect of irradiation on the likelihood of surgical complications. In Suh and colleagues' study, which, to our knowledge, involves the largest series to date, no difference was noted in the 400 cases reviewed based on history of irradiation. As early as 1979, Watson<sup>5</sup> reported a potential detrimental effect due to the healing of microvessel anastomosis after high-dose radiation therapy in an ex-

perimental model. A 54% reduction in venous patency was demonstrated in Watson's study. In a separate series involving 100 patients who received fibular free flap reconstruction for mandibular defects, Choi et al<sup>6</sup> noted a local complication rate of 54%. No statistically significant difference was reported for patients receiving radiation therapy ( $P = .26$ ), whether preoperative or postoperative; however, there did appear to be some increased risk for those who received systemic therapy. In a series of 200 consecutive free flaps, Singh et al<sup>7</sup> reported that prior radiation therapy and pre-morbid conditions were independent factors that led to increased postoperative complications. However, after multivariate analysis, the presence of premorbid conditions was the only factor that remained. Halle et al<sup>8</sup> found a direct relationship between postoperative wound complications and the amount of time from the last radiation treatment.

The existence of premorbid conditions has been the most consistent factor reported to predict an increased risk of perioperative complications due to free tissue transfer.<sup>4,7,9,10</sup> American Society of Anesthe-

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sia (ASA) class.<sup>4,11-15</sup> and the Charlson Comorbidity Index (CCI)<sup>7,12</sup> have been reliable predictors of complications after free tissue transfer in head and neck defects. The presence of diabetes mellitus (DM) has been implicated as an independent risk factor for postoperative complications in free flap surgery.<sup>11,12</sup> The risk of complications has been reported as 5 times higher in patients with diabetes,<sup>12</sup> and free tissue transfer should be avoided if possible in this patient group. In that series, however, Eckardt et al<sup>12</sup> did not report their results with other reconstructive techniques as a comparative alternative.

Age alone has been evaluated in a number of series.<sup>13,15-17</sup> In a review of 197 free flaps, Howard et al<sup>15</sup> evaluated age and ASA class as well as the CCI score. They concluded that the ASA level was not as useful as the CCI for predicting medical and surgical complications, particularly when the CCI took into account alcohol use; yet, age was predictive only of medical complications. Septuagenarians and octogenarians experienced surgical complications that were similar to those of younger patients, while the older group had significantly more medical complications after free flap surgery. Similar findings were noted by Beausang et al,<sup>16</sup> who noted an age-related increase in hospital stay. Ozkan et al<sup>13</sup> concluded that the age-related increase in complications was attributable to an increased likelihood of advanced ASA class in the elderly patients. They also noted a more pronounced increase in medical complications compared with surgical complications based on ASA class.

The purpose of this study was to prospectively identify factors that might predict cervical wound complications in 300 patients who required head and neck reconstruction. The rationale for focusing on cervical wound complications is that they arguably have the greatest impact on overall recovery and outcome of reconstruction. The intent is to narrow group definitions and complications rather than to rely on the results of previously published studies that examined risk factors based on broadly defined groups and criteria.

## METHODS

We retrospectively reviewed a prospectively collected database that included 300 consecutive microvascular head and neck reconstructions performed by a single surgeon (D.S.A.) at a tertiary care academic hospital. The reconstructions, for which microvascular techniques were used, were performed over a 6-year period in patients who were aged 18 years or older.

The microvascular procedures were performed in all cases for large defects that required either composite soft-tissue or soft-tissue and bone reconstruction. A 2-team approach was used, and all reconstructions were performed by the senior author (D.S.A.). Vessels were irrigated intraoperatively with heparinized saline. Cervical recipient vessels from the external carotid system or the transverse cervical artery and the internal or external jugular venous system were used in all cases. Patients were treated with aspirin (81 mg/d) for 7 to 14 days after surgery. Flaps were monitored by a transcutaneous audible Doppler technique and clinical evaluation when possible. Flexible endoscopy was used to routinely examine buried flaps 48 to 72 hours after surgery.

Data collected prospectively included specifics on defect site and size, donor site and type (shown in the tabulation below), vessels used in microvascular anastomosis, and preoperative medical and surgical history.

Donor Site	No.
Radial forearm	171
Fibula	97
Rectus	16
Radial forearm plus serratus/rib	3
Serratus/latissimus	7
Serratus/rib/latissimus	4
Fibula plus radial forearm	1
Anteriolateral thigh	1
Temporoparietal fascia	1

The perioperative conditions, which included the presence of coronary artery disease (CAD), hypertension (HTN), DM, and previous cancer treatment (surgery and/or radiation therapy), are shown below.

Condition	No. (%)
No prior therapy	90 (30.0)
Prior surgery alone	50 (16.7)
Prior radiation therapy alone	86 (28.7)
Both prior surgery and radiation therapy	74 (24.7)
DM	28 (9.3)
CAD	83 (27.7)
HTN	94 (31.3)
Hematocrit <25%	63 (21.0)

The postoperative data included early or late complications, hematocrit during hospitalization, and functional status. Complications were further characterized as surgical or medical. Routine blood cell counts were performed for the first 24 hours after surgery. When the hematocrit was less than 30%, daily or twice-daily measurements were taken. Because data for perioperative anemia were not complete in the database for a large subset of patients, this factor was excluded from the analysis. A multiple regression analysis was used to determine whether previously reported risk factors such as age, CAD, HTN, DM, and prior surgery or radiation treatment were also predictive of postoperative surgical wound complications. Based on the results of the multiple regression analysis, the patients were classified into 4 groups: prior surgery, prior radiation therapy, no prior intervention, or both surgery and radiation therapy. Analysis of covariate analysis was used to determine whether between-group differences in complications were observed, while controlling for a covariate that yielded a predictive value after the multiple regression analysis. Statistical significance was set at  $P = .05$ .

## RESULTS

The mean (SD) patient age was 62 (13.9) years. Age was not correlated with recorded complications ( $P = .75$ ). A total of 110 recipient site complications were recorded in the cohort of 300 patients. Wound complications at the inset site in the head and neck are shown in the **Table**. At least 1 complication was seen in a total of 52 patients (17.3%). There was 1 case of microvascular failure, which resulted in the loss of a skin paddle on a fibula osteocutaneous flap, and 4 cases of partial loss of the skin paddle. The flap survival rates were therefore 99.7% for microvascular success and 98.6% for complete flap survival.

**Table. Cervical Wound Complications**

Complication	No. (%)	Previous XRT	Previous Surgery	DM	CAD	HTN	Hct <25%
Any	52 (17.3)	41	35	12	17	22	20
Infection	32 (10.7)	24	19	7	7	8	9
Cervical skin breakdown	24 (8.0)	18	16	8	7	8	10
Isolated wound dehiscence	6 (2.0)	0	1	1	2	0	1
Cervical skin flap necrosis >4 cm <sup>2</sup>	23 (7.7)	18	15	8	9	8	9
Hematoma	11 (3.7)	7	6	1	3	8	7
Fistula (n=263)	7 (2.7)	6	4	5	4	2	1
Partial flap loss	4 (1.3)	3	2	0	1	0	2
Taken back to OR	3 (1.0)	2	1	0	1	2	3
Flap loss	1 (0.3)	1	0	1	0	1	0
Hardware exposure (n=104)	5 (4.8)	5	5	0	1	1	1
P value <sup>a</sup>	NA <sup>b</sup>	.001	.003	<.001	.30	.20	NA

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; Hct <25%, perioperative anemia with hematocrit less than 25%; HTN, hypertension; NA, not applicable; OR, operating room; XRT, radiation therapy.

<sup>a</sup>The P value is the significance of the correlation to total cervical wound complications.

<sup>b</sup>Isolated wound dehiscence and cervical skin flap necrosis are subsets of the cervical skin breakdown category and are not separately added into the total (see text).

The most common adverse outcome was wound infection, which was seen in 32 patients (10.7%). Incisional breakdown or separation in the cervical skin flaps was seen in 24 cases (8.0%). Frank necrosis of a portion of skin flaps (>4 cm<sup>2</sup>) was also documented in 23 cases. Both incisional breakdown and frank necrosis were observed in the majority of cases (n=18) with a significant skin separation. Six patients had isolated wound separation without skin loss, and 5 had cervical skin loss at a point distal to the incision. There were 11 postoperative hematomas (3.7%), and 3 patients were taken back to the operating room for reexploration of vessel status (1.0%). Perioperative salivary fistulas were considered possible in all patients with oral or pharyngeal defects (n=263). Fistulas were seen in 7 patients (2.7%), and delayed plate or hardware exposure was seen in 5 of 104 patients (4.8%) who received osseous flaps.

Multiple linear regression analyses were conducted to determine whether preexisting medical conditions or prior intervention predicted total complications. The first analysis included prior radiation therapy, prior surgery, DM, CAD, and age. These variables were selected based on previously reported predictive values observed for complications. A backward solution was used to delete individual predictors that did not make significant contributions to the regression. The first analysis included prior radiation therapy and prior surgery, DM, HTN, CAD, and age. Age, HTN, and CAD were removed from the model, as they were nonsignificant ( $P = .54$ ,  $P = .20$ , and  $P = .30$ , respectively). The second model included only significant contributors: radiation therapy, surgery, and DM ( $F_{3,26} = 11.964$ ;  $P < .01$ ). These 3 variables accounted for 11% of the variance in the number of complications and were all statistically significant ( $P < .05$ ).

A 1-way analysis of variance was conducted to determine whether there were between-group differences in the number of complications among the 4 groups based on previous radiation therapy or surgical history. The

independent variable included 4 levels: no prior treatment, prior radiation therapy, prior surgical history, and both radiation therapy and surgical history. The dependent variable was the number of total cervical wound complications. The analysis of variance was significant ( $P = .03$ ). Follow-up tests were conducted to evaluate pairwise differences among the means. A Bonferroni adjustment was used to control for type 1 error. The group of patients with a history of radiation therapy and surgery had statistically significantly more complications than the group of patients with no previous treatment (mean [SD] difference, 0.40 [0.13];  $P = .01$ ). A 1-way analysis of covariance was then performed with DM as the covariate to control for differences in this variable. A preliminary analysis evaluating the homogeneity of slopes assumption indicated that the relationship between DM and complications did not differ significantly as a function of previous treatment ( $F_{3,292} = 0.369$ ; mean squared error [MSE], 0.245;  $P = .78$ ; partial  $\eta^2 = 0.00$ ). The main effect for the group remained significant ( $F_{3,295} = 3.28$ ; MSE, 2.16;  $P = .02$ ). Although not the focus of this analysis, DM was also significant ( $F_{1,295} = 19.41$ ; MSE, 12.79;  $P < .01$ ). While the covariate DM was controlled for, the patients with a history of surgery and radiation therapy had more complications than those without prior treatment. Also, there were more complications in patients with DM than in patients without DM. It must be noted that owing to the small number of patients with DM (n=28), the group sizes were unequal.

Donor site complications, as shown below, were seen in a total of 45 patients, with the most common being a partial "nontake" of the split-thickness skin graft that was used to provide wound coverage.

Donor Site Complication	No. (%)
Any	45 (15.0)
Partial loss of skin graft	41 (16.3)
Infection/cellulitis	7 (2.3)
Hematoma	3 (1.0)

At least 1 of the following medical complications was seen in 18.3% of the patients in this series:

Medical Complication	No. (%)
Any	55 (18.3)
Pulmonary infiltrate/pneumonia	29 (9.7)
Atrial dysrhythmia	14 (4.7)
Non-Q-wave troponin elevation	11 (3.7)
Deep vein thrombus	9 (3.0)
Pulmonary embolus	7 (2.3)
Myocardial infarction	4 (1.3)
Cardiac arrest	2 (0.7)
Renal failure	1 (0.3)

Statistical analysis of these subsets of complications are beyond the scope of the particular study and will be presented separately.

## COMMENT

The outstanding flexibility and reliability of microvascular reconstruction has made it the standard of care for the management of head and neck cancer in patients with large ablative defects. While the successful tissue transfer has been well documented in the literature,<sup>1-4</sup> there are few prospective data regarding the outcomes and complications of these procedures. Our study objectives were to provide data regarding surgical outcomes in cases of microvascular reconstruction and to identify potential perioperative risk factors.

As with most recent large series,<sup>4,7</sup> successful microvascular transfer can be performed with excellent reliability. In this series, only 1 of the 300 flaps had a postoperative vessel failure. Interestingly, the 1 significant flap loss did not occur in the traditional postoperative period. This case involved an angle-to-angle mandibulectomy and a total glossectomy and was reconstructed with the fibula. After a normal postoperative course, the patient was discharged to home on postoperative day 8 and was seen on postoperative day 14, when the flap appeared viable. At a second postoperative visit on day 28, the skin paddle was noted to be necrotic. The bone was viable. Given the very large skin paddle, which was fed by a single perforator in this case, a delayed embolic phenomenon was suspected. The actual anastomotic site continued to have normal flow in both the arterial and the venous segments. While the vascular anastomoses had no failures, partial flap loss was seen in 4 cases, all of which involved flaps with large skin paddles where small segments (<20%) of the flap surface were lost presumably because of technical errors in flap harvest or in planning of the angiosomal distribution. These failures highlight the paramount importance of the preservation of cutaneous perforators off the main vascular pedicle. In the context of this series, these failures were infrequent but clearly more prevalent than anastomotic failures.

Safe free flap transfer, however, does not preclude surgical wound complication at the inset site. In this series, 17.3% of the patients had at least 1 wound complication in the head and neck in the perioperative period. This percentage is within the ranges seen in other large series.<sup>4,16</sup> Specific complications were tracked for their incidence and prevalence in a prospective fashion. While

this method allows accurate and complete data collection from the entire cohort group, it does exclude other complications that were not included in the study variables. These potential exclusions may explain the somewhat lower overall rate of complications that was observed in our group of patients when compared with similar large retrospective series.<sup>4</sup> For the same reason, preoperative comorbidities may also be falsely underestimated. For example, there was no information collected on preoperative pulmonary function status, history of tobacco use, or other previous medical conditions, such as other malignant diagnosis, that might effect immune system response or recovery. Given this limitation, we hope that the comprehensive analysis of studied complications and their relationship to specific preoperative variables in this report will provide new insight into relevant clinical associations.

Another limitation of this series is that adequate information was not obtained over the past 6 years because many patients were unavailable for follow-up. Consequently, conclusions about late complications such as delayed plate exposure are difficult to characterize. Conversely, collecting data prospectively has allowed the collection and retention of other data that could have been prohibitively difficult to collect in a retrospective manner. To perform the study in a prospective manner, the determinates followed have to be preselected based on an initial hypothesis, therefore making it impossible to include every potential risk factor or outcome.

Local wound breakdown, skin dehiscence of the neck incisions, or frank necrosis of the cervical skin flaps was seen quite frequently in our series. Many of the patients had aggressive combined therapeutic protocols and had previously undergone surgical procedures in the neck. A statistical analysis of these complications found a strong association with preoperative surgical and radiation therapy. This finding is in contrast to a few other reported series that did not find radiation therapy to be an independent variable associated with poor postoperative outcomes.<sup>4,6,15</sup> There are some potential explanations for this discrepancy. The first is that the studies are looking at slightly different outcomes. Most of the prior studies examined postoperative complications as a whole and then performed their statistical analysis based on this large, multifaceted group. The specific identification of individual postoperative complications allows the data analysis to identify specific risk factors. The specific adverse outcomes that were tracked were observed much more frequently in patients who had been previously treated. Many of these cases are salvage operations for recurrent or failed radiation or chemoradiation therapy, often with advanced T stage or reoperations. Previous surgery,<sup>4,6,17</sup> recurrent disease,<sup>18</sup> and advanced T stage<sup>17,18</sup> have all been associated with poorer outcomes. Prior surgery in the neck was also a clinically relevant factor that showed some suggestion of an association but only reached significance when it was combined with radiation therapy.

Premorbid medical conditions have been associated with potential increased risk of surgical complications; DM in particular has been cited as a significant factor.<sup>10</sup> The results of this study also found DM to be a signifi-

cant risk factor for cervical wound complications, consistent with previously published results. We also studied CAD and HTN, both of which appeared not to have a clinical association with wound-related complications, with the exception of a relationship with HTN and postoperative hematoma formation.

In conclusion, microvascular reconstruction is safe and effective for treating large ablative defects and has become the treatment of choice. Postoperative complications remain a challenge for patients undergoing major reconstruction of head and neck defects. While general classifications of surgical fitness can help predict those patients who are at risk for developing complications, it is logical that specific complications would have specific predictors of risk. In this study, interest was focused on the complications that have a significant clinical impact on patient recovery. The combination of previous surgery and radiation therapy has the greatest impact on wound complications and has implications for preoperative patient counseling and surgical planning. Furthermore, a significant increase in morbidity is potentiated by the development of multiple complications.

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