Original Article

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Radiation Therapy Does Not Impact Local Complication Rates After Free Flap Reconstruction for Head and Neck Cancer

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Abstract

Objective To determine whether external beam radiation therapy (XRT), administered either before or after surgery, increases the rate and/or severity of local postoperative complications in patients with head and neck cancer who undergo microvascular free flap reconstruction.

Design Retrospective cohort study.

Setting University of Washington Medical Center, Seattle, a tertiary care hospital.

Patients A total of 100 consecutive patients underwent fibular free flap reconstruction of the mandible. The study cohort was divided according to radiation treatment status: (1) no XRT (28 patients), (2) preoperative XRT (37 patients), and (3) postoperative XRT (35 patients). The median follow-up after surgery was 11 months (range, 1-89 months).

Main Outcome Measures Rate and severity of local postoperative complications.

Results Fifty-four patients (54%) had at least 1 postoperative complication. There were no differences among the 3 XRT subgroups in the overall proportion of patients with complications of any severity (15 [54%] of 28 patients in the no XRT group, 24 [65%] of 37 patients in the preoperative XRT group, and 16 [46%] of 35 patients in the postoperative XRT group; $P = .26$, χ^2 analysis). There were also no differences seen when mild and severe complication rates were specifically examined ($P = .58$ and $P = .10$, respectively). No case of complete flap loss was observed. We noted no significant correlations between the rate of postoperative complications and the following covariates: total radiation dose, size of radiation field, disease stage, exposure to chemotherapy, presence of

Conclusions Our experience suggests that XRT can be safely administered before or after surgery to patients undergoing head and neck free flap reconstruction at an experienced surgical referral center. Postoperative complication rates were not significantly affected by administration, timing, dose, or extent of XRT.

Definitive surgical resection of locally advanced squamous cell cancer of the head and neck frequently entails complex bone and soft tissue defects. Free tissue transfer reconstruction with microvascular anastomosis provides reliable repair of such defects and has gained acceptance as standard practice. Comprehensive treatment of these advanced head and neck cancers frequently mandates the use of definitive or adjuvant external beam radiation therapy (XRT). Radiation therapy can damage small vessels and has the potential to adversely affect microvascular anastomoses. Specific vascular damage after XRT includes diminished smooth muscle density, endothelial cell dehiscence, and vessel wall fibrosis.[1,2] The in vivo effect of XRT on free flap viability was initially studied in animal models. Krag et al[3] showed that adminstering XRT to recipient vessels in rabbits before surgery significantly increased free flap failure rates. Other groups have presented conflicting results, showing that radiating recipient vessels in rats before surgery did not adversely effect free flap viability.[4,5] Although there have been several clinical studies suggesting that XRT does not have any obvious adverse effect on the viability of free flap reconstruction,[6-9] controversy remains as to the exact effect of XRT on the rate and severity of local surgical bed complications after free tissue transfers. In this article, we summarize our own experience to ascertain whether XRT has an adverse interaction with free flap reconstruction. We examined the effect of the timing of XRT with respect to surgery, as well as the potential impact of clinical and disease-related risk factors on postoperative complication rates.

Methods

We retrospectively reviewed the charts of 100 consecutive patients who underwent mandibular reconstruction with a free fibular flap reconstruction at the University of Washington Medical Center, Seattle, between 1995 and 2002. All cases were analyzable. We obtained approval for this review from the University of Washington Investigational Review Board. The study subjects were divided into 3 cohorts: (1) those who did not receive any XRT (28 patients), (2) those who had received preoperative XRT (37 patients), and (3) those who received postoperative XRT (35 patients). Potential risk factors for surgical complications, such as age, smoking history, and presence of medical comorbidities (eg, coronary artery disease, hypertension, and/or diabetes mellitus requiring active medical management), were obtained from the medical records. A patient was determined to have a medical comorbidity if he or she was receiving active medical treatment for that condition. Study cohort characteristics are summarized in **Table 1**. Overall, the patients from the preoperative and postoperative XRT groups were well matched as to age, sex, primary site of cancer, histologic type of cancer, history of smoking, and presence of medical comorbidities. Patients who did not receive XRT were more likely to be younger, be nonsmokers, and have benign disease. The most common indication for surgical reconstruction in this subgroup was craniofacial trauma.

Table 1 Cohort Characteristics*

Preoperative and postoperative XRT consisted of megavoltage photon and electron treatment delivered by means of a standard 3-field isocentric technique. Posterior neck electron fields and off-cord photon field boost fields were used to shield spinal cords from doses greater than 50.0 Gy. All patients were treated with once-daily fractionation. Eleven patients received synchronous platinum-based chemotherapy. Seven patients received fast neutron beam radiation therapy for salivary gland or sarcomatous disease. For these patients, a photon equivalent dose was calculated by adjusting the total neutron dose with a relative biologic effectiveness factor of 3.5. The median radiation dose was 66.6 Gy (range, 36.0-77.0 Gy). The median radiation dose for the preoperative XRT cohort was 69.6 Gy (range, 36.0-77.0 Gy). The median radiation dose for the postoperative XRT cohort was 64.0 Gy (range, 50.4-70.2 Gy). The median time between surgery and XRT for the postoperative XRT cohort was 8 weeks (range, 1-39 weeks). Because most patients in the preoperative XRT cohort underwent free flap reconstruction after a post-XRT salvage resection, the median interval between initiation of preoperative XRT and surgery was much longer (167 weeks; range, 23-537 weeks).

Routine surveillance began approximately 1 month after surgical resection, with serial evaluations performed at 1- to 3-month intervals during the first 2 years after surgery. The time between surveillance visits was extended to 4- to 6-month intervals thereafter. The median follow-up period was 11 months (range, 1-89 months). Any deviation from the expected course of local postsurgical wound healing was defined as a postoperative complication. These complications were dichotomized according to severity: (1) mild sequelae that did not require surgical intervention (included in this category was dehiscence that resolved with wound care and/or local infection that resolved with antibiotic treatment), and (2) severe sequelae requiring reoperation (examples included dehiscence leading to surgical revision, exposed bone or graft, orocutaneous fistula, severe fibrosis or hematoma, and complete flap loss). The earliest time to any complication, as well as time to flap loss, was cataloged.

We used a commercially available software package (StatView Version 5.0; SAS Institute, Cary, NC) for all statistical analysis. The complication rates of the 3 groups were formally compared using χ^2 testing. The effects of the total radiation dose and size of the radiation field on the complication rate were analyzed using unpaired *t* testing. The effect of disease stage was analyzed with χ^2 testing, for which the subjects with a classified stage were dichotomized into early-intermediate-stage (American Joint Committee on Cancer stages I-III, n = 19) and advanced-stage (American Joint Committee on Cancer stage IV, n = 41) cohorts. Specific relationships between the presence or absence of serious medical comorbidities, tobacco history, or exposure to systemic therapy and postoperative complication rates were analyzed with χ^2 testing.

Results

Disease characteristics and stage distribution for the different treatment cohorts are summarized in **Table 2**. Seventy-one patients had squamous cell carcinoma. Fourteen patients had nonsquamous malignancies, including adenoid cystic carcinoma, acinic cell carcinoma, renal cell carcinoma, and osteogenic sarcoma.

Table 2 Disease Characteristics for Study Cohort

Disease Characteristics for Study Cohort

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Fifty-four patients (54%) had at least 1 local postoperative complication (Table 3). Eighteen patients (6 in the no XRT group, 8 in the preoperative XRT group, and 4 in the postoperative XRT group) had both mild and severe complications. There was no incidence of complete flap loss in this study. There was no statistical difference among the 3 patient groups in the incidence of overall complications (15 [54%] of 28 patients in the no XRT group, 24 [65%] of 37 patients in the preoperative XRT group, and 16 [46%] of 35 patients in the postoperative XRT group) ($P = .26$, χ^2 analysis). The incidence of mild complications among the 3 groups was 25%, 35%, and 26%, respectively ($P = .58$). The incidence of severe complications was 50%, 46%, and 25%, respectively ($P = .10$).

Table 3 Local Postoperative Complication Rates by Treatment Cohort*

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Correlations between risk factors and complications are summarized in Table 4. We observed no statistical correlations between the total dose of XRT and the incidence of severe ($P = .22$, *t* test) or overall ($P = .99$) postoperative complications. There was no correlation between XRT field size treated and the rate of severe ($P = .32$) or overall ($P = .88$) complications. Systemic therapy did not affect the rate of overall complications ($P = .19$). A history of smoking did not affect the rate of severe ($P = .68$) or overall ($P = .41$) complications. No other consistent relationship was seen between complication rates and other risk factors. This finding also remained consistent for specific medical risk factors, such as the presence or absence of hypertension, coronary artery disease, or diabetes (data not shown).

Table 4 Potential Risk Factors and Postoperative Complication Rates*

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Comment

The true risk of delivering head and neck XRT in patients who undergo free flap reconstruction surgery remains unclear. It is well known that XRT can impair wound healing and promote chronic vascular damage.[1,2] These biologic effects, in theory, may decrease the viability of grafted free tissue transfers. The literature provides mixed evidence as to whether such biologic sequelae lead to tangible postoperative complications. Our results suggest that local postoperative complications are no more common or severe in patients who receive XRT before or after free flap reconstruction than in patients not treated with XRT. Complete flap loss did not occur in any patient treated with XRT, in contrast to the 4% to 6% flap loss rate reported in the literature.

Our overall complication rates appear higher than those described in similar studies.[8,10] While it is difficult to definitively explain discrepancies between institutional series, it is reasonable to speculate that our high overall rates were directly related to our criteria for defining the occurrence of a postoperative complication. We took advantage of systematic, rigorous cataloging of postsurgical wound healing in our institutional database. Any deviation from a completely healed wound was considered to be a complication. We chose to use low threshold criteria to optimize sensitivity for detecting differences between radiation treatment cohorts. Nonetheless, we could not detect significant differences in local postoperative recovery according to radiation exposure or timing.

Our findings agree with those of Bengtson et al,[6] who observed no difference in minor wound complications (21% vs 18%, *P*>.65) or major wound complications (16% vs 11%, *P*>.20) in patients undergoing free tissue transfers in the head and neck region, according to radiation treatment status. Kiener et al[8] also reported that preoperative XRT did not affect the rate of complications after microvascular reconstruction. Complications (excluding flap loss) occurred in 15% of subjects in the XRT group, as opposed to 19% in the no XRT group. Overall flap survival was 90% (88% in the XRT group and 95% in the no XRT group).

However, Deutsch et al[10] recently presented conflicting data from 140 patients who underwent reconstruction that was identical to that in our cohort (fibular flap free reconstruction of the mandible), suggesting inferior results with the addition of XRT either before or after surgery. The patients were divided into 4 groups: (1) no XRT, (2) preoperative XRT followed by immediate reconstruction, (3) preoperative XRT followed by delayed reconstruction, and (4) postoperative XRT. Overall complication rates were as follows: 28% in group 1, 45% in group 2, 46% in group 3, and 47% in group 4. The authors concluded that the timing of the XRT and reconstruction did not affect the rates of complications. However, because formal statistical analysis was not provided, it was not possible to determine if any differences in complication rates between treatment cohorts were significant.

There are few data in the literature to guide judgment regarding potential risk factors to predict increased postoperative risk in patients treated with radiation. The effect of smoking, presence of medical comorbidities, and chemotherapy on free flap survival has been studied to a limited degree. Reece et al[11] evaluated a cohort of elderly patients with cancer (aged >65 years) who underwent free tissue transfer after cancer surgery. The patients were divided into 2 groups: (1) those who had previously received XRT and/or chemotherapy, and (2) those who did not have any previous treatment. The authors found that there was no difference in the surgical complication rates, medical complication rates, or free tissue transfer failure according to XRT or chemotherapy. They also found that active smoking, moderate/heavy alcohol use, medical comorbidities, and treatment with chemotherapy did not affect the complication rate after a free tissue transfer. Eckardt and Fokas,[12] in a recent review of 500 consecutive patients who underwent microvascular free tissue transfer without radiation treatment, also showed that the incidence of "local" complications (defined as those at the surgical site) was not affected by a history of tobacco use (*P* = .18). They did not analyze the effect of the presence of other medical comorbidities on complication risks.

We specifically examined a more complete selection of clinical factors known to affect morbidity after XRT, including radiation dose and field size, history of tobacco use, use of chemotherapy treatment, extent of disease (stage), and presence of significant medical comorbidity (such as hypertension, coronary artery disease, or diabetes mellitus). None of these factors was demonstrated to compound the risk of postoperative complications

subgroup, since all of these patients had no significant medical comorbidities or other risk factors. Our results lead us to speculate that free flap complication rates are considerably more dependent on the quality of surgical technique and perioperative and postoperative management than on any single putative medical or disease-related risk factor.

In conclusion, our findings suggest that XRT can be safely administered before or after fibular free flap reconstruction of the mandible at an experienced surgical referral center. Local postoperative complication rates were not significantly affected by administration, timing, dose, or extent of XRT. Presenting stage of primary disease, use of systemic chemotherapy, presence of medical comorbidities, and history of smoking were not predictors of postsurgical complications. Severe complications were universally managed successfully, and none of our patients had complete flap loss. Additional reports will be necessary to address this long-standing clinical issue more conclusively.

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