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CASE REPORT

Sentinel lymph node biopsy's role in oral cavity cancer: analysis of cases and literature review

O papel do gânglio sentinela nos tumores da cavidade oral: revisão de casos e da literatura

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Abstract

Early-stage oral cavity squamous cell carcinoma (OCSCC) presents with occult metastases in up to 30% of cases. For this reason, a dilemma remains between adopting a watchful waiting approach or a more aggressive strategy with elective neck dissection (END). In recent years, an intermediate option has emerged: sentinel lymph node biopsy (SLNB), which enables ganglionar staging with less morbidity compared to END. This study reviews the related literature and early-stage OCSCC cases from our department, aiming to implement SLNB as a procedure in our institution.

Keywords: *Sentinel lymph node biopsy. Squamous cell carcinoma of the head-and-neck. Neck dissection.*

Resumo

O carcinoma de células escamosas da cavidade oral (CECO) em estadio inicial apresenta metástases ocultas em até 30% dos casos. Por essa razão, nestas situações, permanece a dúvida entre a realização de uma abordagem expectante ou de outras mais interventivas (esvaziamento ganglionar cervical eletivo- ECE). Nos últimos anos, uma opção intermédia surgiu, a Biópsia de Gânglio Sentinela (BGS), o que permitiu a realização de estadiamento ganglionar sem a morbilidade associada ao ECE. Este estudo faz uma revisão da literatura relacionada e dos casos de CECO de estadio inicial do nosso serviço, visando instituir a BGS como procedimento na nossa instituição.

Palavras chave: *Biópsia de linfonodo sentinela. Carcinoma de células escamosas da cabeça e pescoço. Dissecção cervical.*

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Introduction

Oral cavity squamous cell carcinoma (OCSCC) is the most common histological type of oral cavity cancer. While early-stage (cT1-2) OCSCC often presents without clinically detectable cervical lymph node metastasis (cN0), between 20% and 30% of these patients have the risk of concealing occult metastasis[1]. The presence of lymph node metastasis is the most important prognostic factor in OCSCC, reducing by 50% the overall survival rates[2]. Despite the evolution in imaging modalities, neither is yet sufficiently sensitive to detect occult metastasis in a clinically negative neck[3,4]. Therefore, either assessment of cervical lymph node status is achieved with elective neck dissection (END), or a "wait and see" approach is chosen.

Despite being the preferred current practice in cT1-2N0 OCSCC patients, by performing END around 70-80% of these individuals will be overtreated[5]. While END provides pathological staging and offers lower risk of both recurrence and death when compared with watchful waiting, it is associated with considerable morbidity, including shoulder dysfunction, sensory and motor nerve damage, and esthetic concerns[6,7]. This has prompted the investigation of procedures that can accurately stage the neck and guide management decisions while being less invasive than END[8].

Sentinel lymph node biopsy (SLNB) has emerged as a less invasive procedure aimed at identifying the first nodes that drain from the primary tumor–the sentinel lymph nodes (SLN)–which are at highest risk for metastasis[9]. Its application in early stage OCSCC has been the subject of numerous studies and meta-analyses, marking SLNB has a reliable and safe oncological technique for staging these patients[1,10-13]. By using this technique in OCSCC, unnecessary END may be avoided without compromising the prognosis[14]. Furthermore, two other findings emphasize the potential benefit of SLNB in comparison with END: (i) unexpected contralateral lymphatic drainage occurs in a percentage of patients, meaning occult cervical metastases may be missed if ipsilateral END is performed; (ii) Histopathological examination with step-serial sectioning with immunohistochemistry is recommended for identification of micrometastasis and isolated tumor cells, which is less feasible in the analysis of an END[10,14-16].

However, despite these promising results and the fact that this procedure is successfully used in the staging of other cancers, the adoption of SLNB in OCSCC has been gradual, with its availability limited to specialized centers. Concerns regarding the learning curve, standardization of the technique, and the accuracy of SLN identification in the complex lymphatic drainage of the head and neck region have been cited as barriers[15].

The aim of this study is to analyze our experience with cT1-2N0 OCSCC and review the literature regarding SLNB in this pathology, to find which patients could have benefitted from this procedure and start to implement it in our institution.

Materials and methods

This study followed the tenets of the Declaration of Helsinki for biomedical research. We conducted a single-center, retrospective cohort study, of all early stage OCSCC (cT1-2N0M0) that were diagnosed and treated in our Otorhinolaryngology Department between January 2008 and February 2024. Staging was obtained according to the TNM Staging of Head and Neck Cancer[17]. Two groups were created based on the primary tumor staging: group 1 (T1) and group 2 (T2). Patients with previous treatment for a head and neck cancer were excluded. A literature review was conducted to synthesize the available information regarding the usefulness of SLNB in early stage OCSCC.

Results

A total of twenty patients, fifteen male (75%) and five female (25%), were included: eleven in group 1 (cT1N0) and nine in group 2 (cT2N0). Mean age at diagnosis was 64.75 ± 13.24 (mean ± SD). The primary tumor origin was located in the oral tongue in 75% of the patients (n = 15), floor of the mouth in 10% (n = 2), buccal mucosa in 10% (n = 2), and mucosal lip in 5% (n = 1) (Table 1).

Treatment modalities for each group are summarized in table 2. Out of the eleven patients in group 1, eight (72.7%) had tumor resection (TR) alone, two (18.2%) had TR + ipsilateral END, and one (9.1%) had TR + bilateral END. In group 2, six patients (66.7%) had TR + ipsilateral END, and three patients (33.3%) had TR + bilateral END. In two patients (18.1%) from group 1 and in five patients (55.6%) from group 2 there were positive margins or close negative margins following TR, and all these had adjuvant radiotherapy. Every patient who had END (n = 12, 60%) was negative for lymph node metastases (pN0).

Cancer recurrence occurred in five patients (45.5%) from group 1 and in four patients (44.4%) from group

Table 1. Patient demographics and tumor locations

Variable	Total (n = 20) (%)	Group 1: cT1N0 (n = 11) (%)	Group 2: cT2N0 (n = 9) (%)
Male	15 (75)	9 (81.8)	6 (66.7)
Female	5 (25)	2 (18.2)	3 (33.3)
Mean age (years)	64.75	65.55	63.78
Primary tumor location			
Oral tongue	15 (75)	9 (81.8)	6 (66.7)
Floor of the mouth	2 (10)	-	2 (22.2)
Buccal mucosa	2 (10)	1 (9.1)	1 (11.1)
Mucosal lip	1 (5)	1 (9.1)	-

Table 2. Treatment modality for each group

Treatment	Group 1: cT1N0 (n = 11) (%)	Group 2: cT2N0 (n = 9) (%)
Tumor resection	8 (72.7)	0
TR + ipsilateral END	2 (18.2)	6 (66.7)
TR + bilateral END	1 (9.1)	3 (33.3)

TR: tumor resection; END: elective neck dissection.

2. In group 1, four of the patients with recurrence had TR alone and one had TR + ipsilateral END. In group 2, three patients had TR + ipsilateral END and one had TR + bilateral END (Table 3). Of these nine patients, two (22.2%) had exclusively regional lymph node recurrence < 1 year after surgical resection: one from group 1, who had only been treated with TR; and one from group 2, who had bilateral cervical lymph node recurrence after ipsilateral END.

Of the sixteen END that were performed (twelve ipsilateral and four bilateral), one patient suffered from shoulder dysfunction for accessory nerve injury during surgery. No other complications were registered.

Discussion

The treatment of early-stage OCSCC presents a clinical challenge, particularly concerning the management of the clinically negative neck. Traditionally, either a "wait and see" policy or an END was offered[18]. However, with various studies showing that SLNB is an accurate staging technique in early-stage OCSCC, the paradigm shifted and led to the incorporation of this procedure into the National Comprehensive Cancer Network (NCCN) guidelines for stage I to II OCSCC in 2014[19,20]. Thus, our institutions' head and neck group wishes to start offering SLNB for our patients who meet the criteria. Our analysis provides insights into the outcomes of the past 20 patients with early stage OCSCC that our otorhinolaryngology department managed, highlighting areas where SNLB could offer potential benefits.

In our cohort, there was a male predominance, and the oral tongue was the most common primary site, which is consistent with the literature[19]. END was performed in 60% of patients, including every cT2 patient. However, in most cT1 patients a "wait and see" approach was preferred. Although it is true that less pathologic depth of invasion offers a reduced risk of spread to regional lymph nodes, and most patients will not have metastasis, occult lymph nodal disease may still be present and cannot be reliably excluded with physical examination or imaging[15,21,22]. In our cohort, 80% of the five cT1 recurrences were seen in patients who had not had END, one of which presenting exclusively with nodal disease. With that in mind, SLNB could be of particular interest in these patients, offering accurate node staging with a less invasive procedure than END[19,23,24].

In group 2, every patient had an END, whether unilateral (66.6%) or bilateral (33.3%). Four recurrences were seen (two local recurrences, one local recurrence and ipsilateral nodal disease, one bilateral nodal disease), 75% of which in patients who had ipsilateral END. Similarly, to what was seen in group 1, in group 2 one patient also had recurrence exclusively with nodal disease, presenting with bilateral nodal carcinoma after having ipsilateral END. At present, it is

Table 3. Recurrences seen for each group

Recurrence	Total recurrences (n = 9) (%)	Group 1: cT1N0 (n = 5) (%)	Group 2: cT2N0 (n = 4) (%)
After TR	4 (80)	4 (100)	0
After TR + ipsilateral END	3 (60)	1 (20)	3 (50)
After TR + bilateral END	1 (20)	0	1 (25)

TR: tumor resection; END: elective neck dissection.

known aberrant lymphatic drainage that would not be expected is sometimes seen, with sentinel nodes being in the contralateral neck in between 12.4% and 22.6% of cases[7,10,25,26]. This means that ipsilateral END, which is usually the option in tumors not involving the midline, would miss node metastasis in those cases where the contralateral SLN are positive[14]. Furthermore, through the use of step-serial sectioning and immunohistochemistry analysis in the few sentinel nodes that have been excised, identification of micrometastases and isolated tumor cells is possible. This would be unfeasible in the large specimen of END, which is analyzed through routine histopathological examination, thus potentially improving staging in SLNB[14,19].

For experienced head and neck surgeons, END is a routine operation. However, its morbidity is not negligible, as seen in our cohort with one patient with shoulder dysfunction after END. Correspondingly, studies comparing END with SLNB show significantly less post-operative morbidity with decreased length of post-operative hospital stay, better shoulder function, and less impairment from cervical scars in SLNB[8,19,27]. This is another factor that should come to mind when dealing with patients with early stage OCSCC, as it is hypothesized that 70-80% of them will be overtreated with an END[28].

Despite its advantages, proven efficacy, and the inclusion in the NCCN guidelines, the adoption of SLNB in OCSCC in the United States has been sparce, with only 2.9% of patients undergoing SLNB instead of END in a study with 8,328 patients with cT1-T2N0 OCSCC[19,23]. This may be explained due to the lack of training with lymphoscintigraphy and subsequent inconvenience of the procedure, the fact that surgeons take several years of information to become comfortable with new techniques, and the logistical challenges in each institution, with close proximity needed between surgeons and pathologists[19,23]. However, in the recent years SLNB has been increasingly used in Europe with demonstrated oncologic safety, being integrated into the standard of care pathway of countries such as Denmark and France[10,13].

Conclusion

Our study offers a detailed vision on the most recent evidence regarding SLNB for early stage OCSCC, with proven efficacy and safety except for floor of the mouth tumors. By adopting SLNB as a standard of care we hope to be able to offer an intermediate approach between "wait-and-see" and END, meticulously staging the neck while causing less morbidity, since only patients with a positive SLNB will undergo neck dissection.

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Conflicts of interest

There are no conflicts of interest to declare.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Kim DH, Kim Y, Kim SW, Hwang SH. Usefulness of sentinel lymph node biopsy for oral cancer: a systematic review and meta-analysis. Laryngoscope. 2021;131:459-65.
2. Alvi A, Johnson JT. Extracapsular spread in the clinically negative neck (N0): implications and outcome. Otolaryngol Head Neck Surg. 1996;114: 65-70.
3. Brennan PA, Subramaniam S, Tsioryannis C, Green B. An update on the latest evidence for managins the clinically negative neck (cN0) in oral squamous cell carcinoma. Oral Dis. 2017;23:287-91.
4. Stoeckli SJ, Haerle SK, Strobel K, Haile SR, Hany TF, Schuknecht B. Initial staging of the neck in head and neck squamous cell carcinoma: a comparison of CT, PET/CT, and ultrasound-guided fine-needle aspiration cytology. Head Neck. 2012;34:469-76.
5. Liu M, Wang SJ, Yang X, Peng H. Diagnostic efficacy of sentinel lymph node biopsy in early oral squamous cell carcinoma: a meta-analysis of 66 studies. PLoS One. 2017;12:e0170322.
6. Hutchinson IL, Ridout F, Cheung SM, Shah N, Hardee P, Surwald C, et al. Nationwide randomised trial evaluating elective neck dissection for early stage oral cancer (SEND study) with meta-analysis and concurrent real-world cohort. Br J Cancer. 2019;121:827-36.
7. Moya-Plana A, Aupérin A, Guerlain J, Gorphe P, Casiraghi O, Mamelle G, et al. Sentinel node biopsy in early oral squamous cell carcinomas: long-term follow-up and nodal failure analysis. Oral Oncol. 2018;82:187-94.
8. Schiefke F, Akdemir M, Weber A, Akdemir D, Singer S, Frerich B. Function, postoperative morbidity, and quality of life after cervical sentinel node biopsy and after selective neck dissection. Head Neck. 2009;31: 503-12.
9. Hoft S, Maune S, Muhle C, Brenner W, Czech N, Kampen WU, et al. Sentinel lymph-node biopsy in head and neck cancer. Br J Cancer. 2004;91:124-8.
10. Schilling C, Stoeckli SJ, Haerle SK, Broglie MA, Huber GF, Sorensen JA, et al. Sentinel European node trial (SENT): 3-year results of sentinel node biopsy in oral cancer. Eur J Cancer. 2015;51:2777-84.
11. Thompson CF, St John MA, Lawson G, Grogan T, Elashoff D, Mendelsohn AH. Diagnostic value of sentinel lymph node biopsy in head and neck cancer: a meta-analysis. Eur Arch Otorhinolaryngol. 2013;270:2155-22.
12. Govers TM, Hannink G, Merkx MA, Takes RP, Rovers MM. Sentinel node biopsy for squamous cell carcinoma of the oral cavity and oropharynx: a diagnostic meta-analysis. Oral Oncol. 2013;49:726-32.
13. Garrel R, Poissonnet G, Moya-Plana A, Fakhry N, Dolivet G, Lallemant B, et al. Equivalence randomized trial to compare treatment on the basis of sentinel node biopsy versus neck node dissection in operable T1-T2N0 oral and oropharyngeal cancer. J Clin Oncol. 2020;38:4010-8.
14. De Bree R, De Keizer B, Civantos FJ, Takes RP, Rodrigo JP, Hernandez-Prera JC, et al. What is the role of sentinel lymph node biopsy in the management of oral cancer in 2020? Eur Arch Otorhinolaryngol. 2021;278:3181-91.
15. Jang SS, Davis ME, Vera DR, Lai SY, Guo TW. Role of sentinel lymph node biopsy for oral squamous cell carcinoma: current evidence and future challenges. Head Neck. 2022;45:251-65.
16. Rinaldo A, Devaney KO, Ferlito A. Immunohistochemical studies in the identification of lymph node micrometastases in patients with squamous cell carcinoma of the head and neck. ORL J Otorhinolarygol Relat Spec. 2004;66:38-41.
17. American Joint Committee on Cancer. Cancer of the Mucosal Lip and Oral Cavity TNM Staging AJCC UICC 2017. 8th ed. [AJCC Cancer Staging Manual]; 2017.
18. Abu-Ghanem S, Yehuda M, Carmel NN, Leshno M, Abergel A, Gutfeld O, et al. Elective neck dissection vs observation in early-stage squamous cell carcinoma of the oral tongue with no clinically apparent lymph node metastasis in the neck: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg. 2016;142:857-65.
19. Cramer JD, Sridharan S, Ferris RL, Duvvuri U, Samant S. Sentinel lymph node biopsy versus elective neck dissection for stage I or II oral cavity cancer. Laryngoscope. 2019;129:162-9.
20. National Comprehensive Cancer Network. Head and Neck Cancer Clinical Practice Guidelines in Oncology. Available from: https//www.nccn.org/guidelines/guidelines-detail?category=1&id=1437 [Last accessed on 2025 Jan 20].
21. Kane SV, Gupta M, Kakade AC, D'Cruz A. Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. Eur J Surg Oncol. 2006;32:795-803.
22. Broglie MA, Haerle SK, Huber GF, Haile SR, Stoeckli SJ. Occult metastases detected by sentinel node biopsy in patients with early oral and oropharyngeal squamous cell carcinomas: impact on survival. Head Neck. 2013;35:660-6.
23. Eskander A, Dziegielewski PT, Patel MR, Jethwa AR, Pai PS, Silver NL, et al. Oral cavity cancer surgical and nodal management: a review from the American head and neck society. JAMA Otolaryngol Head Neck Surg. 2024;150:172-8.
24. Schilling C, Sahovaler A, Lai SY. Sentinel node biopsy in oral cancer-indications, analysis, and outcomes-reply. JAMA Otolaryngol Head Neck Surg. 2024;150:634.
25. Flach GB, Bloemena E, Klop WM, Van-Es RJ, Schepman KP, Hoekstra OS, et al. Sentinel lymph node biopsy in clinically N0 T1-T2 staged oral cancer: the Dutch multicenter trial. Oral Oncol. 2014;50:1020-4.
26. Mølstrøm J, Grønne M, Green A, Bakholdt V, Sørensen JA. Topographical distribution of sentinel nodes and metastases from T1-T2 oral squamous cell carcinomas. Eur J Cancer. 2019;107:86-92.
27. Murer K, Uber GF, Haile SR, Stoeckli SJ. Comparison of morbidity between sentinel node biopsy and elective neck dissection for treatment of the N0 neck in patients with oral squamous cell carcinoma. Head Neck. 211;33:1260-4.
28. De Bree R, Takes RP, Shah JP, Hamoir M, Kowalski LP, Robbins KT, et al. Elective neck dissection in oral squamous cell carcinoma: past, present and future. Oral Oncol. 2019;90:87-93.