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Research Article

Sentinel Lymph Node Biopsy in Intraoral Squamous Cell Cancer-Validation Study and our Experience

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Abstract

Purpose: The objective of the study was the validation of the sentinel lymph node biopsy technique for intraoral squamous cell cancer.

Methods: A descriptive study of the patients treated with a sentinel lymph node biopsy for intraoral squamous cell cancer during the year 2021 at the Virgen de las Nieves University Hospital in Granada was done. As the technique was being validated, homolateral elective neck dissection of levels IA, IB, IIA, IIB, III and IV was performed in all patients.

Results: The study presents 31 patients (17 men and 14 women) with early-stage intraoral squamous cell carcinoma (cT1/cT2 N0), obtaining 32.6% (10) of sentinel nodes positive for squamous cell carcinoma. The sensitivity was 90% and the specificity 100%. The most frequent location was the left lingual lateral border, with the migration of the radiotracer unilaterally. The mean hospital stay was 4.7 days and the mean surgical time was 237.7 minutes. There were two cases of postoperative cervical hematoma and two cases of shoulder pain syndrome, which improved with physiotherapy.

Conclusion: We conclude that it is a useful technique for detecting occult metastases in the early stage (T1/T2 N0) intraoral squamous cell cancer, avoiding unnecessary neck dissections, reducing morbidity and hospital costs, without having a negative impact on patient survival.

Keyword: • Occult metastases, • Radiotracer migration, • Morbidity, • Homolateral elective neck dissection

Introduction

Intraoral squamous cell cancer is the eight most common cancer worldwide and has a high metastatic potential. Cervical lymph node metastasis is one of the most significant prognosis factors, because the presence of a single positive node can reduce disease-free survival at 5 years by 50% [1]. Management of the clinically node-negative (N0) neck in early -stage (T1-T2) has evolved considerably over the last few decades [2]. While the primary tumor is typically treated making a wide local excision, the Elective Neck Dissection (END) has always been controversial. It is estimated that nearly 20%-30% of early-stage (T1-T2) node negative (N0) cancer will have occult metastases in the cervical draining lymph nodes (even when they are clinically and radiologically clear), which is the single most important prognostic factor for disease-related outcomes. Therefore, elective surgical management of the N0 neck improves survival in early stages when compared with watchful waiting [3]. Nevertheless, elective neck dissection is an unnecessary operation in nearly 70% of early-stage cancer and morbidity and diverse postoperative complications have been reported: shoulder syndrome (60%-80%), muscle disorders, sternoclavicular problems, skiing numbness and surgical scars [4].

Sentinel Lymph Node Biopsy (SLNB) was first described by Gould et al [5] and it aims to establish the metastatic status of the first lymph node that drains the primary tumor though detailed histological study. SLNB has emerged in the last decade as an intermediate approach between elective neck dissection and watchful waiting, allowing accurate identification of occult neck nodal metastases. Presence of metastases in the sentinel node mandates surgical removal of remaining nodes completing de elective neck dissection, whereas negative sentinel node obviates the need for any further neck surgery [6]. Three different medical procedures are successively applied in selective sentinel node biopsy: lymphoscintigraphy with tracer injection and subsequent imaging tests, surgery, and histopathological study, which implies having a multidisciplinary team of professionals with at least Nuclear Medicine, Pathological Anatomy and Maxillofacial Surgeons [7]. The main objective of the sentinel node biopsy is to find those 20%-30% of occult metastases in early-stage cancer, avoiding the unnecessary 70% of cervical neck dissections and its complications [8]. By the way, National Institute for Health and Care Excellence (NICE) guidelines have endorsed the recommendation of SLNB to patients when access for the neck for free-flap reconstruction is not required. It follows that these T1-T2 N0 patients should be offered either SLNB or END [9].

We present a study carried out in Hospital Universitario Virgen de las Nieves (Granada, Spain) to validate the sentinel node technique for the intraoral squamous cell cancer during the year 2021, performing selective sentinel node biopsy of early-stage cancer (T1/T2 N0) and posterior unilateral or bilateral cervical dissection, until the results were analyzed for technique validation.

Materials and Methods

A descriptive study of the patients who underwent sentinel node biopsy for squamous cell cancer of the oral cavity during the year 2021 at the Virgen de las Nieves University Hospital in Granada was performed. The Hospital Ethics Committee approved the study and the patients signed the informed consent for the procedure.

The inclusion criteria for the study were: intraoral squamous cell cancer, clinically and radiologically T1/T2 N0, no prior treatment, written consent being provided and age >18 years. Exclusion criteria included: clinically and radiologically T3/T4 or N1 tumors, a history of radiation therapy for the neck, planned o current pregnancy or lactation, recurrence after definitive treatment, age <18 and written consent not being provided.

The study presents 31 patients with squamous cell cancer from different locations in the oral cavity (floor of mouth, tongue and buccal mucosa) who were injected with peritumoral radiotracer (99 mTc-nanocolloids) 12-16 hours before the surgery. Subsequently, an early and late SPECT/CT-scan and lymphoscintigraphy were performed to locate the migration of the radiotracer to the sentinel node. Then, the sentinel lymph node(s) was (were) marked in the neck of the patients prior going to the operating room. Once the sentinel node was identified and excised in the operating room, elective neck dissection of levels IA, IB, IIA, IIB, III and IV was done (unilateral or bilateral) according the usual technique, because our sentinel node biopsy technique was being validated until the results were analyzed.

Results

After carrying out the study of the samples by pathological anatomy service of our hospital, the results obtained were the following:

31 patients were included (mean age: 64.39 years ± 13.02 years) with 17 men and 14 women (54.8% men, 45.2% women) in the study. The primary tumor was most frequently located on the lateral border of the tongue (61.3%) followed by the floor of the mouth (29%) and buccal mucosa (9.7%), while the most frequent affected side was the left side of the tongue (48.4%). Well-differentiated squamous cell carcinoma was presented in 58.1%, with pT2 being the most frequent stage (54.8%) (Table 1 and 2).

Table 1. Tumor characteristics by gender.

Sex					
		Frequency	Percentage	Valid percentage	Accumulated percentage
Valid	Men	17	54.8	54.8	54.8
	Women	14	45.2	45.2	100
	Total	31	100	100	-

Table 2. Distribution of tumor locations and affected sides.

Location					
		Frequency	Percentage	valid percentage	Accumulated percentage
Valid	Floor of the mouth	9	29	29	29
	Lateral border of the tongue	19	61	61.3	90
	Yugal mucosa	3	9.7	9.7	100
	Total	31	100	100	-

In all cases, migration of the tracer to the SLN was observed in both early and late imaging in SPECT/CT and lymphoscintigraphy (100% identification of the SLNB), being bilateral in 11/31 (35.5%) cases. The mean number of SLNs identified was 3 and the most frequent location were cervical levels II and III (65.4%) (Table 3-5).

Table 3. SLN migration and identification.

Laterality of cervical findings					
		Frequency	Percentage	valid percentage	Accumulated percentage
Valid Laterality of cervical findings	Right	12	38.7	38.7	38.7
	Left	15	48.4	48.4	87.1
	Central	4	12.9	12.9	100
	Total	31	100	100	-

Table 4. Number of SLNs identified.

Clinical Stage					
		Frequency	Percentage	valid percentage	Accumulated percentage
Valid	cT1N0	14	45.2	45.2	45.2
	cT2N	17	54.8	54.8	100
	Total	31	100	100	-

Table 5. SLN locations.

Laterality of cervical findings					
		Frequency	Percentage	valid percentage	Accumulated percentage
Valid	Homolateral	20	64.5	64.5	64.5
	Bilateral	11	35.5	35.5	100
	Total	31	100	100	-

32.3% presented a positive result for squamous cell carcinoma in the anatomopathological study. The mean number of nodes removed in neck 32lymphadenectomy was 31.6. (Table 6).

The sensitivity of our results was 90%, with a positive predictive value of 100%. The specificity of our results was 100% with a negative predictive value of 95%. There was a case of false negative of the sentinel node with a positive squamous cell carcinoma in a node of the cervical dissection. So that, the false negative rate was 9.09%.

Table 6. Diagnostic performance for squamous cell carcinoma.

Sentinel node results					
		Frequency	Percentage	valid percentage	Accumulated percentage
Valid	Negative	21	67,7	67,7	67,7
	Positive	10	32,3	32,3	100,0
	Total	31	100,0	100,0	

The only factor associated with a greater probability of presenting a positive result in the SLNB, in the binary logistic regression model was the female sex (OR: 14.63, p=0.019).

In the postoperative period, there were two cases (6.4%) of cervical hematoma during the first 24 hours after surgery, the cause was an increase in blood pressure. Hemostasis was done in the operating room without any further problems. There were no other complications during the immediate postoperative period. The mean hospital stay of the patients was 4.7 days. The mean surgery duration was 237.7 minutes. Seven patients received radiotherapy, two patients received radiotherapy + chemotherapy and 22 patients were followed up in consultation without complementary treatment (Table 7).

Table 7. Postoperative outcomes and treatment details.

Treatment after surgery					
		frequency	percentage	valid percentage	accumulated percentage
Valid	Follow-up	22	70.9	70.9	70.9
	RT	7	22.6	22.6	93.5
	RT+QT	2	6.5	6.5	100
	Total	31	100	100	-
Total		31	100	-	-

During the follow-up of the patients in the next 12 months, there weren´t cases of local or locoregional recurrence. Two patients had shoulder syndrome after the surgery (6.4%) and both improved their symptoms after performing physiotherapy exercises until almost disappeared completely in the 12-month review.

Discussion

The management of the neck of patients with oral squamous cell cancer has evolved from radical surgery towards selective or conservative neck dissection [10]. Currently, elective neck dissection has been acknowledged as a standard approach for oral squamous cell cancer in early stage (T1/T2 N0) because its survival outcomes are better than the observation strategy [5,11]. More recently, SLNB has emerged as a minimally invasive mode of accurately evaluating the status of the cervical lymph nodes without compromising oncologic prognosis [12].

According to the literature, early-stage (T1/T2 N0) squamous cell cancer presents 20-30% of occult cervical metastases [3,13]. In our results, we observed that 32.3% presented a positive result. Therefore, near 70% of patients do not present cervical metastases, so elective cervical dissection could have been avoided. After the elective neck dissection, morbidity and diverse postoperative complications have been reported: shoulder syndrome (60-80%), muscle disorders, sternoclavicular problems, skiing numbness and surgical scars [4]. In our study, there were two cases (6.4%) of cervical hematoma during the first 24 hours and two patients had shoulder syndrome after the surgery (6.4%). Govers et al [14] investigated the quality of life after different procedures for neck management through the EuroQo1-5d questionnaire and concluded that SLNB had high health utility as a dominant role in oral cancer. A similar discovery was reported by Schiefke et al [15]. Despite being a lower result than those described in the literature, these numbers could be further reduced if only sentinel node biopsy had been performed in the patients included in our study.

The sensitivity of our results was 90%, with a positive predictive value of 100%. The specificity of our results was 100% with a negative predictive value of 95%. Schilling et al and Kim et al reported a sensitivity of 90-95% in their sentinel node biopsy study [16-20]. On the other hand, Ding et al made a systematic review of prospective studies about sentinel lymph node biopsy vs elective neck dissection in squamous cell cancer in the oral cavity, reporting a sensitivity mean of 67.14%, being much lower than in our study [20]. So that, our results can be considered acceptable.

The false negative rate was 9.09% having a case of a negative sentinel node biopsy and a positive node in another cervical level during the analysis of the elective neck dissection. Bowe et al reported a false negative rate of 14% (16). Antonio et al reported a false negative rate of 5.2%. Furthermore, they described that after years of experience in several centers, it is accepted that the percentage of false-negative should be below 5% [17,18]. Therefore, our false negative percentage is above the ideal. The patient who presented the false negative was the third in our study (3/31), therefore, it could be related to the lack of experience when injecting the peritumoral radiotracer prior to the surgery. If the radiotracer is not injected correctly, the migration to the cervical node could be to one that isn´t the real sentinel node.

Hasegawa et al reported a randomized, multicenter and non-inferiority trial about the Sentinel Lymph Node Biopsy (SLNB) vs Elective Neck Dissection (END) in early-stage cancer with 271 patients. The primary end point was the 3-year overall survival rate and secondary end points included postoperative neck functionality and complications and 3-year disease-free survival. The 3-year overall survival in the SLNB group 87.9% was noninferior that in the END group 86.6% (p for noninferiority < 0.001). The 3-year disease-free survival rate was 78.7% and 81.3% in the SLNB and END groups, respectively (p for noninferiority <0.001). The scores of neck functionality in the SLNB group were significantly better than those in the END group. They conclude that SLNB may replace the END without a survival disadvantage and a reduced postoperative neck disability in patients with early-stage intraoral squamous cancer [21].

Finally, when performing the sentinel lymph node biopsy, the surgical time is reduced near 40% and the patient's hospital stay is also reduced near 50% [22]. Therefore, the costs associated with surgical intervention are reduced. In our study, the mean hospital stay of the patients was 4.7 days and the mean surgery duration was 237.7 minutes, both could be reduced if only sentinel node biopsy had been done. O'Connor et al measured the financial impact of the two treatment pathways, SLNB and END, that are considered ontologically comparable by evaluating costs relative to each other; data from a treatment model showed that the cost of SLNB was only 48% of the traditional method and explained that it conferred an economic dividend in addition to the clinical Benefit [23].

Conclusion

We conclude that it is a useful technique for detecting occult metastases at an early stage (cT1/T2 N0) intraoral squamous cell cancer, avoiding unnecessary neck dissections, reducing morbidity and hospital costs, without having a negative impact on patient survival. However, more studies should be carried out with a larger number of patients.

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