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Surgery Remains the Best Treatment for Floor of Mouth Squamous Cell Carcinoma

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ABSTRACT

Aims: This review seeks to define if radiotherapy is comparable to surgery in eradicating Floor of Mouth (FOM) carcinomas.

Materials and Methods: This ethics approved study-audited information on patients with a FOM squamous cell carcinoma. Data was sourced from the electronic medical record (EMR) system (MOSAIQ) for each patient, hospital notes, and referral correspondence. Analysis was performed using Pearson Chi-square or Fisher's Exact Test. The Kaplan-Meier method described time-to-event data, with the log rank test used to assess differences between curves. Endpoints were local/ultimate local control, overall/cancer-specific survival, and time-to-development of second malignancy.

Results: Eligible were 184 patients. The majority were males with a smoking history. Surgery was used in 150 (82%) patients, with 32 treated with radiotherapy alone. There was no difference in patient and disease factors between the two populations. Five-year ultimate local control for patients treated with radiotherapy alone was 46% versus 84% for surgery alone, and 68% when combined with radiotherapy (p=0.001). There was a high likelihood of developing a second malignancy. A new primary was evident in 53 (29%) patients, with a median time to development of 4.4 years.

Conclusions: Surgery is a superior modality to radiotherapy alone to address FOM carcinoma.

Keywords: Head and neck cancer; Floor of mouth; Carcinoma; Surgery; Radiotherapy; Recurrence

INTRODUCTION

The floor of mouth (FOM) defines an anatomical subunit of the oral cavity. The majority of malignancies arise near the anterior midline with spread inferiorly into the muscular compartment of the floor. There is a smoking aetiology,[1] although pre-malignant non-smoking conditions can be evident,[2] these can be relatively bulky at initial presentation. Treatment has the focus on cancer eradication and preservation of tongue function. There is increasing use of sentinel node biopsy to define nodal spread, when not clinically apparent.[3,4]

Surgical resection has been the mainstay of management for many years,[5] with various types of free flap reconstructions now utilized to address surgical defects.[6] Imaging assessment to determine mandibular involvement is appropriate now, influencing whether reconstruction will be soft tissue, or a composite bone-soft tissue mix.[7] Radiotherapy has traditionally played a lesser role, however the use of brachytherapy or intensity-modulated radiotherapy (IMRT) enables a higher dose to be delivered with potentially greater impact.[8,9]

This center's earlier experience in addressing this malignancy reported the superiority of surgery in achieving better local control figures.[10] The aim of this review is to define whether this philosophy should continue or are there other factors (patient or disease related) that are the true determinants of outcome.

MATERIALS AND METHODS

This is an ethics approved retrospective study (South Eastern Local Health District 10/040) of predominantly prospectively collected data with patients treated from September 1967-June 2017 allowing a minimum two-year follow-up period.

Eligible patients were defined by the following criteria: definitively managed at the Prince of Wales Cancer Centre (POWCC), squamous cell carcinoma (SqCC) (including in-situ disease), floor of mouth origin (even if involving other structures), and age 18 years or older, with minimum two-year follow-up. Patients were excluded if referred with current/progressive disease or had distant metastases at presentation. All staging was via the 2009 Union for International Cancer Control TNM 7th edition manual.

Data utilized in this audit is housed in the Prince of Wales Cancer Centre Head and Neck Cancer Database, which is anatomically site orientated, and grouped into three categories: patient, disease, and treatment information. This was sourced from the electronic medical record (EMR) system (MOSAIQ) for each patient, hospital notes, and referral correspondence. Older paper-based records were deposited in the EMR. Following treatment, patients were routinely followed up at 3-4 month intervals during the first two years, 4-6 months to 5 years, and 12 monthly thereafter. Follow-up information addressing recurrence/progression of disease was sought from EMR and involved clinicians. Death information was obtained from the New South Wales Registry of Births, Death and Marriages, and the National Death Index (E02017/5/392).

Treatment

All patients had management decisions documented at a multidisciplinary (MDT) Head and Neck Clinic with imaging input, this information being recorded for the last 20 years in the patients EMR, previously in paper records.

Surgery was performed by experienced Head and Neck surgeons with all flap repair considerations available by comparably experienced reconstructive surgeons. Maintenance of function was an important consideration with Allied Health input.

Radiotherapy with appropriate head fixation was delivered 5 days per week, all fields treated daily, at 2-2.5 gray (Gy) per fraction, progressively moving from 2D to 3D, and more recently IMRT. Brachytherapy was performed infrequently.

Nodal sites were addressed as dictated by the clinical situation. Palpable disease was usually addressed surgically, if the primary site warranted post-operative radiotherapy, and no palpable disease, this was included in the radiotherapy volume.

Outcomes

All dates were measured from the initial date of treatment. The primary endpoint was time to local failure and subsequently to ultimate local failure. Local failure was defined as persistent disease within the FOM after treatment, or a local recurrence after a complete response (CR) (a macroscopically complete resection). Ultimate local failure was declared when there was a local failure and salvage treatment was not performed, or salvage treatment was performed, however the cancer recurred. Similar criteria were applied to nodal and ultimate nodal failure.

Cancer-specific survival (CSS) was a secondary endpoint, defined as survival or death in patients without head and neck cancer (no primary, regional recurrence, or distant metastasis). Overall survival (OS) recognized the subsequent fate of the patient without defining the cause of death.

The tertiary endpoint was the development of further malignancy unrelated to the defined FOM carcinoma.

Statistical evaluation

Statistical analysis was performed using SPSS Statistics 26.0 (IBM, Armonk, New York). The Shapiro-Wilk test determined data distribution for continuous variables. The mean (range) and median interquartile range (IQR) values were reported for normally and non-normally distributed data respectively. Categorical variables were reported as frequencies and analyzed using Pearson Chi-square or Fisher's Exact Test. Time-to-event analysis was performed using the Kaplan-Meier method. The log rank test assessed differences between curves, when present; the Mann-Whitney U test identified the difference between two groups, for all groups. The level of significance for all tests was set to $P<0.05$ and all P-values are two-sided.

RESULTS

The oral cavity subunit of the Head and Neck Cancer Database has a total population of 1052 patients registered between September 28, 1967 and June 28, 2017, of which 184 patients fulfilled all of the eligibility criteria. Demographic patient data is listed in Table 1. Of note is that males constituted 77% of patients, and 92% had defined smoking history. Nearly all patients were fit for surgery (using modified Charlson comorbidity indices) and had operable cancer.

Disease characteristics

Early stage disease (T1-2) was present in 145 of 184 (79%) patients. Nodal disease was present in 60 (32%) patients, only one patient having contralateral nodal disease, and 9 patients with bilateral disease (Figure 1). Level I was more frequently involved in the FOM than for other anatomical sub-units of the oral cavity. The median largest node size was 25 mm (IQR 15-40 mm). Clinical stage at diagnosis is depicted in Table 1.

Surgical treatment

Surgical resection to the primary took place in 150 of 184 patients (82%). Reconstruction procedures used are depicted in Table 2. A neck dissection was performed in 102 (68%) patients, with a selective dissection (level I-III, unilateral) in 21 (14%), unilateral (level I-IV) in 31 (21%), and bilateral (level I-III) in 50 (33%).

Radiotherapy treatment

Radiotherapy was the only treatment in 32 (17%) patients and combined with surgery in 70 (38%) patients. As evidenced in table 2, for those 27 patients having conventional radiotherapy as the only treatment, the median dose was 60 Gy (IQR 50-60 Gy) in 25 fractions (IQR 24-28 fractions), and a median treatment duration of 42 days (IQR 36-50 days), with three patients having a treatment interruption greater than one week. Those patients having conventional post-operative radiotherapy (69 patients) received a median dose of 56 Gy (IQR 55-62 Gy) in 28 fractions (IQR 28-31 fractions), and a median treatment duration of 40 days (IQR 38-44 days), with 5 patients having a treatment interruption greater than one week. Brachytherapy was used in 9 patients (median dose 60 Gy (IQR 60-71 Gy), over a median of 5 days), 5 as the only treatment and one combined with surgery, and in three patients combined with external conventional radiotherapy.

Chemotherapy treatment

Two patients had chemotherapy as definitive treatment, not for palliation.

Pathology

There were negative (5 mm or greater) margins for the primary in 62 (41%) patients having surgery, in-situ disease in 10 (7%), close margins in 40 (26%), positive margins in 25 (17%), and 13 (9%) unknown margins. The median depth of invasion was 5 mm (IQR 3-8 mm).

Of the 102 patients having neck dissection, no tumour was found in 41, intracapsular disease in 29, focal extracapsular disease in 15, gross extracapsular extension in 6, and 5 patients with unknown extension.

Treatment outcomes

Outcomes consequent to treatment are displayed in Table 3 and related to T stage in Figure 2, with the number of patients at-risk presented in supplement Table 1. At a time point after initial treatment, 162 (88%) patients had no evidence of malignancy.

Local control

A local recurrence occurred in 47 (25%) patients, persistent disease in 17 (9%), and 1 unknown outcome, thus there was an initial local control figure of 119 (65%). The median time to local failure from a CR was 6.8 months. All local failures included the initial disease site, irrespective of their initial treatment. Local control was significantly better with early stage disease compared to T3 (T1 73%, T2 67%, T3 36%, T4 60% at 5 years, $p<0.001$), and with lower stage disease (74% stage I vs 60% stage IV at 5 years, $p=0.040$). It was significantly better with surgery (with or without radiotherapy) than radiotherapy alone (63% vs 74% vs 38% respectively at 5 years, $p<0.001$). Close margins had a significantly lower local control rate compared to negative margins (55% vs 82% respectively at 5 years, $p=0.005$). For those patients treated by radiotherapy, there was a trend for worse local control with the presence of a treatment interruption greater than one week (38% vs 56% respectively at 5 years, $p=0.384$).

Nodal recurrence occurred in 31 (17%) patients with 8 (4%) having persistent nodal disease, for initial nodal control in 144 (78%) patients. Median time to nodal failure was 7.5 months. Of the 31 patients, nodal recurrence occurred in the ipsilateral node in 19 (61%), contralateral node in 8 (26%), bilateral nodes in three (10%), with one unknown. For the 8 patients with persistent disease, it was ipsilateral in four and bilateral in four.

Distant metastatic disease became apparent in 10 (5%) patients, with a median time to development of 15.1 months. The lungs were the dominant site of metastatic disease (n=5).

Ultimate local control

For those patients with non-controlled disease, 49 received further local treatment (surgery in 24, radiotherapy only in 15, and post-operative radiotherapy in 10), and 7 with palliative chemotherapy. Ultimate local control (ULC) was achieved in 132 (72%) patients, thus 51 (28%) failed with one unknown outcome (Table 3). Ultimate nodal control (UNC) was achieved in 152 (83%) patients. Figure 2A and 2B graph ULC by T stage (T1 81%, T2 76%, T3 36%, T4 80% at 5 years, p<0.001) and overall stage (I 83%, II 78%, III 58%, IV 59% at 5 years, p=0.006), demonstrating the anticipated decline in control by increasing T and overall stage.

The impact of treatment modality is demonstrated in Figure 2C with 16 of 32 patients treated by radiotherapy as initial definitive treatment failing locally for a 46% 5-year ULC figure. This contrasts with surgery in any form, 84% as the only treatment, and 68% when combined with radiotherapy (p=0.001), at 5 years. More likely, combined treatment is for more advanced disease. Other factors that influenced ULC were margins, comparing negative to close margins (86% vs 68% respectively at 5 years, p=0.031) (Figure 2D). For those patients having radiotherapy, there was a trend for worse ULC with a treatment interruption greater than one week (38% vs 64% at 5 years, p=0.095).

For the whole cohort, UNC was uninfluenced by N0 or N1-3 stage (81% vs 83% respectively at 5 years, p=0.529). However, UNC was significantly higher for patients with T1-2 versus T3 where radiotherapy only was used (T1 70%, T2 79%, T3 33% at 5 years, p=0.035) (Figure 2E), with no difference for those patients having surgery of any nature (T1 87%, T2 84%, T3 81%, T4 100%, p=0.527) (Figure 2F). UNC was worse for patients treated with radiotherapy only with late stage disease (I 88%, II 75%, III 56%, IV 25% at 5 years, p=0.007), whereas there was no difference in UNC by stage for those patients having surgery as their main treatment (I 78%, II 85%, III 89%, IV 85% at 5 years, p=0.886).

Cancer-specific survival

With a median follow-up of 4.1 years, 66 patients died with or related to their FOM cancer, and 95 died of events unrelated to their FOM cancer (Table 3). CSS by T stage is depicted in Figure 2G with T4 better than T3 (55% vs 39% respectively at 5 years, p<0.001), more likely a reflection of small T4 numbers. The same declining survival pattern is evident for N stage (only two patients were N3) (N0 69%, N1 76%, N2 46%, N3 100% at 5 years, p=0.115), and overall stage (I 80%, II 72%, III 60%, IV 49% at 5 years, p=0.023). The influence of treatment modality on CSS is included in Figure 2H, with those patients having radiotherapy as definitive treatment doing worse (radiotherapy only 52%, surgery only 81%, post-operative radiotherapy 61% at 5 years, p=0.004). Interestingly, one of the two patients who had chemotherapy only as definitive treatment was a long-term survivor.

Overall survival

T stage (T1 50%, T2 54%, T3 32%, T4 40% at 5 years, p=0.099), overall stage (I 50%, II 55%, III 53%, IV 32% at 5 years, p=0.403), and treatment modality (radiotherapy 38%, surgery only 53%, post-operative radiotherapy 48% at 5 years, p=0.555) curves were less differentiated from each other when death by any means was evaluated.

Tertiary outcome

A new primary malignancy was evident in 53 patients with the median time to this being 4.4 years (Table 3). This is represented in time-to-development of a second malignancy with those patients presenting prior to

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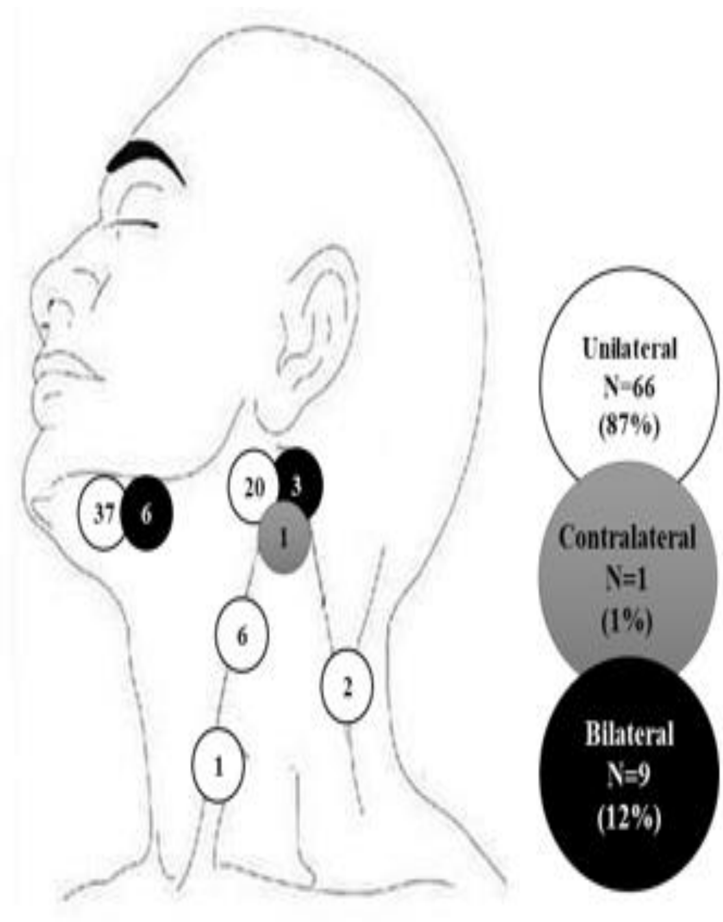
diagnosis being included (Figure S1). A new head and neck primary was diagnosed in 26 (49%) patients and a lung cancer in 15 (28%).

A simple conclusion from the data would be that patients having radiotherapy as the only treatment had worse patient and disease factors, the reason for the differences in the outcomes. Table 1 addresses this, defining that there are no significant differences between the two groups, demonstrating the superiority of including surgery in the management for patients with all stage disease.



Floor of Mouth Neck Node Distribution by Level I-V (60 patients)

Level I	Level II	Level III	Level IV	Level V	Total Nodes
43 (56%)	24 (32%)	6 (8%)	1 (1%)	2 (3%)	76

Figure 1: Neck node distribution by level.

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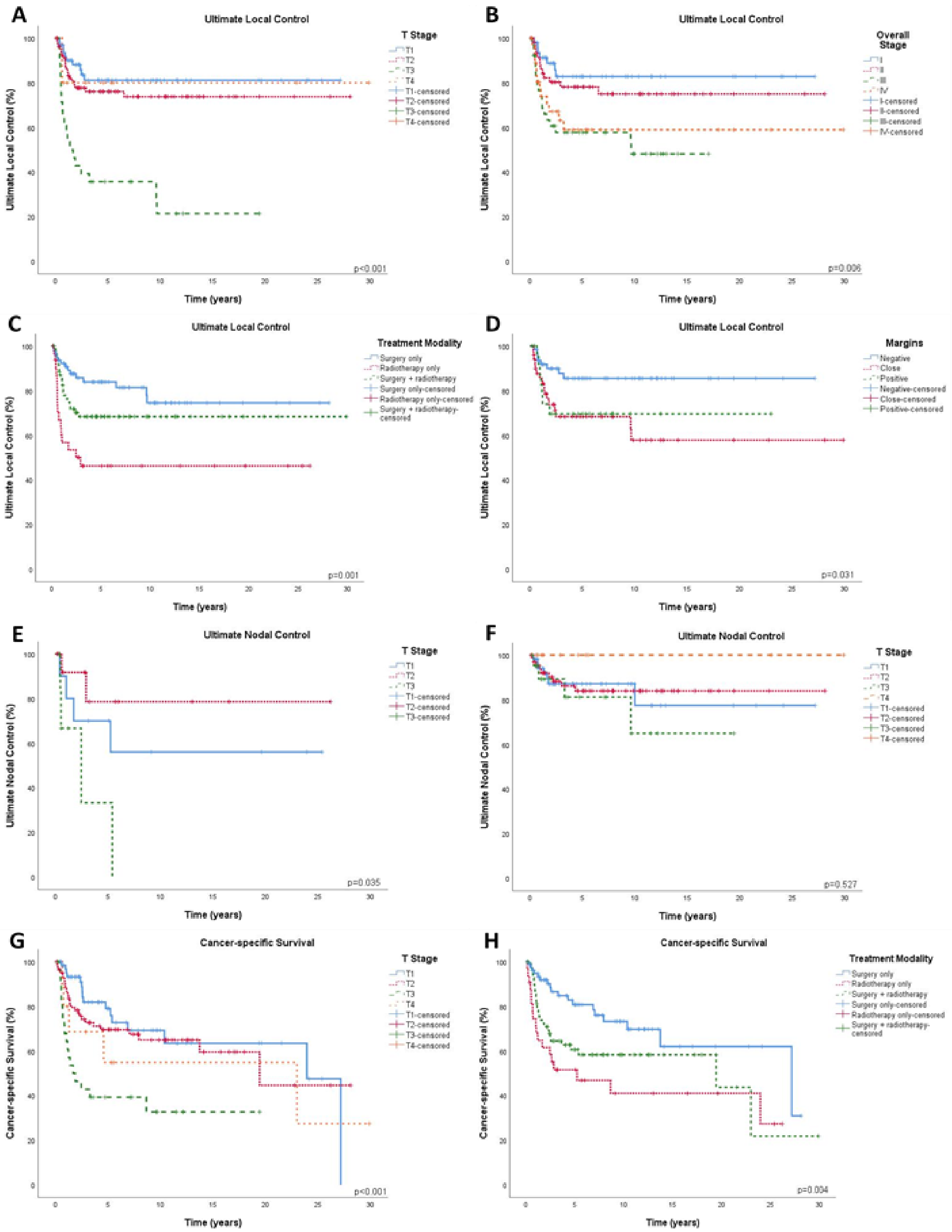

Figure 2: Ultimate local control by A) T stage, B) overall stage, C) treatment modality, and D) tumour margins, ultimate nodal control by T stage in patients treated with E) radiotherapy only, and F) surgery with or without radiotherapy, and cancer-specific survival by G) T stage, and H) treatment modality.

Table 1: Patient demographics and tumour features by treatment.

Factors	Whole cohort (n=184)	Radiotherapy only (n=32)	Surgery ± radiotherapy[a] (n=150)	P-value[b]
Age at presentation, years, mean (range)	61 (39-84)	61 (41-83)	61 (39-84)	0.857
Gender				
Male	141 (77%)	27 (84%)	113 (75%)	0.27
Female	43 (23%)	5 (16%)	37 (25%)	
Previous tumour				
Head and neck	34 (19%)	4 (13%)	30 (20%)	0.323
Lung	3 (2%)	0	3 (2%)	1.000[c]
Other	15 (8%)	3 (9%)	12 (8%)	0.730[c]
Comorbidities[d]				
Diabetes	9 (5%)	0	9 (6%)	0.360[c]
Hypertension	40 (22%)	1 (3%)	39 (26%)	**0.006**
Hypothyroidism	0	0	0	NC
Tobacco use				
Never smoked	6 (3%)	0	5 (3%)	0.105[c]
Ex-smoker, not for two years	30 (16%)	3 (9%)	27 (18%)	
Current or recent smoker	139 (76%)	25 (78%)	113 (76%)	
Unknown	9 (5%)	4 (13%)	5 (3%)	
Alcohol consumption				
Nil	17 (9%)	0	17 (11%)	0.218[c]
Social only	17 (9%)	3 (9%)	13 (9%)	
Daily drinker	133 (73%)	26 (82%)	106 (71%)	
Unknown	17 (9%)	3 (9%)	14 (9%)	
Performance (ECOG) status				
0-Normal	77 (42%)	11 (34%)	65 (44%)	0.379[c]
1-Symptoms/self-care	76 (41%)	16 (50%)	59 (39%)	
2-Ambulatory <50%	3 (2%)	1 (3%)	2 (1%)	
3-Ambulatory >50%	3 (2%)	1 (3%)	2 (1%)	
4-Bedridden	0	0	0	
Unknown	25 (13%)	3 (10%)	22 (15%)	
Cancer operable	182 (99%)	30 (94%)	150 (100%)	**0.030**[c]
Fit for operation	180 (98%)	28 (88%)	150 (100%)	**0.001**[c]
Tumour grade				
Well differentiated	33 (18%)	8 (25%)	24 (16%)	**<0.001**
Moderately well differentiated	93 (50%)	6 (19%)	87 (58%)	
Poorly differentiated	29 (16%)	5 (16%)	24 (16%)	
Unknown	29 (16%)	13 (40%)	15 (10%)	
T stage (7th edition)				
T1	63 (34%)	10 (31%)	53 (35%)	0.362
T2	82 (45%)	15 (47%)	65 (43%)	
T3	29 (16%)	7 (22%)	22 (15%)	
T4	10 (5%)	0	10 (7%)	
N stage (7th edition)				
N0	124 (68%)	25 (78%)	97 (65%)	0.102[c]
N1	30 (16%)	1 (3%)	29 (19%)	
N2	28 (15%)	6 (19%)	22 (15%)	
N3	2 (1%)	0	2 (1%)	
Size largest node, mm, median (IQR)	25 (15-40)	33 (23-53)	20 (15-38)	0.13

Overall stage (7th edition)				
I	48 (26%)	8 (25%)	40 (27%)	0.979
II	59 (32%)	11 (34%)	46 (30%)	
III	40 (22%)	7 (22%)	33 (22%)	
IV	37 (20%)	6 (19%)	31 (21%)	

ECOG: Eastern Cooperative Oncology Group; IQR: Interquartile Range; mm: Millimetres; NC: Not Calculable

P-value compares differences between treatment groups (patients treated with chemotherapy only (n=2) are excluded)

[a]Patients treated with radiotherapy plus adjuvant surgery (n=4) are included

[b]Pearson Chi-square, bold values indicate statistical significance, 2-sided p<0.05

[c]Fisher's Exact Test, bold values indicate statistical significance, 2-sided p<0.05, replaces Pearson Chi-square when ≥ 20% of cells have an expected count less than five

[d]Not mutually exclusive, patients may have multiple comorbidities

Table 2: Treatment details.

Factors	**N (%)**
Treatment modality	
Surgery	80 (44%)
Radiotherapy	32 (17%)
Surgery plus adjuvant radiotherapy[a]	70 (38%)
Chemotherapy	2 (1%)
Radiotherapy treatment (± surgery)	**102**
Conventional	93 (91%)
Brachytherapy	6 (6%)
Conventional and brachytherapy	3 (3%)
Conventional radiotherapy details (radiotherapy only)	**27**
Dose, gray, median (IQR)	60 (50-60)
Fractions, median (IQR)	25 (24-28)
Treatment length, days, median (IQR)	42 (36-50)
Treatment interruptions >1 week	3 (11%)
Conventional radiotherapy details (surgery plus adjuvant radiotherapy)[a]	**69**
Dose, gray, median (IQR)	56 (55-62)
Fractions, median (IQR)	28 (28-31)
Treatment length, days, median (IQR)	40 (38-44)
Treatment interruptions >1 week	5 (7%)
Brachytherapy details	**9**
Dose, gray, median (IQR)	60 (60-71)
Depth, mm, median (IQR)	5 (5-5)
Treatment length, days, median (IQR)	5 (5-38)
Surgical treatment (± radiotherapy)	**150**
Surgery to primary site	150 (100%)
Neck dissection only	0
Neck dissection	**150**
None	48 (32%)
Limited	21 (14%)
Unilateral	31 (21%)
Bilateral	50 (33%)
Neck dissection pathology	**102**
No tumour found	41 (40%)
Intracapsular	29 (28%)

Focal (extracapsular extension)	15 (15%)
Gross (extracapsular extension)	6 (6%)
Tumour present, unknown extent	5 (5%)
Unknown	6 (6%)
Depth of invasion, mm, median (IQR)	**5 (3-8)**
Reconstruction to primary	**150**
Nil	3 (2%)
Primary closure	35 (24%)
Radial forearm flap	37 (25%)
Jejunal flap	12 (8%)
Skin graft	9 (6%)
Deltoid pectoralis flap	5 (3%)
Tongue flap	12 (8%)
Pectoralis major flap	1 (1%)
Buccal flap	4 (3%)
Nasolabial flap	4 (3%)
Lateral arm flap	2 (1%)
Lateral thigh flap	0
Submandibular skin flap	0
Other	2 (<1%)
Unknown	24 (16%)

IQR: Interquartile Range, mm: Millimetres

[a]Surgery plus adjuvant radiotherapy group includes 4 patients treated with radiotherapy plus adjuvant surgery

Table 3: Treatment outcomes and follow up.

Factors	**N (%)**
Treatment response	
Complete response	162 (88%)
Partial response	4 (2%)
Stable disease	5 (3%)
Progressive disease	12 (6%)
Unknown	1 (1%)
Local recurrence	
No	119 (65%)
Yes	47 (25%)
Persistent disease	17 (9%)
Unknown[a]	1 (1%)
Time to local failure[b], months, median (IQR)	6.8 (1.8-14.5)
Nodal recurrence	
No	144 (78%)
Yes	31 (17%)
Persistent disease	8 (4%)
Unknown[a]	1 (1%)
Time to nodal failure[b], months, median (IQR)	7.5 (2.6-30.6)
New primary	
No	131 (71%)
Yes	53 (29%)
Time to new primary, years, median (IQR)	4.4 (0.7-8.9)
Site of new primary[c]	**53**
Head and neck	26 (49%)
Lung	15 (28%)
Other	17 (32%)
Time to new head and neck primary, years, median (IQR)	4.5 (0.5-9.5)
Time to new lung primary, years, median (IQR)	3.0 (0.6-7.7)

Time to new other primary, years, median (IQR)	3.6 (1.3-10.4)
Ultimate local failure	
Ultimate local control	132 (72%)
Ultimate local fail	51 (28%)
Unknown[a]	1 (<1%)
Time to ultimate local failure[d], months, median (IQR)	11.0 (6.3-19.9)
Ultimate nodal failure	
Ultimate nodal control	152 (83%)
Ultimate nodal fail	31 (17%)
Unknown[a]	1 (<1%)
Time to ultimate nodal failure[d], months, median (IQR)	15.9 (6.5-34.8)
Follow up status	
Alive	20 (11%)
Dead, not with head and neck cancer	95 (52%)
Dead, with head and neck cancer	66 (36%)
Dead, cause unknown	3 (1%)
Follow up interval, years, median (IQR)	4.1 (1.3-9.6)
Survival interval, years, median (IQR) [e]	4.8 (3.4-10.2)

IQR: Interquartile Range

[a]The unknown is for an overseas patient

[b]Local and nodal failure include patients with recurrence and persistent disease at first local and nodal sites respectively

[c]Not mutually exclusive, patients can have multiple new primaries

[d]Ultimate local failure and ultimate nodal failure include patients with recurrence and persistent disease at second local and nodal sites respectively, and those patients who did not receive treatment for first local and/or nodal recurrence respectively

[e]Survival interval for 20 alive patients

Supplement Table 1: Number of patients at-risk of death.

		Number of patients					
Figure	**Variable**	**0 years**	**5 years**	**10 years**	**15 years**	**20 years**	**25 years**
2A	T1 stage	63	25	12	7	5	2
	T2 stage	82	41	24	9	3	2
	T3 stage	29	7	3	1	0	0
	T4 stage	10	4	2	2	2	1
2B	Stage I	48	20	12	7	5	2
	Stage II	59	30	17	7	3	2
	Stage III	40	16	8	1	0	0
	Stage IV	37	11	4	4	2	1
2C	Surgery only	80	38	21	7	4	2
	Radiotherapy only	32	10	6	5	3	2
	Surgery + radiotherapy	70	28	13	7	3	1
2D	Negative margins	62	30	19	7	3	1
	Close margins	40	16	8	3	2	2
	Positive margins	25	11	2	1	1	0
2E	T1 stage	10	6	3	3	2	1
	T2 stage	15	5	3	2	1	1
	T3 stage	7	1	0	0	0	0
2F	T1 stage	53	19	8	4	3	1
	T2 stage	65	36	20	7	2	1
	T3 stage	22	7	3	1	0	0

	T4 stage	10	4	2	2	2	1
2G	T1 stage	63	26	12	7	5	2
	T2 stage	82	42	24	9	3	2
	T3 stage	29	8	3	1	0	0
	T4 stage	10	4	2	2	2	1
2H	Surgery only	80	39	21	7	4	2
	Radiotherapy only	32	12	6	5	3	2
	Surgery + radiotherapy	70	28	13	7	3	1

DISCUSSION

The typical patient who presents with a FOM SqCC is an older male with a cigarette smoking background.[6] Although anatomically close to the oral tongue, there are some differences clinically within the literature, such as a greater likelihood of mandibular involvement (necessitating consideration of resection and appropriate bone reconstruction), as well as level I being part of the nodal resection.[11] More typically, these two anatomical sites are presented together, blurring any significance to these clinical differences.[12,13]

Local control is an important feature to achieve with its attendant impact on OS and CSS.[13] Attempting to preserve anatomical structures related to quality of life (QOL) may adversely impact upon local control.[14] This center's earlier report detailed a significantly better outcome for patients where surgery is a component of the initial treatment.[10] This updated review with more patients and longer follow-up reports comparable outcomes. Where surgery was the only treatment, the ULC rate was 84% at 5 years, and 68% combined with radiotherapy. There are many factors influencing the outcomes at this center (margins, T stage and overall stage), comparable to that reported in the literature. For those patients having radiotherapy only, 50% of patients failed locally, an outcome influenced by many factors specifically the presence of a treatment interruption.[15] A more aggressive treatment approach using intra-arterial chemotherapy and radiotherapy in a small patient population recorded a more favorable outcome with better QOL.[16]

The presence of nodal disease has a significant impact upon outcomes.[11] This may be apparent at presentation, or defined by investigative procedures, such as a sentinel node biopsy.[17] The specific location (i.e. relationship to the midline) can influence the likelihood of contralateral nodal development,[18] and the depth of infiltration.[19] Balasubramanian reported that whilst neck dissection is appropriate for oral tongue cancers greater than 4 mm thickness, for FOM, the defining depth is 2 mm.[20] Elective neck dissection for the node negative neck has its advocates with a randomized study demonstrating a statistically significant survival advantage for those patients having a dissection, versus those patients observed.[21]Wang noted that a discontinuous neck dissection (in relation to the local resection) had a higher locoregional failure rate than those patients having an in-continuity neck dissection.[22] In this series, when the whole cohort was considered, the presence and extent of nodal disease did not influence UNC. Stage III-IV disease had worse nodal control where radiotherapy was used as the main control, whereas this had no impact where surgery was the initial treatment.

Early stage disease at presentation was more evident for FOM (compared to patients presenting with oral tongue carcinoma at this center [unpublished data]), and carried a more favorable outlook for ULC, UNC, and CSS, being more profound for surgery rather than radiotherapy. However, there are differences in the population that may be a determinant of outcome rather than the treatment itself. Patient comorbidities and treatment toxicities that could lead to treatment interruptions are notable examples.[23,24] Even small tumors within the FOM may have bone invasion, and thus extension into the medullary cavity.[7]

These patients have poor OS, a reflection of the overwhelming majority of patients being cigarette and alcohol consumers. In this series, this manifests with a proportion of patients presenting with a prior malignancy, and developing a subsequent malignancy, the proportion that progressively increases over time. The proportion of patients unfit for surgery was low in this review compared to other sites.[24] Treatment interruptions for patients having radiotherapy created an adverse outcome that may reflect upon the toxicity of treatment, including the patient's nutritional status.[13,15,25]

A limiting feature to interpretation of the results in this study is the timeframe over which the patient population was accrued. However, all patients were clinically staged, and there was a consistency of conclusions following discussion at the MDT meetings. The only missing link in the recording of the MDT discussion was the reason for choosing radiotherapy over surgery. A time variation in the literature support for surgery versus radiotherapy could be an explanation.

A stated purpose of this audit was to determine if, with more patients seen and treated, and more follow-up on those previously treated; this would modify the prior conclusion. There need be no change as surgery is still superior to a radiotherapy only approach in the circumstance where there is no difference in patient and disease factors between the two groups. OS remains poor with new primaries being a big contributing factor, this almost negating whatever benefit surgery provides. Impacting upon this is likely to have greater benefit for the patient than any variations in the way surgery and/or radiotherapy is delivered.

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