Multicentric Prospective Study on the Prevalence of Sublevel IIB Metastases in Head and Neck Cancer

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Objective: To evaluate the prevalence of sublevel IIB lymph node (LN) metastases for head and neck primary tumors in a large cohort of patients.

Design: Prospective study.

Setting: One referral university hospital and 2 national institutes of oncology.

Patients: Between 2003 and 2005, 297 patients (male to female ratio, 3.5:1; mean age, 58.8 years [range, 18-89 years]) affected by head and neck cancer were treated by surgery on the primary tumor and/or the neck. Primary site distribution included the following: oral cavity in 111 patients, larynx in 92, oropharynx in 32, thyroid gland in 22, skin of the lateral face or scalp in 16, hypopharynx in 11, unknown primary in 7, and parotid gland in 6. Sublevel IIB was evaluated for the number of LNs and pathologic N (pN) status.

Interventions: All patients underwent unilateral or bilateral neck dissection (ND) with therapeutic or elective intent according to the primary site and clinical T (cT) and clinical N (cN) status. Sublevel IIB was selectively dissected at the beginning of ND, labeled, and processed independently.

Main Outcome Measures: The distribution of metastases among the different levels was analyzed. The influence of several factors (institution in which the surgical procedure was performed, sex of the patient, site of primary, histotype, pathologic T [pT] status, cN status, lower level involved in the neck together with sublevel IIB, association with sublevel IIA metastasis, ipsilateral number of involved levels, and previous surgical treatment limited on the primary site) on the prevalence of sublevel IIB metastasis was statistically evaluated by the Pearson χ^2 test or Fisher exact test.

Results: A total of 443 NDs were performed (unilateral in 151 patients and bilateral in 146). Among the patients, the tumors were staged cN0/pN0 in 27%, cN+/pN+ in 50%, cN+/pN0 in 7%, and cN0/pN+ in 16%. The mean number of LNs collected at sublevel IIB was 5.4 (range, 0-24). The overall prevalence of sublevel IIB metastases was 5.6% (26 neck sides). Tumor histologic type in the sublevel IIB+ population was squamous cell carcinoma in 80%, papillary carcinoma in 8%, melanoma in 8%, and adenocarcinoma in 4%. The χ^2 test showed a significantly higher risk for LN metastases at sublevel IIB in patients affected by parotid gland primary tumors (33%), tumors of the skin or scalp (25%), unknown primary tumors (14%), and cancers of the oral cavity (10%) ($P=.02$) and in those clinically staged as cN+ ($P<.001$).

Conclusions: Sublevel IIB dissection is strongly recommended for all patients with cN+ tumors and in those affected by tumor of the parotid gland, skin, and scalp scheduled for elective ND. Patients affected by laryngeal cancer scheduled for elective ND can be considered the ideal candidates for preservation of sublevel IIB. However, whether this policy could be associated with a better functional outcome remains to be demonstrated by prospective studies on a large series of patients.

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In 1905 and 1906, George Crile[1,2] published 2 milestone articles emphasizing the crucial role of cervical lymph node (LN) metastasis in the natural history and prognosis of head and neck tumors. He asserted that a "block dissection" of all lymphatic structures from level I to V encompassing the sternocleidomastoid muscle, the internal jugular vein, and the spinal accessory nerve had to be systematically performed to improve the survival rate for patients with clinical N (cN)+ tumors and those with cN0 tumors.[1,2] The idea that neck dissection (ND) may be modulated in relation to specific clinical settings was subsequently developed by Hayes Martin, who introduced the concept of partial ND.[3] Over the next decades, functional (or modified radical)[4,5] and selective NDs[6] were introduced with the intent to combine the oncologic control of disease with improved functional results.

Recently, technical advances in preoperative neck evaluation by ultrasound sonography, computed tomography, and magnetic resonance imaging, a better understanding of metastatic spread along the different levels and sublevels, and the observation of persistent shoulder functional impairment even after spinal accessory nerve–sparing procedures, led to the suggestion of performing a highly selective ND in specific clinical settings, with preservation of submuscular recess fat pad referred to as sublevel IIB.[7-18]

We report herein the results of the largest prospective study, to our knowledge, on patients with head and neck cancer scheduled for sublevel IIB fat pad dissection prior to completion of the surgical procedure on the neck, with the purpose of evaluating the prevalence of metastasis at this site in elective as well as in therapeutic NDs.

METHODS

Between January 2003 and December 2005, 297 consecutive patients (male to female ratio, 3.5:1; mean age, 59 years [range, 18-89 years]) affected by head and neck cancer were treated by surgery on the primary site and/or the neck in 3 different Italian centers: the Department of Otorhinolaryngology at the University of Brescia in Brescia, the Head and Neck Department at the European Institute of Oncology in Milan, and the Department of Otorhinolaryngology at the Regina Elena Institute of Oncology in Rome.

The inclusion criteria for the study were no previous surgery on the lateral compartment of the neck for either benign or malignant lesions, no previous radiation therapy or induction chemotherapy for the malignant neoplasm considered, no previous surgical and/or radiation treatment for other head and neck primary tumors, and the technical feasibility of isolation and dissection of sublevel IIB fat pat from the remainder of the ND (ie, patients with massive metastatic localization involving level II were excluded).

All primary tumors and neck metastases were staged according to the sixth edition of the American Joint Committee on Cancer TNM staging system.[19]

In general, bilateral ND was performed in all cases of medullary carcinoma, in papillary carcinomas with evidence of bilateral nodal disease, and in those squamous cell carcinomas (SCCs) of the upper aerodigestive tract crossing the midline or with preoperative detection of contralateral suspicious LNs. The extent of ND was modulated according to the site of the primary and clinical neck status. Clinical staging of the neck was accomplished by physical examination, combined with ultrasound sonography, computed tomography, or magnetic resonance imaging. Neck dissections were classified according to the latest ND classification update.[20]

The sublevel IIB fat pad was isolated and dissected at the beginning of the surgical procedure, according to the anatomic landmarks provided in the latest ND classification update[20]: starting from the level of the skull base and dissecting posterior and lateral to the vertical plane defined by the spinal accessory nerve back to the posterior border of the sternocleidomastoid muscle. The muscular fascia of the levator scapulae and splenius defined the deep plane of dissection. The LNs isolated over and behind the spinal accessory nerve were always included in sublevel IIB. Once dissected, the fat pad was removed before completing the remainder of the ND, labeled, and processed separately for histopathologic permanent section analysis. This procedure was applied with the specific intent to minimize the bias deriving from separating sublevel IIB from the entire ND specimen without precise anatomic markers. The ND was subsequently completed and the specimen divided in the different levels by the surgeon to improve the accuracy in localization of metastatic disease. All levels were histopathologically evaluated in standard fashion by assessing the overall number of LNs, the number of metastatic LNs, and the presence of extracapsular spread. As agreed by the different pathologists involved in the study, serial sections of the specimen were obtained to identify the lymphatic tissue. The LNs were harvested, and 1 or 2 slices (in relation to LN size) were obtained at the level of the longest axis of each isolated node and stained with hematoxylin-eosin.

Statistical analysis was performed using a commercially available computer software package (SPSS for Windows version 10.0.1; SPSS Inc, Chicago, Illinois). The influence of different factors (institution in which the surgical procedure was performed, sex of the patient, site of primary, histotype, pathologic T [pT] status, cN status, lower level involved in the neck together with sublevel IIB, association with sublevel IIA metastasis, ipsilateral number of involved levels, and previous treatment) on the prevalence of sublevel IIB metastasis was statistically evaluated by cross-tabulation using the Pearson χ^2 test or Fisher exact test when at least 1 cell was expected to count less than 5. $P < .05$ was considered significant.

RESULTS

A wide spectrum of primary sites and histologic types with different propensity to lymphatic spread were included. The primary site distribution included the following: oral cavity in 111 patients (38%), larynx in 92 (31%), oropharynx in 32 (11%), thyroid gland in 22 (8%), skin of the lateral face or scalp in 16 (5%), hypopharynx in 11 (4%), unknown primary in 7 (2%), and parotid gland in 6 (2%). The histologic type of the lesions was SCC in 90% (n=267), papillary carcinoma in 5% (n=15), medullary carcinoma in 2% (n=7), and adenocarcinoma of the parotid gland and melanoma of the skin of the lateral face and scalp in 1.5% (n=4) each.

A total of 443 NDs (unilateral in 151 patients and bilateral in 146) were performed in 166 patients with a clinically positive neck and in 131 for an elective purpose. Surgery on the neck included 11 radical NDs from level I to V including the internal jugular vein, sternocleidomastoid muscle, and spinal accessory nerve; 127 modified radical NDs from level I to V preserving 1, 2, or 3 of the aforementioned nonlymphatic structures; and 305 different selective NDs. Taking into account the entire population, the tumors were staged cN0/pathologic N (pN)0 in 27% (true negatives), cN+/pN+ in 50% (true positive), cN+/pN0 in 7% (false positive), and cN0/pN+ in 16% (occult metastasis). These data are summarized in relation to the site of the primary tumor in **Table 1**.

The mean number of LNs isolated at sublevel IIB was 5.4 (range, 0-24). The overall prevalence of sublevel IIB metastases was 8.4% and 5.8% when patients (25 of 297) or neck sides (26 of 443) were considered, respectively (**Table 2**). The oral cavity was the site of primary tumor in 11 cases (10 cN+ and 1 cN0), skin of the lateral face and scalp in 4 (4 cN+), oropharynx in 2 (1 cN+ and 1 cN0), larynx in 2 (1 cN+ and 1 cN0), parotid gland in 2 (2 cN+), thyroid gland in 2 (2 cN+), hypopharynx in 1 (1 cN+), and unknown primary in 1 (1 cN+). Only 1 case of bilateral involvement of sublevel IIB was observed (see patient 22 in Table 2). Adjunctive details concerning the different levels involved in association with sublevel IIB are listed in Table 2.

The histologic type in the sublevel IIB+ population was SCC in 80% of patients, papillary carcinoma in 8%, mela-

Table 1. Relationship Between Clinical N (cN) and Pathologic N (pN) Lymph Node Status by Site of the Primary Tumor[a]

	cN and pN Status			
Site of Primary Tumor	cN0/pN0	cN+/pN+	cN+/pN0	cN0/pN+
Oral cavity (n=111)	28 (25)	49 (44)	8 (7.5)	26 (23.5)
Larynx (n=92)	35 (38)	33 (36)	9 (10)	15 (16)
Oropharynx (n=32)	5 (24)	20 (54)	2 (10)	5 (12)
Thyroid gland (n=22)	1 (4.5)	20 (91)	0	1 (4.5)
Scalp (n=16)	7 (44)	8 (50)	0	1 (6)
Hypopharynx (n=11)	2 (18)	7 (64)	0	2 (18)
Unknown primary (n=7)	0	7 (100)	0	0
Parotid gland (n=6)	1 (17)	3 (50)	0	2 (33)

[a] Data are given as number (percentage) of patients.

Table 2. Data on the 25 Patients Positive for Metastatic Disease at Sublevel IIB

Patient No.	Site	Histotype	Levels Clinically Involved	Levels Histopathologically Involved	R Neck Levels Dissected	L Neck Levels Dissected	pTNMG	Previous Treatment
1	Tongue	SCC	L: II, III, IV	L: I, IIA, IIB	I-IV	I-V	T2N2b ecs+M0G3	None
2	Cheek, RMT	SCC	R: I, II	R: I, IIA, IIB	I-IV	NP	T3N2b ecs+M0G3	None
3	Tongue	SCC	L: I, II, V	L: I, IIA, IIB, V	NP	I-V	T2N2bM0G2	None
4	Tongue	SCC	R: I	R: I, IIA, IIB, V L: IIA, IV	I-V	I-V	T4aN2cM0G3	None
5	Tongue	SCC	Bilateral nodes	R: IIA, III L: IIA, IIB, III, IV	I-V	I-V	T4aN2cM0G2	None
6	Tongue	SCC		L: IIA, IIB, III	I-V	I-IV	T3N2bM0G1	None
7	FOM	SCC	R: II	R: IIA, IIB	I-V	NP	T1N2bM0G2	None
8	Tongue	SCC	R: II L: II	R: I, IIA, III, IV L: IIB	I-V	I-V	T4aN2cM0G2	None
9	Tongue	SCC	R: II	R: IIA, IIB, IV	I-V	I-III	T4aN2bM0G2	None
10	RMT	SCC	N1	R: IB, IIB, III	I-V	NP	T4aN2bM0G2	None
11	Inferior gingiva	SCC	L: IB	L: IB, IIB	NP	I-V	T4aN2bM0G2	None
12	Scalp	Melanoma	L: II	L: IIB, nucha	NP	II-V	T4aN2bM1	None
13	Scalp	Melanoma	R: II, V	R: IIB, V	II-V	NP	T0N2bM0	Surgery
14	Scalp	SCC	L: II	L: IIA, IIB	NP	II-V	T0N2bM0	Surgery
15	Scalp	SCC	R: II	R: IIA, IIB, IV	II-V	NP	T3N2bM0G3	None
16	Tongue base	SCC	Bilateral nodes	R: IIA, V L: IIB, III, IV	I-V	II-V	T3N2cM0G3	None
17	Tongue base	SCC		L: IIB	NP	II-V	T3N1M0G2	None
18	Supraglottis	SCC	L: II, III, IV	L: IIA, IIB	II-V	I-V	T3N2b ecs+M0G3	None
19	Glottis (transglottic)	SCC		R: IIB	II-IV+VI	NP	T3N1M0G3	None
20	Parotid gland	SCC	L: II, V	L: IIA, IIB, V	NP	II-V	T4aN2b ecs+M0G1	None
21	Parotid gland	AC	R: II, III, V	R: IIA, IIB, V	I-V	NP	T4aN2b ecs+M0	None
22	Thyroid gland	Papillary	R: II, III, IV L: II, III, IV	R: IIB, III, IV, VI L: IIA, IIB, III, IV	II-V+VI	II-IV+VI	T4aN1bM0	None
23	Thyroid gland	Papillary	R: III	R: IIA, IIB, III	II-III	NP	T0N2bM0	Surgery
24	Hypopharynx	SCC	L: II, III	L: IIA, IIB	II-V	II-V	T4aN2bM0G3	None
25	Unknown	SCC	R: II L: II	R: IIA, IIB L: IIA	I-V	II-V	TxN2cM0	None

Abbreviations: AC, adenocarcinoma; ecs, extracapsular spread; FOM, floor of mouth; L, left side; NP, not performed; pTNMG, pathologic TNM and grading; R, right side; RMT, retromolar trigone; SCC, squamous cell carcinoma.

noma in 8%, and adenocarcinoma in 4%. All 3 cases (1% of the patient population and 0.7% of the dissected neck sides) that were cN0/pN+ at sublevel IIB (2 pN1 and 1 pN2b) had a locally advanced SCC of the upper aerodigestive tract (see patients 6, 17, and 19 in Table 2). In 2 cases, metastasis exclusively involved 1 LN at sublevel IIB.

The results of the statistical analysis evaluating the impact of several clinical factors on sublevel IIB LN involvement are reported in **Table 3**. A higher risk for metastasis at sublevel IIB was detected in the parotid gland, skin of the lateral face and scalp, and unknown primary tumors ($P = .02$). The oral cavity was the primary site among those of the upper aerodigestive tract, with the highest prevalence of metastasis at this sublevel (10%); by contrast, the lowest prevalence (2%) was observed in laryngeal cancers.

A comparison between SCC and non-SCC histologic type did not reach statistical significance ($P = .11$). Con-

Table 3. Analysis by Pearson χ^2 Test or Fisher Exact Test of the Impact of 9 Variables on the Prevalence of Sublevel IIB Metastatic Involvement

Factor	Prevalence of IIB metastasis, No./Total No. (%)	*P* Value
Institution in Italy		
Brescia	11/141 (8)	.49
Milan	12/117 (10)	
Rome	2/39 (5)	
Sex		
Male	17/230 (7)	.23
Female	8/67 (12)	
Site		
Unknown	1/7 (14)	.02
Oral cavity	11/111 (10)	
Skin/scalp	4/16 (25)	
Hypopharynx	1/11 (9)	
Larynx	2/92 (2)	
Oropharynx	2/32 (6)	
Parotid gland	2/6 (33)	
Thyroid gland	2/22 (9)	
Histotype (1)		
SCC	20/267 (8)	.11
Non-SCC	5/30 (17)	
Histotype (2)		
SCC	20/267 (8)	.02
Adenocarcinoma	1/4 (25)	
Melanoma	2/4 (50)	
Medullary carcinoma	0/7	
Papillary carcinoma	2/15 (13)	
pT status		
pT0	3/29 (10)	.13
pT1	0/33	
pT2	3/69 (4)	
pT3	6/75 (8)	
pT4	12/82 (15)	
pTx	1/7 (14)	
cN status		
cN0	3/131 (2)	<.001
cN+	22/166 (13)	
Lower level involved		
I	1/17 (6)	.74
II	7/65 (11)	
III	3/41 (7)	
IV	5/40 (12.5)	
V	6/27 (22)	
VI	1/7 (14)	
Sublevel IIA involved		
Yes	19/131 (14)	.08
No	4/66 (6)	
Ipsilateral involved levels		
1 Level	8/107 (7)	.15
2 Levels	10/55 (18)	
3 Levels	4/23 (17)	
4 Levels	1/9 (11)	
5 Levels	0/3	
Previous surgical treatment on the site of primary		
Yes	2/32 (6)	>.99
No	23/265 (9)	

Abbreviations: cN, clinical N; SCC, squamous cell carcinoma; pN, pathologic N; pT, pathologic T.

versely, when all different histotypes (SCC, adenocarcinoma, melanoma, medullary, and papillary carcinoma) were considered, the results paralleled those obtained by analysis of primary sites ($P = .02$). This probably reflects the preference of the different histologic types for specific sites.

Moreover, the possibility to find a metastatic localization at sublevel IIB in a patient without clinical evidence of LN metastasis (cN0) was significantly lower than the probability of the same finding in patients staged as cN+ ($P < .001$). When considering synchronous metastatic involvement of sublevel IIA and IIB, in our series, this finding was observed in 65% (17 of 26) NDs and 63% (10 of 16) NDs of all head and neck primary tumors and SCCs of the upper aerodigestive tract, respectively, although the finding was nonsignificant ($P = .08$).

COMMENT

The pN status is generally considered the most important prognostic factor in patients with head and neck cancer and, in fact, the presence of nodal metastasis is estimated to decrease determinate survival by about 50%.[21,22] Nevertheless, ND is a surgical procedure with remarkable sequelae that can influence the residual quality of life. Shoulder disability is one of the most important morbidities traditionally associated with radical ND characterized by shoulder drop, scapular flaring, pain, and weakness. A large spectrum of different procedures is presently available for treatment of LN metastasis, but the anatomic preservation of the spinal accessory nerve is not always associated with normal shoulder function. In fact, only 70% to 75% of patients who underwent to nerve-sparing dissections did not report any shoulder disability.[23,24] The clearance of the submuscular recess inevitably causes mechanical traction and ischemic trauma on the cranial portion of the spinal accessory nerve running from the skull base to its entrance into the sternocleidomastoid muscle. In fact, the vascular supply to the nerve originates from the surrounding fat tissue with a segmental pathway, with unavoidable ischemic insult when dissection of both sublevels IIA and IIB is performed. The analysis of our data and review of the literature on the prevalence of sublevel IIB metastasis for head and neck SCC and non-SCCs (**Table 4**) suggests that for a specific subset of patients dissection of sublevel IIB could be reasonably avoided with the intent of minimizing functional impairment of the shoulder.

Kraus et al[7] prospectively evaluated the prevalence of occult nodal metastasis in selective ND specimens (levels I-III) for oral and oropharyngeal primary tumors, with only 1 case (2.1%) observed in a patient affected by a cT3N0 tonsil cancer who had concomitant occult disease at both sublevels IIA and IIB. Two years later, Talmi et al[8] studied a series of patients with different head and neck primary tumors and attempted to define risk factors for metastasis involving LNs of the submuscular recess. Based on the observation of metastasis at this level in only 4 patients with cN2-cN3 tumors (3.9%), they concluded that dissection of this lymphatic station could be avoided in elective NDs. In 2 of the 4 cases, the oral cavity was the site of the primary tumor. Chone et al[9] reported SCC metastatic spread to sublevel IIB in 6.5% of NDs, which was always in conjunction with other lym-

Table 4. Metastatic Involvement of Sublevel IIB: Review of the Literature

Source	Type of Study	No. of NDs	Type of NDs	Sites	Histotype	IIB+, No. (%)	Exclusive IIB+, No.	Remarks
Kraus et al,[7] 1996	Prospective	47	Elective	OC, OP	SCC	1 (2.1)	0	. . .
Talmi et al,[8] 1998	Prospective	102	Elective and therapeutic	OC, OP, L, S, UP, others	SCC	4 (3.9)	0	. . .
Chone et al,[9] 2000	Retrospective	62	Elective and therapeutic	OC, OP, HP, L, UP	SCC	4 (6.5)	0	Significant correlation between IIB Mets and IIA-III Mets ($P<.05$)
Talmi et al,[10] 2001	Prospective	37	Elective and therapeutic	TG, PG, S, others	Non-SCC	6 (16)	0	100% Of cases with IIA Mets also reported IIB Mets
Koybasioğlu et al,[11] 2002	Prospective	53	Elective and therapeutic	L	SCC	0 (0)	0	. . .
Silverman et al,[12] 2003	Prospective	90	Elective and therapeutic	OC, OP, HP, L, UP, others	SCC	4 (4.4)	0	Significant correlation between IIB Mets and high pN status ($P=.003$) and between IIB Mets and IIA Mets ($P=.001$)
Coskun et al,[13] 2004	Prospective	113	Elective	L	SCC	0	0	. . .
Lim et al,[14] 2004	Prospective	74	Elective	OC	SCC	4 (5.4)	0	. . .
Corlette et al,[15] 2005	Prospective	160	Elective and therapeutic	OC, OP, HP, L, S, PG	SCC	30 (18.7)	10 (S, PG)	Significant correlation between IIB Mets and S and PG primary tumors ($P<.05$)
Elsheikh et al,[16] 2005	Prospective	74	Elective	OC	SCC	5 (6.7)	0	Molecular analysis of lymphatic tissue
Elsheikh et al,[17] 2006	Prospective	51	Elective	L	SCC	1 (2)	1 (L)	Molecular analysis of lymphatic tissue
Lim et al,[18] 2006	Prospective	125	Elective and therapeutic	L	SCC	8 (6.4)	0	Significant correlation between IIB Mets and cN+ status ($P<.001$) and between IIB Mets and presence of other metastatic LNs ($P=.001$)
Present series, 2006	Prospective	443	Elective and therapeutic	OC, OP, HP, L, PG, TG, S, UP	SCC and non-SCC	26 (5.6)	2 (1 OP, 1 L)	Significant correlation between IIB Mets and cN+ status ($P<.001$) and IIB Mets and the site of primary tumor ($P=.02$)

Abbreviations: cN, clinical N; HP, hypopharynx; L, larynx; Mets, metastasis; LNs, lymph nodes; NDs, neck dissections; OC, oral cavity; OP, oropharynx; PG, parotid gland; pN, pathologic N; S, skin/scalp; SCC, squamous cell carcinoma; TG, thyroid gland; UP, unknown primary.

phatic localizations, with 1 case only of occult disease. They concluded that dissection of the "apex" is especially warranted in patients with cN+ tumors and pharyngeal lesions. The limitations of that study were its retrospective nature and the tagging of the sublevel IIB made on the ND specimen.

Silverman et al,[12] considering SCC of all head and neck sites, found metastatic localization at sublevel IIB in 4 NDs (4.4%), but only 1 of these cases (1.6%) was clinically staged as N0 and therefore affected by occult metastasis. They reported a higher prevalence of sublevel IIB metastasis in patients with advanced pN status ($P=.003$) and in those with metastatic disease involving sublevel IIA ($P=.001$). They concluded that sublevel IIB fat pad dissection could be avoided during elective NDs or for limited nodal disease not involving sublevel IIA.

In one of the most extensive series reported in the literature, Corlette et al[15] demonstrated that the prevalence of sublevel IIB metastasis may increase as high as 18.7% because of the inclusion of the parotid gland and skin of the lateral face and the scalp among the primary sites considered, with overall values of 50% for both sites. In contrast, no cases of laryngeal and hypopharyngeal primary tumors with sublevel IIB metastatic spread were reported.

In 2001, Talmi and coworkers[10] expanded their experience on the issue, focusing on non-SCC of the head and neck region. The sites analyzed are listed in Table 4, and the prevalence of sublevel IIB metastasis was 16%. Most of the cases were cN+ (78%), and at least 1 other level was always involved in tumor spread. In the absence of statistical analysis, it was concluded that in the case of cN+ primary tumors of the parotid and thyroid glands, with a prevalence of submuscular recess metastatic spread of 43% and 11%, respectively, sublevel IIB dissection should be strongly advocated. This concept was also confirmed by our data: in fact, 91% of thyroid gland and 50% of parotid gland primary tumors were cN+, with a prevalence of sublevel IIB metastasis of 33.3% and 8.7%, respectively. Whenever primary tumors arising from the parotid gland, the skin of the lateral face, and the scalp were included in the analysis, the prevalence of submuscular recess metastatic spread increased, not only because of the high percentage of cN+ cases[10,15] but also because, independently of histologic type, this LN echelon is one of the first involved by tumor spread from these specific sites.[20]

Several reports have specifically focused on laryngeal primary tumors, considering both elective and therapeutic settings.[11,13,17,18] Exclusive sublevel IIB metastatic localization was detected in 1 specimen

(2%) from 51 elective NDs after molecular analysis by nested reverse transcription polymerase chain reaction for cytokeratin 19 and cytokeratin 20.[17] In contrast, in a larger series of laryngeal primary tumors, a 6.4% prevalence of sublevel IIB involvement was detected, 1% for patients scheduled for elective NDs and 30% for those scheduled for therapeutic NDs, with no cases of exclusive sublevel IIB localization.[18] These data provide a high degree of evidence for the negligible involvement of submuscular recess LNs in patients scheduled for elective ND for laryngeal primary tumors. In our series, considering the 50 patients affected by cN0 laryngeal cancer, only a single case (2%) of exclusive sublevel IIB metastatic localization was observed (patient 19 in Table 2).

There are only 2 studies that have focused on SCC of the oral cavity: in both reports, only elective NDs were evaluated with a relatively high frequency of sublevel IIB occult localization (5.4% and 6.7%, respectively).[14,16] Our experience also indicates that the oral cavity has the highest overall prevalence of sublevel IIB metastasis (10%) among SCCs arising from the upper aerodigestive tract (Table 3), but with a lower prevalence in the cN0 setting (2%) compared with those reported in the literature.

In conclusion, our multicentric prospective study analyzed a wide range of head and neck cancers with squamous and nonsquamous histologic type, involving most primary sites (except paranasal sinuses and nasopharynx), with the intent to provide information on sublevel IIB metastatic involvement. The data collected reinforce the concept already reported in the literature that sublevel IIB dissection is strongly recommended for all patients with cN+ tumors and in those with a tumor of the parotid gland, skin of the lateral face, and scalp scheduled for elective ND.

A major limitation in our study is the small number of patients considered for some specific sites, such as the hypopharynx and parotid gland, which can be considered a source of bias for statistical analysis. The reasons for this distribution can be identified in our management policy, which mainly includes chemoradiation for the primary treatment of hypopharyngeal cancer and rarely requires ND for parotid primary tumors.

Furthermore, patients with cN0 laryngeal primary tumors scheduled for elective ND appeared to be the ideal population for further studies aimed at prospective assessment of whether preservation of sublevel IIB is associated with an improvement in shoulder function using clinical and electromyographic evaluations.

Data from the first preliminary report concerning this issue did not provide encouraging results, with no functional shoulder improvement and a similar axonal deterioration in patients who did not undergo sublevel IIB dissection.[25] However, the small number of patients (n=10) and the early timing of postoperative control (third postoperative month) suggest that further investigations on a large cohort of patients with adequate timing for postoperative evaluation are required. Moreover, additional measures could be adopted to reduce shoulder disability, such as meticulous preservation, when possible, of cervical branches (C2-C4) during ND and a systematic postoperative physical therapy.

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REFERENCES

1. Crile GW. On the surgical treatment of cancer of the head and neck: with a summary of one hundred and twenty-one operations performed upon one hundred and five patients. *Trans South Surg Gynecol Assoc*. 1905;18:108-127.
2. Crile GW. Excision of cancer of the head and neck—with special reference to the plan of dissection based on one hundred and thirty-two operations. *JAMA*. 1906;47:1780-1786.
3. Martin HE, Del Valle B, Ehrlich H, et al. Neck dissection. *Cancer*. 1951;4(3):441-499.
4. Suarez O. El problema de las metastasis linfaticas y alejadas del cancer de laringe e hipofaringe. *Rev Otorrinolaringol*. 1963;23:83-99.
5. Bocca E. Supraglottic laryngectomy and functional neck dissection. *J Laryngol Otol*. 1966;80(8):831-836.
6. Shah JP. Patterns of cervical lymph node metastasis from squamous cell carcinomas of the upper aerodigestive tract. *Am J Surg*. 1990;160(4):405-409.
7. Kraus DH, Rosemberg DB, Davidson BJ, et al. Supraspinal accessory lymph node metastases in suprahomohyoid neck dissection. *Am J Surg*. 1996;172(6):646-649.
8. Talmi YP, Hoffman HT, Horowitz Z, et al. Patterns of metastases to the upper jugular lymph nodes (the "submuscular recess"). *Head Neck*. 1998;20(8):682-686.
9. Chone CT, Crespo AN, Rezende AS, Carvalho DS, Altemani A. Neck lymph node metastases to the posterior triangle apex: evaluation of clinical and histopathological risk factors. *Head Neck*. 2000;22(6):564-571.
10. Talmi YP, Horowitz Z, Wolf M, et al. Upper jugular lymph nodes (submuscular recess) in non-squamous-cell cancer of the head and neck: surgical considerations. *J Laryngol Otol*. 2001;115(10):808-811.
11. Koybasioğlu A, Uslu S, Yilmaz M, Inal E, Ileri F, Asal K. Lymphatic metastasis to the supraretrospinal recess in laryngeal squamous cell carcinoma. *Ann Otol Rhinol Laryngol*. 2002;111(1):96-99.
12. Silverman DA, El-Hajj M, Strome S, Esclamado RM. Prevalence of nodal metastases in the submuscular recess (level IIb) during selective neck dissection. *Arch Otolaryngol Head Neck Surg*. 2003;129(7):724-728.
13. Coskun HH, Erisen L, Basut O. Selective neck dissection for clinically N0 neck in laryngeal cancer: is dissection of level IIb necessary? *Otolaryngol Head Neck Surg*. 2004;131(5):655-659.

14. Lim YC, Song MH, Kim SC, Kim KM, Choi EC. Preserving level IIb lymph nodes in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg*. 2004;130(9):1088-1091.
15. Corlette TH, Cole IE, Albsoul N, Ayyash M. Neck dissection of level IIb: is it really necessary? *Laryngoscope*. 2005;115(9):1624-1626.
16. Elsheikh MN, Mahfouz ME, Elsheikh E. Level IIb lymph nodes metastasis in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma: a molecular-based study. *Laryngoscope*. 2005;115(9):1636-1640.
17. Elsheikh MN, Mahfouz ME, Salim EI, Elsheikh EA. Molecular assessment of neck dissections supports preserving level IIB lymph nodes in selective neck dissection for laryngeal squamous cell carcinoma with a clinically negative neck. *ORL J Otorhinolaryngol Relat Spec*. 2006;68(3):177-184.
18. Lim YC, Lee JS, Koo BS, Choi EC. Level IIb lymph node metastasis in laryngeal squamous cell carcinoma. *Laryngoscope*. 2006;116(2):268-272.
19. Greene FL, Page DL, Fleming ID, et al. *AJCC Cancer Staging Manual.* 6th ed. New York, NY: Springer; 2002.
20. Robbins KT, Clayman G, Levine PA, et al; American Head and Neck Society; American Academy of Otolaryngology–Head and Neck Surgery. Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology–Head and Neck Surgery. *Arch Otolaryngol Head Neck Surg*. 2002;128(7):751-758.
21. Shah JP, Andersen PE. Evolving role of modifications in neck dissection for oral squamous carcinoma. *Br J Oral Maxillofac Surg*. 1995;33(1):3-8.
22. Puri SK, Fan CY, Hanna E. Significance of extracapsular lymph node metastases in patients with head and neck squamous cell carcinoma. *Curr Opin Otolaryngol Head Neck Surg*. 2003;11(2):119-123.
23. Leipzig B, Suen JY, English JL, Barnes J, Hooper M. Functional evaluation of the spinal accessory nerve after neck dissection. *Am J Surg*. 1983;146(4):526-530.
24. Cappiello J, Piazza C, Giudice M, De Maria G, Nicolai P. Shoulder disability after different selective neck dissections (levels II-IV versus levels II-V): a comparative study. *Laryngoscope*. 2005;115(2):259-263.
25. Koybasioğlu A, Bora Tokcaer A, Inal E, Ulsu S, Kocak T, Ural A. Accessory nerve function in lateral selective neck dissection with undissected level IIb. *ORL J Otorhinolaryngol Relat Spec*. 2006;68(2):88-92.