MRI and frozen section evaluation of mylohyoid muscle in determining surgical approach for T2–T3 floor of the mouth cancer

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Abstract

Purpose The choice of surgical approach for floor of the mouth (FOM) cancer, particularly for intermediate-stage tumors (cT2–cT3), remains controversial. This study aims to evaluate a method considering mylohyoid muscle (MM) invasion as a determinant for surgical approach selection, utilizing magnetic resonance imaging (MRI) preoperatively and frozen section (FS) analysis intraoperatively.

Methods This observational retrospective cohort study analyzed patients undergoing surgical resection of cT2 and cT3 FOM squamous cell carcinoma (SCC) between January 2013 and June 2023. MM infiltration assessed by preoperative MRI determined the surgical approach: clear infiltration led to compartmental surgery (CS), while doubtful or absent infiltration led to transoral surgery (TOS). Conversion from TOS to CS occurred intraoperatively based on macroscopic evidence or positive FS. Data collected included demographic, clinical, surgical, and pathological variables. Survival analysis was conducted using Kaplan–Meier method.

Results Among 44 patients included, majority had cT2 tumors (59.1%). MM resection was necessary in 22.7% of cases. Overall survival (OS) and progression-free survival (PFS) did not significantly differ between TOS and CS groups. Radiological depth of invasion (rDOI) < 10 mm is correlated with MM preservation in 89% of cases, while rDOI > 10 mm is correlated with MM resection only in 23.8% of cases. Pathological depth of invasion (pDOI) discrepancies were observed in the two groups: in CS group is shown a higher pDOI (> 10 mm) confirmation (90%). Surgical complications and functional outcomes differed between TOS and CS groups.

Conclusion Considering MM invasion for surgical approach selection in cT2–cT3 FOM tumors appears oncologically safe, with better functional outcomes in muscle preservation. Preoperative MRI for MM assessment combined with intraoperative FS analysis provides reliable guidance for surgical decision-making.

Keywords Oral cancer · Floor of the mouth · Floor of the mouth cancer · Transoral surgery · Oral cavity

Introduction

With a worldwide estimated age-standardized incidence of 4.1 per 100,000 and an estimated number of 377,731 and 177,757 new cases and deaths in 2020, respectively, oral cavity and lip cancers are the most common malignancies developing from the upper aero-digestive tract and squamous cell carcinoma (SCC) represents the 80% of all these tumors [1–3]. Among oral cavity subsites, the floor of the mouth (FOM) is the second most commonly affected site following the oral tongue [4, 5]. It is globally accepted that a radical surgery is the keystone of oral SCC management with the goal being to achieve cancer resection with clear margins [6]. Surgical approach, together with neck

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stage and depth of invasion (DOI), significantly influenced survival in surgically treated patients with oral cancer [7]. However, the ideal surgical approach to SCC of the FOM is still a matter of controversy. While it is widely accepted that T1 tumors can be approached by a transoral surgery (TOS) and that advanced tumors are generally treated with compartmental surgery (CS), the debate on surgical strategies for intermediate categories (T2–T3) is still open. CS was proposed with the intent to remove the tumor en-bloc, together with the tumor-neck tract (so called T-N tract) [8] and the draining lymph nodes regardless of the T stage, sustaining that this approach represents the safest one even in intermediate stages (T2–T3) [9–11]. Nevertheless, this approach is considered as an invasive technique that required a reconstruction with free flap. Alongside this technique, other authors have observed that survival and locoregional control in oral SCC were equally good after a more conservative TOS combined with a discontinuous neck dissection, compared to an en-bloc resection [2]. The authors who sustain the CS often adopted the 10 mm DOI evaluated by preoperative MRI (called radiologic DOI, rDOI) as the ideal cut-off to shift from a transoral approach to a CS, irrespective of the superficial extension of the lesion, therefore irrespective of the clinical stadiation/stage [10–13]. DOI is often difficult to be precisely calculated by preoperative imaging and, by now, there is not a standardized method for its measurement in a preoperative setting [12]. To date, there are no guidelines that consider DOI as an indicator for choosing the type of surgical approach.

Due to the lack of guidelines or clear indications, the surgical approach of intermediate-stage tumors (T2/T3) of the FOM mostly depends on the surgeon decision and skills, making the choice not univocal and laying the foundations for different functional results between centers [2, 10]. In our center, we utilize the assessment of the mylohyoid muscle (MM), both radiologically and through frozen section (FS), to guide the type of resection and potentially convert it during surgery from TOS to CS. The primary aim of this study is to report the outcomes of this surgical approach, both in terms of oncologic survival and functional results. Second, we aim to compare the assessment of the MM with the DOI as criteria for selecting the surgical approach.

Materials and methods

This observational retrospective cohort study adhered to the principles outlined in the Declaration of Helsinki (1964). All patients provided consent for the anonymous use of anamnestic and clinical data. The study received approval from the local ethical committee (IRB nr.121/2022).

Inclusion criteria

Patients undergoing surgical resection of cT2 and cT3 SCC the FOM at the Clinic of Otolaryngology-Head and Neck Surgery of Trieste University Hospital between January 2013 and June 2023 were included. All FOM cancer patients who underwent preoperative MRI evaluation were considered. Patients with clear infiltration of the MM were excluded as candidates for CS; patients with MRI demonstrating doubtful or absent infiltration of the MM were included in the study. Patients with a history of head and neck surgery or radiotherapy were excluded.

Resection criteria and surgical protocol

Patients underwent a 1.5 Tesla MRI, where the radiologist provided DOI and evaluated MM infiltration. Surgery type was determined based on MM infiltration indicated by MRI: clear infiltration led to CS, while the patients with MRI demonstrating doubtful or absent infiltration of the MM led to TOS. The conversion from TOS to CS occurred in cases where there was macroscopic evidence of infiltration of the MM during surgery or if the FS on the muscle were positive. Surgery used narrow-band imaging (NBI) for defining superficial resection margins. Tumors were resected with a 10 mm margin from the suspicious vascular pattern in NBI [14–16]. Deep margin assessment used a margin mapping system through strips-and-bowl FS [17–19]. Intraoperative evaluation determined whether to proceed with resection or maintenance of the MM; specifically when the geniohyoid muscle is included in the tumoral resection area, biopsies for FS are performed there. If they result positive, the geniohyoid muscle is resected, and we perform biopsies on the MM. If FS on the MM result positive, we resect this muscle too, performing in this way a CS. On the other hand, if the MM results free, we do not resect it, maintaining in this way a transoral approach (Fig. 1). The reconstruction of the surgical defect occurred with a local flap or a free flap depending on the defect that has to be filled. Finally, concordances between rDOI and pathological DOI (pDOI), and between MM infiltration and pDOI were observed.

Outcomes

Clinical, surgical, and pathological data were collected from electronic health records. Subgroups were identified based on surgical approach: (1) transoral surgery group (TOS group); (2) compartmental surgery group (CS group). Variables, including age, preoperative MRI information, surgical approach, reconstruction type, pathological stage, and postoperative complications, were compared. Complications

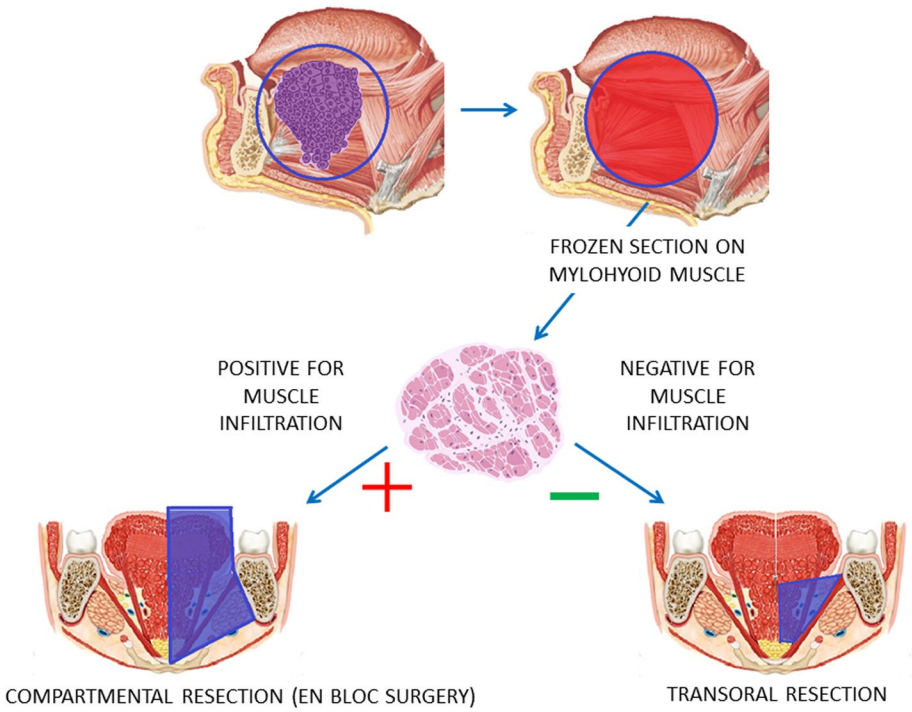

Fig. 1 Role of frozen section on mylohyoid to guide the type of resection

included salivary oro-cervical fistula, hematoma or seroma formation, abscess or dehiscence of the surgical wound, and flap necrosis. Follow-up data included nasogastric tube and tracheostoma permanence, surgery duration, and hospitalization time. Overall survival (OS), and progression-free survival (PFS) were estimated for survival analysis.

Statistical analysis

Qualitative variables were reported as proportions and differences across strata were evaluated though Fisher's exact test. Quantitative data were reported as median value with interquartile range (Q1–Q3), and differences across strata were evaluated though Mann–Whitney test.

For each patient, the time at risk was calculated from the surgery to the occurrence of the event of interest, death, or end of follow-up, whichever occurred first. The event of interest was the death for OS, and recurrence or death for PFS. Survival probabilities were estimated according to the Kaplan–Meier method and differences between curves were evaluate through log-rank test.

Results

Population and surgical outcomes

The final sample included 44 patients, 13 female and 31 males, with a median age of 65 years (range 43–95); Table 1 summarizes the socio-demographic and clinical characteristics of the sample. In the majority of the cases, the stage of the tumor was cT2 (59.1%), while 18 cases were cT3 (40.9%). In 10 (22.7%) cases, the MM had been resected during the surgical intervention, since FS showed malignant involvement, while in 34 (77.3%) cases, this structure was preserved.

In 16 patients, a free flap was used, in 13 a local flap, in one patient was used a Thiersch graft, and in 14 was need no reconstruction to feel the surgical defect. Table 2 delineates the specific flap types employed within patient subgroups based on surgical approach and T stages.

Mylohyoid resection and survivals

Kaplan–Meier curves reported the OS and PFS estimated with Kaplan–Meier method, showing that the difference among the two groups were not statistically significant ($p = 0.65$, $p = 0.58$) (Figs. 2, 3).

Mylohyoid resection and MRI findings

In 8 (89%) patients with an rDOI < 10 mm, the MM has been resected, while in 16 (76%) patients with an rDOI > 10 mm, the MM has been preserved (Table 3).

Mylohyoid resection and DOI

From our data, there is no discrepancy between the two groups concerning the rDOI ($p = 0.81$), whereas a notable distinction is observed in the pDOI ($p < 0.01$) (Table 1).

Table 1 Socio-demographic and clinical characteristics of the sample

Characteristics	*n* (%)	Mylohyoid resection		
		No	Yes	Fisher's exact test
		n (%)	*n* (%)	
Gender				
Female	13 (29.6)	11 (32.4)	2 (20.0)	$p=0.70$
Male	31 (70.5)	23 (67.7)	8 (80.0)	
Age (years)				
< 65	23 (52.3)	17 (50.0)	6 (60.0)	$p=0.72$
≥ 65	21 (47.7)	17 (50.0)	4 (40.0)	
Laterality				
Anterior	10 (22.7)	10 (29.4)	0 (0.0)	$p=0.04$
Left	14 (31.8)	8 (23.5)	6 (60.0)	
Right	20 (45.5)	16 (47.1)	4 (40.0)	
cT				
cT2	26 (59.1)	23 (67.7)	3 (30.0)	$p=0.06$
cT3	18 (40.9)	11 (32.4)	7 (70.0)	
pN				
N0	26 (59.1)	21 (61.8)	5 (50.0)	$p=0.12$
N1	5 (11.4)	5 (14.7)	0 (0.0)	
N2	7 (15.9)	4 (11.8)	3 (30.0)	
N3	3 (6.8)	1 (2.9)	2 (20.0)	
Nx	3 (6.8)	3 (8.8)	0 (0.0)	
Pathological DOI (mm)				
< 10	29 (65.9)	28 (82.4)	1 (10.0)	$p<0.01$
≥ 10	15 (33.1)	6 (17.7)	9 (90.0)	
Radiological DOI (mm)				
< 10	9 (20.5)	8 (23.5)	1 (10.0)	$p=0.81$
≥ 10	21 (47.7)	16 (47.1)	5 (50.0)	
Missing	14 (31.8)	10 (29.4)	4 (40.0)	

DOI Depth of Invasion

Specifically, we observe that in only 1 case (10%), despite resecting the MM, the pathological examination revealed a pDOI < 10 mm. Instead, in 90% of cases where the MM was resected, the pathological examination confirmed a pDOI > 10 mm**.** We can see also that in all patients where the pDOI was > 10 mm, the rDOI agreed (Table 4)**.**

Functional and recovery outcomes

Nasogastric tube days, tracheostomy days, surgery duration, and hospitalization are significantly longer in cases in which the MM has been resected (Table 5). Particularly, the median hospitalization days increase from 17 in the patient group with preserved MM to 21 in those where the MM was resected. Additionally, there was a significant increase in surgery duration between the two groups, with the duration extending from 303 to 548 min in the group where the MM was resected. There were 2 complications flap-related (one case of flap dehiscence and a flap necrosis), one hemorrhage and two cases of sieroma formation. In four patients, the MM was left unresected, while in only one patient, the MM was resected. However, there is no significant difference between the two groups concerning surgical complications.

Discussion

The choice of surgical approach for FOM cancer remains a topic of intense debate in the literature, particularly regarding intermediate-stage tumors (cT2–cT3). In this study, we present the results of a method that considers MM invasion as the determining factor in the choice of approach, specifically evaluating its invasion using MRI imaging in the preoperative setting and FS analysis in the intraoperative setting.

The MM represents the most critical anatomical boundary between the oral cavity and the neck, and its preservation

Table 2 Type of reconstruction according to mylohyoid muscle status

Mylohyoid muscle status (*n*; %)	Reconstruction technique (*n*)	
Preserved (34; 77%)	Free flap (6)	ALT flap (5) UFFF (1)
	Local flap (14)	Nasogenial flap (2) FAMM (9) Skin graft (1) Submental (2)
	No flap (14)	14 (suture/collagen membrane)
Resected (10; 23%)	Free flaps (10)	ALT Flap (5) RFFF (3) ALT flap + RFFF (1) Fibula flap (1)

ALT Anterolateral Thight*; UFF* Ulnar Forearm Flap*; FAMM* Facial Artery Muscolo-Mucosal*; RFFF* Radial Forearm Free Flap

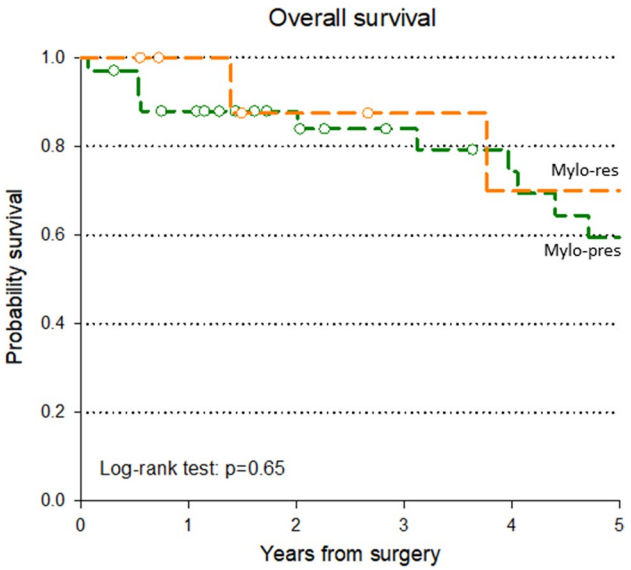

Fig. 2 Overall survival according to surgery. *Mylo-res* Resected Mylohyoid, *Mylo-pres* Preserved Mylohyoid

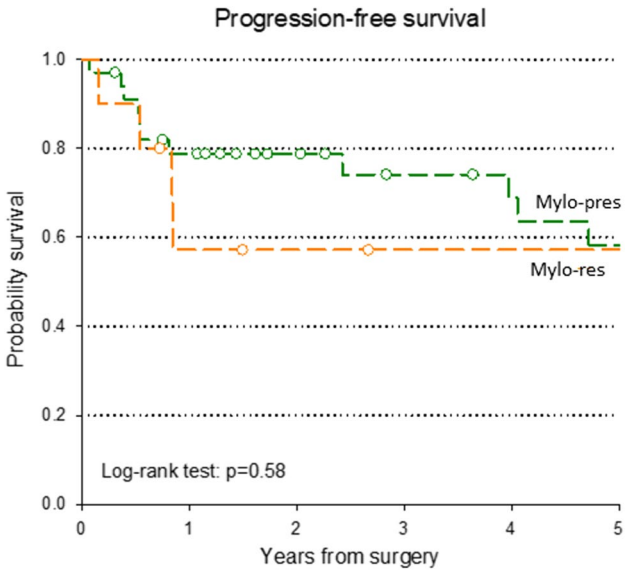

Fig. 3 Progression-free survival according to surgery. *Mylo-res* Resected Mylohyoid, *Mylo-pres* Preserved Mylohyoid

Table 4 Radiological depth of invasion (DOI) and mylohyoid resection according to pathological DOI

	Pathological DOI (mm)	
	< 10	≥ 10
	n (%)	*n* (%)
Radiological DOI (mm)		
< 10	9 (45)	0 (0)
≥ 10	11 (55)	10 (100)
Missing	9	5
Mylohyoid resection		
No	28 (96.6)	6 (40)
Yes	1 (3.4)	9 (60)

DOI Depth of invasion

enables TOS, associated with discontinuous ND, thus avoiding a compartmental approach. TOS is known to yield better functional outcomes and a higher quality of life. Therefore, provided equivalent oncological outcomes to more invasive surgeries can be achieved, transoral surgery should always be pursued when possible [2, 20]. The indications for CS are not unambiguous, and different criteria are reported in the literature depending on the authors. Some authors advocate the degree of T and N, others the infiltration of the extrinsic muscles of the tongue, and still others the value of preoperative DOI [9, 11, 13, 21]. Due to its soft-tissue resolution, MRI is widely applied in the assessment of clinical DOI; however, it is a parameter that has been found to be generally larger than histopathological DOI due to peritumor edema or inflammation, leading to overestimated clinical T staging [22–26]. According to these findings, in our case series, we also observed a high percentage of disagreement between rDOI and definitive histologic measurements, thus suggesting an alternative cut-off point to guide surgeons in the decision process for treating T2–T3 FOM cancer.

In our study, we preoperatively investigated MM invasion using MRI, the preferred examination for studying this structure [27]. In all cases where the muscle was clearly infiltrated, the patient underwent CS; conversely, in all cases where the MRI indicated no clear MM infiltration, FS was performed intraoperatively. If necessary,

Table 3 Functional and recovery outcomes according to type of treatment

	All	Mylohyoid resection		
		No	Yes	
	Median (Q_1–Q_3)	Median (Q_1–Q_3)	Median (Q_1–Q_3)	KW test
Nasogastric tube (days)	11 (7–16)	10 (7–14)	13 (13–17)	$p = 0.03$
Tracheostomy (days)	11 (4–15)	10 (0–14)	15 (13–20)	$p = 0.01$
Surgery duration (min)	355 (215–485)	303 (193–404)	548 (480–570)	$p < 0.01$
Hospitalization (days)	20 (14–22)	17 (12–22)	21 (20–29)	$p = 0.01$

Table 5 Functional and recovery outcomes according to type of treatment

	All	Mylohyoid resection		
		No	Yes	
	Median (Q_1–Q_3)	Median (Q_1–Q_3)	Median (Q_1–Q_3)	KW test
Nasogastric tube (days)	11 (7–16)	10 (7–14)	13 (13–17)	$p=0.03$
Tracheostomy (days)	11 (4–15)	10 (0–14)	15 (13–20)	$p=0.01$
Surgery duration (min)	355 (215–485)	303 (193–404)	548 (480–570)	$p<0.01$
Hospitalization (days)	20 (14–22)	17 (12–22)	21 (20–29)	$p=0.01$

KW Kruskal–Wallis test

resection was expanded, and surgery was eventually converted from TOS to CS. The method followed was bed-driven frozen section analysis, which, in our experience, provides more reliable results in this subregion [28]. The specimen-driven method has often been associated with failures in detecting the true margin to be expanded, as well as no improvement in survival rates and recurrence [29]. Unlike the observed high degree of disagreement between rDOI and pDOI, indication for CS based on MM infiltration has shown high sensitivity and specificity. In fact, in 9 out of 15 cases where pDOI exceeded 10 mm, a CS was performed, and in 6 case (40%) was a TOS performed in a patient with a final pDOI exceeding 10 mm. Conversely, when pDOI was lower in 28 out of 29 cases, the mylohyoid was preserved, and in only 1 case, it was removed. These findings highlight how considering the mylohyoid rather than rDOI as a factor influencing the choice of approach leads to a lower rate of overtreatment. The primary outcome of the study was to verify that there were no differences in survival rates between patients undergoing resection involving the MM (CS) and patients undergoing muscle preservation (TOS), ensuring that transoral resection for these stages of the disease did not negatively impact overall survival and disease-free survival at 5 years. From our results, there was no difference in overall survival and disease-free survival. These data are consistent with what has already been reported by our group in a larger general case series and with findings reported by other authors [2, 20, 30]. It is worth noting that there were no significant differences between the two groups we compared in terms of stage and lymph-node involvement. Functional outcomes showed that in CS, nasogastric tube permanence, surgery duration, and hospitalization were all significantly longer than in the subgroup treated with a more conservative approach. Tracheostomy permanence, however, was similar between the two groups, indicating that, regardless of the type of reconstruction, oral surgery that violated the FOM required approximately 11–19 days to restore a physiologic airway. No relevant post-operative complications occurred in both groups. Looking at the survival analysis, there were no significant differences among subgroups divided by surgical approaches and reconstructions. In this scenario, the indication regarding the best surgical approach to choose in the treatment of T2–T3 FOM cancers is still a tricky phase, because, although survival is equal, functional outcomes and post-operative quality of life are known to vary greatly depending on the surgical approach. In our experience, MM involvement by the primary tumor might be suggested by imaging, but this indication requires proof by intraoperative frozen section. MM involvement could represent a possible anatomical/oncologic limit to minimally invasive TOS, suggesting proceeding with a more demolitive surgery. This indication goes beyond the classic procedure of establishing the appropriate surgical procedure based on the staging of the tumor, aiming to offer a tailored strategy to the patients.

Conclusions

From our data, it emerges that considering MM invasion as the determining factor in the choice of surgical approach for cT2–cT3 FOM tumors is oncologically safe, and the preservation of the muscle is more favorable in terms of functional outcomes. Studying the MM in the preoperative setting with MRI appears to be a more reliable method than obtaining radiological DOI. This, combined with precise execution of bed-driven frozen section analysis on the muscle, could represent a reliable method in guiding surgical decision-making.

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Declarations

Conflict of interest No sponsorships or competing interests have been disclosed for this article.

Ethical approval This study adhered to the principles outlined in the Declaration of Helsinki (1964) and has been approved by the local university ethical committee.

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