HEAD AND NECK

Sentinel lymph node biopsy in squamous cell carcinoma of the head and neck: 10 years of experience

Il linfonodo sentinella nel carcinoma squamocellulare della testa e collo: 10 anni di esperienza

J.K. ANTONIO, S. SANTINI, D. POLITI, S. SULFARO¹, R. SPAZIANTE², A. ALBERTI², M. PIN, L. BARZAN S.C. Otorinolaringoiatria, Azienda Ospedaliera Santa Maria degli Angeli, Pordenone, Italy; ¹ S.C. Anatomia Patologica, Azienda Ospedaliera Santa Maria degli Angeli, Pordenone, Italy; ² S.C. Medicina Nucleare, Azienda Ospedaliera Santa Maria degli Angeli, Pordenone, Italy

SUMMARY

Sentinel node (SN) biopsy of head and neck cancer is still considered investigational, and agreement on the width of the surgical sampling has not yet been reached. From May 1999 to Dec 2009, 209 consecutive patients entered a prospective study: 61.7% had primary tumour of the oral cavity and 23.9% of the oropharynx. SN was not found in 26 patients. Based on these data and definitive histopathological analysis, we proposed six hypothetic scenarios to understand the percentage of neck recurrences following different treatments Among patients with identified SN, 54 cases were pN+: 47 in SN and 7 in a different node. Considering the six hypothetic scenarios: "only SN removal", "SN level dissection", "neck dissection from the tumour site to SN level", "selective neck dissection of three levels (SND)", "dissection from level I to IV" and "comprehensive I-V dissection", neck recurrences could be expected in 6.5%, 3.8%, 2.18%, 2.73%, 1.09% and 1.09% of cases, respectively. SN biopsy can be considered a useful tool to personalize the surgical approach to a N0 carcinoma. The minimum treatment of the neck is probably dissection of the levels between the primary tumour and the level containing the SN(s). Outside the framework of a clinical study, the best treatment can still be considered SND.

KEY WORDS: Neck dissection • Sentinel node • Squamous cell carcinoma • Head and neck cancer • Nodal metastasis

RIASSUNTO

La biopsia del linfonodo sentinella (SN) nel carcinoma squamocellulare della testa e collo è ancora considerata investigazionale e non è stata raggiunta unanimità su quanto ampio debba essere il prelievo da utilizzare. In questo studio prospettico, dal maggio 1999 al dicembre 2009, sono stati analizzati 209 pazienti consecutivi: 61,7% con tumore primitivo della cavità orale e 23,9% dell'orofaringe. Il SN non è stato identificato in 26 pazienti. Sulla base dei referti istopatologici definitivi, vengono creati sei scenari per ipotizzare quale sarebbe stato il tasso di ricorrenza nel collo se fossero stati impiegati i diversi trattamenti, più o meno invasivi. Dal totale di pazienti in cui è stato localizzato il SN, 54 casi sono stati pN+: 47 nel SN e 7 in un altro linfonodo. Considerando i sei scenari ipotetici: "rimozione solo SN", "dissezione livello contenente il SN", "svuotamento laterocervicale dal sito del tumore al livello del SN", "svuotamento selettivo di tre livelli (SND)", "svuotamento dei livelli I-IV" e "svuotamento dei livelli I-V", si sarebbero potute attendere rispettivamente 6,5%, 3,8%, 2,18%, 2,73%, 1,09% e 1,09% di recidive nel collo. La biopsia del SN può essere considerato uno strumento utile per personalizzare l'approccio chirurgico di un carcinoma squamocellulare N0 della testa e collo. Il trattamento minimo del collo è probabilmente la dissezione dei livelli fra il tumore primitivo ed il livello che contiene SN(s). Al di fuori di studi clinici, il miglior trattamento rimane lo SND.

 $\label{eq:parole} \textit{PAROLE CHIAVE: Svuotamento cervicale} \bullet \textit{Linfonodo sentinella} \bullet \textit{Carcinoma squamocellulare} \bullet \textit{Carcinoma testa e collo} \bullet \textit{Metastasi linfonodale}$

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Introduction

Head and neck squamous cell carcinoma (SCC) has a high metastatic potential, and lymph node metastasis is one of the most significant prognostic factors: the presence of a single positive lymph node can reduces disease-free survival at 5 years by 50% ¹⁻⁷. Correct diagnosis and adequate treatment of the neck are crucial for determining

prognosis. In recent decades, improved knowledge of the patterns of lymphatic drainage has allowed assessment of the levels at a higher risk of metastases for various primary sites, and therefore dissection can be limited to these levels. In the treatment of a N0 neck, the policy has shifted from radical neck dissection to modified radical neck dissection (MRND), and now to selective neck dissection

(SND) ^{8 9 10}. Biopsy of the sentinel node (SNB) as a staging procedure and decision tool to establish whether surgical treatment of the lymphatic area is to be performed or not is now recognized as the gold standard in melanoma and breast cancer. Although the methodology of SNB has been well known for more than 10 years and many prospective studies with a significant number of patients have been published, it has not been accepted worldwide for head and neck SCC, where it is still considered investigational. Moreover, there is also debate regarding sites of primary tumour (T) and stages that could be eligible: at present, the general consensus is restricted to T1 and T2 SCC of the oral cavity and the upper part of the oropharynx. Probably the most challenging issue is evaluation not only of the more uptaking single sentinel node (SN), but of all the uptaking nodes and possible surrounding nodes: if they are multiple and at different levels, the procedure may eventually be the same as formal SND.

This paper will report the results of a single-centre series of SNB in head and neck SCC examining the feasibility and utility of the procedure. Furthermore, hypothesizing different scenarios, evaluation can be performed depending of different widths of surgical sampling.

Patients and methods

From May 1999 to December 2009, 209 consecutive patients treated in the Unit of Otorhinolaryngology, Azienda Ospedaliera Santa Maria degli Angeli, Pordenone (Italy), were included in this prospective study after obtaining their informed consent.

Eligibility criteria included histologically proven, previously untreated, SCC of the oral cavity, oropharynx, hypopharynx, larynx, scheduled for surgery (T + N) with either:

- clinical c2N0 (i.e. degree 2 of certainty: clinical evaluation always documented by CT scan) and candidates for monolateral or bilateral selective neck dissection, or
- midline or paramedian T, monolateral neck disease and candidates for elective treatment of the contralateral neck

The mean age of patients was 61 years, ranging from 36 to 91 years, with a male:female ratio of 3:1. The tumour site was 61% in the oral cavity, 23% in the oropharynx, 8.6% in the larynx and 5.8% in the hypopharynx. Moderate degree of tumour differentiation – G2 – was observed in 54.5% of patients and G3 in 38.3%. Tumours were staged as T1 in 47 patients (22.5%), T2 in 100 (47.9%), T3 in 35 (16.7%) and T4 in 27 (12.9%). One hundred and forty-three patients (68.4%) were clinically staged as c2N0, 32 (15.3%) as c2N1 and 24 (11.5%) as c2N2b.

The technique of injection and evaluation of the SN is well known and has already been published also by our group ⁹ ¹¹. None of the patients were candidates for removal of a

single node, but received evaluation of the SN within the context of some type of neck dissection. A MRND was performed in 13 cases, SND in 135, dissection of the level(s) containing the SN in 39, dissection of the level(s) containing the SN + SND in 12 and a SND (on the same side of the SN) + MRND (on the side of the paramedian tumour) in 10 patients. Nodes were considered "sentinel" if the radioactivity level was at least 4 times over background level. The different levels of the neck nodes were carefully marked with threads during dissection, divided by the surgeon at the end of the procedure and sent to the pathologist in separate containers. If the SN was not found, the patient was submitted to traditional treatment of the neck. Even if in many patients intraoperative frozen sections were examined, the present paper evaluates only the results of the definitive histopathologic workup with multiple serial sections and immunohistochemistry. Recurrences were always assessed by CT scan and histologically proven.

Combining clinical, histopathological data and the followup of patients, with the aim to shed light on still-debated issues, six hypothetical scenarios were taken into consideration: patients would be submitted to more or less extended surgical neck treatment to estimate the probability of neck recurrence.

Statistical analysis

A contingency table analysis between all considered variables and follow-up was done. A chi-square test based on the permutation technique was used. The results of the six scenarios were compared by a chi-square test based on permutation technique, Z test for proportions and Fisher's exact test ¹²⁻¹⁴.

Results

Among the 209 patients, the SN was not identified in 26 cases, 11 in the first two years, 14 from the second to the fifth year and only one after five years. Of the 183 patients with an identified SN, histological analysis showed the presence of metastases in 54 cases, of which 47 were in the SN and 7 in a different node in the same or adjacent level. Of these 47 patients, other positive nodes were identified in the same level of the SN in 10 cases, while additional metastatic nodes were present in a different level in another 10 patients. Eight of these were in adjacent levels (1 above, 6 below and 1 case above and below) (Fig. 1). In 129 patients (70.5%), the SN was negative. In 5 cases (27%), the SN was negative, but histological examination found an adjacent positive node in the same level, and in 2 patients (1.1%) a positive node was found in adjacent levels (Fig. 1). An average of 1.86 SN per patient were found.

No SN was identified at level V and no pN+ was demonstrated at level V. A SN at level IV was detected in 8 pts:

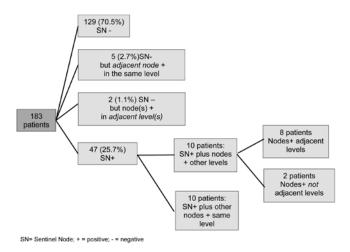


Fig. 1. Patients with localized SN.

6 had multiple SNs also identified in other levels, 2 had tumour in the floor of the mouth with isolated SN at level IV but histologically negative. In patients with N0 neck and well lateralized tumour (> 1 cm from the midline), a SN in the contralateral neck was identified in 3 cases (all histologically negative).

According to the protocol of adjuvant treatment in our hospital, 100 patients received postoperative radiotherapy, and 10 also underwent concurrent chemotherapy. Radiotherapy was indicated for histopathological features of the tumour (involved or close surgical margins, poor differentiation, angio-lymphatic or neural invasion), and for multiple positive nodes or with extra-capsular spread. In the present series, adjuvant treatment was indicated based on pN features in 51 patients, even though it is our policy to irradiate both the bed of the tumour and node.

A total of 35 patients (16.7%) experienced relapse during follow-up (Table I). Among the 9 patients with relapse on N or N+M, four had relapse within 6 months of follow-up, 3 patients from 6 months to 2 years and 2 patients after 2 years. Among these 9 cases, only 5 had recurrence in the same side of SN (the other 4 in the contralateral neck side, where the presence of N+ was known).

Table I. Site of relapse.

		Frequency	Percentage	Cumulative percentage
	No relapse	174	83.3	83.3
Relapse	T	16	7.6	90.9
	N	8	3.8	94.7
	M	7	3.3	98.0
	T+N	2	1.0	99.0
	N+M	1	.5	99.5
	T+M	1	.5	100.0
	Total	209	100.0	

No relapse occurred in level V or in patients with SCC of oropharynx, larynx or hypopharynx.

Of the 7 pts with recurrence in the same neck side of the SN, 2 cases were associated with T relapse. The following analysis attempted to verify the reliability of SN methods, provided that in these 2 cases the nodal relapse was not a growth of cells missed at the time of SNB, but colonization from the relapsed tumour, these cases are not further considered. On the other hand, if neck relapse allows for subsequent metastatic spread, the patient with nodal relapse and metastasis was considered in the analysis.

One hundred and forty-nine pts (71.3%) were followed-up for longer than 2 years. At the time of writing, 68.4% of patients are free of disease (Fig. 2).

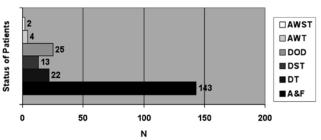
Considering vital status, no statistical difference between men and women was found (Chi square = 2.25, p = 0.48) or among tumour sites (Chi square = 18.21, p = 0.013). Patients staged as pN+ had the worst prognosis (Chi square = 38.88, p = 0.001).

The sensitivity and specificity of the SN method were, respectively, 87% and 100%; the false negative rate was 5.1%. If we also consider the 5 patients with neck recurrence in the same side of the SN, the sensitivity was 79.6% with a false negative rate of 8.5%.

On the basis of the available data, the following scenarios were considered to answer specific questions:

Scenario 1

How many patients would develop neck relapse if only the SN had been removed? How many patients would have neck relapse in the same side of the neck side as the SN? If we consider the 183 patients in whom it was possible to identify the SN, and we would have systematically done only SN removal in patients in which the SN was negative (at intra-operative or definitive histological analysis), we would have expected at least 12 recurrences. Five patients would have another positive node in the same level of SN and another 2 patients would have positive nodes in adjacent levels. Moreover, there were also 5 cases that developed neck metastases (Fig. 3): A case submitted to



A&F = Alive and free of disease; DT = Death for tumour; DST = Death for second tumour; DOD = Death for other disease; AWT = Alive with tumour; AWST = Alive with second tumour.

Fig. 2. Status of patients.

Table II. Patients with relapse in the neck side of SN.

No. patients	Primary site	рТ	Side of SN	SN level	pΝ	Type of neck dissection	Side of the recurrence	Level of the recurrence
1	OC	рТ3	Bilateral	I/II Left None SN Right	pN+	SND	Left	Parapharynx
2	OC	pT1	Right	II Right	pN0	SN level	Right	Level I
3	OC	pT1	Bilateral	I/II Right IV Left	pN0	SND (left side) + SN level Right	Right	Level III
4	OC	pT1	Bilateral	II/III Right I Left	pN0	SND (right side) + SN level	Right	Level I
5	OC	pT1	Left	l Left	pN0	SN level	Left	Level IV

SND = Selective Neck Dissection; OC = Oral Cavity.

SN dissection (level II right) that developed a late metastases in level I.

A patient with SN identified on levels I and II right (pN0) and level IV left (pN0) that was submitted to SND (I-IV) on the left side and SN dissection on the right side. This patient developed neck recurrence in level III right.

A patient with SN identified on levels I and III right and level I left, submitted to SND (I-III) on the right side (pN0) and SN level dissection on the left side (pN0). The relapse occurred in level I on the right side.

A case with SN identified on levels I and II left that was submitted to bilateral SND. This patient developed recurrence in a parapharyngeal node on the left side. A patient with SN identified on level I left that was submitted to dissection of only the SN level. This patient developed neck recurrence in level IV left. Thus, if only SN removal in patients with negative SN had been performed, 12 recurrences (6.5%) could be expected.

Scenario 2

With the hypothesis of some difficulties in precise identification of the single SN and aiming to harvest a larger tissue sample containing the SN, the entire neck level containing the SN might be removed. *How many patients*

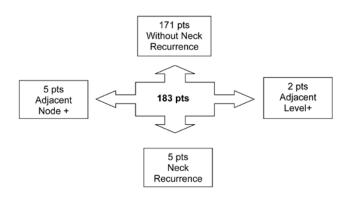


Fig. 3. Patients in scenario 1.

would develop neck recurrence if only the entire level containing the SN would have been dissected? How many patients have a negative SN but other positive nodes in other levels? How many patients would have neck recurrence in the same side of the SN?

If we consider all 183 patients in which it was possible to identify the SN, and if we had only SN level dissection in patients in which the SN was negative, we would have expected at least 7 cases of relapse. Two patients had positive nodes in adjacent levels and 5 patients had neck recurrence, as previously described. In those cases, the recurrence did not affect the SN level but an adjacent level (Fig. 4).

Thus, if we had done only SN level dissection, we would have expected 7 relapses (3.8%).

Scenario 3

If the neoplastic cells migrate from the tumour to the SN, one would argue that microscpic foci might be missed if all tissues between the tumour and node are not removed. The SN procedure would have the aim of indicating how distant from the tumour one must arrive with the selective removal of neck levels.

How many patients would have developed neck recurrence if we had done neck dissection from the tumour site to SN level?

If we consider all 183 patients in which it was possible to identify the SN, and if we had done neck dissection from the tumour site to SN level in patients in which the SN was negative, we should have expected at least 4 neck recurrences (2.18%):

One patient with tumour in the oral cavity and SN in levels I and II that developed neck relapse in level III.

One patient with a SN identified on level I left that was submitted to dissection only at the level of the SN. This patient developed neck relapse in level IV left.

One patient submitted to SND (I-III) who, despite this, developed a neck relapse in level I.

^{*} The patients with neck recurrence in the contralateral neck or with recurrence in T+N have been excluded.

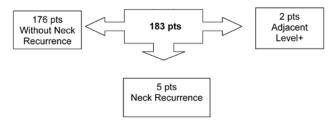


Fig. 4. Patients in scenario 2.

One patient submitted to SND who developed neck relapse (parapharynx).

In these latter two cases, neck recurrence could not have been avoided even with more extensive surgery.

Scenario 4

How many patients would have developed neck relapse if the usual SND of three levels for any tumour site was performed?

If we had performed traditional SND (levels I-III for oral cavity and levels II-IV for the pharynx and larynx) in 183 patients, we could have expected at least 5 neck relapses (2.73%):

- Two patients with tumour in the oropharynx who had a
 positive node in level I (both identified by SN method).
- Two patients submitted to SND that developed neck relapse on level I and parapharyngeal nodes.
- One patient with SN identified on level I left and submitted to dissection of the SN level only. This patient developed neck relapse in level IV left.

Scenario 5

How many patients would have developed neck relapse if we had always done dissection from level I to level IV? If we had used the neck dissection from level I to level IV in the 183 patients, we could have expected at least two neck relapses (1.09%):

• Two patients submitted to SND that developed neck relapse on level I and parapharyngeal nodes.

Scenario 6

How many patients would have developed neck relapse if we had always done dissection from level I to level V? If we had used comprehensive MRND (level I-V) for the 183 patients, we could have expected at least 2 neck relapses (1.09%):

Two patients submitted to SND that developed neck recurrence on I level I and parapharyngeal nodes.

No neck recurrence was observed on level V.

Using scenarios 4, 5 or 6, we would have dissected many"disease free" levels: if we compare these possibilities with "scenario 3", we would have dissected more (1.26, 2.10 and 3.43) levels/patient, respectively, in scenarios 4, 5 and 6.

Tab. 3 shows the significant differences in relapse rate among the various scenarios: there was no difference

between scenario 1 and 2 using any statistical method; however, there was a difference between scenario 1 and scenarios 5 or 6. Only the Chi square method showed a significant difference between scenarios 2 and 5 or between scenarios 2 and 6 (Table III).

Discussion

Between the routine use of elective neck dissection in all N0 neck and a "wait and see" policy, SNB in HNSCC has been suggested as a method to improve the accuracy of staging and tailor treatments. Furthermore functional outcome after SNB is recognized as significantly better compared to SND ¹⁵, even if the quality of life perceived from the patients is similar ¹⁶. Nevertheless, we should not forget that we are dealing with a group of patients with a good prognostic factor, namely a N0 neck. Therefore, all our efforts to improve the quality of life must not affect prognosis.

Although in melanoma and breast cancer the SN procedure is widely employed, for SCC of the head and neck the most active proponents state that it is "safe and accurate with... *the potential to become* the new standard of care" ¹⁷.

The first data worthy of note in the present series is the absence of either pN+ or relapse in level V, further confirming that in c2N0 pts with SCC of the oral cavity, oro and hypo-pharynx and larynx, elective treatment of level V is unnecessary. A second consideration is that unexpected lymphatic drain arriving from the site of the tumour to distant levels is very rare: in this series, no metastatic cells were found in the contralateral neck of lateralized tumours and no isolated metastases occurred at level IV.

The technique of SN was started in our hospital 10 years ago within the collaborative framework of a multidisciplinary team. At the beginning, the SN was not identified in a quite high percentage of patients: the common learning curve ^{1 18 19} was particularly prolonged in our hands and these patients were treated with MRND. Perhaps one of the more rewarding results is the assembly of a interested, motivated and efficient team.

Another fact to note is the feasibility and safety of the technique in tumours of the larynx, oropharnyx and hypopharynx and for study of the contralateral neck in patients with a paramedian tumour and homolateral N+: no relapse on the SN side was observed in these cases, but the small number of patients must be considered as a source of possible bias. Even if the majority of studies on SNB are focused on the oral cavity and oropharynx with NO, nevertheless some authors also consider different tumour sites and nodal classes ²⁰ ²¹. We chose to include laryngeal and hypopharyngeal SCC to evaluate the feasibility of the procedure even in these cases; the small number of patients enrolled is due to the large number of nonsurgical protocols usually adopted for these localizations

Table III. Significance of differences of relapse between the scenarios using Chi Square Test based on permutation technique, Z test for proportions and Fisher's exact test.

Scenario	Chi Squ	Chi Squared		Z Test	
	Chi Squared Value	Probability	Z Value	Probability %	
1X2	1.39	p = 0.140	0.94	65.0	p = 0.34
1X3	4.18	p = 0.006	1.78	92.6	p = 0.07
1X4	3.00	p = 0.024	1.49	86.4	p = 0.13
1X5	7.42	p = 0.000	2.45	98.6	p = 0.01
1X6	7.42	p = 0.000	2.45	98.6	p = 0.01
2X3	0.83	p = 0.290	0.61	46.0	p = 0.54
2X4	0.34	p = 0.532	0.30	61.7	p = 0.77
2X5	2.84	p = 0.028	1.36	82.5	p = 0.17
2X6	2.84	p = 0.028	1.36	82.5	p = 0.17
3X4	0.11	p = 0.726	0.01	0.30	p = 1.00
3X5	0.67	p = 0.361	0.42	32.0	p = 0.68
3X6	0.67	p = 0.361	0.42	32.0	p = 0.68
4x5	1.39	p = 0.140	0.76	55.0	p = 0.44
4X6	1.39	p = 0.140	0.76	55.0	p = 0.44
5X6	0.00	p = 1.00	0.00	0.00	p = 1.00

^{*} Bold identifies significant probability.

in our hospital. Likewise, as for other studies of SNB in the literature ²²⁻²⁶, herein SNB was also performed in the same context of a neck dissection: this was not a limiting factor, but provided better safety and more information about adjacent nodes.

Of the 183 patients in whom SN was identified, in 5(2.7%)it was histologically negative, whereas a metastatic node was found in an adjacent node in the same level. The positivity of a node different from the "hottest" reach 13% in the experience of Gallegos-Hernadez ²² may be related to the difficulty in identifying the SN, and may suggest the indication to dissect the entire level containing the SN. However, this is not the opinion of the authors who consider that non-sentinel nodes should be removed only if they represent a "hurdle" for SN resection 8. Different radioactivity uptake thresholds have been suggested to determine the indication for tissue removal, either 3 or 4 times the background or more than 10% of background 127, or more than one-tenth of the hottest node8. The question of how many SNs must be removed if they are multiple and at different levels is still unanswered, and may lead to an extensive procedure that is not very different from a formal SND. Werner advocates biopsy of 1 to 3 "hot" lymph nodes to reduce the possibility of false-negative results 28, and Atula 29 also judges that only the three hottest nodes require sampling to stage the neck accurately. Following Gallegos-Hernandez, if more than two SN are identified and examined, there are fewer probabilities of having positive non-sentinel nodes ²⁴. Furthermore, one may speculate that the presence of a SN in levels distant from the tumour would suggest the possibility of distant metastatic cells that might be neglected between the tumour and node. One possibility would be to limit SND from the site of the tumour to the level of the identified SN, also removing the intervening levels (scenario 3), which may minimize the risk of regional recurrence to the percentage seen with formal SND.

Of the 47 patients with a positive SN, we observed 10 cases with the presence of other positive nodes at the same SN level and 10 cases at other levels, adjacent or not, but never at level V. This may suggest the indication of performing a dissection of all levels in patients with a positive SN, in agreement with the opinion of other authors ³⁰, possibly sparing level V. Burns reports that the number of metastases to level V would be very low for the oral cavity and oropharynx, even in patients with a positive SN, and that the comprehensive dissection is thus unnecessary ¹⁶. Some previous studies have advocated using SNB only for N0 pts and for early T 31 32, as used outside these circumstances, SNB may cause errors and inconsistencies. In addition, large tumours would hardly be surrounded by radiotracer and would drain to multiple lymphatic basins 8 31. We use the technique for negative sides of the neck, even in larger tumours and have not found any major difficulties. The use of SNB is also possible in patients with tumours close to the midline, with one clinically positive side, where it is necessary to clarify the actual need of contralateral dissection. In this case, there is still no consensus on the best option, and certainly SN can be of assistance 11. Prognosis of patients is poor if the SN is histologically metastatic (pN+) ³², compared to pN-, but this is in agreement with the general consensus that pN-have better outcomes than pN+.

The sensitivity of the method in the present study was satisfactory (87%), with a false negative rate of 5.2%. Today, after years of experience in several centres, with improvements in the method, it is accepted that the percentage of false-negative SN should be below 5% ⁸. Considering the suggested scenarios, even if these are purely hypothetical conditions, this data can be compared with the possible regional recurrence rate with the more recent literature and with data from our previous experience.

Regional recurrences are reported after elective dissection of a N0 neck by the meta-analysis of Fasunla ³³ in 6-30% of cases, by Liu ³⁴ in 14.8%, by Ebrahimi ³⁵ in 7% and by Deganello ³⁶ in 6.25%. In a previous analysis of comprehensive neck dissection, we ³⁷ reported regional recurrences in 3.2% (8/250) of cases after elective dissections; in a subsequent report of elective SND, we had only 1/310 isolated nodal recurrence (unpublished data, presented at Round Table Elective Neck Treatment at SIO Annual Meeting, Bologna 2006).

In the hypothesis that only SN would be resected (Scenario 1), the probability of neck relapse would be 6.5%. Comparing Scenario 2 to the other scenarios, i.e. where we would have hypothetically made dissection from the tumour to the level of SN (Scenario 3), performed SND (Scenario 4), made dissection from level I to IV (Scenario 5) or systematically dissected from level I to V (Scenario 6), the only statistical difference as between scenario 2 and 5 or scenario 2 and 6, which are obviously safer, although more extended.

More extended surgery means a considerable number of levels will be unnecessarily dissected, in addition to longer surgical time, higher costs and greater morbidity. Postoperative morbidity should not be disregarded if it does not add a significant advantage. Functional outcomes after SNB are recognized as significantly better than after SND. However, this is not reflected in the score of quality of life questionnaires ¹⁵, and the perception of the patient is probably as important as all functional items. A convenient compromise for NO patients needing elective neck treatment may be dissection from the site of tumour to the level containing the SN(s).

Conclusions

SNB is technically feasible, and after the initial acquisition of experience by a multidisciplinary team can be safely used. Nevertheless, the role of SNB in HNSCC is still undecided. Surgeons should be aware that these patients have a N0 neck and good prognosis, and that elective SND has proven reliability and worldwide acceptance. The SN concept defines the surgical approach to a N0 neck, tailoring the dissection on the lymphatic drainage pattern to the specific patient.

The minimum investigational treatment of the neck is likely to be dissection of the levels from the site of tumour to the level containing the SN(s). At any rate, while awaiting the results of large prospective studies, clearly demonstrating the utility of the procedure as for the cutaneous melanoma, the definitive practical conclusion should be left to the surgeon who may consider risks and benefits faced by the individual patient with head and neck N0 cancer.

References

- ¹ Kuriakose MA, Trivedi NP. *Sentinel node biopsy in head and neck squamous cell carcinoma*. Curr Opin Otolaryngol Head Neck Surg 2009;17:100-10.
- ² Layland MK, Sessions DG, Lenox J. The influence of lymph node metastasis in the treatment of squamous cell carcinoma of the oral cavity, oropharynx, larynx and hypopharynx: NO versus N+. Laryngoscope 2005;115:629-39.
- ³ Farias TP, Peryassu BC, Rezende JF, et al. Analise critica da aplicação da pesquisa do linfonodo sentinela no tratamento do cancer inicial de boca. Rev Bras Cir Cabeça e Pescoço 2009;38:98-102.
- Stoeckli SJ, Alkureishi LWT, Ross GL. Sentinel node biopsy for early oral and oropharyngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol 2009;266:787-93.
- Chone CT, Sampaio MH, Gripp FM, et al. *Estudo da biopsia* de linfonodo sentinela em pacientes com carcinoma epidermoide de cabeça e pescoço com pescoços N0. Rev Bras Cir Cabeça e Pescoço 2006;35:51-6.
- 6 Alkureishi LWT, Ross GL, MacDonald DG, et al. Sentinel node in head and neck cancer: use of size criterion to upstage the N0 neck in head and neck squamous cell carcinoma. Head Neck 2007;29:95-103.
- Hart RD, Nasser JG, Trites JR, et al. Sentinel lymph node biopsy in NO squamous cell carcinoma of the oral cavity and oropharynx. Arch Otolaryngol Head Neck Surg 2005;131:34-8.
- 8 Alkureishi LWT, Burak Z, Alvarez JA, et al. Joint practice guidelines for radionuclide lymphoscintigraphy for sentinel node localization in oral/oropharyngeal squamous cell carcinoma. Ann Surg Oncol 2009;16:3190-210.
- ⁹ Barzan L, Sulfaro S, Alberti F, et al. *Gamma probe accuracy in detecting the sentinel lymph node in clinically NO squamous cell carcinoma of the head and neck*. Ann Otol Rhinol Laryngol 2002;111:794-8.
- Hoft S, Maune S, Muhle C, et al. Sentinel lymph-node biopsy in head and neck cancer. Br J Cancer 2004;91:124-8.
- Barzan L, Sulfaro S, Alberti F, et al. An extended use of the sentinel node in head and neck squamous cell carcinoma: results of a prospective study of 100 patients. Acta Otorhinolaryngol Ital 2004;24:145-9.
- Estabrook CB, Estabrook GF. Actus: a solution to the problem of small samples in the analyses of two-way contingency tables. Historical Meth 1989;82:5-8.
- Fleiss JL, Levin B, Cho Paik M. Statistical methods for rates and proportions. Hoboken, NJ: Wiley; 2003. p. 798.
- ¹⁴ Burba N, Feoli E, Malaroda M. MATEDIT: a software to in-

- tegrate information in decision making progress. In Neves R, Baretta JW, Mateus M. Perspectives on Integrated Coastal Zone Management in South America. Lisboa: IST Press; 2008. p. 123-7.
- Schiefke F, Akdemir M, Weber A, et al. Function, postoperative morbidity, and quality of life after cervical sentinel node biopsy and after selective neck dissection. Head Neck 2009;31:503-12.
- Murer K, Huber GF, Haile SR, et al. 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 2011;33:1260-4.
- Stoeckli SJ, Alkureishi LW, Ross GL. Sentinel node biopsy for oreal and oropharyngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol 2009;266:787-93.
- Burns P, Foster A, Walshe P, et al. Sentinel lymph node biopsy in node-negative squamous cell carcinoma of the oral cavity and oropharynx. J Laryngol Otol 2009;123:439-43.
- ¹⁹ Ross GL, Shoaib T, Soutar DS, et al. The first international conference on sentinel node biopsy in mucosal head and neck cancer and adoption of a multiceter trial protocol. Ann Surg Oncol 2002;9:406-10.
- Werner JA, Dünne AA, Ramaswamy A, et al. Number and location of radiolabeled, intraoperatively identified sentinel nodes in 48 head and neck cancer patients with clinically staged N0 and N1 neck. Eur Arch Otorhinolaryngol 2002;259:91-6.
- ²¹ Hu G, Zhong S, Xiao Q, et al. Radiolocalization of sentinel lymph nodes in clinically N0 laryngeal and hypopharyngeal cancers. Ann Otol Rhinol Laryngol 2011;120:345-50.
- Stoeckli SJ, Alkureishi LWT, Ross GL. Sentinel node biopsy for early oral and oropahryngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol 2006;266:787-93.
- ²³ Werner JA, Dünne AA, Ramaswamy A, et al. *The sentinel node concept in head and neck cancer: solution for the controversies in the N0 neck?* Head Neck 2004;26:603-1.
- ²⁴ Gallegos-Hernandez JF, Hernandez-Hernandez DM, Flores-Diaz R, et al. *The number of sentinel nodes identified as* prognostic factor in oral epidermoid cancer. Oral Oncol 2005;41:947-52.
- ²⁵ Bilde AB, von Buchwald C, Therkildsen MH, et al. *Need for*

- intensive histopathologic analysis to determine lymph node metastases when using sentinel node biopsy in oral cancer. Laryngoscope 2008;118:408-14.
- ²⁶ Keski-Säntti H, Kontio R, Törnwall J, et al. Sentinel node biopsy or elective neck dissection for patients with oral squamous cell carcinoma? Eur Arch Otorhinolaryngol 2008;265(Suppl):S13-S17.
- Stoeckli SJ. Sentinel node biopsy for oral and oropharyngeal squamous cell carcinoma of the head and neck. Laryngoscope 2007;117:539-51.
- Werner JA. Selective sentinel lymphadenectomy for head and neck squamous cell carcinoma. Cancer Treat Res 2005;127:187-206.
- Atula T, Shoaib T, Ross GL, et al. How many sentinel nodes should be harvested in oral squamous cell carcinoma? Eur Arch Otorhinolaryngol 2008;265 Suppl:S19-S23.
- ³⁰ Shoaib T, Soutar DS. Sentinel node biopsy in head and neck cancer. Curr Opin Otolaryngol Head Neck Surg 2001;9:79-84.
- ³¹ Stoeckli SJ, Pfaltz M, Ross GL, et al. *The second international conference on sentinel node biopsy in mucosal head and neck cancer*. Ann Surg Oncol 2005;12:919-24.
- ³² Kovacs AF, Stefenelli U, Seitz O, et al. Positive Sentinel Lymph nodes are negative prognostic factor for survival in T1-2 Oral/Oropharyngeal cancer – A long-term study on 103 patients. Ann Surg Oncol 2009;16:233-9.
- ³³ Fasunla AJ, Greene BH, Timmesfeld N, et al. A meta-analysis of the randomized controlled trials on elective neck dissection versus therapeutic neck dissection in oral cavity cancers with clinically node-negative neck. Oral Oncol 2011;47:320-4.
- ³⁴ Liu TR, Chen FJ, Yang AK, et al. Elective neck dissection in clinical stage I squamous cell carcinoma of the tongue: does it improve regional control or survival time? Oral Oncol 2011;47:136-41.
- Ebrahimi A, Ashford BG, Clark JR. Improved survival by elective neck dissection in thick early stage oral squamous cell carcinoma. Head Neck 2011; DOI:10.1002/hed. 21809.
- Deganello A, Gitti G, Meccariello G, et al. Effectiveness and pittfalls of elective neck dissection in N0 laryngeal cancer. Acta Otorhinolaryngol Ital 2011;31:216-21.
- Barzan L, Talamini R. Analysis of prognostic factors for recurrence after neck dissection. Arch Otolaryngol Head Neck Surg 1996;122:1299-302.

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Address for correspondence: Dr. Luigi Barzan, Azienda Ospedaliera "Santa Maria degli Angeli", Struttura Complessa ORL, Padiglione B, via Montereale 24, 33170 Pordenone, Italy. Tel. +39 0434 399510, +39 0434 399568. Fax +39 0434 399753. E-mail: luigi.barzan@aopn.fvg.it