Original Article

BREAST CANCER SURGICAL MANAGEMENT OF THE AXILLA: A NATIONAL PORTRAIT COMPARED TO INTERNATIONAL CONSENSUS (PART 2)

TRATAMENTO CIRÚRGICA DA AXILA NO CANCRO DA MAMA: UM RETRATO NACIONAL COMPARADO COM O CONSENSO INTERNACIONAL (PARTE 2)

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Received: 17/04/2024 *Accepted:* 06/06/2024 *Published online:* 27/07/2024

ABSTRACT

Purpose: The Chapter on Breast Surgery of the Portuguese Society of Surgery aimed to find out from hospitals that treat breast cancer (BC) their contemporary surgical management of the axilla. **Methods:** Forty-five hospitals were invited to participate in a nationwide survey in March 2023. A qualitative and quantitative description was made. A complementary comparison with national and international BC clinical guidelines was performed. **Results:** We received 38 responses (84.4%). To define a negative axilla, 65.8% required physical examination plus axillary ultrasound (US).

ISSN: 1646-6918 eISSN: 2183-1165

A positive axilla requires lymph node US-guided biopsy (core biopsy in 76.3% and fine-needle cytology in 52.6%). Most (94.7%) used a combined dual tracer for sentinel node biopsy (SNB). Tc99 plus Patent Blue was the most common (76.3%). Intraoperative pathology was routinely performed in 52.6%. Omission of SNB was consensual in DCIS (86.8%), 68.4% considered it in older patients, but only 2.6% proposed it in low-risk invasive BC. There was a consensus (92.1%) to omit axillary lymph node dissection (ALDN) when one or two positive sentinel nodes were identified intraoperatively in an initially c/uN0 axilla. To perform a targeted axillary dissection (TAD) in a suspicious/positive axilla, 42.1% reported that one or two nodes were biopsied and marked. The most common localization technique was a titanium clip in 84.2% (only 36.8% were US-visible clips). For the cN1 axilla, the majority preferred ALND for upfront surgery (60.5%) or in the absence of a radiological complete response (uCR) after primary systemic therapy (PST)(63.2%). For uCR after PST, 86.8% favoured SNB plus TAD, with a consensus (92.1%) to omit ALND for pathologic complete response in the axilla. Our survey was unable to assess the morbidity of axillary surgery as outcome registries were found in only 42.1% of hospitals. **Conclusion:** De-escalation of surgical management of the axilla has been followed in most hospitals in this national portrait. SNB has long been the standard of care for cN0 axilla. A trend toward more conservative multidisciplinary management of positive axilla has also been noted, with the progressive omission of ALND in favour of TAD and axillary RT.

Keywords: *breast cancer units, organization, surgical management of the axilla.*

RESUMO

Introdução: O Capítulo de Cirurgia da Mama da Sociedade Portuguesa de Cirurgia procurou avaliar, junto dos hospitais portugueses que tratam cancro da mama, qual é sua atual abordagem cirúrgica da axila. **Métodos:** Quarenta e cinco hospitais foram convidados a participar num inquérito a nível nacional em março de 2023. Foi feita uma descrição qualitativa e quantitativa. Adicionalmente realizou-se uma comparação com as atuais recomendações científicas nacionais e internacionais. **Resultados:** Tivemos 38 (84,4%) respostas. Para definir clinicamente uma axila como negativa (c/uN0), 65,8% consideraram ser necessário complementar o exame físico com uma ecografia axilar. Considerar uma axila positiva, obriga a uma biópsia ecoguiada de um gânglio axilar (por agulha grossa em 76,3% e por citologia em 52,6%). Para a biópsia do gânglio sentinela (SNB), a maioria (94,7%) recorreu a um marcador duplo, sendo a combinação Tecnésio99 e Azul patente a mais usada (76,3%). O estudo patológico intraoperatório foi realizado por rotina em 52,6%. Houve um consenso (86,8%) na omissão da SNB no carcinoma ductal insitu (DCIS). Uma maioria (68,4%) também a considerou em doentes mais velhas, mas apenas 2,6% a defenderam num carcinoma invasor de baixo risco. Verificou-se um consenso (92,1%) para a omissão do esvaziamento axilar (ALND) perante a identificação intraoperatória de um ou dois gânglios sentinela positivos, numa axila inicialmente c/uN0. Para realizar uma disseção axilar dirigida (TAD) numa axila inicialmente suspeita ou positiva, 42,1% defenderam que um ou dois gânglios devem ser biopsados e marcados. Um clipe de titânio foi a técnica de marcação mais usada (84,2%, dos quais apenas 36,8% eram clipes ecovisíveis). Numa axila cN1, o ALND foi a primeira opção quando se decidiu avançar primariamente para cirurgia (60,5%) ou perante a ausência de resposta imagiológica completa (uCR) após a terapêutica primária sistémica (PST)(63,2%). Quando houve uCR após PST, a opção foi fazer SNB associado ao TAD por 86,8%, com consenso (92,1%) na omissão do ALND perante uma resposta patológica completa (pCR) na axila. Não conseguimos avaliar a morbidade da cirurgia axilar, por falta de registos adequados (42,1%). **Conclusão:** Neste retrato nacional, constatou-se um desescalar do estadiamento cirúrgico da axila na maioria dos hospitais nacionais. A SNB é o procedimento standard na axila c/uN0. Também se observou uma tendência para uma abordagem multidisciplinar mais conservadora na axila positiva, com a omissão progressiva do ALND em favor da TAD e da radioterapia axilar.

Palavras chave: *unidades de cancro da mama, organização, tratamento da axila*

ISSN: 1646-6918

eISSN: 2183-1165

INTRODUCTION

The Chapter of Breast Surgery of the Portuguese Society of Surgery (SPCIR) has invited hospitals treating breast cancer (BC) to participate in a nationwide survey on the contemporary surgical management of the axilla.

The aim was a national portrait to find out current clinical practice in different regions of the country and in different Portuguese public and private hospitals. It was not an audit of best practices, but rather a collective assessment of daily routines or uncertainties. The ethical and educational imperative to know, compare and disseminate the organizational structure and scientific trends, namely surgical training and differentiation, in different hospitals that treat BC in Portugal at SPCIR also needed to be put in perspective with international standards. The results of this survey were publicly presented at the XLIII National Congress of Surgery in March 2023 and are now being compared with some recently published national and international guidelines and consensus.

Breast surgeons have witnessed a remarkable evolution in the management of the axilla over the past 30 years. Sentinel node biopsy (SNB) was a paradigm shift at the end of the twentieth century[1-3]. The clinical validation of a fine theoretical idea was very gratifying. It was a real-life implementation of a functional concept against a dogmatic anatomical impossibility. The initial prospective randomized clinical trials that validated the SNB have been tested and reproduced in almost all national and international breast units, ensuring local reproducibility and clinical safety. Its low false-negative rate has established SNB as a staging alternative to axillary lymph node dissection (ALND) in node-negative (c/uN0) invasive BC with non-inferior survival outcomes. By eliminating routine ALND, SNB allowed for more conservative surgical staging of the axilla, minimizing functional and sensory morbidity and the feared lymphedema. A cN0 / pN0sn staging became the consensus standard. Over the years, the SNB concept allowed further de-escalation of axillary management. Even in the presence of a positive sentinel lymph node, the possibility of avoiding unnecessary ALND was studied. From the first predictive nomograms to calculate the probability of finding additional positive non-sentinel lymph nodes, to practice-changing randomized trials such as the earlier ACOSOG Z0011 (Z11) and EORTC AMAROS, or the subsequent, more comprehensive SENOMAC trial, which validated the non-inferiority of routine omission of ALND in presence of one or two sentinel node macrometastases[4-6]. Additionally, major advances in breast imaging, targeted systemic treatment, and radiation therapy (RT) have contributed to the current trend toward sparing the axilla, with no impact on long-term BC-specific survival and a non-significant marginal impact on regional recurrence. Several expert consensus and evidence-based medicine proposed it in selected c/uN0 low-risk invasive BC, but only the SOUND trial recently proved a 5-year non-inferiority of omitting surgical axillary staging, even SNB, in cT1N0 tumors regardless of molecular subtype[7]. On the other hand, the predictability of pathologic complete response in a previously positive axilla after primary systemic treatment (PST) in specific BC molecular subtypes has made it tempting to avoid the usual ALND. Recently, two retrospective observational studies have recommended replacing ALND after PST with SNB or targeted axillary dissection (TAD) of previously positive and marked axillary lymph nodes based on oncological safety reported at 2.5 and 5-year in their large real-world cohorts[8-9]. However, this recommendation is not supported by prospective randomized trials[10].

Lastly, as surgeons following the philosophical trend from "maximum tolerable" to "minimum effective"[11], priority should be given to optimal oncological outcome. Surgeons must be involved in collaborative clinical trials to minimize possible bias of altruistic de-escalation of multimodal treatment, where omission of one therapeutic modality

ISSN: 1646-6918 eISSN: 2183-1165

compels compensation by another[12]. Importantly, we should not overlook the need for continuous educational training in ALND surgical skills, which will continue to be an essential surgical tool, albeit increasingly in selected cases.

MATERIAL AND METHODS

The Chapter of Breast Surgery of the SPCIR invited 45 hospitals treating BC in Portugal to participate in a nationwide survey on the surgical management of the axilla.

The "Google Forms" methodology was used to complete the online survey, quickly and anonymously during March 2023, just before the XLIII National Congress of Surgery. In a national geographical distribution, in alphabetical order and using their names at the time, 38 hospitals responded, 12 from the North of Portugal (CH Médio Ave, VN Famalicão; CHU S. João, Porto; CHU St. António, Porto; CH Tâmega e Sousa, Penafiel; CH VNGaia e Espinho; H. Braga; CH Póvoa de Varzim-Vila do Conde; H. Senhora da Oliveira, Guimarães; H. St. Luzia, Viana do Castelo; H. St. Maria Maior, Barcelos; IPO-Porto; ULS Pedro Hispano, Matosinhos), 4 from the Center (CHU Coimbra; H. S. Sebastião, Feira; H. S. Teotónio, Viseu; IPO-Coimbra) and 21 from the South, of which 12 were public (CHU Algarve; H. Espírito Santo de Évora; H. Garcia de Orta, Almada; H. Litoral Alentejano, Santiago do Cacém; H. Nossa Senhora Rosário, Barreiro; H. Portalegre; H. St. Maria / Lisboa Norte; H. Santarém; H. S. Bernardo, Setúbal; H. S. Francisco Xavier, Lisboa Ocidental; H. St. Luzia de Elvas; IPO-Lisboa) and 9 private (Fundação Champalimaud, Lisboa; H. CUF Descobertas, Lisboa; H. CUF Santarém; H. CUF Sintra; H. Lusíadas, Lisboa; H. Luz, Lisboa; H. Luz Tejo, Lisboa; H. Luz, Setúbal; Joaquim Chaves Saúde – Clínica de Carcavelos). From Madeira, H. Nélio Mendonça, Funchal, responded.

All questions concerned the axillary approach exclusively, regardless of the breast surgery performed. All data queried reports on the volume of care they provide through 2022. An anonymized qualitative and quantitative description of the answers was made. Descriptive statistics were not performed. Ethics committee approval was not sought as no individual patient data were involved.

A complementary comparison was made with national and international consensus: the BC National Consensus of the Portuguese Society of Senology (SPS)[13]; the Early BC Clinical Practice Guideline of the European Society for Medical Oncology (ESMO)[14]; the BC Clinical Practice Guidelines of the National Comprehensive Cancer Network (NCCC)[15]; the Society of Surgical Oncology (SSO), in conjunction with Choosing Wisely[16]; the Lucerne Toolbox (LT) multidisciplinary expert consensus[17,18]; and the Oncoplastic Breast Consortium (OPBC) joint venture with the European Breast Cancer Research Association of Surgical Trialists (EUBREAST-network) expert consensus[19].

RESULTS

Of 45 hospitals invited, 38 (84.4%) agreed to participate in the survey. Table 1 describes technical details and morbidity of axillary surgery. Most hospitals (94.7%) use a combined dual tracer for SNB. Technetium 99 combined with Patent Blue was the most popular method (76.3%). Five (13.2%) hospitals used more than one SNB identification technique in different clinical situations. Only nine reported the use of a sole tracer. The tracer injection site was almost exclusively (92.1%) in the subareolar plexus of Sappey, even with dual tracer. Only 13.2% performed synchronous subareolar tracer injection plus separate second tracer peritumoral injection. Intraoperative pathologic study of the sentinel node was performed routinely in 52.6% and only in selected cases in 26.3%. Frozen section histology was the most used (52.9%) intraoperative pathology technique, followed by imprint / citology analysis

ISSN: 1646-6918

eISSN: 2183-1165

Table 1 – **Technical details and morbidity of axillary surgery.**

		(n)	(%)	Compliance with
SNB identification technique (n=38)	Dual tracer (Tc99+Blue)	29	76.3%	NCCN
	Dual tracer (Blue+ICG)	4	10.5%	
	One tracer (Tc99)	4	10.5%	
	One tracer (Magnetic iron oxide)	4	10.5%	
	Dual tracer (Blue+Iron oxide)	2	5.3%	
	Dual tracer (Te99+Iron oxide)	1	2.6%	
	One tracer (Blue)	1	2.6%	
SNB tracer injection site (n=38)	Subareolar (dual tracer)	28	73.7%	NCCN
	Subareolar (one tracer)	7	18.4%	NCCN
	Subareolar+peritumoral (dual tracer)	5	13.2%	NCCN
SNB intraoperative pathology exam (n=38)	Yes, as a routine	20	52.6%	
	Yes, in selected cases	9	23.7%	ESMO, NCCN
	No	8	21.1%	
	Yes, if mastectomy	1	2.6%	
Intraoperative pathology (n=34)	Frozen section histology	18	52.9%	
	Imprint / cytology	14	41.2%	
	OSNA	11	32.4%	
Estimated axillary op. morbidity? (n=38)	Yes	16	42.1%	ESMO, NCCN
	No	22	57.9%	
% lymphedema after SNB? (n=16)	0%	6	37.5%	
	<1%	3	18.8%	
	1-2%	4	25.0%	
	3-5%	2	12.5%	
	<10%	1	6.3%	
% lymphedema after SNB plus adjuvant RT? (n=14)	0%	3	21.4%	
	≤1%	2	14.3%	
	3-5%	5	35.7%	
	10%	1	7.1%	
	20-30%	1	7.1%	
	Unknown	2	14.3%	
% lymphedema after ALND? (n=15)	5-10%	3	20.0%	
	10-15%	7	46.7%	
	20-30%	4	26.7%	
	Unknown	1	6.7%	
% lymphedema after ALND plus adjuvant RNI? (n=17)	5-10%	2	11.8%	
	15-20%	6	35.3%	
	25-30%	6	35.3%	
	>30-40%	2	11.8%	
	Unknown	1	5.9%	

(41.2%) and one-step nucleic acid amplification (OSNA) assay in 32.4%.

Regarding morbidity assessment for axillary surgery, only 42.1% of hospitals were able to estimate based on a prospective registry of operative complications. When questioning the proportion of lymphedema after SNB, 56.3% reported a zero (or <1%) probability, but 43.8% estimated between 1-10%. This null probability (or <1%) decreases to 35.7%, although two hospitals report a value of 10-30% when adjuvant nodal RT is performed after SNB. After ALND, 20% report a 5-10% likelihood of lymphedema, while the majority (73.3%) estimate a 10-30% rate. These figures rise to 15-40% in 82.4% of hospitals when adjuvant RNI is performed after ALND in a positive axilla.

Table 2 describes the axillary surgical management. As previously reported, this decision-making was always discussed in the MDM, as were all other therapeutic decisions. To define a negative axilla (c/uN0), physical examination and axillary ultrasound (US) were used in 65.8% of hospitals. Some (31.6%) included magnetic resonance imaging (MRI). Lymph node US-guided biopsy was required to define a positive axilla (cN+) in most centers (76.3% by histologic core-biopsy; and 52.6% by fine-needle aspiration for cytology), while five (13.2%) defined physical examination alone as appropriate for this definition. When suspicious axillary lymph nodes were identified by US, we queried how many of them would be biopsied and marked: 42.1% reported one or two lymph nodes, 39.5% up to three lymph nodes, and 18.4% only one axillary lymph node. To perform TAD in a suspicious or positive axilla, the most common preoperative localization technique was a titanium clip in 84.2% (of which only 36.8% were intraoperative US-visible clips). Fifteen (39.5%) centers used more than one localization method in different clinical situations, mainly a two-step conventional clip placed at the time of biopsy followed by preoperative wire-guided localization. No one uses radioactive seeds. Preoperative localization of suspicious or positive axillary lymph nodes was not performed in 15.8%. Assessment of axillary imaging response after PST was mostly (63.2%) performed by US plus MRI before and after PST. Another 31.6% performed MRI alone.

When questioned on different clinical conditions in which omission of SNB could be considered in an axilla c/uN0, there was a strong consensus (86.8%) that SNB should not be performed in DCIS. Likewise, a majority (68.4%) stated that SNB should be omitted in older patients. In contrast, in a low-risk invasive BC, a luminal G1 cT1N0 tumor, only one center considered omitting SNB.

Several real-world therapeutic decisions were questioned. If one or two positive sentinel nodes are identified on intraoperative pathology in a previous c/uN0 axilla, there was consensus to omit ALDN (71.1% based on Z11 criteria, 21.1% on AMAROS trial, 10.5% by tumor biology, and 7.9% by OSNA total tumor load count). In this scenario, only 13.2% proceeded to an ALND. Other scenario was the identification of one or two positive lymph nodes at the time of BC diagnosis. When a patient had a c/uN1 axilla and was proposed for upfront surgery, the majority (60.5%) performed ALND and 47.4% adopted more conservative axillary approach. In the same scenario, if the patient was initially proposed for PST and did not have a complete imaging response (uCR) after this treatment, the majority (63.2%) also performed ALND. However, if the patient had uCR, the surgical approach shifted radically (86.8% underwent SNB plus TAD, 7.9% TAD, and 5.3% SNB). For this c/uN1 scenario, two additional questions were discussed. In this setting, in a patient with uCR after PST proposed for SNB, we wanted to know when it was safe to avoid an ALND. There was a strong consensus (92.1%) to omit ALND for ypN0sn (76.3% favored 1-2 negative lymph nodes, but 15.8% preferred a more representative sample of 3-4 negative nodes). Eleven (28.9%) centers omitted ALND when isolated tumor cells (ypN0itc) or micrometastatic disease (ypN1mi) were detected on sentinel lymph nodes. In contrast, only one center

ISSN: 1646-6918 eISSN: 2183-1165

Table 2 – **Characterization of axillary surgical management.**

		(n)	(%)	Compliance with
Axilla c/uN0	Physical exam + US	25	65.8%	ESMO, NCCN, OPBC, LT
Definition of cN0	Physical exam + US + MRI	12	31.6%	ESMO, NCCN, OPBC
(n=38)	Physical exam only	1	2.6%	
When omitting the SNB?	DCIS	30	78.9%	ESMO, NCCN (if BCS)
(n=38)	Older age with life expectancy ←5y	16	42.1%	
	Older age ↗ 80y	7	18.4%	NCCN (↗70y), LT (↗75y), SSO
	Older age with life expectancy ↗5-8y	2	5.3%	
	Small DCIS (←3-4cm)	2	5.3%	ESMO, NCCN
	Stage IV invasive carcinoma	2	5.3%	
	Low-risk invasive ca.(T1, G1, Luminal)	1	2.6%	
	Low grade DCIS	1	2.6%	ESMO, NCCN
	Older age ↗ 70y	1	2.6%	NCCN (↗70y), SSO
	TN / HER2 invasive ca. for PST	1	2.6%	
Surgical options for 1-2	ALND omission, like Z11	27	71.1%	ESMO, NCCN, OPBC
positive SN detected	ALND omission, like Amaros	8	21.1%	ESMO, NCCN
intraop. (in cN0 axilla)	ALND	5	13.2%	
(n=38)	ALND omission, by tumor biology	4	10.5%	
	ALND omission, by OSNA TTL	3	7.9%	
Axilla c/uN1				
Definition of a positive	US guided core-biopsy	29	76.3%	ESMO, NCCN, LT
axilla (c/uN+)	US guided fine-needle biopsy	20	52.6%	ESMO, NCCN, LT
(n=38)	US	7	18.4%	
	MRI	6	15.8%	
	Physical exam	5	13.2%	
No. lymph nodes	1-2 suspicious lymph nodes	16	42.1%	SPS
biopsied / localized?	Up to 3 lymph nodes	15	39.5%	
(n=38)	Only one lymph node	7	18.4%	
Lymph node localization	Titanium clip, non-specified	18	47.4%	ESMO
technique	US-visible clip	14	36.8%	
(n=38)	Wire-guided localization	10	26.3%	
	None	6	15.8%	
	Radiofrequency (RFID) Localizer	2	5.3%	
	Carbon marking	2	5.3%	ESMO
	Magnetic tracer	2	5.3%	

		(n)	(%)	Compliance with
Surgical options (if	ALND	23	60.5%	ESMO, NCCN
upfront) for 1-2 positive	SNB plus TAD	15	39.5%	ESMO
lymph nodes?	TAD	2	5.3%	ESMO
(n=38)	SNB	1	2.6%	ESMO
How to assess axilla	US+RMI (before and after)	24	63.2%	ESMO, NCCN, LT
response after PST?	MRI (before and after)	12	31.6%	ESMO, NCCN
(n=38)	US (before and after)	3	7.9%	ESMO, NCCN
	Physical exam during treatment	1	2.6%	
	SNB plus TAD	1	2.6%	
Surgical options for 1-2	ALND	24	63.2%	ESMO, NCCN
positive nodes and no	SNB plus TAD	13	34.2%	
uCR after PST?	TAD	2	5.3%	
(n=38)	SNB	1	2.6%	
Surgical options for 1-2	SNB plus TAD	33	86.8%	ESMO, NCCN, OPBC, LT
positive nodes with uCR	TAD	3	7.9%	ESMO, NCCN, OPBC, LT
after PST?	SNB	2	5.3%	ESMO, NCCN
(n=38)	ALND	1	2.6%	
In a cN1 axilla with uCR	1-2 negative SN/TAD nodes (ypN0)	29	76.3%	ESMO, NCCN, OPBC, LT
after PST, when is safe	1-2 SN/TAD nodes with itc (ypN0itc)	6	15.8%	
to omit an ALND?	1-2 SN/TAD nodes with mic (ypN1mi)	5	13.2%	LT
(n=38)	3 negative SN/TAD nodes (ypN0)	3	7.9%	ESMO, NCCN
	4 negative nodes (in a sampling)	3	7.9%	ESMO, NCCN
	Never	1	2.6%	
If a cN1 axilla becomes	Yes, based on initial stage (cN1)	18	48.6%	ESMO, NCCN
ypN0 after PST, is	No, based on final stage (ypN0)	12	32.4%	NCCN, LT
adjuvant RT indicated?	Yes, based on AMAROS trial	4	10.8%	ESMO, NCCN
(n=38)	No, based on Z11 trial	3	8.1%	ESMO, NCCN
	No, an ALND was done	1	2.7%	
Axilla c/uN2				
Surgical options (if	ALND	38	100%	ESMO, NCCN
upfront)? (n=38)	Only if PST refused/contra-indicated	2	5.3%	
Surgical options if no	ALND	36	94.7%	ESMO, NCCN
uCR after PST? (n=38)	SNB plus TAD	2	5.3%	
Surgical options if uCR	ALND	29	76.3%	ESMO, NCCN
after PST? (n=38)	SNB plus TAD	8	21.1%	
	SNB	1	2.6%	
	TAD	1	2.6%	

never considered omitting ALND. The other issue was the formal indication for adjuvant RNI: a slight majority (57.9%) defended it based on initial staging (cN1) or AMAROS trial criteria, while 42.1% did not consider it based on final staging after PST (ypN0) or Z11 eligibility trial criteria. The last scenario was cN2. Regardless of imaging response to PST, ALND was the standard approach in an initially cN2 axilla. Only 8 (21.2%) favored performing SNB plus TAD in the setting of uCR after PST.

DISCUSSION

Axillary staging remains one of the strongest prognostic factors in BC. However, multidisciplinary management of the axilla has evolved significantly in recent years. Several international recommendations promote surgical de-escalation strategies. For cN0 / pN1sn, we have matured 10-year data from the Z11 and AMAROS trials showing similar regional recurrence and survival outcomes between ALND and SNB plus axillary RT[4,5]. In the AMAROS trial, unlike the Z11 trial, the non-ALND randomized arm was intentionally treated with comprehensive RNI volumes. However, the ESMO guidelines assumed that in Z11 trial radiation is delivered to the lower axilla[14]. Similarly, advances in PST have allowed this trend toward a targeted axillary approach, potentially avoiding ALND in many initially metastasized axillae. After nearly a century as the standard of care, ALND is disappearing from daily practice. Nowadays, it is only indicated in selected cases. Therefore, ongoing surgical training in ALND should not be overlooked.

In our survey regarding the SNB surgical technique, there was a strong consensus (94.7%) for the combined use of a dual tracer, especially the combination of Tc99-Blue (76.3%). There was also a strong consensus (92.1%) for subareolar injection of the tracer. However, this technical detail deserves some reflection. By injecting both tracers at the same site, we minimize the likelihood of identifying alternative lymphatic pathways. Accurate localization of one or more sentinel nodes, and thus the predictive value of SNB, could be maximized by injecting one tracer into the subareolar lymphatic plexus and the other tracer peritumorally, as originally postulated (and preferred by only 13.2% in our survey). Another technical issue was the purpose of intraoperative sentinel lymph node assessment. Considerable variation was noted between national hospitals. Given the observed strong consensus trend to omit ALND (only 13.2% decided to do it intraoperatively), we consider it pertinent to discuss why most centers continue to prolong operative time with this pathologic work-up (only 21.1% never do). Also, its technical standardization should be discussed, especially when 52.9% use a more time-consuming laboratory technique such as frozen section.

Historically, the reported incidence of upper extremity lymphedema in BC survivors after ALND has ranged from 9-41% and remains at 4-10% even after the first decade of SNB[20]. Recently, axillary surgery has been increasingly performed by dedicated breast surgeons. However, because these procedures are often combined with adjuvant RNI, uncertainty remains regarding the long-term morbidity of axillary surgery. Limited evidence is available only on secondary endpoints in some clinical trials[5,21]. Our survey was unable to provide this assessment. Outcome registries were found in only 42.1% of hospitals. This lack of prospective non-oncological data mirrors our previous Part 1 nipple-sparing mastectomy survey. Nevertheless, lymphedema remains a reality: after SNB, the estimated probability ranges from 0% to an excessive rate of 10% maximum; after SNB plus axillary RT, it ranges from 0-30%; after ALND, there is variability between 5-30%; and finally, in a positive axilla undergoing ALND plus RNI, the estimated probability ranges from 5-40%. All these upper limits for lymphedema in our survey may seem overestimated, but they are comparable to the AMAROS 10-year morbidity outcomes. Like

https://doi.org/10.34635/rpc.1036

ISSN: 1646-6918

eISSN: 2183-1165

our Part 1 survey of breast units, this survey did not query oncological outcomes or participation in external quality programs, which are strongly recommended by ESMO, OPBC, and the Lucerne Toolbox consensus.

All discussions concerning the real-world scenarios presented to evaluate axillary management were conducted regardless of whether breast conservative surgery (BCS) or mastectomy was performed. Clinical practice settings in which SNB may be omitted were discussed. Consistent with ESMO and NCCN recommendations, there was a strong consensus (86.8%) not to perform SNB in DCIS. Conversely, only one center considered omitting SNB in cN0 low-risk invasive BC. This reflects insufficient published evidence at the time of this survey. The Society of Surgical Oncology, in conjunction with Choosing Wisely, has not recommended routine SNB in women ≥70 years of age with cT1N0 luminal tumors since 2016, based on prospective studies highlighting that SNB had no impact on regional recurrence or BC-specific mortality. The Lucerne Toolbox consensus supports that SNB can be omitted in selected older patients ≥75 years with comorbidities who are not candidates for chemotherapy with low-risk unifocal cT1N0 tumors, regardless of tumor biology. Compliance with these recommendations was not clear from our survey. To minimize ageism, we asked about 2 topics: age itself and life expectancy. When asked for a specific chronological age limit, only one center advocated omitting SNB in women ≥ 70 years, and seven (18.4%) omitted it in women ≥ 80 years. When asked differently according to life expectancy in older women, the answers were similar. When predicted life span was ≥ 5-8 years, only two centers advocated omitting SNB, but when predicted life span was < 5 years, 42.1% omitted it.

No question was provided about the cN0 / pN0sn scenario. ESMO guidelines and Lucerne Toolbox consensus support SNB after PST as the standard of care for initially cN0 axilla. A more challenging scenario discussed was a cN0 axilla where intraoperative pathology revealed one or two sentinel nodes with macrometastases. Omitting ALDN, but using different criteria, had a strong consensus (92.1%) nationwide. Recommended by ESMO and NCCN, this is a well-supported intention. Interestingly, in our survey, 71.1% used the Z11 criteria, but 21.1% preferred the AMAROS eligibility criteria. Only 7.9% used their own OSNA criteria.

Another scenario was the management of a positive axilla at initial diagnosis. ESMO or NCCN guidelines state that suspicious lymph nodes must be marked at the time of diagnosis for later surgical excision and ultimately avoid ALDN after PST. Contrary to ESMO and NCCN, the SPS national consensus specifies a predefined number of one or two suspicious nodes that should be biopsied and marked for subsequent TAD. The Lucerne Toolbox consensus supports that only one involved node needs to be marked when planning TAD after PST. In our survey, there was no consensus on the number of suspicious nodes that should be biopsied and marked (42.1% for up to two, but 39.5% for up to three and 18.4% for a single suspicious node). In addition, as evidenced by the lack of consensus in the Lucerne Toolbox, a non-standardized technique for marking suspicious lymph nodes was evident nationwide. ESMO guidelines consider SNB safe in cN1 axilla converted to uCR after PST based on the results of the ACOSOG Z1071, SENTINA, GANEA 2, SN FNAC prospective trials[22-25]. The Lucerne Toolbox consensus supports the safety of SNB plus TAD for ≤3 suspicious nodes in selected patients. However, this is controversial. A cautious review of these non-randomized trials does not support oncologic safety, given discrepancies in study design, false-negative rates (validating primary endpoints), and no survival data [10]. For cN1 axilla, a majority in our survey preferred ALND for upfront surgery (60.5%) or in the absence of uCR after PST (63.2%). When uCR occurred after PST, according to ESMO, NCCN, and SPS, all but one center opted to omit ALND in favor of a more conservative surgical

ISSN: 1646-6918

eISSN: 2183-1165

approach to the axilla. For pathologic complete response in the axilla (ypN0sn), there was a strong consensus (92.1%) to omit ALND after PST. Not recommended by ESMO, NCCN, or SPS, if tumor deposits such as isolated tumor cells (ypN0itc) or micrometastatic disease (ypN1mi) were detected in sentinel nodes after PST, 28.9% of national centers were more liberal and considered omitting ALND. A similar proportion of experts (25%) in the Lucerne Toolbox consensus considered the same for micrometastasis. Finally, contrary to ESMO, NCCN, and SPS guidelines, no consensus has been observed regarding adjuvant RNI when the axilla is initially cN1 and becomes ypN0 after PST: 57.9% advocated it based on initial staging or AMAROS inclusion criteria, while 42.1% did not consider it based on final staging or Z11 eligibility criteria.

The last scenario, the cN2 axilla, was the most straightforward. Consistent with limited evidence (due to under-representation of cN2 tumors in clinical trials) and ESMO, NCCN, and Lucerne Toolbox recommendations, there was 100% consensus to perform ALND. Only 26.3% considered a more conservative axillary surgical approach for uCR after PST in an initially cN2 axilla in specific BC molecular subtypes.

CONCLUSION

With this second national portrait, also imperfect, the Chapter of Breast Surgery of the SPCIR has demonstrated that national hospitals treating BC have de-escalated the surgical management of the axilla. SNB, with some possible technical improvements, has long been the standard of care for the cN0 axilla. Coordinated multidisciplinary management of a positive axilla has been evidenced by the progressive omission of ALND in favor of more conservative TAD or axillary RT as a clearly established emerging trend.

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ISSN: 1646-6918

eISSN: 2183-1165