Research Article

Comparative accuracy of intraoperative ultrasound vs. clinical tumor palpation in the determination of the depth of invasion in patients with T1-T3 squamous cell carcinoma of the tongue

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Abstract...

Background: Determining the exact size of the tongue tumor and its resection with an adequate margin is an essential determinant of patient survival. We conducted a randomized comparative study of the accuracy of intraoperative ultrasound vs. clinical examination in T1-T3 tongue tumor depth of invasion compared to tumor margins determined by the histopathologic study as a reference standard.

Methods: 64 patients with oral tongue cancer were randomly assigned to either ultrasound-guided resection or conventional tumor resection. Adequacy of tumor margins was compared based on histopathology results. We also prospectively followed the groups for tumor recurrence at one year.

Results: The positive predictive value for inadequate ultrasound resection of tongue tumor margin was 93% compared to 68% for clinical examination alone.

Conclusion: Intraoperative ultrasound accurately estimated adequate tumor margins among patients with stage T1-T3 tongue cancer.

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Introduction

Squamous cell carcinoma is the most prevalent non-skin malignancy of the head and neck, accounting for 90 percent of the oral cavity and oropharyngeal malignancies [1] with an increased incidence, especially among women [2]. Treatment is planned according to disease staging and is based on surgical resection with a margin of 1 to 2 centimeters. Neck dissection might also be recommended in cases with lymph node involvement or a high risk of latent metastasis [3]. Lymph node metastasis is an essential prognostic factor in these patients. The thickness and depth of the tumor are two important factors not only in terms of prognosis but also as a predictor for lymph node metastasis [4-8]. Several studies have reported a significant association between surgical margins of 5 or more millimeters and the patient's survival and a reduction in local recurrence [9,10].

The conventional method for surgical tumor resection is to remove the tissue based on clinical examination, CT-scan, or MRI, none of which guarantee removal of the tumor margin when it comes to deep lesions [4,11]. Given the substantial role of sufficient margin removal in improved patient outcomes, intraoral ultrasound has shown promise as a rapid, easily repeatable, relatively cheap tool to demarcate tongue tumors with acceptable accuracy [7,12,13]. Several studies show a strong positive correlation between ultrasonography results and histopathology in estimating tumor depth [14-18]. However, it is not clear whether ultrasound-guided tumor resection improves detection of tumor removal margins and reduces the rate of tumor recurrence compared to conventional tumor resection, which relies on direct palpation of the tumor.

In this clinical trial, we aimed to compare the diagnostic accuracy of intraoperative ultrasound vs. conventional surgery in estimating tumor depth and determining adequate resection margins in stage T1-T3 tongue SCC.

Methods

Study design

Sixty-four patients diagnosed with T1-T3 oral tongue SCC were consecutively enrolled in the study and randomized to either preoperative ultrasound or conventional manual clinical examination for tumor invasion depth and surgical margin calculation. All patients underwent resection of their tumors with a 1-1.5 cm margin, and all the samples were sent for pathological review (reference standard) by the same pathologist at the same hospital. The institutional ethical review board approved this study at Tehran University of Medical Sciences.

Participants

All patients with tissue-diagnosed previously untreated T1-T3 oral tongue SCC based on the American Joint Committee Criteria referred to Amir-Alam Hospital in Tehran, Iran, from December 2014 to December 2017 were enrolled in this study after informed signed consent. Patients with a previous history of tongue surgery, the base of tongue involvement, and patients with stage 4 disease were excluded.

All patients completed a questionnaire that comprised items

on their demographic characteristics, medical history, surgical history, and chemotherapy/radiotherapy history with assistance from a clinician investigator.

Conventional tumor resection

The surgeon resected the tumor with a 1-1.5 cm margin based on the depths determined by physical examination and palpation of tongue mass.

Ultrasound-guided tumor resection

In the operating room, a radiologist gently placed a US transducer-covered with a sterile sheath with a small amount of sonography gel inside the cover- on the surface of the tongue tumor that was covered with sterile lidocaine gel to obtain a clear image of the oral tongue tumor. The tumor was identified by ultrasound and differentiated from the surrounding normal tissue as a hypoechoic mass that disrupts typical echogenic tongue tissue architecture. Subsequently, the head and neck surgeon inserted a blue needle into the tumor tissue (1 cm depth), the tip of the needle was visualized by ultrasound, and the needle was adjusted to the point that it was 1-1.5 cm away from the tumor surface. The needle was then fixed, and the surgeon cauterized the tissue via the needle to mark the margin. This procedure was repeated for the four surfaces and the tumor's basal surface. If the tumor border was irregular or unclear, we considered the deepest point from the surface as the margin. Finally, the surgeon resected the tumor based on the depths determined by the needles placed under ultrasound guidance.

Tissue analysis

The intact resected tissue samples from patients of both groups were sent for frozen section and permanent histopathological review to assess for positive tumor margin or a smaller than 5 mm tumor margin (near margin) intraoperatively. The pathologists who performed the tissue analysis were masked to the patients' assignments and unaware of the estimated margin results detected by either conventional clinical examination or ultrasonographic study. However, the pathologists were informed regarding patients' clinical information.

Statistical analysis

A statistician calculated the sample size based on the results of a pilot study. One of 7 patients who underwent ultrasound-guided tumor resection had a positive tumor margin, whereas three of seven randomly selected patients who underwent conventional resection had positive tumor resection margins. The sample size was calculated as 32 in each group aiming for an 80% power and 5% type 1 error and assuming the base rates obtained in the pilot study.

Data entered into SPSS version 25. Data descriptions are based on frequency tables and related graphs. Frequency and percentage have been used to describe qualitative characteristics, mean and standard deviation have been used to describe quantitative characteristics.

An independent t-test was used to compare quantitative variables. Mann-Whitney test was used to compare ordinal variables. The Chi-square test was used to compare Nominal

Table 1: Baseline Characteristics of the study participants.

Patient characteristics		The conventional clinical palpation group N(%)	The ultrasound group N(%)
Tumor stage	T1	6(18.75%)	10(31.25%)
	T2	18(56.25%)	1631.25%)
	T3	8(25%)	6(18.75%)
Lymph node involvement	Positive	23(71.9%)	27(84.4%)
	Negative	9(28.1%)	5(15.6%)
Smoking		23(71.87%)	25(78.12%)
Neoadjuvant chemo-radiotherapy		4(6.25%)	4(6.25%)
Mean tumor size (cm)		3.64	3.82
Gender	Male	21(65.62)	20(62.5%)
	Female	11(34.37)	12(37.5%)

Table 2: The cross-tabulation table.

	Surgical margin		
Study Group	Positive	Negative	Total
Ultrasound-guided resection	2	30	32
Conventional resection	10	22	32
Total	12	52	64

variables. The significance level in all tests was considered P-value <0.05.

Results

In this diagnostic accuracy trial, a total number of 64 patients ranging from 25 to 80 (mean age: 49.7) years old with stage T1-T3 tongue cancer were randomized to two groups of 32. Forty-four (68%) patients had negative tumor margins, 8 (12.5%) patients had a near-margin, and 11 (19%) patients had appositive tumor margin according to histopathology. Table 1 shows the baseline demographic and clinical characteristics of participants in each group.

Only one person (6.3%) in the ultrasound-guided resection group compared to 10 (31.3%) people in the conventional tumor resection group had positive tumor margins. Also, five people in the ultrasound-guided group and three in the control group had a near-margin (a margin less than 5 cm from tumor edge). There was a positive correlation between intra-operative ultrasound and a negative tumor margin on histopathology (p value=0.001). Table 2 shows the cross-tabulation of the results of the two margin detection methods by histopathology results.

The positive predictive value for accuracy of tumor margin was about 93% in the ultrasound-guided resection group and 68% in the conventional resection group (P-value=0.001).

At one-year follow-up, the local recurrence rate was 10 out of 32 in the control group and 2 out of 32 in the ultrasound-guided resection group.

Discussion

We found that intraoperative ultrasound has a higher predictive value than an examination by palpation for intraoperative estimation of adequate resection margins for tongue tumors. Also, ultrasound-guided surgery significantly decreased the rate of recurrence in comparison with conventional resection.

A similar study by Helbig et al. suggested the superiority of the ultrasound-assisted approach over the conventional-palpation method, which is consistent with our results [17]; they filled the oral cavity with normal saline, whereas we covered the probe with ultrasonography gel and placed it directly on the lesion and found similar accuracy.

The results from Kodama et al. [19] and Baek et al. [4] were consistent with ours. In the study conducted by Shintani et al. [7], the results from ultrasonography were shown to be more consistent with the histologic study than that of CT and MR imaging, which makes it preferable not only over the conventional method probably over the standard imaging methods.

In the study by Tarabichi et al. [13], 12 patients underwent ultrasonography-assisted hemiglossectomy. The results from this study also confirm the superiority of ultrasound-guided resection over the conventional method. The size of the unaffected margin was measured in millimeters in this study, while in our study, we only studied the positivity or negativity of the margin as a dichotomous measure.

Although the use of ultrasound is not technically complex, the current approach requires a medical ultrasound machine in the operating room and a sonologist-at least until the surgery team is well trained to use the machine. Also, the use of ultrasound during surgery has been shown to add little extra time to the time of operation [13,20].

Another downside is that intraoral ultrasonography cannot give reliable information in cases of lesions extending to the base of the tongue or the floor of the mouth. The images obtained by different operators and from different tissues vary; for example, pressing the probe (versus just placing it, applying no pressure) on the lesion can compress it and underestimate the tumor thickness. Also, physical pressure on the lesion can cause tissue distortion that can influence histologic study.

Conclusion

The results from our study suggest that surgeons may remove a more precise and more reliable margin (particularly with deeper tumors) from the lesion by ultrasound guidance. Intraoperative ultrasound can, in turn, improve patient survival decrease recurrence rate and need for re-operation, which eventually decreases the burden both on the patient and the healthcare system.

Declarations

Conflicts of interest: The authors declare no conflict of interest.

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Ethical approval: This study was approved by the ethics committees of the collaborating hospitals. Informed consent was obtained from all participants.

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