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The high stakes of head and neck surgery following radiation and chemotherapy – An assessment of complications and survival

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ABSTRACT

Objectives: To investigate variables that predict medical and surgical complications in patients undergoing salvage surgery after primary organ-preserving therapy for head and neck cancer and to investigate the effect of complications on 5-year overall survival.

Materials and methods: A retrospective study was conducted on patients undergoing salvage surgery after primary organ-preserving therapy for head and neck cancer at a tertiary institution from 2006 to 2011. Multivariable regression analysis was used to assess association between independent variables and medical and surgical complications. A Kaplan-Meier survival curve was plotted to assess effect of surgical and medical complications on 5-year overall survival.

Results: One hundred thirty-six patients undergoing salvage surgery after primary organ-preservation surgery met inclusion criteria. Surgical complications occurred in 68/136 (50.0%) of patients. After adjusting for confounders, young age and history of hypothyroidism were significant predictors of surgical complications ($p < 0.05$). Medical complications occurred in 37/136 (27.2%) of patients. After adjusting for confounders, older age and history of hepatic disease were significant predictors of having a medical complication ($p < 0.05$). Patients with no complications had better overall survival than patients with medical complications ($p = 0.009$). There was no difference in overall survival between patients without complications and patients with surgical complications only ($p = 0.259$).

Conclusion: Risk factors for medical and surgical complications include history of hypothyroidism, liver disease, and age. Survival outcomes are not affected by surgical complications but are significantly affected by medical complications highlighting the importance of personalized patient care and medical co-management.

Introduction

The use of upfront radiation and chemoradiation therapy for head and neck squamous cell carcinoma is rising [1–3]. However, anywhere from 5% to 40% of patients undergoing organ-preserving therapy, including all subsites, will eventually have persistent or recurrent disease [4–9]. Salvage surgery is often the best therapeutic option to control locoregional disease in this setting despite its associated high morbidity with rates reported from 17% to 71% [10–19]. Moreover, as salvage surgery has become commonplace in a head and neck surgeon's practice, more attention to optimizing outcomes and care is necessary. It is well known these patients have more complications, longer hospital stays, and more costly treatments than the primary surgery patient. In this study, we aim to investigate variables that predict increased rate of complication in a population of high-risk patients undergoing salvage surgery after primary organ-preserving therapy. Additionally, we aim to investigate the effect medical and surgical complications have on 5-year overall survival at a single, high-volume, tertiary care center.

Abbreviations: AJCC, American Joint Committee on Cancer; CAD, coronary artery disease; CCI, Charlson comorbidity index; CI, confidence interval; EBL, estimated blood loss; IQR, interquartile range; LOS, length of stay; NSQIP, National Surgical Quality Improvement Program; OR, odds ratio; ORN, osteoradionecrosis; OSUWMC, Ohio State University Wexner Medical Center

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Methods

Study sample

After approval by The Ohio State University Wexner Medical Center (OSUWMC) Institutional Review Board, a retrospective study was conducted on adult patients undergoing head and neck surgery following primary radiation or chemoradiation therapy for head and neck cancer between January 2006 and December 2011. The dates were selected to allow survival analysis for all patients greater than five years out from surgery. Patients with unresectable metastatic disease at the time of surgery were excluded from the study.

Study variables

Patient charts were reviewed for demographics, pre-operative comorbidities, pre-surgical treatment course, surgical details, diagnoses, functional outcomes, complications, and survival. Our primary outcome, complications, was divided into medical and surgical complications. Surgical complications were further divided into minor and major complications as previously outlined by Sassler et al. [12]. Major complications included life-threatening systemic and local complications that required surgical intervention, prolonged hospital stay, or readmission. Minor complications were non–life-threatening, local complications that did not require additional surgery. Moreover, overall survival was defined as the time from the date of surgery to the date of death, with patients alive at the date of the last observation censored.

The independent variables used to predict the outcome included: age; gender; history of tobacco and alcohol use; pack years smoking history; history of hypothyroidism, coronary artery disease, diabetes mellitus, pulmonary disease, renal disease, and liver disease; previous head and neck surgery; primary tumor location; AJCC stage at time of salvage surgery; pathology; history of chemotherapy; need for pre-operative feeding tube; indication for salvage surgery; neck dissection; time since completion of radiation therapy; need for flap; and intraoperative estimated blood loss.

Statistical analysis

Descriptive statistics were used to characterize the study population and summarize surgical characteristics and outcomes. Data is displayed as mean ± standard deviation or median (IQR). A univariable logistic regression analysis was conducted between the independent variables and the outcomes: surgical complications and medical complications. Odds ratios (OR) and 95% confidence intervals (CI) are reported. Variables that were found to be significant at the $\alpha = 0.20$ level in the univariable models were considered for the multivariable analysis using a backward selection algorithm to estimate odds ratio. Co-linearity amongst the independent variables was assessed using variance inflation factor before inserting them into the multivariable model. p-values were two-tailed, and significance was set to 0.05 alpha. A survival curve was plotted using the Kaplan-Meier method to assess effect of surgical and medical complications on overall survival. All statistical analysis was conducted in SPSS version 25 (IBM, Armonk, NY).

Results

Patient characteristics

One hundred thirty-six patients undergoing salvage head and neck surgery after primary chemoradiation met inclusion criteria (Table 1). The median age of the entire sample was 61 (55.3, 69.8). Most patients, 104/136 (76.5%), were male. Additionally, 122/136 (91.0%) and 94/136 (69.6%) of patents had a history of smoking and alcohol use, respectively, with a median pack year of 40 (30, 60). The primary tumor occurred in the larynx in 58/136 (42.6%) of cases, the oral cavity in 34/136 (25.0%), the oropharynx in 21/136 (15.4%), the hypopharynx in 14/136 (10.3%), the sinonasal cavity in 6/136 (4.4%), the skin, the nasopharynx, and minor salivary gland each in 1 (0.7%) case. In terms of staging, 34/136 (25.0%) patients had AJCC stage I/II, and 99/136 (72.8%) patients had AJCC stage III/IV. Finally, reasons for salvage surgery included recurrence in 95/136 (69.9%), secondary primary in 21/136 (15.4%), and persistent disease in 20/136 (14.7%).

Table 1
Patient characteristics.

Characteristics (n = 136)		N (%) or Median (IQR)
Age in years		61 (55.3, 69.8)
Gender	Male	104 (76.5)
	Female	32 (23.5)
Tobacco use (n = 134)		122 (91.0)
Pack years (n = 126)		40 (30, 60)
Alcohol use (n = 135)		94 (69.6)
Past Medical History	Pulmonary disease	89 (65.4)
	Coronary artery disease	39 (28.7)
	Diabetes mellitus	26 (19.1)
	Hypothyroidism	17 (12.5)
	Hepatic disease	9 (6.6)
	Renal disease	8 (5.9)
Age-adjusted CCI		5 (3, 5.75)
Previous head/ neck surgery (n = 135)		90 (66.7)
Primary tumor location	Larynx	58 (42.6)
	Oral Cavity	34 (25.0)
	Oropharynx	21 (15.4)
	Hypopharynx	14 (10.3)
	Sinonasal	6 (4.4)
	Other	3 (2.2)
AJCC Stage at time of surgery	Unknown	3 (2.2)
	I/II	34 (25.0)
	III/IV	99 (72.8)
Pathology	Squamous cell carcinoma	133 (97.8)
	Adenoid cystic carcinoma	2 (1.5)
	Myoepithelial carcinoma	1 (0.7)
Chemotherapy		73 (53.7)
Reason for salvage surgery	Recurrence	95 (69.9)
	Secondary primary	21 (15.4)
	Persistent disease	20 (14.7)
Time since completion of therapy (months)		16.5 (6, 49.5)

Notes: CCI, Charlson comorbidity index.

Surgical characteristics and post-operative courses are included in Table 2. An intraoperative tissue flap was performed in 101/136 (74.3%) of patients, 71/101 (70.3%) of these patients had a free flap, 30/101 (29.7%) had a regional, pedicled flap, and 1/101 (0.99%) patient had both. Patients remained in the hospital for a median of 8 days (7, 11.8). In 39/136 (28.7%) of cases, patients were readmitted within 60 days of the operation and in 74/136 (54.4%) of cases, patients were readmitted within 6 months of the operation.

Surgical complications occurred in 68/136 (50.0%) of patients (Table 3). Surgical complications were classified as major in 41/136 (30.1%) and minor in 27/136 (19.9%) of cases. The most common major surgical complication was fistula formation, which occurred in 24/136 (17.6%) of all patients. The most common minor surgical complication was wound dehiscence, which occurred in 14/136 (10.3%) of all patients. In 27/136 (19.9%) of cases, patients required further surgical intervention with regional pedicled flap being the most common, 11/136 (8.1%), additional intervention. Medical complications occurred in 36/136 (27.2%) of cases.

Table 2
Surgical characteristics and post-operative course.

Surgical characteristics (n = 136)		N (%) or Median (IQR)
Neck Dissection	Not performed	50 (36.8)
	Unilateral	51 (37.5)
	Bilateral	35 (25.7)
Pre-operative feeding tube		36 (26.5)
Intraoperative flap	Not performed	34 (25.0)
	Free flap	71 (52.2)
	Regional pedicled flap	30 (22.1)
	Both	1 (0.7)
EBL (mL)		300 (200, 413)
LOS (days)		8 (7, 11.8)
Hospital Readmission (60 days)		39 (28.7)
Hospital Readmission (6 months)		74 (54.4)
Length of follow up (months)		7 (3, 15)

Notes: EBL, estimated blood loss; mL, milliliters; LOS, length of stay.

Table 3
Complications stratified by surgical and medical complications.

Complications (n = 136)		N (%) or Median (IQR)[a]
Overall surgical complications		68 (50.0)
Major surgical complications		41 (30.1)
	Fistula	24 (17.6)
	Wound dehiscence	22 (16.1)
	Infection	14 (10.2)
	Flap compromise	10 (7.4)
	Major vessel rupture	6 (4.4)
Minor surgical complications		27 (19.9)
	Dehiscence	14 (10.3)
	Infection	12 (8.8)
	Superficial skin necrosis	4 (2.9)
	Hematoma (non-op)	2 (1.5)
Additional surgical intervention		27 (19.9)
	Regional pedicled flap	11 (8.1)
	Wound debridement	10 (7.4)
	Revision of anastomosis	8 (5.9)
	Closure of fistula	6 (4.4)
	Major vessel ligation	3 (2.2)
Medical complications		37 (27.2)
	Pulmonary	20 (14.7)
	Mental status change	10 (7.4)
	Cardiac	9 (6.6)
	Genitourinary	5 (3.7)
	Endocrine	3 (2.2)
	Gastrointestinal	1 (0.7)

[a] Patients had more than 1 complication.

Predicting surgical and medical complications

An overall surgical complication univariable logistic regression analysis identified age in years (OR, 0.96; CI 95%, 0.92–0.99; $p = 0.013$), history of pulmonary disease (OR, 0.55; CI 95%, 0.27–1.13; $p = 0.106$), history of coronary artery disease (OR, 1.66; CI 95%, 0.78–3.53; $p = 0.186$, history of diabetes mellitus (OR, 1.79; CI 95%, 0.74–4.48; $p = 0.194$), history of hypothyroidism (OR, 2.7; CI 95%, 0.90–8.14 l; $p = 0.078$), primary tumor subsite (oral cavity vs other; OR, 0.31; CI 95%, 0.07–1.46; $p = 0.138$), and history of chemotherapy (OR, 1.93; CI 95%, 0.97–3.82; $p = 0.060$), as variables to include in the multivariable model based on an alpha of < 0.20 (Table 4). After adjusting for confounders, young age (OR, 0.95; CI 95%, 0.91–0.99; $p = 0.014$) and history of hypothyroidism (OR, 3.37; CI 95%, 1.01–11.3; $p = 0.049$) were significant predictors of surgical complications.

A medical complications univariable logistic regression analysis identified age in years (OR, 1.04; CI 95%, 1.00–1.09; $p = 0.033$), history of tobacco use (OR, 0.33; CI 95%, 0.10–1.10; $p = 0.068$), history of alcohol use (OR, 0.59; CI 95%, 0.26–1.32; $p = 0.197$), history of diabetes mellitus (OR, 2.37; CI 95%, 0.97–5.79; $p = 0.059$), history of renal disease (OR, 2.88; CI 95%, 0.68–12.2; $p = 0.15$), history of hepatic disease (OR, 3.71; CI 95%, 0.94–14.7; $p = 0.062$), and AJCC stage at time of surgery (stage III/IV vs stage unknown/I/II status; OR, 1.86; CI 95%, 0.74–4.7; $p = 0.189$) as variables to include in the multivariable model based on an alpha < 0.20 (Table 5). After adjusting for important confounders, age (OR, 1.05; CI 95%, 1.00–1.10; $p = 0.032$) and history of hepatic disease (OR, 5.23; 1.09–25.2; $p = 0.039$), were both significant predictors of having a medical complication.

Overall survival by surgical and medical complications

Overall survival rates at 1, 3, and 5 years for our patient sample was 60.3%, 40.4%, and 31.6% (Fig. 1). The overall survival for patients with surgical complications at 1, 3, and 5 years is 66.7%, 43.1%, and 33.3%. The overall survival for patients with medical complications at 1, 3, and 5 years is 45.0%, 25.0%, and 20.0%. The overall survival for patients with both medical and surgical complications at 1, 3, and 5 years is 23.5%, 5.9%, and 5.9%. The overall survival for patients without any complications at 1, 3, and 5 years is 72.9%, 56.3%, and 43.8%. Overall survival was statistically significantly different between patients with different complication types (log rank $p < 0.0005$). In particular, patients with surgical complications had improved overall survival than patients with both medical and surgical complications ($p < 0.0005$). Similarly, patients with no complications had improved overall survival than patients with medical complications ($p = 0.009$) and patients with both medical and surgical complications ($p < 0.0005$). There was no difference in overall survival between patients without complication and patients with surgical complication only ($p = 0.259$).

Discussion

Salvage head and neck surgery continues to be a source of challenge in our field. The overall rate of postoperative surgical complications in our cohort was 50.0%, which is comparable to those reported in other studies [10–19]. The most commonly encountered surgical complications include infection, wound dehiscence, flap compromise, hematoma, fistula, and major vessel rupture. Overall, our rate of fistula was 17.6% (n = 24) which supports the gradual decline that has been observed likely due to advances in radiotherapy and surgical technique, specifically with free tissue transfer reconstruction [14–16,20]. For this reason, we chose this cohort of patients, dating from 2006 to 2011 in order to fully evaluate patients within the free flap era and to assess predictors of complications and the effects these post-operative complications have on patient survival at a single, busy, tertiary care center. Most notably, we discovered surgical complications alone were not found to worsen overall patient survival.

Nevertheless, the issues these patients experience following salvage surgery should not be understated. Even when complications do not arise, these patients still suffer from issues such as delayed wound healing, trismus, xerostomia, dysphagia, dysphonia, unsightly appearance and much more. Identifying key risk factors and addressing each of these peri-operatively is critical in order to strive and achieve our goal for the most optimal oncologic and post-surgical outcome.

As stated, half of patients experience some type of complication during the post-operative period and many require re-admission at some point. Surprising to find in this cohort, younger age was a significant risk factor for having a surgical complication. This is in contrast to previous studies that reported no association between age and

Table 4
Univariable and multivariable analysis of surgical complications (50.0%).[a]

Predictor	No surgical complications (n = 68)	Surgical complications (n = 68)	Univariable analysis		Multivariable analysis	
			Odds Ratio CI (95%)	p-value	Odds Ratio CI (95%)	p-value
Age (years)	**64.6 ± 9.4**	**60.2 ± 10.3**	**0.955 (0.921–0.990)**	**0.013**	**0.948 (0.909–0.989)**	**0.014**
Male sex	52 (76.5)	52 (76.5)	1.000 (0.453–2.209)	1.000		
Tobacco use (n = 134)	61 (91.0)	61 (91.0)	1.000 (0.305–3.274)	1.000		
Smoke pack years (n = 126)	42.2 ± 22.6	41.7 ± 24.7	0.999 (0.984–1.014)	0.917		
Alcohol use (n = 135)	45 (67.2)	49 (72.1)	1.261 (0.604–2.630)	0.537		
Past Medical History						
Pulmonary disease	49 (72.1)	40 (58.8)	0.554 (0.270–1.134)	0.106		
Coronary artery disease	16 (23.5)	23 (33.8)	1.661 (0.783–3.526)	0.186		
Diabetes mellitus	10 (14.7)	16 (23.5)	1.785 (0.744–4.278)	0.194		
Hypothyroidism	**5 (7.4)**	**12 (17.6)**	**2.700 (0.896–8.141)**	**0.078**	**3.370 (1.006–11.29)**	**0.049**
Renal disease	5 (7.4)	3 (4.4)	0.582 (0.133–2.536)	0.471		
Hepatic disease	4 (5.9)	5 (7.4)	1.270 (0.326–4.948)	0.731		
Previous head & neck surgery (n = 135)	43 (64.2)	47 (69.1)	1.249 (0.610–2.559)	0.543		
Primary tumor subsite						
Other	3 (4.4)	6 (8.8)	Ref			
Oral cavity	21 (30.9)	13 (19.1)	0.310 (0.066–1.457)	0.138		
Hypo/larynx/oropharynx	44 (64.7)	49 (72.1)	0.557 (0.131–2.361)	0.427		
AJCC Stage at time of surgery						
Unknown	1 (1.5)	2 (2.9)	Ref			
I/II	21 (30.9)	13 (19.1)	0.310 (0.025–3.764)	0.358		
IIII/IV	46 (67.6)	53 (77.9)	0.576 (0.051–6.562)	0.657		
Original pathology						
Squamous cell carcinoma	67 (98.5)	66 (97.1)	Ref			
Other	1 (1.5)	2 (2.9)	2.030 (0.180–22.93)	0.567		
Chemotherapy	31 (45.6)	42 (61.8)	1.928 (0.974–3.818)	0.060		
Pre-operative feeding tube	15 (22.1)	21 (30.9)	1.579 (0.731–3.410)	0.245		
Neck dissection						
Not performed	25 (36.8)	25 (36.8)	Ref			
Unilateral	29 (42.6)	22 (32.4)	0.759 (0.346–1.661)	0.490		
Bilateral	14 (20.6)	21 (30.9)	1.500 (0.626–3.596)	0.363		
Time since completion of therapy (months)	43.7 ± 58.6	36.5 ± 50.1	0.998 (0.991–1.004)	0.445		
Free/pedicled flap	49 (72.1)	53 (77.9)	1.370 (0.628–2.990)	0.429		
EBL, mL	322 ± 176	373 ± 349	1.001 (0.999–1.002)	0.293		

Abbreviations: CCI, Charlson comorbidity index; EBL, estimated blood loss; mL, milliliters; ORN, osteoradionecrosis.

[a] Categorical variables presented as number (%) and continuous variables as mean ± SD unless otherwise indicated. All variables with $p < 0.20$ in the univariable analysis were considered in the multivariable analysis algorithm. Bold values demonstrate statistical significance in the final multivariable model.

postoperative complications [11,21,22]. One reason for this significance could be that younger patients are more likely to have more aggressive disease and organ-preserving treatment leading to more complications. In contrast, as expected, older age was a significant predictor of medical complication as chronic medical issues overall increase with advancing years.

It should not be any surprise, that patients with more medical comorbidities (diabetes, hypothyroidism, and heart disease) were more likely to suffer surgical complications. The higher association of post-operative issues in patients with these chronic medical issues has been previously reported and was confirmed in our study [23,24].

With this in mind, methods to reduce these complications must be employed and should begin at the pre-operative assessment. At our institution, comprehensive pre-operative clinic attendance has been found to reduce complications and overall cost for head and neck patients [25]. For this reason, all patients undergoing major surgery have since been referred to this clinic for pre-operative clearance with peri-operative medical recommendations for the past several years. Prospective analysis of a systematic pre-operative medical optimization system is therefore warranted and will be beneficial in further justifying the associated costs of this clinic.

Importantly, we found there was no effect on survival when comparing patients with a surgical complication to those with no complications, which differs from previous reports [26]. Obviously, survival can be looked at in many different ways (i.e. with or without tracheostomy, feeding tube or recurrence) but it is important to note that it is the medical complications, not the surgical complication in this cohort that worsened overall survival by more than 10% at 5-years. Certainly, there are numerous variables at play however the effect of post-operative medical complications has also been seen on a larger scale using the National Surgical Quality Improvement Program (NSQIP) database [27]. It is also reassuring and invaluable information for around half of these salvage surgery patients being managed closely for a post-surgical wound issue as the delayed time course can be time and energy consuming.

Looking closer at the medical complication effects, we found, at 3 and 5-year intervals patients suffering a medical complication had reduced survival from 56.3% to 25.0% and from 43.8% to 20.0%

Table 5
Univariable and multivariable analysis of medical complications (27.2%). [a]

Predictor	No medical complications (n = 99)	Medical complications (n = 37)	Univariable analysis		Multivariable analysis	
			Odds Ratio CI (95%)	p-value	Odds Ratio CI (95%)	p-value
Age (years)	**61.3 ± 9.88**	**65.5 ± 10.2**	**1.043 (1.004–1.085)**	**0.033**	**1.049 (1.004–1.097)**	**0.032**
Male sex	75 (75.8)	29 (78.4)	1.160 (0.468–2.875)	0.749		
Tobacco use (n = 134)	92 (93.9)	30 (83.3)	0.326 (0.098–1.087)	0.068		
Smoke pack years (n = 126)	40.9 ± 22.1	44.8 ± 27.4	1.007 (0.990–1.024)	0.415		
Alcohol use (n = 135)	72 (72.7)	22 (61.1)	0.589 (0.264–1.315)	0.197		
Past medical history						
Pulmonary disease	66 (66.7)	23 (62.2)	0.821 (0.375–1.801)	0.623		
Coronary artery disease	30 (30.3)	9 (24.3)	0.739 (0.311–1.755)	0.494		
Diabetes mellitus	15 (15.2)	11 (29.7)	2.369 (0.969–5791)	0.059		
Hypothyroidism	11 (11.1)	6 (16.2)	1.548 (0.528–4.540)	0.426		
Renal disease	4 (4.0)	4 (10.8)	2.879 (0.681–12.17)	0.150		
Hepatic disease	**4 (4.0)**	**5 (13.5)**	**3.711 (0.939–14.669)**	**0.062**	**5.232 (1.088–25.15)**	**0.039**
Previous head & neck surgery (n = 135)	64 (65.3)	26 (70.3)	1.256 (0.554–2.847)	0.586		
Primary tumor subsite						
Other	5 (5.1)	4 (10.8)	Ref			
Oral cavity	21 (21.2)	13 (35.1)	0.774 (0.175–3.418)	0.735		
Hypo/larynx/oropharynx	73 (73.7)	20 (54.1)	0.342 (0.084–1.395)	0.342		
AJCC Stage at time of surgery						
Unknown/I/II	30 (30.3)	7 (18.9)	Ref			
III/IV	69 (69.7)	30 (81.1)	1.863 (0.737– 4.712)	0.189		
Pathology						
Squamous cell carcinoma	97 (98.0)	36 (97.3)	Ref			
Other	2 (2.0)	1 (2.7)	1.347 (0.119–15.31)	0.810		
Chemotherapy	54 (54.5)	19 (51.4)	0.880 (0.413–1.874)	0.740		
Pre-operative feeding tube	26 (26.3)	10 (27.0)	1.040 (0.443–2.439)	0.928		
Neck dissection						
Not performed	35 (35.4)	15 (40.5)	Ref			
Unilateral	38 (38.4)	13 (35.1)	0.798 (0.333–1.911)	0.613		
Bilateral	26 (26.3)	9 (24.3)	0.808 (0.306–2.130)	0.666		
Time since completion of therapy (months)	37.0 ± 50.5	48.4 ± 63.8	1.004 (0.997–1.010)	0.281		
Free/pedicled flap	72 (72.7)	30 (81.1)	1.607 (0.632–4.090)	0.319		
EBL, mL	336 ± 285	380 ± 252	1.001 (0.999–1.002)	0.415		

Abbreviations: CCI, Charlson comorbidity index; EBL, estimated blood loss; mL, milliliters.

[a] Categorical variables presented as number (%) and continuous variables as mean ± SD unless otherwise indicated. All variables with $p < 0.20$ in the univariable analysis were considered in the multivariable analysis algorithm, but only the final model is presented. Bold values demonstrate statistical significance in the final multivariable model.

respectively (Fig. 1). Comparably, the overall survival for all patients undergoing salvage surgery was 60.3%, 40.4%, and 31.6% at 1, 3 and 5-years. In response to this, our institution has developed a system where head and neck patients are admitted directly to a head and neck specialty trained floor rather than the intensive care unit. The value of this approach has been previously reported [28]. This inpatient volume for the head and neck service can range anywhere from the mid-single digits to high-20′s at any time point. This volume of patients would be un-reasonable to manage by only the head and neck team and as such a medical co-management system has been developed with the medical consultant service. These consultants help manage patients in these high-risk cohorts in order to optimize their chronic medical conditions post-operatively and to guide that critical transition from hospital to home care. This service has been invaluable improving both patient care as well as the global sense of medical collaboration. The goals of this approach are to foresee and reduce the medical issues these patients face following high-risk salvage surgery. These results will be reviewed independently but clinically has been a very positive experience for all parties.

Conclusion

Salvage head and neck surgery is fraught with complications secondary to patient, disease and previous treatment characteristics. We have identified several risk factors that are prone to surgical and medical complications and have instituted a system of pre-operative comprehensive evaluation and optimization as well as medical co-management after surgery in order to control these factors better. Survival outcomes are not affected by surgical complications but are significantly affected by medical complications at 1, 3 and 5-year marks highlighting the importance of personalized patient care and the value in medical co-management of these patients.

Declaration of Competing Interest

None declared by any of the authors.

	Overall survival rates			
	1 year (%)	3 year (%)	5 year (%)	
Overall	60.3	40.4	31.6	
Surgical complications	66.7	43.1	33.3	
Medical complications	45.0	25.0	20.0	
Medical and surgical complications	23.5	5.9	5.9	
No complications	72.9	56.3	43.8	

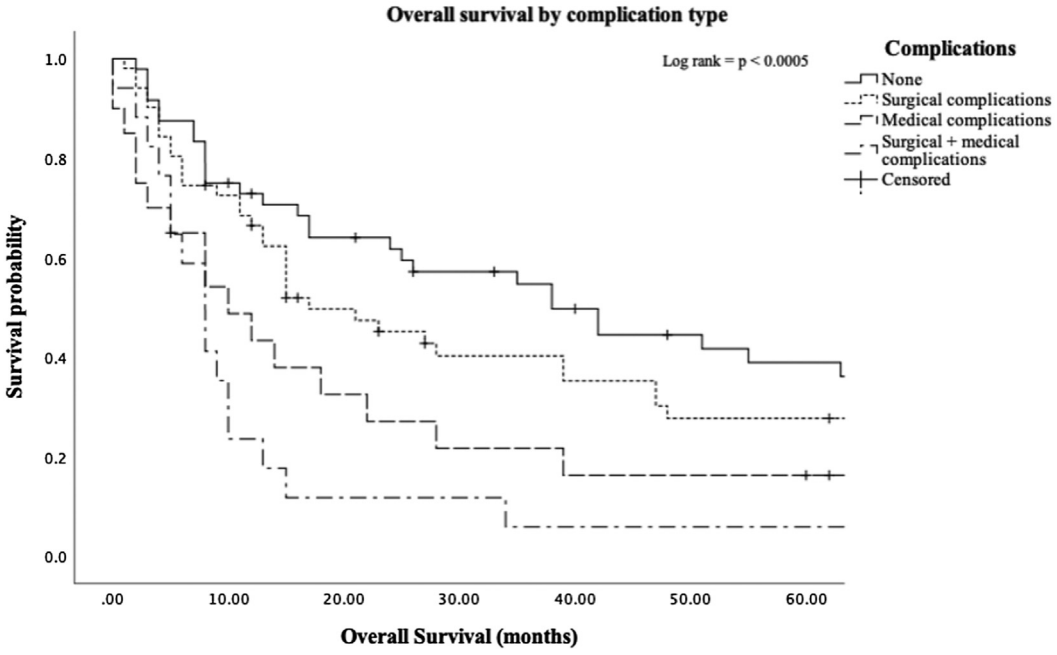

Fig. 1. Caption: Overall survival stratified by medical and surgical complications. Description: ** Log rank p = 0.009. Overall survival for patients with no complications vs patients with medical complications. * Log rank p < 0.0005. Overall survival for patients with no complications vs patients with both medical and surgical complications and patients with surgical complications vs patients with both medical and surgical complications.

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References

[1] Spaulding MB, Fischer SG, Wolf GT. Tumor response, toxicity, and survival after neoadjuvant organ-preserving chemotherapy for advanced laryngeal carcinoma. The Department of Veterans Affairs Laryngeal Cancer Study Group. J Clin Oncol 1994;12:1592–9.
[2] The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med 1991; 324: p. 1685–90.
[3] Chen AY, Schrag N, Hao Y, Stewart A, Ward E. Changes in treatment of advanced oropharyngeal cancer, 1985–2001. Laryngoscope 2007;117:1–21.
[4] Shah JP, Loree TR, Kowalski L. Conservation surgery for radiation failure carcinoma of the glottic larynx. Head Neck 1990;12:326–31.
[5] Lydiatt WM, Shah JP, Lydiatt KM. Conservation surgery for recurrent carcinoma of the glottic larynx. Am J Surg 1996;172:662–4.
[6] Le QT, Fu KK, Kroll S, et al. Influence of fraction size, total dose, and overall time on local control of T1–T2 glottic carcinoma. Int J Radiat Oncol Biol Phys 1997;39:115–26.
[7] Small Jr W, Mittal BB, Brand WN, et al. Results of radiation therapy in early glottic carcinoma. Radiology 1992;183:789–94.
[8] McLaughlin MP, Parsons JT, Fein DA, et al. Salvage surgery after radiotherapy failure in T1–T2 squamous cell carcinoma of the glottic larynx. Head Neck 1996;18:229–35.
[9] Yiotakis J, Stavroulaki P, Nikolopoulos T, et al. Partial laryngectomy after irradiation failure. Otolaryngol Head Neck Surg 2003;128:200–9.
[10] Morgan JE, Breau RL, Suen JY, Hanna EY. Surgical wound complications after intensive chemoradiotherapy for advanced squamous cell carcinoma of the head and neck. Arch Otolaryngol Head Neck Surg 2007;133(1):10–4.
[11] Agra IM, Carvalho AL, Pontes E, et al. Postoperative complications after en bloc salvage surgery for head and neck cancer. Arch Otolaryngol Head Neck Surg 2003;129(12):1317–21.
[12] Sassler AM, Esclamado RM, Wolf GT. Surgery after organ preservation therapy. Analysis of wound complications. Arch Otolaryngol Head Neck Surg 1995;121(2):162–5.
[13] Richey LM, Shores CG, George J, et al. The effectiveness of salvage surgery after the failure of primary concomitant chemoradiation in head and neck cancer. Otolaryngol Head Neck Surg 2007;136(1):98–103.
[14] Stoeckli SJ, Pawlik AB, Lipp M, Huber A, Schmid S. Salvage surgery after failure of nonsurgical therapy for carcinoma of the larynx and hypopharynx. Arch Otolaryngol Head Neck Surg 2000;126(12):1473–7.
[15] Weber RS, Berkey BA, Forastiere A, et al. Outcome of salvage total laryngectomy following organ preservation therapy: the Radiation Therapy Oncology Group trial 91–11. Arch Otolaryngol Head Neck Surg 2003;129(1):44–9.
[16] Ganly I, Patel S, Matsuo J, et al. Postoperative complications of salvage total laryngectomy. Cancer 2005;103(10):2073–81.
[17] Fung K, Teknos TN, Vandenberg CD, et al. Prevention of wound complications following salvage laryngectomy using free vascularized tissue. Head Neck 2007;29(5):425–30.
[18] Kostrzewa JP, Lancaster WP, Iseli TA, Desmond RA, Carroll WR, Rosenthal EL. Outcomes of salvage surgery with free flap reconstruction for recurrent oral and oropharyngeal cancer. Laryngoscope 2010;120(2):267–72.
[19] Furuta Y, Homma A, Oridate N, et al. Surgical complications of salvage total

laryngectomy following concurrent chemoradiotherapy. Int J Clinic Onc 2008;13(6):521–7.
[20] Bresson K, Rasmussen H, Rasmussen PA. Pharyngo-cutaneous fistulae in totally laryngectomized patients. J Laryngol Otol 1974;88:835–42.
[21] Clayman GL, Eicher SA, Sicord MW, Razmpa E, Goepfert H. Surgical outcomes in head and neck cancer patients 80 years of age and older. Head Neck 1998;20:216–23.
[22] Kowalski LP, Alcantara PS, Magrin J, Parise Junior O. A case-control study on complications and survival in elderly patients undergoing major head and neck surgery. Am J Surg 1994;168:485–90.
[23] Tsou Y, Hua C, Lin M, Tseng H, Tsai M, Shaha A. Comparison of pharyngocutaneous fistula between patients followed by primary laryngopharyngectomy and salvage laryngopharyngectomy for advanced hypopharyngeal cancer. Head Neck 2010;32:1494–500.
[24] Miller MC, Agrawal A. Hypothyroidism in postradiation head and neck cancer patients: incidence, complications, and management. Curr Opin Otolaryngol Head Neck Surg 2009;17(2):111–5.
[25] Dziegielewski PT, et al. Predictors and costs of readmissions at an academic head and neck surgery service. Head Neck 2016;38(Suppl 1):E502–10.
[26] de Melo GM, Ribeiro KC, Kowalski LP, Deheinzelin D. Risk factors for postoperative complications in oral cancer and their prognostic implications. Arch Otolaryngol Head Neck Surg 2001;127:828–33.
[27] Mulvey CL, Brant JA, Bur A. Complication associated with mortality after head and neck surgery: an analysis of the NSQIP database. Otolaryngol Head Neck Surg 2017;156(3):504–10.
[28] Arshad H, Ozer HG, Thatcher A, et al. Intensive care unit versus non-intensive care unit postoperative management of head and neck free flaps: comparative effectiveness and cost comparisons. Head Neck 2014 Apr;36(4):536–9.