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ORIGINAL ARTICLE – BREAST ONCOLOGY

Evolution of the Use of Completion Axillary Lymph Node Dissection in Patients with T1/2N0M0 Breast Cancer and Tumour-Involved Sentinel Lymph Nodes Undergoing Mastectomy: A Cohort Study

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ABSTRACT

Background. In breast cancer, completion axillary lymph node dissection (cALND) was previously recommended for patients with at least one tumour-affected sentinel lymph node (SLN). Several prospective trials predominantly in patients undergoing breast-conserving surgery showed no benefit and increased arm morbidity with this procedure. We report the influence of these trials on clinical practice of patients undergoing mastectomy.

Methods. We analysed prospectively collected data from patients with primary invasive breast cancer treated at German breast cancer units between January 2008 and December 2015. Time trends of cALND rates were analysed in patients undergoing mastectomy for T1/2N0M0 breast cancer with one or two tumour-involved SLNs. Multivariable logistic regression was used to determine factors influencing the decision not to perform cALND.

Results. Among the entire study cohort of 166,074 patients treated at 179 breast cancer units, 4093 patients (2%) had T1/2N0M0 breast cancer with one or two tumour-involved SLNs and underwent mastectomy. cALND rates decreased from 89.9% in 2010 to 55.5% in 2015 ($p < 0.001$). Rates decreased from 82% to 8% in patients with micrometastatic SLN disease and from 93% to 63% in those with macrometastasis ($p < 0.001$). In multivariable analysis, factors associated with omission of cALND were treatment at a general, nonacademic hospital, pT1 status, older age, higher number of removed SLNs, fewer tumour-affected SLNs, and SLN micrometastasis (all $p < 0.001$).

Conclusions. Despite limited evidence from prospective trials relating to the omission of cALND specifically in patients undergoing mastectomy, our nationwide data show that use of cALND decreased in these patients in routine clinical practice.

In patients with breast cancer, evaluation of the axillary lymph nodes provides prognostic information used to estimate the risk of breast cancer relapse and informing clinical decision-making regarding the need for adjuvant systemic therapy and radiotherapy.[1–3] Until the beginning of the new millennium, axillary lymph node dissection (ALND) was a standard surgical approach in breast cancer, together with surgical removal of the primary tumour. The introduction of sentinel lymph node (SLN) dissection (SLND) for patients with clinically node-negative axillary lymph nodes allowed a less invasive procedure for nodal staging.[4] Lymphoedema with arm swelling and restricted movement causes a substantial decrease in quality of life in 20% of patients with ALND compared with less than 5% of patients following SLND.[5] Prospective trials confirmed that completion ALND (cALND) provides no benefit in patients with pathologically confirmed node-negative

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SLNs.[4,6] However, for patients with clinically lymph node-negative disease but at least one tumour-affected SLN, cALND remained the standard of care.

Several randomised, controlled trials have challenged the need for this further axillary surgery. First, the prospective American College of Surgeons Oncology Group (ACOSOG) randomised Z0011 trial examined outcomes in patients who did not undergo cALND for positive SLNs.[7] The trial included patients with clinical T1/2N0M0 breast cancer with one or two tumour-affected SLNs, treated with breast-conserving surgery (BCS) and whole-breast irradiation without neoadjuvant chemotherapy. The initial results were reported in 2010 and long-term results published in 2017 confirmed that survival in patients treated with SLND alone was noninferior to that observed with cALND. At a median follow-up of 9.3 years, the 10-year overall survival rates were 86.3% with SLND alone and 83.6% with cALND. The 10-year locoregional relapse-free survival rate was 83.0% in the SLND arm and 81.2% in the ALND arm.[7,8]

The After Mapping of the Axilla: Radiotherapy Or Surgery? (AMAROS) trial published in 2014 by Donker et al.[9] compared axillary recurrence in patients with tumour-affected SLN(s) treated with SLND following axillary radiotherapy (ART) or cALND. The trial included patients with cT1/2 breast cancer and clinically node-negative axillary lymph nodes. In this trial, 248 of 1425 patients (17%) underwent mastectomy. ART was associated with similar disease control and less morbidity than cALND. At a median follow-up of 6.1 years, the 5-year axillary recurrence rate was 0.43% (4/744 patients) in the cALND group compared with 1.19% (7/681 patients) in the ART group. The 5-year overall survival rate was 93.3% in the cALND arm versus 92.5% in the ART arm. Furthermore, patients in the cALND arm had significantly higher rates of lymphoedema than those in the ART arm (23% vs. 11% at 5 years; $p < 0.0001$).

The Optimal Treatment of the Axilla Surgery or Radiotherapy (OTOASOR) trial published in 2017 by Sávolt et al.[10] also included patients with positive SLN(s) and compared outcomes in those treated with either regional nodal irradiation or cALND. This trial included patients with tumours < 3 cm, of whom 74 of 474 (16%) underwent a mastectomy. The OTOASOR trial confirmed findings from AMAROS, showing similar rates of axillary recurrence (2.0% with cALND vs. 1.7% with regional nodal irradiation; $p = 1.00$) and 8-year overall survival (77.9% vs. 84.8%, respectively; $p = 0.06$) in the two study arms.

Results from these trials led to practice-changing recommendations for the omission of cALND in patients with tumour-involved SLNs, enabling decreased surgical radicalness, leading to decreased paraesthesia and reduced arm swelling, without compromising oncological outcomes. The American Society of Clinical Oncology guidelines state that "Women with one to two metastatic SLNs who are planning to undergo BCS with whole-breast radiotherapy should not undergo ALND (in most cases)."[11] However, these guideline recommendations do not apply for patients undergoing mastectomy.

The AMAROS and OTOASOR trials included few patients with mastectomy (17% and 16%, respectively), and these patients were excluded from the ACOSOG Z0011 trial. Therefore, there is only limited information available relating to the omission of cALND in patients undergoing mastectomy. The purpose of our study was to explore the influence of these trials on cALND rates in routine clinical practice among patients undergoing mastectomy for T1/2N0M0 breast cancer with one or two tumour-involved SLNs.

METHODS

Study Design and Data Collection

Hospitals with a focus on breast cancer care and breast cancers units in Germany were invited to participate on a voluntary basis in an external, independent, scientific benchmarking system developed by the German Cancer Society (DKG) and the German Society of Senology (DGS). For each patient treated at the participating institutions, clinical, surgical, and pathological variables were collected prospectively by staff members. All data were collected centrally and analysed by the West German Breast Center (WBC)/German Oncology Center. Quality indicators, based on national guidelines, were reported twice a year in a benchmarking report.

The study was approved by the ethics committee of the University of Heidelberg in accordance with the Declaration of Helsinki. Because the study was deemed as without risk, including only anonymised analysis of routinely collected data, the ethics committee of the University of Heidelberg did not request approval for consent.

Quality Control

The credibility of data was assessed in twice-yearly in-house data monitoring visits by clinical research associates. During these monitoring visits, the electronic documentation extracted from each patient's medical records was checked for correctness and completeness to ensure that the database was valid and suitable for further analysis. Data recording was discussed and staff members at the participating institutions were advised on issues related to the

documentation process to ensure the high quality of the database.

Patient Selection

Data were extracted from the WBC database for patients with a diagnosis of primary invasive breast cancer who were treated between January 1, 2008 and December 31, 2015. This dataset was then screened to select patients matching the inclusion criteria for the above-mentioned prospective trials examining the omission of cALND in patients with metastatic SLNs (T1/2N0M0 breast cancer with 1 or 2 tumour-affected SLNs).

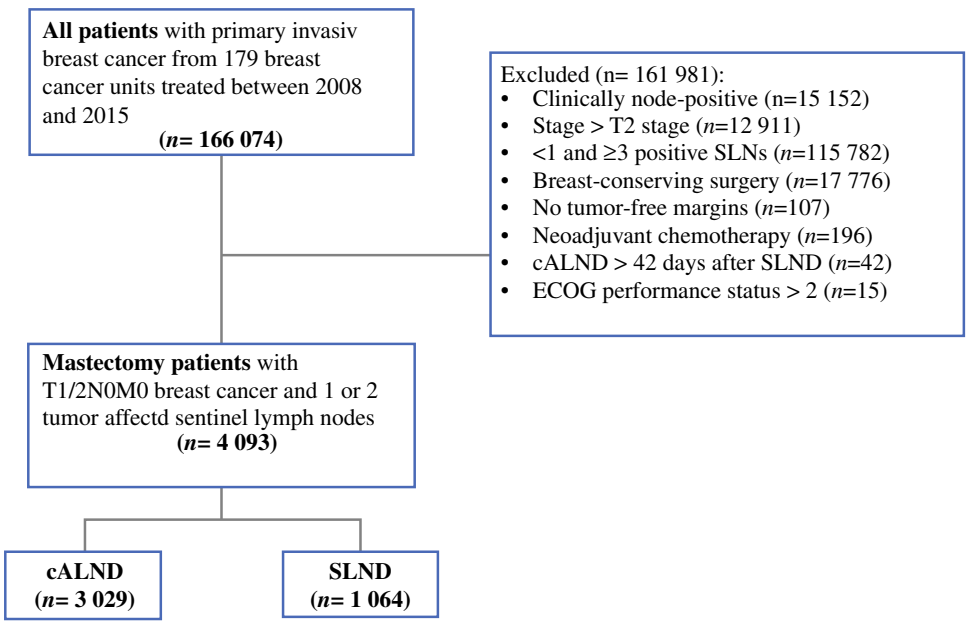
Statistical Analysis

Data are presented as mean ± standard deviation or as frequencies and percentages, unless otherwise noted. Descriptive statistics are provided for clinical, surgical, and pathological variables. Annual percentages of cALND use were calculated and are presented as a longitudinal time-trend analysis for the period from 2008 to 2015. Multivariable logistic regression was used to determine factors associated with the omission of cALND in patients with T1/2N0M0 breast cancer and one or two tumour-affected SLNs. A p value < 0.05 was considered to be statistically significant. All statistical analyses were performed with R software, version 3.4.1.[12]

RESULTS

The entire study cohort comprised 166,074 patients with primary invasive breast cancer treated at 179 specialist breast cancer units in Germany between 2008 and 2015. Of these, 161,981 patients were excluded for the reasons shown in Fig. 1, leaving 4093 patients (2%) with T1/2N0M0 breast cancer and one or two tumour-affected SLNs who underwent mastectomy. Baseline characteristics of the mastectomy cohort are shown alongside those of the entire cohort in Table 1. The majority of patients in the mastectomy cohort had hormone receptor-positive HER2-negative grade II disease. Compared with the entire study cohort, patients in the mastectomy cohort were older and more likely to have lymphovascular invasion. Other clinicopathological variables were similar in the two cohorts (Table 1).

Among the 4093 patients in the mastectomy cohort with T1/2N0M0 breast cancer and one or two tumour-affected SLNs, 3029 (74%) underwent cALND and 1064 (26%) were treated with SLND alone (Table 2). Patients undergoing cALND were younger than patients with SLND alone, were more likely to have two tumour-affected SLNs and macrometastatic SLNs, and were more likely to have



cALND=completion axillary lymph node dissection; ECOG=Eastern Cooperative Oncology Group; SLN=sentinel lymph node; SLND=sentinel lymph node dissection.

FIG. 1 CONSORT diagram. *cALND* completion axillary lymph node dissection; *ECOG* Eastern Cooperative Oncology Group; *SLN* sentinel lymph node; *SLND* sentinel lymph node dissection

TABLE 1 Comparison of patient characteristics between the entire study cohort and patients with T1/2N0M0 breast cancer undergoing mastectomy

	Invasive breast cancer (n = 166,074)	T1/2N0M0 breast cancer undergoing mastectomy (n = 4093)
Age, year		
Median (range)	63 (18–72)	68 (21–95)
Missing	0	0
Age, year		
≤ 50	36,085 (21.7)	846 (20.7)
> 50	129,989 (78.3)	3247 (79.3)
No. of affected SLNs		
1	20,195 (12.2)	3087 (75.4)
2	6114 (3.7)	1006 (24.6)
SLN metastasis[a]		
Micrometastasis	4225 (14.4)	619 (15.1)
Macrometastasis	25,177 (85.5)	3470 (84.8)
Missing	20 (0.1)	4 (0.1)
Tumor stage		
T0	3541 (2.1)	–
T1	92,071 (55.4)	1244 (30.4)
T2	56,088 (33.8)	2849 (69.6)
T3/4	13,553 (8.2)	–
Tis	593 (0.4)	
Missing	228 (0.1)	
HER2 status		
Positive	20,434 (12.3)	516 (12.6)
Negative	142,186 (85.6)	3516 (85.9)
Missing	3454 (2.1)	61 (1.5)
Oestrogen receptor status		
Positive	139,093 (83.8)	3710 (90.6)
Negative	26,596 (16.0)	382 (9.3)
Missing	385 (0.2)	1 (< 0.1)
Progesterone receptor status		
Positive	121,175 (73.0)	3226 (78.8)
Negative	44,483 (26.8)	864 (21.1)
Missing	416 (0.3)	3 (0.1)
Lymph invasion		
Yes	36,416 (21.9)	1752 (42.8)
No	115,846 (69.8)	2030 (49.6)
Missing	13,812 (8.3)	311 (7.6)
Grade		
I	23,102 (13.9)	329 (8.0)
II	95,460 (57.5)	2709 (66.2)
III	45,801 (27.6)	1051 (25.7)
Missing/unknown	1711 (1.0)	4 (0.1)
Tumour type		
Infiltrating ductal	135,106 (81.4)	3236 (79.1)
Infiltrating lobular	22,776 (13.7)	778 (19.0)
Other	8192 (4.9)	79 (1.9)
Radiotherapy		
Performed/planned	131,115 (79.0)	1940 (47.4)
Not performed/planned	33,250 (20.0)	2114 (51.6)
Missing	1709 (1.0)	39 (1.0)

Data are n (%) unless otherwise stated

SLN sentinel lymph node

[a]For the calculation of the relative frequencies only patients with a tumour involved sentinel were applied

radiotherapy planned or performed. Distribution of tumour biology, including grading, HER2, and hormone-receptor status, was similar in the two subgroups (Table 2).

Rates of cALND remained constant from 2008 (89.7%) to 2010 (89.9%). In subsequent years, the rate of cALND decreased gradually from 74.9% in 2011 to 55.5% in 2015 ($p < 0.001$; Fig. 2). This decrease was most pronounced in patients with micrometastasis in the SLN, declining from 82% in 2010 to 26% in 2012 and 8% in 2015 ($p < 0.001$). In patients with macrometastasis, the decrease in cALND rate was less pronounced, decreasing from 93% in 2010 to 63% in 2015 ($p < 0.001$; Fig. 3).

A multivariable logistic regression analysis was used to determine independent predictors for omitting cALND in patients with T1/2N0M0 breast cancer and one or two tumour-involved SLND undergoing mastectomy in clinical routine management (Table 3). The following factors were associated with omission of cALND: treatment at a general, nonacademic hospital, pT1 status, older age, more removed SLNs, only one tumour-affected SLN, and micrometastasis of the SLN (all $p < 0.001$). No statistically significant influence was detected for annual hospital case load, lymphovascular invasion, grading, hormone receptor status, or HER2 status.

DISCUSSION

In this study, we explored the impact of results from prospective clinical trials on cALND rates in patients with T1/2N0M0 breast cancer and one or two tumour-involved SLNs undergoing mastectomy. Despite the limited evidence for patients with mastectomy, our data show a constant decrease in cALND rates in clinical routine management.

TABLE 2 Patients with mastectomy and T1/2N0M0 breast cancer who underwent cALND or SLND alone

	cALND (n = 3029)	SLND alone (n = 1064)
Age, year		
Median (range)	67 (21–95)	73 (29–94)
≤ 50	680 (22.4)	166 (15.6)
> 50	2349 (77.6)	898 (84.4)
Affected SLN		
1	2198 (72.6)	889 (83.6)
2	831 (27.4)	175 (16.4)
SLN metastasis		
Micrometastasis	223 (7.4)	396 (37.2)
Macrometastasis	2804 (92.6)	666 (62.6)
Missing	2 (< 0.1)	2 (0.2)
Tumour stage		
T1	875 (28.9)	367 (34.5)
T2	2154 (71.1)	695 (65.3)
Missing	0	2 (0.2)
HER2 status		
Positive	403 (13.3)	113 (10.6)
Negative	2586 (85.4)	930 (87.4)
Missing	40 (1.3)	21 (2.0)
Oestrogen receptor status		
Positive	2729 (90.1)	981 (92.2)
Negative	299 (9.9)	83 (7.8)
Missing	1 (< 0.1)	0
Progesterone receptor status		
Positive	2364 (78.0)	862 (81.0)
Negative	663 (21.9)	201 (18.9)
Missing	2 (0.1)	1 (0.1)
Lymph invasion		
Yes	1349 (44.5)	403 (37.9)
No	1439 (47.5)	591 (55.5)
Missing	241 (8.0)	70 (6.6)
Grade		
I	220 (7.3)	109 (10.2)
II	1991 (65.7)	718 (67.5)
III	815 (26.9)	236 (22.2)
Missing/unknown	3 (0.1)	1 (0.1)
Tumour type		
Infiltrating ductal	2413 (79.7)	823 (77.3)
Infiltrating lobular	559 (18.5)	219 (20.6)
Other	57 (1.9)	22 (2.1)
Missing	0	0
Radiotherapy		
Planned/performed	1617 (53.4)	323 (30.4)
Not performed/planned	1385 (45.7)	729 (68.5)
Missing	27 (0.9)	12 (1.1)

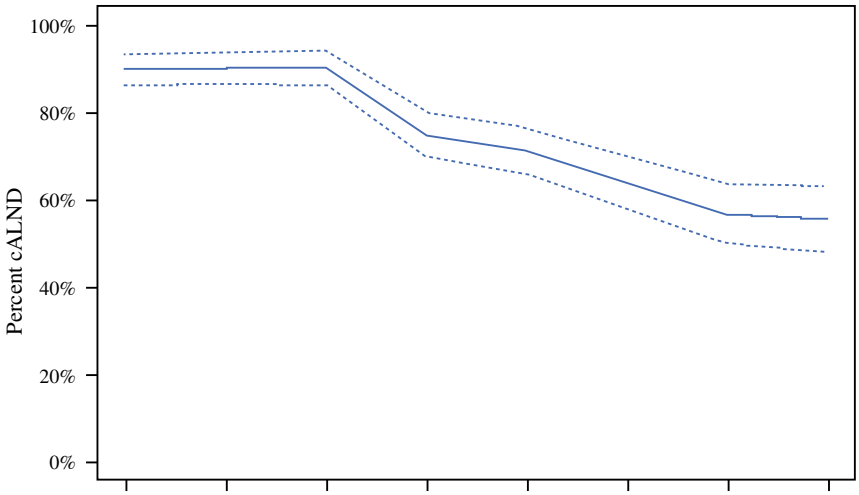
Data are n (%) unless otherwise stated

cALND completion axillary lymph node dissection, *SLN* sentinel lymph node, *SLND* sentinel lymph node dissection

The ACOSOG Z0011 trial was the first randomised controlled trial showing no benefit from cALND in patients with clinical T1 or T2 invasive breast cancer, no palpable axillary adenopathy, and one or two positive SLNs. In our time-trend analysis, the first significant decrease in cALND rates among patients undergoing mastectomy was in 2011, the year after initial publication of results from ACOSOG Z0011.[7] Furthermore, the time-trend analysis shows a constant reduction in cALND rates during subsequent years. This suggests that in clinical routine decision-making, the results of the ACOSOG Z0011 trial also have been gradually adopted for patients undergoing mastectomy, although this patient population was not included in ACOSOG Z0011. Positive lymph nodes are an important prognostic factor and lymph node status informs clinical decisions for adjuvant systemic therapy and radiotherapy. However, the decrease in cALND rates in patients undergoing mastectomy may reflect physicians' confidence in the general concept that even a positive lymph node left in situ will not develop into further metastases.[13] Thus, a more conservative approach to nodal staging could be possible, reducing arm morbidity without compromising oncological safety.

An analysis of the National Cancer Database (NCDB) included 34,243 patients from 2004 to 2015 with clinical T1/2N0M0 invasive breast cancer who underwent mastectomy with 1–2 positive lymph nodes. In this study, the cALND rate significantly decreased from 79% (2004) to 55% (2015) ($p < 0.001$), which is comparable to our study. The results from the NCBD database showed that survival outcomes did not differ by axillary treatment for patients with lymph node micrometastasis without axially radiotherapy and for patients who received postmastectomy radiotherapy.[14] Furthermore, several single institutions have analysed the outcomes of patients undergoing mastectomy with tumour-affected SLN(s) who did not receive cALND. They confirmed the findings from the prospective trials of equivalent overall and locoregional-free survival rates irrespectively from the surgical treatment of the axilla.[15–18]

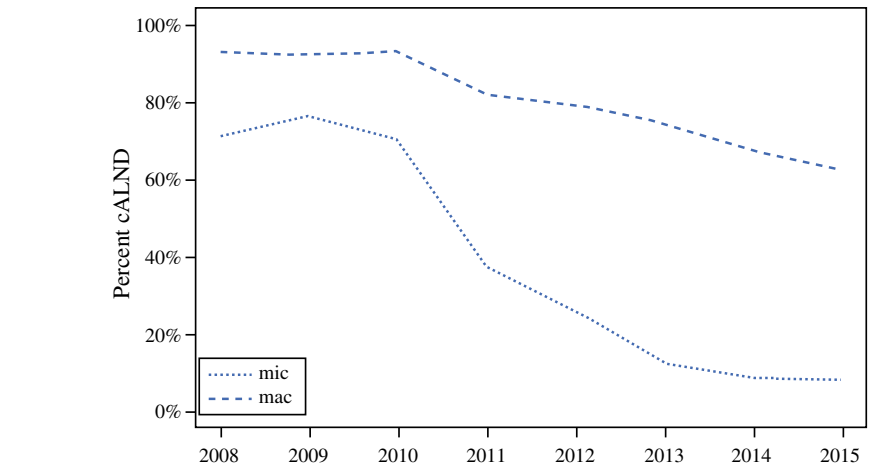
A recent report from Poodt et al. examined trends in axillary surgery in a nationwide Dutch cancer registry. They reported a marked and sustained decrease in cALND rates among patients with T1/2N0M0 breast cancer and positive SLN(s) undergoing BCS. This decrease also was seen in patients undergoing mastectomy, although to a lesser extent. The Dutch study reported a cALND rate in 2011 of 72% in the BCS group compared with 79% in the mastectomy group.[19] The authors concluded that variation between the surgical procedures is attributable to the small numbers and proportions of patients undergoing mastectomy in the existing randomized, controlled trials



cALND %	89.72	89.94	89.94	74.92	71.15	63.75	56.67	55.50

cALND=completion axillary lymph node dissection; SLN=sentinel lymph node.

FIG. 2 cALND rate in patients with T1/2N0M0 breast cancer and one or two tumour-affected SLNs undergoing mastectomy between 2008 and 2015. The dashed line shows the 95% confidence interval. *cALND* completion axillary lymph node dissection; *SLN* sentinel lymph node



cALND Macrometastasis (%)	92.94	91.04	93.02	81.87	79.20	74.41	67.57	62.65
cALND Micrometastasis (%)	71.19	76.47	82.46	36.96	25.81	12.26	8.43	7.84

cALND=completion axillary lymph node dissection; SLN=sentinel lymph node

FIG. 3 cALND rate in patients with micrometastasis versus macrometastasis from T1/2N0M0 breast cancer with one or two tumour-affected SLNs treated with mastectomy between 2008 and 2015. *cALND* completion axillary lymph node dissection; *SLN* sentinel lymph node

examining the omission of a cALND in patients with limited metastatic disease of the SLN [248 (17%) in AMAROS and 74 (16%) in OTOASOR].[9,10]

In 2011, the National Comprehensive Cancer Network (NCCN) guideline recommended no further axillary surgery for patients with T1/2N0M0 breast cancer and one or two tumour-affected SLNs treated with BCS and whole-breast radiotherapy.[20] It was not until 2015 that the NCCN guideline stated that for patients with a metastatic SLN undergoing mastectomy, axillary radiation could replace axillary dissection for regional disease control.[21] Similarly, the German Society of Gynecological Oncology (AGO) guidelines suggested omitting cALND in patients undergoing BCS and whole-breast radiation who met the ACOSOG Z0011 inclusion criteria as an option from 2011. It was not until 2015 that omitting cALND was recommended as an option for patients undergoing mastectomy

TABLE 3 Multivariable analysis on the influence of performing cALND in patients with T1/2N0M0 breast cancer and one or two tumour-affected SLNs undergoing mastectomy

Variable		Odds ratio (95% CI)	*p* value
Type of hospital	Academic teaching hospital	Reference	
	General, nonacademic hospital	0.57 (0.45–0.72)	< 0.001
	University hospital	1.21 (0.76–1.93)	0.41
Annual hospital caseload	< 150	Reference	
	150–249	0.99 (0.75–1.29)	0.92
	≥ 250	1.06 (0.81–1.40)	0.66
Age, year		0.97 (0.97–0.98)	< 0·001
pT stage	1	Reference	
	2	1.55 (1.21–1.99)	< 0.001
Type of metastasis	Macro	Reference	
	Micro	0.06 (0.04–0.08)	< 0.001
SLN removed	1	Reference	
	2	0.60 (0.44–0.82)	0.001
	3	0.38 (0.27–0.53)	< 0.001
	≥ 4	0.22 (0.16–0.31)	< 0.001
No. of metastatic SLNs	1	Reference	
	2	1.82 (1.39–2.40)	< 0.001
Grade	1	Reference	
	2	1.93 (0.79–1.78)	0.39
	3	1.25 (0.79–1.97)	0.34
Lymphovascular invasion	No	Reference	
	Yes	1.11 (0.88–1.38)	0.38
Histological subtype	Ductal	Reference	
	Lobular	0.66 (0.50–0.87)	0.002
	Other	1.11 (0.51–2.53)	0.79
HER2 status	Negative	Reference	
	Positive	0.91 (0.64–1.30)	0.62
Surgical procedure	Mastectomy	Reference	
	Mastectomy with re-excision	1.25 (0.21–10.81)	0.82
ECOG performance status	0	Reference	
	1	0.81 (0.61–1.08)	0.15
	2	0.63 (0.39–1.02)	0.06
Hormone receptor status	Negative	Reference	
	Positive	0.84 (0.54–1.28)	0.42

ECOG Eastern Cooperative Oncology Group, *pT* pathological tumour stage

for T1/2N0M0 breast cancer with one or two tumour-affected SLNs. This recommendation was based on results from the AMAROS trial following axillary radiation.[22]

In our time-trend analysis, we also examined the cALND rate separately for patients with macrometastasis versus micrometastasis of the SLN in the mastectomy cohort. The decrease in cALND rate was clearly more distinct among patients with micrometastasis than macrometastasis. In patients with minimal SLN involvement, defined as one or more micrometatastic SLNs (≤ 2 mm), the International Breast Cancer Study Group (IBCSG) 23-01 trial examined whether cALND is necessary in patients with a tumour measuring ≤ 5 cm.[23,24] In this trial, which was first presented at the San Antonio Breast Cancer Symposium in 2011, 9% of patients underwent mastectomy. The trial showed no benefit for cALND in patients with only micrometastasis of the SLN, consistent with results in non-mastectomy patients in the ACOSOG Z0011 trial. In addition, a smaller, randomised trial (AATRM 048/13/2000) that involved 247 patients with clinical node-negative breast cancer, tumours measuring < 3.5 cm in diameter, and micrometastases in the

SLN also reported no difference in disease-free survival between patients assigned to cALND versus those assigned to clinical follow-up alone.[25]

The 2017 version of the NCCN guidelines incorporates findings from the IBCSG 23-01 trial to recommend omitting cALND for patients with positive SLNs if the disease is limited to micrometastases independent of the surgical procedure.[26] AGO has made the same recommendation since 2011. The rapid implementation of these guidelines in patients undergoing mastectomy is reflected by the marked decline in cALND rates for patients with SLN micrometastasis in our time-trend analysis.

In addition to the size of SLN metastasis, another important factor that influenced treatment decisions in our multivariable analysis was nodal tumour burden, determined by the number of involved SLNs and the number of removed SLNs. In routine clinical practice, physicians were more comfortable with omitting cALND in patients with one rather than two tumour-affected SLNs [odds ratio 1.82; 95% confidence interval (CI) 1.39–2.40] and a higher number of removed SLNs (e.g., > 4 nodes odds ratio 0.22; 95% CI 0.16–0.31), presumably representing patients with a higher likelihood of no further non-sentinel metastasis. The nodal ratio has been shown to be an important determinant for predicting additional nodal disease and has been established in several nomograms.[27,28]

In clinical decision-making, the probability of omitting cALND decreases with decreasing age. This shows that physicians treat the axilla more aggressively in younger patients with the aim of minimising locoregional recurrence while increasing the risk of arm morbidity and the associated deterioration in quality of life. In breast cancer, local control is linked to overall survival.[29] Although in the randomised controlled trials to examine the omission of a cALND the axillary recurrence was low and ranges between 1 and 1.7% in 5–10 years follow-up data.[8–10]

Interestingly, in multivariable analysis hormone and HER2 receptor status showed no significant association with omitting cALND, suggesting that tumour biology was not a critical factor determining the clinical decision to perform cALND. This observation is perhaps surprising given that hormone-receptor status was a significant factor in multivariable analyses of overall survival in ACOSOG Z0011.[8]

These prospectively collected data from a nationwide cohort of patients treated for breast cancer in clinical routine management are high quality because of the extensive validation and monitoring. Nevertheless, there are limitations. No information on overall survival is available, precluding outcome analysis. Furthermore, data on radiation fields (e.g., chest wall vs. regional lymph nodes) are not consistently available. Therefore, it was not possible to explore routine clinical practice regarding axillary radiation in patients undergoing mastectomy, which should be taken into account when discussing treatment options.

CONCLUSIONS

Despite the limited evidence from prospective trials relating to omission of cALND in patients undergoing mastectomy, our data from routine clinical practice show a gradual decrease in the use of cALND in this patient population, similar to the decrease observed in patients undergoing BCS and whole-breast irradiation.

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ETHICAL APPROVAL The study was approved by the ethics committee of the University of Heidelberg and was conducted in accordance with the Declaration of Helsinki. The study was deemed to be without risk, including only anonymised analysis of routinely collected data; consequently the ethics committee of the University of Heidelberg did not request approval for consent.

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