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Outcomes after definitive surgery for mandibular osteoradionecrosis

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Abstract

Objectives: To analyze charges, complications, survival, and functional outcomes for definitive surgery of mandibular osteoradionecrosis (ORN).

Materials and Methods: Retrospective analysis of 76 patients who underwent segmental mandibulectomy with reconstruction from 2000 to 2009.

Results: Complications occurred in 49 (65%) patients and were associated with preoperative drainage (odds ratio [OR] 4.40, 95% confidence interval [CI] 1.01–19.27). The adjusted median charge was $343 000, and higher charges were associated with double flap reconstruction (OR 8.15, 95% CI 2.19–30.29) and smoking (OR 5.91, 95% CI 1.69–20.72). Improved swallow was associated with age <67 years (OR 3.76, 95% CI 1.16–12.17) and preoperative swallow (OR 3.42, 95% CI 1.23–9.51). Five-year ORN-recurrence-free survival was 93% while overall survival was 63% and associated with pulmonary disease (HR [hazard ratio] 3.57, 95% CI 1.43–8.94).

Conclusions: Although recurrence of ORN is rare, surgical complications are common and charges are high. Poorer outcomes and higher charges are associated with preoperative factors.

KEYWORDS
hospital charges, mandibular, osteoradionecrosis, outcomes, survival

1 | INTRODUCTION

The application of radiation therapy for the treatment of head and neck cancer has significantly increased over the last several decades.[1] Although this has resulted in improvements in recurrence and survival rates, significant toxicities have been associated with this treatment.[2–5] Among these, osteoradionecrosis (ORN) of the mandible has been shown to have a substantial impact on patients' quality of life.[6] Estimated to occur in 6%–8% of patients with oropharyngeal cancer within 5 years of radiation treatment, ORN is a condition in which the bone becomes devascularized and exposed,

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resulting in chronic osteomyelitis with poor penetration of antibiotics and wound healing.[7–11] Tumor characteristics, patient factors, and pre-treatment management of dentition influence the development and severity of ORN.[3,12,13]

Early ORN can be managed conservatively with therapies such as oral hygiene, antibiotics, local debridement, and hyperbaric oxygen.[14,15] However, when progression of ORN results in pathologic fracture, fistulization, and/or severe pain, the most common treatment is resection of involved segments of bone and reconstruction with free tissue transfer.[16–18] Despite this intervention serving as the gold standard for definitive treatment, there is a paucity of data evaluating outcomes, including the incidence of recurrent ORN.[19,20] Few studies to date have evaluated the impact of definitive surgical management of ORN on functional outcomes, such as speech and swallowing. Furthermore, to our knowledge, no study to date has explored hospital charges associated with this major surgical intervention.[21]

The purpose of this study was to assess functional outcomes, complications, survival, and hospital charges associated with the definitive surgical management of mandibular ORN related to radiation therapy for head and neck cancer.

2 | METHODS

2.1 | Patient characteristics

After Institutional Review Board approval, 76 patients were identified who were treated for mandibular ORN with definitive surgery and reconstruction at a tertiary care center between 2000 and 2009. Inclusion criteria were patients with head and neck cancer with: (i) previous definitive or adjuvant radiation therapy for head and neck cancer, (ii) radiographic and clinical evidence of mandibular ORN, (iii) definitive surgery for ORN at our institution, and/or (iv) no evidence of cancer at the time of treatment for ORN. Exclusion criteria included patients: (i) unable to undergo definitive surgical management for ORN, (ii) active cancer, (iii) definitive ORN treatment performed at an outside facility, and/or (iv) necrosis not related to radiation.

2.2 | Covariates

The covariates of interest were age at presentation, sex, prior cancer disease site, TNM classification of previous head and neck cancer, previous treatment of head and neck cancer, type and dose of radiation, dental extraction timing, previous treatment for ORN, smoking status (never vs. past [quit >6 months ago] vs. current smoker), and alcohol status (never vs. past [quit >6 months ago] vs. current [> 2 drinks/day]). Three time points were assessed based on the date of last radiation (initial or re-irradiation), date of first documented diagnosis of ORN, and the date of definitive surgery for ORN.

2.3 | Outcomes

ORN recurrence was defined as clinical and radiographic evidence of ORN. Follow-up time for ORN or cancer recurrence (i.e., disease-specific survival [DSS]) was recorded from the time of surgery for ORN until first recurrence of ORN or cancer with censor at date of last clinical evaluation. Postoperative functional measures were performed at the final assessment for each patient. The metric 80% intelligible was a priori defined and measured by speech pathology as functional speech quality. Follow-up time for overall survival (OS) was recorded from the time of surgery to death for any cause with censor at last encounter.

Minor complications were defined as those requiring limited treatment that did not require a procedure to be done in the operative theater. These included wound infection, wound dehiscence, skin graft failure, seroma, partial flap loss, fistula managed conservatively, and donor site complication. Major complications were defined as any unforeseen treatment that required the procedure to be done in the operating theater, such as washout for hematoma or infection, fistula, partial flap loss, total flap loss, or carotid blowout. Perioperative deaths were recorded within 90 days of surgery, whether inpatient or outpatient. Hospital and professional charges were collected and categorized based on hospital and professional charges associated with surgical resection and reconstruction, hospital charges associated with management of complications, and overall total hospital charges. Hospital charges are corrected based on average consumer price index inflation from 2005 to 2021 based on US Bureau of Labor and Statistics.[22]

2.4 | Statistical analysis

Descriptive statistics for scaled values and frequencies of study patients within the categories for each of the parameters of interest were enumerated with the assistance of commercial statistical software. Comparisons of scaled parameters between groups were done via one-way ANOVA followed by factorial ANOVA to assess the interactive effects of multiple categorical variables.

Correlations between categorical parameters and endpoints were assessed by the two-tailed Fisher exact test. Univariate and multivariate odds ratios were calculated by logistic regression. Cox regression was used to calculate hazard ratios for survival data. The Kaplan–Meier method and the log-rank test were used to generate curves describing time-to-event outcomes and to test for differences in the survival functions between strata defined by clinical variables. The statistical significance of differences between the actuarial curves was tested by the logrank test. A two-tailed *P*-value of 0.05 or less was considered statistically significant. These statistical tests were performed with the assistance of the Statistica (TIBCO, Inc., Palo Alto, CA) and SPSS (IBM SPSS, IBM Corporation, Somers, NY) statistical software applications.

3 | RESULTS

3.1 | Demographics and treatment characteristics

Table 1 illustrates demographic and cancer history for the 76 patients treated for ORN. Of these, 76% of patients originally had advanced stage (III and IV) squamous cell carcinoma of the oropharynx or oral cavity. Only 8% had definitive radiation alone. Three patients (3%) had re-irradiation after locoregional failure, while the vast majority (96%) received surgery with adjuvant radiation or chemoradiation. At the time of surgery, 22 (29%) patients were current smokers, 34 (45%) patients were former smokers, and 20 (26%) patients were never smokers.

The most common presenting symptoms of ORN were pain (96%), oral ulceration (78%), exposed mandibular bone (78%), and trismus (57%). Pathologic fracture (49%), fistula (38%), and purulent discharge (25%) were present in a minority of patients. A total of 22 (29%) patients were edentulous at presentation. Previous trauma was noted in 22 patients (29%), including dental extraction, following radiation therapy that could have impacted the development of ORN. Prior treatments for ORN included oral hygiene/antibiotics (17%), debridement/sequestrectomy (38%), hyperbaric oxygen (70%), and previous attempt at definitive resection at another institution (17%).

3.2 | Surgery and reconstruction

All patients underwent a segmental mandibulectomy. The median defect size was 9 cm (range 3–18 cm). Hemimandibulectomy was the most common resection (32%) followed by midline to angle (17%), midline to ramus (15%), body to ramus (12%), body to body (9%), angle to angle (5%), hemimandibulectomy to contralateral body (5%), ramus to ramus (3%), hemimandibulectomy to ramus (1%), and total mandibulectomy (1%). Reconstruction was performed in all 76 patients: 47 (62%) patients with an osteocutaneous free flap, 20 (26%) patients with a fasciocutaneous/myocutaneous free flap, and nine (12%) patients with a pectoralis major pedicled flap. Soft tissue reconstruction was not regularly performed with mandibular reconstructive bars. One (1%) patient was tracheostomy tube dependent at the time of surgery. At the time of surgery, 70 (91%) patients required a tracheotomy for perioperative management of the airway; eight (11%) patients remained permanently tracheostomy dependent after reconstruction. The median operative time was 11 h (range 4.0–19.5). Patients were hospitalized a median of 8 days (range 3–43) after definitive surgery.

3.3 | Complications

At least one complication occurred in 49 (65%) patients, and 20 (24%) patients had at least two postoperative complications. Take-back to the operating room occurred in 35 (47%) patients (range 0–10/per patient). Donor site complication (16%), wound dehiscence (11%), and wound infections (9%) were the most common complications. Partial flap necrosis occurred in three (4%) patients. Total flap loss occurred in three (4%) patients. Flap thrombosis with salvage occurred in five (7%) patients. Second flaps for complications occurred in 12 patients (7 free flaps and 5 pectoralis major flaps). Two (3%) patients developed subsequent contralateral osteoradionecrosis, requiring additional surgery.

There was one death within 30 days of surgery (1.3%) and three deaths within 90 days (3.9%). Two patients died prior to discharge from the hospital (major bleed postoperative day 8 and pneumonia postoperative day 43), while a third patient with a history of coronary artery disease died of an acute myocardial infarction as an outpatient less than 90 days after definitive surgery. Table 2 describes univariate and multivariate analyses of factors associated with complications. On multivariate analysis, only presentation with purulent drainage was significantly associated with the development of a minor complication.

Time from the end of radiation to diagnosis of ORN, time from end of radiation to definitive surgery for ORN, and time from diagnosis of ORN to definitive surgery were calculated (Table 3). Compared to patients with complications, patients without complications had a significantly shorter median time from radiation therapy to

TABLE 1 Patient tumor and treatment characteristics

Characteristic	Number	%
Total	76	–
Median follow-up time	44.3 months (0.3–110)	
Median age (range)	60.4 years (29–89)	–
Sex		
Male	54	71
Female	22	29
Original tumor site	$n = 75$	
Oral cavity	33	43
Oropharynx	30	40
Sinonasal	4	5
Salivary gland	3	4
Skin	2	3
Larynx	2	3
Unknown primary	1	1
Nasopharynx	1	1
Tumor pathology	$n = 76$	
Squamous cell carcinoma	61	80
Other[a]	15	20
Cancer treatment history	$n = 75$	
Surgery + adjuvant radiation	31	41
Surgery + adjuvant CRT	24	32
Definitive radiation	6	8
Definitive chemoradiation	14	18
Staging		
T-Classification	$n = 64$	
1	5	8
2	24	38
3	13	20
4	19	30
0	1	2
x	2	3
N-Classification	$n = 62$	
N0	24	39
N1	8	13
N2a	4	7
N2b	10	16
N2c	12	19
N3	4	7
Stage	$n = 60$	
I	3	57
II	11	18
III	9	15
IV	37	62

TABLE 1 (Continued)

Characteristic	Number	%
Radiation		
Type of radiation	$n = 76$	
Traditional	65	86
IMRT	8	11
Brachytherapy	2	3
XRT + brachytherapy	1	1
Radiation dose	$n = 64$	
<60	7	11
>60Gy	57	89
Median dose (range)	65 Gy (25–130)	–
Mean dose	66.7 Gy	
Risk factors	$n = 76$	
Alcohol		
Current	10	13
Former	6	8
Never	60	79
Tobacco	$n = 76$	
Current	22	26
Former	34	45
Never	20	26
Comorbidities	$n = 64$	
Diabetes	8	11
Hypertension	35	46
Cardiac disease	14	18
Pulmonary disease	7	9

[a]Other pathology includes salivary gland, sarcoma, melanoma, lymphoma, and metastatic breast.

surgery (34 vs. 59 months, $p = 0.016$) and ORN diagnosis to surgery (5 vs. 12 months, $p = 0.027$).

3.4 | Hospital-associated charges

Adjusted hospital charges by complication are found in Table 4. The median surgical charge was $343 000. On univariate analysis, total overall charges were significantly associated with operative time >12.6 h ($p = 0.001$), lack of trismus ($p = 0.008$), and double free flap reconstruction ($p = 0.011$). Similarly, when assessing charges greater than the 50th percentile (>$343 000), double free flap reconstruction ($p < 0.001$), current smoking ($p = 0.003$), lack of trismus ($p = 0.15$), and operative time ≥12.6 h ($p = 0.032$) were all significantly associated with increased charges. Multivariate analysis identified the

TABLE 2 Regression analysis for charges, functional, and complication outcomes

Outcome, N = 76 Variable (*n* positive)	Univariate Odds ratio	Univariate *P*-value	Multivariate Odds ratio	Multivariate 95% CI	Multivariate *P*-value
Regular final diet					
Regular preoperative diet (57)	3.84	0.009	3.42	1.23–9.51	0.018
Age < 67.4 at surgery (58)	4.33	0.012	3.76	1.16–12.17	0.027
Fistula (35)	0.41	0.089			
80 + % intelligible speech					
Was a second flap used? (39)	0.15	0.0025			
OR time ≥12.6 h (53)	0.31	0.066			
Total charges ≥ $343 000					
Second flap (39)	7.94	<0.001	8.15	2.19–30.29	0.002
Current smoker (11)	5.75	0.003	5.91	1.69–20.72	0.006
Trismus (34)	0.24	0.015	–	–	ns
OR time ≥12.6 h (38)	3.76	0.032	–	–	ns
Preoperative speech ≥80% intelligible (15)	0.17	0.076	–	–	ns
Major complication					
OR time ≥12.6 h (38)	4.95	0.024	–	–	ns
Defect ≥12 cm (27)	0.26	0.08	–	–	ns
Minor complication					
Purulent discharge (57)	4.83	0.048	4.40	1.01–19.27	0.049
Current smoker (11)	3.93	0.043	–	–	ns
Non-squamous cell (20)	4.07	0.090	–	–	ns

Abbreviation: ns, not significant.

TABLE 3 Type of complication by time between radiation, osteoradionecrosis (ORN), and surgery

N = 76 (*n* positive)	Median time (months) Radiation-ORN	Radiation-surgery	ORN-surgery
Overall (range)	36.1 (0.1–2445)	52.8 (2.9–249)	8.0 (0.03–200)
No complications (27)	22.3 (0–153)	34.3 (4–1570)	4.8 (0–28)
Any complication (49)	43.49 (2–245)	59.4 (8–249)	11.6 (0–201)
Minor complication (32)	5.9 (2–245)	74.8 (8–249)	14.2 (1–201)
Major complication (17)	36.4 (4–166)	56.5 (13–218)	8.4 (0–58)

TABLE 4 Adjusted hospital charges by complication

N = 76 (*n* positive)	Mean charges Surgery	Complications	Total[a]
Overall (range)	$233 096 (62 466–807 902)	$161 473 (963–101 618)	$299 084 (62 466–1 389 197)
No complications (27)	$206 660 (62 466–360 117)	–	$218 969 (62 466–360 117)
Any complication (49)	$247 662 (81 884–807 902)	$161 473 (963–1 123 618)	$343 229 (81 884–1 389 197)
Minor complication (32)	$227 767 (81 884–807 902)	$126 631 (14 661–284 703)	$279 211 (81 884–807 902)
Major complication (17)	$285 113 (156 931–642 962)	$189 783 (17 265–1 123 618)	$463 733 (196 056–1 389 197)

[a]Includes other nonsurgical and non-complication charges.

double free flap reconstruction (HR 8.15, 95% CI 2.19–30.29, $p = 0.002$) and current smoking (HR 5.91, 95% CI 1.68–20.72, $p = 0.006$) as independent variables associated with higher charges. Comparing mean charges for patients with and without complications, patients without complications had significantly lower overall charges ($p = 0.004$). Likewise, patients with major complications had significantly greater overall charges compared to patients with no complications ($p < 0.0001$) and minor complications ($p = 0.003$). There was no statistically significant difference in charges between patients with minor complications and no complications ($p = 0.41$).

3.5 | Functional outcomes

Figure 1A compares pre-treatment and post-treatment swallowing and speech function. There was no difference in gastrostomy-tube dependency (21% vs. 23%, $p = 0.81$); however, there was a significant improvement postoperatively in frequency of regular/soft diet (49% vs. 60%, $p = 0.009$). On multivariate analysis (Table 2), preoperative regular diet ($p = 0.018$, OR 3.40, 95% CI 1.23–9.51) and age <67 years ($p = 0.027$, OR 3.76, 95% CI 1.16–12.17) were independently associated with a regular final diet.

There was a non-significant decline in the number of patients with speech intelligibility greater than 80% between pretreatment and post-treatment speech evaluation (93% vs. 77.5%, $p = 0.31$) (Figure 1B). Patients who required two flaps for reconstruction had significantly worse speech outcomes compared to those with only one flap ($p = 0.002$). Of the 70 patients who required perioperative tracheostomy, only 8 (11%) patients were tracheostomy tube dependent 30 days after surgery.

3.6 | Survival

The median follow-up time after surgery was 43 months (range 0.3–110.6). For the entire cohort, 3- and 5-year OS were 77% and 63%, respectively (Figure 2A). Excluding patients who developed cancer recurrence (11 patients), 3- and 5-year OS were 74% and 64%, respectively. Three- and 5-year DSS were 92% and 88%, respectively (Figure 2C). Multivariate analysis (Table 5) demonstrated only the presence of preoperative pulmonary disease to be associated with poorer 5-year OS (29% vs. 67%, $p = 0.009$). The presence of any complication or type of complication (minor vs. major) had no effect on survival. ORN recurrence was 7% at 5 years (Figure 2D). There were no predictive factors associated with ORN recurrence.

4 | DISCUSSION

This study evaluates the morbidity associated with definitive surgical management of ORN and is among the first to assess hospital charges and functional outcomes in this patient population. Although recurrence was rare, two-thirds of patients experienced complications, with fewer

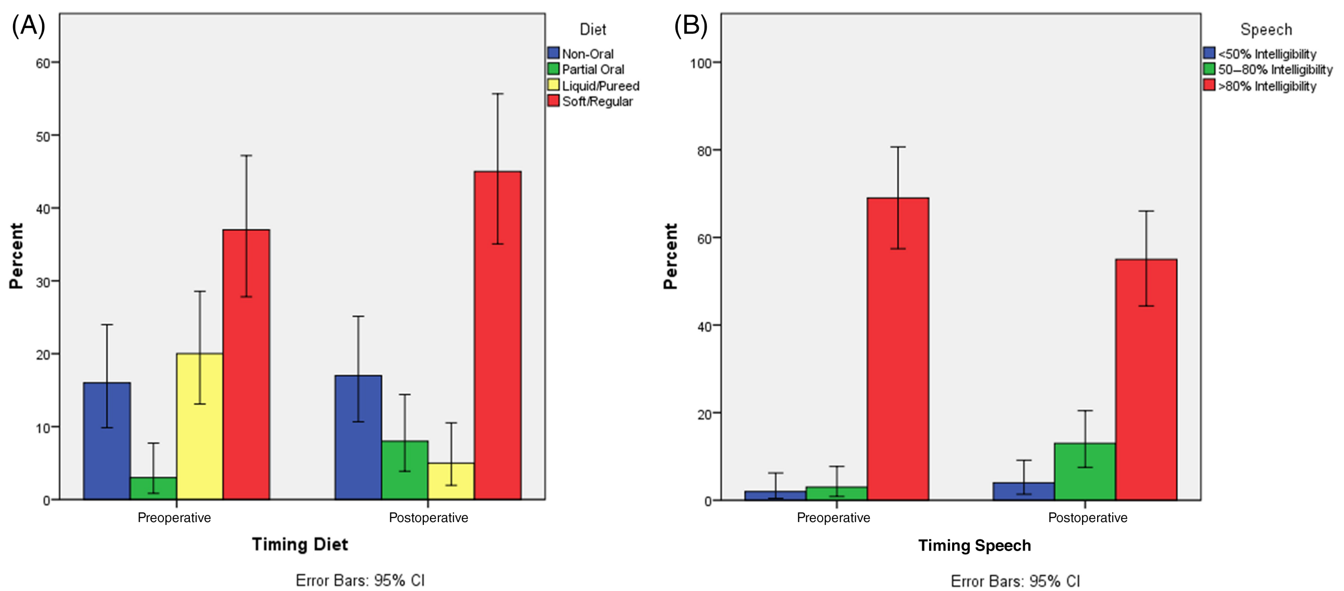

FIGURE 1 Functional outcomes for diet (A) and speech (B) between preoperative and final postoperative [Color figure can be viewed at wileyonlinelibrary.com]

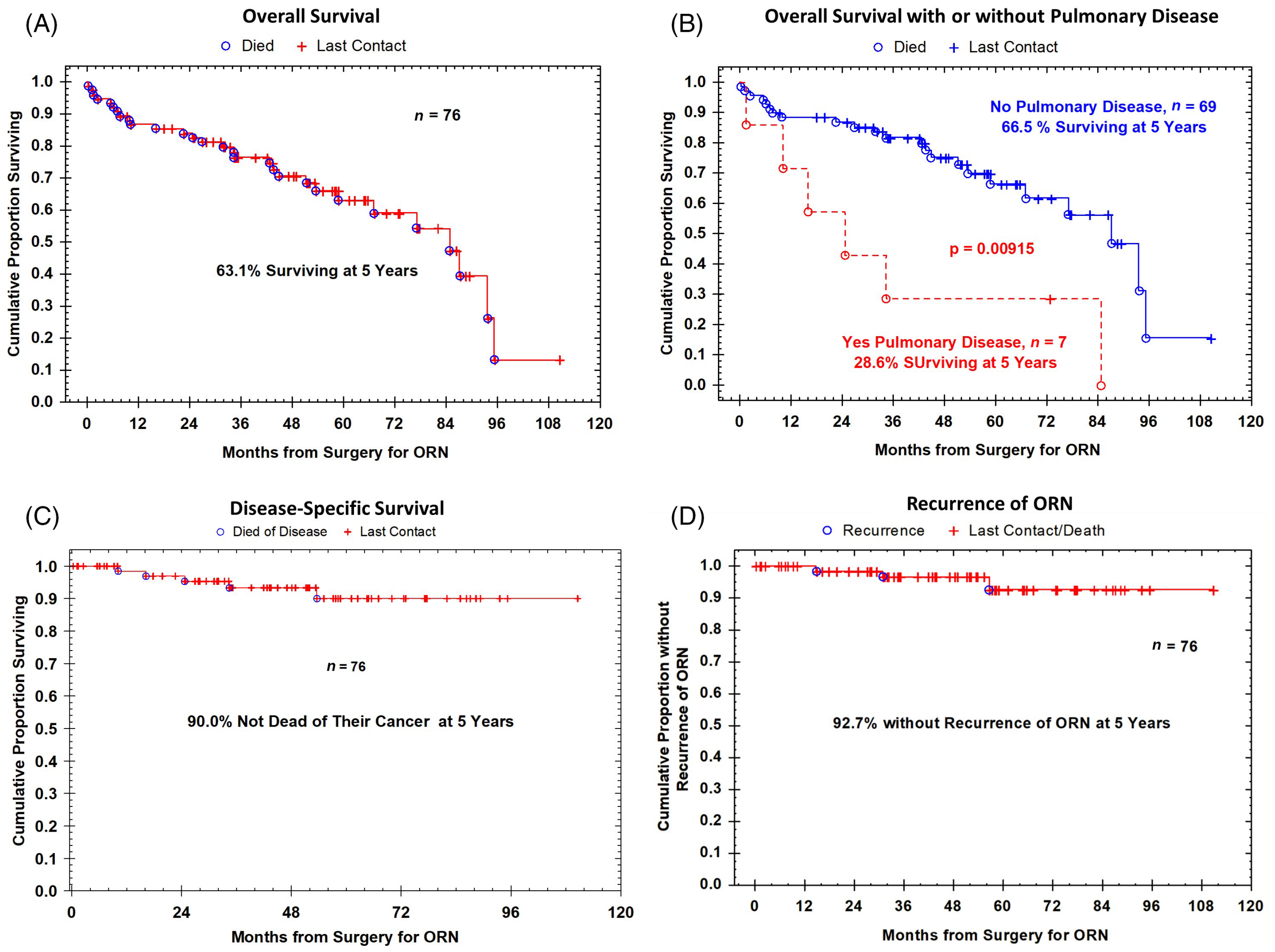

FIGURE 2 Survival outcomes, including overall survival (A), overall survival stratified by pulmonary disease (B), disease-specific survival (C), and recurrence of osteoradionecrosis (ORN) (D) [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 5 Multivariate regression for overall survival

Variable, $N = 76$ (*n* positive)	Hazard ratio	95% CI	*P*-value
Pulmonary disease (7)	3.57	1.43–8.94	0.009
Comorbid conditions (43)	1.39	0.64–3.04	0.41
Any complication (49)	0.75	0.36–1.59	0.45
Complication type			
None (27)	0.81	0.36–1.83	
Minor (32)	0.65	0.22–1.92	
Major (17)	1.34	0.42–3.95	
Age ≥67.4 years (18)	1.06	0.45–2.50	0.89

complications in patients treated sooner for ORN. Five-year OS was 63% and mediated by pulmonary disease. Median total charges were $343 000 with nearly half related to complications and higher charges associated with the need for multiple free flaps and active smoking. Improved postoperative swallowing function correlated with preoperative swallow function and age.

4.1 | Complications

Two-thirds of patients developed a complication, whether minor or major. This is more than the majority of prior studies ranging between 25% and 68%, although documentation, particularly of minor complications, was less stringent in prior reviews.[20,21,23] On univariate analysis, complications were related to previous radiation, smoking, prolonged operative time, large defects, diabetes, and poor preoperative speech quality. Smoking, previous radiation, and diabetes are well-established risk factors for poor wound healing and subsequent complications, such as fistula, wound dehiscence, and need for operative take-back. However, these factors did not retain statistical significance on multivariate analysis, consistent with previously published studies.[24,25] Likewise, prolonged operative time, larger defects, and poor preoperative speech are surrogates for the complexity of the surgery and likely contribute to complications but do not retain significance on multivariate analysis.

The only independent marker predictive of complications in the multivariate analysis was preoperative purulent drainage. Surgical intervention in an infected bed potentially increases the risk of postoperative wound infection. Excluding minor donor site complications, wound dehiscence and infection were the most common perioperative complications.

While the incidence of complications was high, this may be related to the relative health and comorbidities of this patient population. One study evaluating free tissue reconstruction in a matched sample of patients with and without ORN, found higher rates of local complications (47%) and the need for removal of hardware (45%) in the ORN cohort.[19] A large multi-institutional sample found lower albumin, higher TSH, and substance abuse to be associated with higher rates of complications.[26] Our rates of partial and total flap failure (8%) for ORN were comparable to prior studies, ranging from 6% to 16%.[19,20]

Longer time intervals between radiation and surgery and between diagnosis and surgery were found to be associated with increased risk of complications. This is consistent with prior studies.[23] While this may suggest that "preemptive" surgical intervention may improve outcomes, this has not been proven.[27] In the current study, all patients had "absolute indications" for definitive surgery (i.e., fistula, pathologic fracture, and/or intractable pain). Chinn et al. evaluated the efficacy of pre-emptive surgical intervention prior to presentation with fistula, fracture, or intractable pain, and found no difference in complications.[28] Therefore, the optimal timing for definitive surgical intervention in patients with ORN remains unclear. The time from diagnosis of ORN to surgery may be a modifiable variable independent of symptoms, with the possibility that earlier definitive surgical intervention may reduce postoperative morbidity in these patients.

4.2 | Hospital charges

While hospital charges have been previously studied in oropharyngeal cancer, the current study was the first to analyze hospital charge data for patients with ORN.[29] Median overall charges of $343 000 provide a context for the fiscal impact of definitive treatment of this condition. Complications made up 45% of hospital and surgical charges, and major complications were significantly associated with increased charges. Any complication increased hospital charges by 1.2-fold, and charges associated with patients with major complications were 1.5 times higher than charges in patients with minor complications. Given the medical and surgical complexity of these patients, complications are expected to have a significant impact on their hospital course. In the current study, we found complications to be directly related to increased hospital charges.

Major factors associated with increased charges included multiple trips to the operating room, smoking, the use of a second flap, lack of trismus, operative time, and poor preoperative speech. These factors expectedly overlapped with factors that influenced the complications. The use of a second flap, multiple operating room trips, operative time, and poor preoperative speech suggest a higher level of surgical complexity. Smoking is a known risk factor for poor wound healing and other medical complications. Seemingly counterintuitive, the presence of trismus was associated with lower charges. However, the presence of trismus is related to radiation-induced fibrosis of the pterygoid and masseter muscles. The posterior muscles of mastication are often in the radiation field for oropharyngeal or posterior oral cavity cancers, and trismus coupled with a posteriorly based defect often drives free flap selection from osteocutaneous to fasciocutaneous.[30] The use of fasciocutaneous flaps is often associated with shorter operative time and does not require expensive reconstruction plates. While many of the factors are associated with the complexity of surgery, only smoking is a modifiable variable that should be emphasized preoperatively to improve the chances of a "complication-free" hospital course. Furthermore, with the improved survival associated with HPV-related oropharyngeal cancer, further study into deintensification of radiation may further reduce the burden of ORN on patients with head and neck cancer.

4.3 | Functional outcomes

Speech and swallowing function are significant factors in the overall quality of life after treatment for head and neck cancer.[31,32] While advances in radiation have sought to minimize the deleterious effects on speech and swallowing function, ORN represents an extreme sequela of radiation.[6] In the current study, nearly all evaluated presenting symptoms have a propensity to impact speech and swallow function. Pain, specifically, was the most common presenting symptom of patients in this study, a factor which has been shown not only to affect speech and swallowing function but also to significantly impact overall quality of life and survival.[32] There was a significant difference in preoperative versus postoperative swallowing function, with an absolute improvement of 11% in patients eating a regular diet, but no difference in gastrostomy tube dependency. This is consistent with Sweeny et al., who reported 15% and 26% of patients reported improved diet function at 3 months and 5 years, respectively.[33] Despite no significant improvement in gastrostomy tube dependency, the postoperative gastrostomy tube dependency rate was 23%, which compares favorably to the reported 34% gastrostomy tube dependency rate for major oral cavity cancer ablative and reconstructive surgery.[34]

Analysis of speech function demonstrated no significant difference between preoperative and postoperative speech. However, there was a trend for poorer speech intelligibility after surgical intervention for ORN. This may be related to the gross bulk of vascularized tissue in the oral cavity, fibrosis, and significant long-term lymphedema in the setting of previous radiation therapy, both of which can severely alter tongue mobility and affect speech articulation. Vascularized tissue bulk is dependent on the amount of muscle, fat, and skin employed to reconstruct the defect. Muscle generally atrophies approximately 50% over time, whereas skin and fat only atrophy 10%–15%.[35,36] Subsequent flap debulking or long-term speech analysis after flap atrophy may improve speech intelligibility. Hanasono et al. evaluated patients who were reconstructed with microvascular free flap after major ablative surgery for advanced-stage oral cavity cancer and found 72% could communicate via spoken word alone. In the current study of ORN patients, 80% of the patients who were reconstructed after ablation for ORN could communicate via spoken word alone.[34]

4.4 | Survival

Five-year OS was 63% for the entire cohort and 64% among those who did not have a cancer recurrence. Even after removing the effect of cancer recurrence, 5-year survival remained comparable to the 60% generally quoted 5-year survival of patients with oral cancer, suggesting the physiologic stress of chronic infection and major surgery had a significant effect on survival, despite the patients in this cohort being largely free of cancer.[37] Causality for this, however, is difficult to prove. Complications associated with surgical management and reconstruction for ORN are high and demonstrate a direct effect on hospital and surgical charges. However, there was no difference in survival among patients who had complications versus those who did not.

Perioperative mortality was found to be 4%. This is in line with prior studies ranging from 0% to 8%,[20,21,27] but higher than surgery for advanced oral cavity cancer, suggesting that the ORN patient population may be at a higher risk for perioperative death.[37] The average age of the cohort was 61 years, which is comparable to most patients with head and neck cancer, and age was not significantly associated with survival. The survival and perioperative mortality in the ORN population suggest that these patients are at increased risk of non-cancer-related death after surgery, largely due to their medical comorbidities and the long-term effects of years of treatment for their head and neck cancer. Patients with pulmonary disease, in particular, had lower long-term survival after definitive surgery for ORN, possibly related to long-term effects of aspiration, pneumonia, and chronic lung disease in this patient population.

Despite suboptimal survival, there was only a 7% 5-year ORN-recurrence rate. This supports the well-established importance of complete resection of devitalized bone and reconstruction with vascularized tissue. Since the development of ORN is hypothesized to be related to hypoxia, hypocellularity, and hypovascularity, resection of necrotic bone with fibrotic soft tissue and replacement with viable vascularized tissue is essential.[38]

4.5 | Limitations

While this is the largest single-institution cohort to date and multivariate analysis was used to control for confounding variables, the overall number of patients in the study limits the power to detect modest differences in outcomes. Although charges have been adjusted for time, historical bias is also acknowledged, as this population underwent surgery from 2000 to 2009, allowing for a longer duration of follow-up. This may have resulted in a relatively higher incidence of complications and lower hospital charges compared to currently. Although surgical management has not vastly changed over this period, the majority of patients received 3D conformal radiation therapy, with only 11% receiving IMRT and no patients receiving proton therapy. This likely most impacted the incidence of ORN, which was not evaluated in this study. While IMRT may reduce the risk of ORN, once ORN develops, it is unclear if patients who had been treated with IMRT have differing outcomes.[3,9] This study does not assess biochemical measures of morbidity, such as malnutrition or hypothyroidism, which would aid in the quantification patients' underling poor health.[33] Postoperative functional measures were the final assessment performed for each patient. Although this gives the best representation of ultimate outcome, variability in the time that patients were measured limits the reproducibility and predictability of these functional measures. This population is limited to patients undergoing free tissue transfer for mandibular osteoradionecrosis; however, additional studies are needed to compare outcomes and charges associated with other treatments or preventions.[14,15,17,39–41]

5 | CONCLUSIONS

This study represents one of the largest cohorts to date who underwent definitive management of ORN of the mandible and is among the first to evaluate charge and functional outcomes. Median overall charges were $343 000 with nearly half of this related to complications. Charges were higher for smokers and those with complications. Perioperative morbidity is high, with almost two-thirds of patients experiencing at least one postoperative complication and almost half requiring a return to the operating room. However, complications were fewer in patients treated sooner for ORN. Although recurrence of ORN is rare, over one-third of patients died within 5 years of surgery and 4% died within 90 days of surgery. Modest worsening of speech but improvement in swallowing is expected.

CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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