St Gallen 2019 guidelines undercover the axilla in lobular breast cancer: a population-based study

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Abstract

Background: The St Gallen 2019 guidelines for primary therapy of early breast cancer recommend omission of completion axillary lymph node dissection (cALND), regardless of histological type, in patients with one or two sentinel lymph node (SLN) metastases. Concurrently, adjuvant chemotherapy is endorsed for luminal A-like disease with four or more axillary lymph node (ALN) metastases. The aim of this study was to estimate the proportion of patients with invasive lobular cancer (ILC) versus invasive ductal cancer of no special type (NST) with one or two SLN metastases for whom cALND would have led to a recommendation for adjuvant chemotherapy.

Methods: Patients with ILC and NST who had surgery between 2014 and 2017 were identified in the National Breast Cancer Register of Sweden. After exclusion of patients with incongruent or missing data, those who fulfilled the St Gallen 2019 criteria for cALND omission were included in the population-based study cohort.

Results: Some 1886 patients in total were included in the study, 329 with ILC and 1507 with NST. Patients with ILC had a higher metastatic nodal burden and were more likely to have a luminal A-like subtype than those with NST. The prevalence of at least four ALN metastases was higher in ILC (31.0 per cent) than NST (14.9 per cent), corresponding to an adjusted odds ratio of 2.26 (95 per cent c.i. 1.59 to 3.21). Luminal A-like breast cancers with four or more ALN metastases were over-represented in ILC compared with NST, 52 of 281 (18.5 per cent) versus 43 of 1299 (3.3 per cent) (P < 0.001).

Conclusion: Patients with ILC more often have luminal A-like breast cancer with at least four nodal metastases. Omission of cALND in patients with luminal A-like invasive lobular cancer and one or two SLN metastases warrants future attention as there is a risk of nodal understaging and undertreatment in one-fifth of patients.

Lay summary

Nowadays patients who have breast cancer with one to two metastases in the first draining axillary lymph nodes are not recommended to undergo completion surgery of the axilla if they have breast-conserving surgery and will have adequate postoperative oncological treatment. Lobular breast cancer is the second most common type of breast cancer, and this study shows that patients with this type have an increased risk of having lymph node metastases remaining if completion surgery is omitted. The diagnosis of additional lymph node metastases is importance for guidance regarding adjuvant oncological therapy in lobular cancer with a hormonally sensitive low proliferative subtype.

Introduction

Invasive lobular cancer (ILC) comprises approximately 10–15 per cent of all invasive breast cancers1. It has distinct clinicopathological and genomic features with different responsiveness to systemic treatment, distinguishing it from ductal cancer of no special type (NST)2–4. The majority of ILCs are classified as luminal A-like2,5. The long-term prognosis appears the same for ILC and NST, although there is a tendency towards a higher incidence of late recurrences in ILC3,6,7.

ILC has a characteristic growth pattern, with single files of tumour cells diffusely infiltrating benign tissue8. Both primary tumours and axillary lymph node (ALN) metastases tend to be...
non-palpable and difficult to detect by imaging, or fine-needle aspiration or core needle biopsy. The sensitivity of axillary ultrasound imaging for detection of ALN metastases is lower in ILC, especially in patients with a high metastatic nodal burden. The clinical value of breast MRI and PET–CT for clinical staging remains unclear. Patients with ILC are often diagnosed at a more advanced stage, have a tendency towards having four or more ALN metastases, and more non-sentinel lymph node (SLN) metastases. Despite these differences, current treatment guidelines are similar for ILC and NST.

Nodal staging is one of the cornerstones in the diagnostic work-up of breast cancer as ALN metastasis is an important negative prognostic factor. In patients with clinically node-negative (cN0) breast cancer, axillary staging has been done by SLN biopsy followed by completion ALN dissection (cALND) in those with metastases. Two RCTs on ALN management, the American College of Surgical Oncology Group Z0011 trial and the International Breast Cancer Study Group 23-01 trial, showed that omitting cALND in patients with clinically node-negative but SLN-positive T1–2 breast cancer did not affect recurrence and survival rates during the first 10 years of follow-up. Furthermore, the AMAROS RCT, in which patients with clinically node-negative T1–2 breast cancer and at least one SLN metastasis were randomized to either cALND or axillary radiotherapy, showed no differences in recurrence or survival rates with 10 years of follow-up. The findings from these trials have led to a change in practice for axillary management, irrespective of histological subtype.

In the St Gallen 2019 guidelines for primary therapy of early breast cancer, all histological subtypes were included in the extended indication for cALND omission. Completion ALND can thus be omitted in clinically T3, N0 breast cancer with one or two SLN metastases, provided that the patient receives adjuvant systemic treatment and regional nodal irradiation. In addition, the St Gallen 2019 guidelines recommend adjuvant chemotherapy for patients with luminal A-like tumours and four or more ALN metastases. The number patients with ILC was small in the above-mentioned RCTs (8.0 per cent, 334 of 4192), and so the applicability these data as criteria for omitting cALND in patients with ILC is unclear.

The aim of the present study was to compare the prevalence of at least four ALN metastases and the number of non-SLN metastases in ILC and NST in a large population-based cohort from a validated register. A further aim was estimate the prevalence of luminal A-like tumours with at least four ALN metastases in ILC and NST among patients who met the criteria for omission of cALND according to the St Gallen 2019 guidelines or the Z0011 trial.

Methods

The present study was approved by the local ethics committee (2019–02139) and adheres to the STROBE guidelines for observational studies. Clinicopathological characteristics were retrieved from the Swedish National Breast Cancer Register for patients with primary breast cancer. The register is validated and covers 99.99 per cent of all breast cancers diagnosed in Sweden. The interval 2014–2017 was chosen based on cALND still being recommended in patients with SLN metastases by the Swedish treatment guidelines for breast cancer, and on key variables being available in the register. The study was registered in the ISRCTN registry (ISRCTN14341750).

Study populations

Women diagnosed with unilateral primary breast cancer classified as ILC, NST, or mixed ILC/NST, who underwent breast and axillary surgery as primary treatment, were identified. Patients who underwent SLN biopsy and subsequent cALND but who would have been eligible for omission of cALND according to the St Gallen 2019 criteria (clinically T1–3 N0 with 1–2 SLN metastases of which at least one was a macrometastasis) were included in the main study cohort (St Gallen 2019 cohort). In addition, a Z0011 cohort comprised patients who underwent breast-conserving surgery and SLN biopsy (with clinically T1–2 N0 and 1–2 SLN metastases of which at least one was a macrometastasis). Patients with node-negative disease and those with data from only SLN biopsy or ALND were excluded. The study flow chart is shown in Fig. 1.

Pathological assessment and surrogate molecular subtypes

Pathological assessments of the primary tumour, SLNs, and ALNs were performed in accordance with the Swedish Quality Document for Pathology. ILC was identified by specified morphological criteria. In the event of macrometastasis in an uncertain specimen showing a lobular growth pattern, complementary immunohistochemical E-cadherin staining was performed. ALNs were prepared identically irrespective of histological subtype, but in ILC the SLNs were stained using both haematoxylin–eosin and complementary cytokeratin staining. Oestrogen receptor (ER) and progesterone receptor (PR) positivity were defined by at least 10 per cent stained nuclei, and in accordance with Prat and colleagues, FR staining of 20 per cent or more was considered high. Human epidermal growth factor receptor 2 (HER2) positivity was defined as HER2 in situ hybridization test-positive, and, if this test was missing, by immunohistochemical 3+ scoring. The Ki-67 percentage was categorized into three groups—low, intermediate and high—based on local laboratory percentile-based cut-offs, and Nottingham histological grade (NHG) was evaluated according to Elston and Ellis.

Lymph node micrometastasis was defined as a cancer cell deposit larger than 0.2 mm but not larger than 2 mm consisting of at least 200 cancer cells, and a macrometastasis as a deposit larger than 2 mm. Deposits of 0.2 mm or smaller and/or consisting of fewer than 200 cancer cells were defined as isolated tumour cells. Patients with isolated tumour cells in the SLN were classified as having N0 disease. Patients with micrometastases (216, 10 per cent) were excluded (Fig. 1), as current clinical guidelines do not recommend cALND for these patients.

The modification of the St Gallen 2019 guidelines and classification proposed by Maisonneuve et al. (including ER, PR, HER2, Ki-67, and NHG) were used to define surrogate molecular subtypes as luminal A-like, luminal B-like, HER2-positive, and triple-negative breast cancer (Table S1).

Statistical analysis

The primary endpoint was prevalence of at least four ALN metastases in patients with ILC and NST. A secondary endpoint was to estimate the proportion of patients with luminal A-like tumours with four or more ALN metastases in ILC and NST, in patients meeting the criteria for omission of cALND according to the St Gallen 2019 guidelines.

Differences in categorical variables, including patient and tumour characteristics, between the histological subtypes (ILC versus NST) were evaluated using Pearson’s χ² test, Fisher’s exact test, and the Wilcoxon rank sum test. All tests were two-sided and a P-value of 0.05 was considered significant.
test if one or more of the expected counts in the contingency table was below 5, or Pearson’s \( \chi^2 \) test for trend for ordinal variables with more than two categories. Variables measured on a continuous scale were evaluated using the Mann–Whitney \( U \) test. Univariable and multivariable analyses were performed using logistic regression. 

\[ P \text{ values, which were not adjusted for multiple testing, should be interpreted as level of evidence, on a continuous scale from 0 to 1, against the null hypothesis without reference to a cut-off for significance.} \]

**SPSS** version 25.0 (IBM, Armonk, NY, USA) and Stata version 16 (StataCorp, College Station, TX, USA) were used for statistical calculations.

**Results**

**Demographics and non-sentinel node metastases by histological subtype in cohort based on St Gallen 2019 guidelines**

Of a total of 20,139 women with unilateral ILC, NST, or mixed ILC/NST primary breast cancer, who underwent breast and axillary surgery as primary treatment, 1886 were included in the St Gallen 2019 cohort (Fig. 1). Among 329 patients with pure ILC and 1507 with pure NST with one or two metastatic SLNs, several differences in clinicopathological characteristics were identified (Table 1). Patients with ILC were older, and more often had a mastectomy. The tumours were larger, more often multifocal, and the metastatic burden in ALNs was higher. Additionally, the proportion of luminal A-like tumours was higher. The characteristics of the mixed ILC/NST group (50 patients) are shown separately, the biomarker profile in this group was closer to that of pure ILC than NST.

The number of excised ALNs did not differ by histological subtype (Table 1). One or more non-SLN metastases in the axillary specimen was, however, more common in ILC than NST: 165 of 329 (50.2 per cent) versus 545 of 1507 (36.2 per cent) \((P < 0.001; \text{ odds ratio (OR) 1.78, 95 per cent confidence interval c.i. 1.40 to 2.26})\). Similarly, a higher proportion of patients with ILC than NST had four or more ALN metastases: 102 of 329 (31.0 per cent) and 224 of 1507 (14.9 per cent) respectively \((P < 0.001; \text{ OR 2.57, 1.96 to 3.38})\) (Table 1, Fig. S1a, and Fig. 2a). In patients with one or more non-SLN metastases, the number of non-SLN metastases was also higher in ILC than NST: median 3 (i.q.r. 1–7) versus 2 (1–3) (Table 1 and Fig. S1b).

**Four or more nodal metastases by histological and surrogate subtype in cohort based on St Gallen 2019 guidelines**

Patients with the luminal A-like subtype and four or more ALN metastases were over-represented in the group with ILC, 52 of 281 (18.5 per cent) compared with 43 of 1299 patients with NST (3.3 per cent) \((P < 0.001; \text{ OR 6.63, 95 per cent confidence interval c.i. 4.32 to 10.17})\) (Table 1 and Fig. 2b). The relative frequency of at least four ALN metastases in all the different surrogate molecular subtypes was higher in ILC (Table 1 and Fig. 2c). The adjusted odds of at least four ALN metastases in patients with the luminal A-like subtype was higher in ILC compared with NST (OR 2.92, 1.73 to 4.94).
Table 1 Clinicopathological characteristics of patients eligible for omission of completion axillary lymph node dissection according to the St Gallen 2019 criteria

|                          | NST (n = 1507) | ILC (n = 329) | P (ILC versus NST) | Mixed ILC/NST (n = 50) |
|--------------------------|----------------|---------------|-------------------|------------------------|
| Age at surgery (years)*  | 62 (52–71)     | 65 (54–72)    | 0.011$          | 60 (48–70)             |
| Detected by screening    |                |               | 0.549            |                        |
| No                       | 799 (53)       | 180 (55)      |                  | 25 (50)                |
| Yes                      | 707 (47)       | 148 (45)      |                  | 25 (50)                |
| Missing                  | 1              | 1             |                  | 0                      |
| Type of breast surgery   |                |               | <0.001           |                        |
| BCS                      | 861 (57)       | 113 (34)      |                  | 17 (34)                |
| Mastectomy               | 646 (43)       | 216 (66)      |                  | 33 (66)                |
| Multifocal tumour        |                |               | 0.012            |                        |
| No                       | 1142 (76)      | 223 (69)      |                  | 28 (57)                |
| Yes                      | 362 (24)       | 99 (31)       |                  | 21 (43)                |
| Missing                  | 3              | 7             |                  | 1                      |
| T category               |                |               | <0.001           |                        |
| T1 (≤ 20 mm)             | 832 (55)       | 85 (26)       |                  | 19 (38)                |
| T2 (> 20 to 50 mm)       | 627 (42)       | 175 (53)      |                  | 25 (50)                |
| T3 (> 50 mm)             | 48 (3)         | 69 (21)       |                  | 6 (12)                 |
| No. of SLNs excised†     | 2 (1–9)        | 2 (1–8)       | 0.025§           | 2 (1–9)                |
| No. of SLN metastases    |                |               | 0.374            |                        |
| 1                        | 1148 (76)      | 243 (74)      |                  | 38 (76)                |
| 2                        | 359 (24)       | 86 (26)       |                  | 12 (24)                |
| No. of nodes excised*    | 13 (10–17)     | 12 (10–16)    | 0.362§           | 12 (1–16)              |
| No. of non-SLN metastases|                |               | <0.001           |                        |
| No (0)                   | 962 (64)       | 164 (50)      | <0.001           | 31 (61)                |
| Yes (≥1)                 | 545 (36)       | 165 (50)      | <0.001           | 19 (39)                |
| 1                        | 250 (17)       | 42 (13)       | <0.001           | 8 (16)                 |
| 2                        | 107 (7)        | 29 (9)        |                  | 6 (12)                 |
| ≥ 3                      | 188 (12)       | 94 (29)       |                  | 5 (10)                 |
| 1–2                      | 357 (24)       | 71 (22)       | <0.001           | 14 (28)                |
| ≥ 3                      | 188 (12)       | 94 (96)       | <0.001           | 5 (10)                 |
| Median (i.q.r.) if > 0   | 2 (1–3)        | 3 (1–7)       | <0.001§          | 2 (1–3)                |
| N category, 3 groups     |                |               | <0.001           |                        |
| N1 (1–3 ALN metastases)  | 1283 (85)      | 227 (69)      |                  | 43 (86)                |
| N2 (4–9 ALN metastases)  | 181 (12)       | 69 (21)       |                  | 6 (12)                 |
| N3 (≥ 10 ALN metastases) | 43 (3)         | 33 (10)       |                  | 1 (2)                  |
| Nodal category, 2 groups |                |               | <0.001           |                        |
| N1 (1–3 ALN metastases)  | 1283 (85)      | 227 (69)      |                  | 43 (86)                |
| N2 (≥ 2 ≥ 4 ALN metastases) | 224 (15)  | 102 (31)      |                  | 7 (14)                |
| Molecular subtype (all patients)† | 484 (37) | 176 (63) | <0.001           | 26 (62)                |
| Luminal A-like           |                |               |                  |                        |
| Luminal B-like           | 501 (39)       | 88 (31)       |                  | 14 (33)                |
| HER-positive             | 210 (16)       | 13 (5)        |                  | 2 (5)                  |
| TNBC                     | 104 (8)        | 4 (1)         |                  | 0 (0)                  |
| Missing                  | 208            | 48            |                  | 8                      |
| Molecular subtype (patients with ≥ 4 ALN metastases) | <0.001 | |
| Luminal A-like           | 43 (23)        | 52 (60)       |                  | 2 (33)                 |
| Luminal B-like           | 91 (48)        | 25 (29)       |                  | 4 (67)                 |
| HER2-positive            | 42 (22)        | 7 (8)         |                  | 0 (0)                  |
| TNBC*                    | 15 (8)         | 3 (3)         |                  | 0 (0)                  |
| Missing                  | 33             | 15            |                  | 1                      |
| Luminal A-like and ≥ 4 ALN metastases | <0.001 | |
| No                       | 1256 (97)      | 229 (81)      |                  | 40 (95)                |
| Yes                      | 43 (3)         | 52 (19)       |                  | 2 (5)                  |
| Missing                  | 208            | 48            |                  | 8                      |
| Luminal A-like           |                |               | <0.001           | 24 (92)                |
| <4 ALN metastases        | 441 (91)       | 124 (70)      |                  | 2 (8)                  |
| ≥ 4 ALN metastases       | 43 (9)         | 52 (30)       |                  | 2 (8)                  |
| Luminal B-like           |                |               | 0.026            |                        |
| <4 ALN metastases        | 410 (82)       | 63 (72)       |                  | 10 (71)                |
| ≥ 4 ALN metastases       | 91 (18)        | 25 (28)       |                  | 4 (29)                 |
| HER2-positive            |                |               | 0.004            |                        |
| <4 ALN metastases        | 168 (80)       | 6 (46)        |                  | 2 (100)                |
| ≥ 4 ALN metastases       | 42 (20)        | 7 (54)        |                  | 0 (0)                  |
| TNBC                     |                |               | 0.001            |                        |
| <4 ALN metastases        | 89 (86)        | 1 (25)        |                  | 0 (0)                  |
| ≥ 4 ALN metastases       | 15 (14)        | 3 (75)        |                  | 0 (0)                  |

(continued)
Multivariable analyses of axillary nodal burden in cohort based on St Gallen 2019 guidelines

The odds of one or more non-SLN metastases remained higher for ILC than NST after adjustment for other relevant predictors including age, detection by screening, T category, multifocality, number of SLNs with macrometastases, and surrogate molecular subtypes (OR 1.55, 95 per cent c.i. 1.15 to 2.08; P = 0.004) (Table 2). The odds of at least four ALN metastases was higher in ILC than in NST after adjustment for the same variables (OR 2.26, 1.59 to 3.21; P = 0.001) (Table 2 and Fig. 3). Tumour stage, multifocality, surrogate molecular subtypes, and number of SLNs with macrometastases were confirmed as predictors of at least four ALN metastases, along with ILC (Table 2 and Fig. 3).

Demographics and nodal metastatic burden in subcohort based on Z0011 trial criteria

Clinicopathological data for the Z0011 subcohort of 975 patients (Table S2) and the entire cohort retrieved from the register (Table S3) showed essentially the same differences between pure ILC and pure NST cases as the cohort based on the St Gallen 2019 guidelines.

In the Z0011 cohort (105 ILC, 854 NST), 41.9 per cent of patients with ILC and 31.0 per cent with NST had one or more non-SLN metastases (P = 0.025; OR 1.60, 95 per cent c.i. 1.06 to 2.43), and the proportion of patients with at least four ALN metastases was higher in ILC (25.7 versus 10.7 per cent; P < 0.001; OR 2.90, 1.78 to 4.73). The total number of non-SLN metastases in those with one or more non-SLN metastases was higher in ILC than NST (Table S2). Patients in the cohort based on the Z0011 trial with the luminal A-like subtype and at least four ALN metastases were predictors of axillary nodal burden (Table 2 and Fig. 3).

Table 1. (continued)

| Molecular subtype missing | NST (n = 1507) | ILC (n = 329) | P (ILC versus NST)‡ | Mixed ILC/NST (n = 50) |
|---------------------------|---------------|--------------|---------------------|------------------------|
| <4 ALN metastases         | 175 (84)      | 33 (69)      |                     | 7 (88)                 |
| ≥ 4 ALN metastases        | 33 (16)       | 15 (31)      |                     | 1 (12)                 |

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). Eligible patients underwent breast-conserving surgery (BCS) or mastectomy, and had T1–3 cN0 tumours, and one or two sentinel lymph node (SLN) metastases, of which at least one was a macrometastasis. †Based on a modification of the St Gallen 2019 guidelines and the classification proposed by Maisonneuve et al., tumours were defined as: luminal A-like (oestrogen receptor (ER)+, human epidermal growth factor receptor 2 (HER2)−, Nottingham histological grade (NHG) 1, or ER+, HER2−, NHG 2, Ki-67 low, or ER+, HER2−, NHG 2, Ki-67 intermediate, and progesterone receptor (PR) at least 20 per cent), luminal B-like (ER+, HER2−, NHG 3, or ER+, HER2−, NHG 2, Ki-67 high, or ER+, HER2−, NHG 2, Ki-67 intermediate and PR below 20 per cent), HER2-positive (all HER2+ independent of ER, NHG, Ki-67, and PR status), or triple-negative breast cancer (TNBC) (ER−, PR− and HER2−). NST, invasive ductal cancer of no special type; ILC, invasive lobular cancer; ALN, axillary lymph node. ‡Pearson’s χ² test (linear by linear association test if more than 2 ordered categories), except §Mann–Whitney U test.
metastases were also over-represented in ILC compared with NST: 13 of 83 (16 per cent) versus 21 of 738 (2.8 per cent) (P < 0.001; OR 6.34, 3.04 to 13.21) (Table S2).

In multivariable analyses, ILC remained an independent predictor of non-SLN metastases even after adjustments (OR 1.81, 1.11 to 2.98; P = 0.018) (Table S4). Finally, the adjusted odds of at least four ALN metastases was higher in ILC than in NST (OR 2.94, 1.56 to 5.54; P = 0.001) (Table S4).

### Discussion

This population-based Swedish registry study showed that, when the St Gallen 2019 guidelines for omitting cALND were applied, the presence of non-SLN metastases and proportion of patients with at least four ALN metastases were higher among patients with ILC than those with NST. These findings highlight that the St Gallen 2019 guidelines for omission of cALND are associated with understaging of ALN status, and a subsequent risk of undertreatment, especially of ILCs with the luminal A-like subtype. Most patients with NST had benign non-SLNs after cALND, whereas half of the patients with ILC had non-SLN involvement in the axillary specimen. Similar results were seen for the narrower but more generally accepted Z0011 criteria for omitting cALND. Importantly, ILC was an independent predictor of non-SLN metastases and at least four ALN metastases after adjustment for validated predictors of non-SLN metastases in both cohorts.

Breast cancer classified as luminal A-like with at least four ALN metastases was more frequent in patients with ILC than those with NST. In patients with a luminal A-like subtype, the recommendation for adjuvant chemotherapy depends on ALN staging even in the era of genomic testing. Although patients with luminal B-like and HER2-positive subtypes had a higher risk of having at least four ALN metastases than those with the luminal A-like subtype, the staging information from cALND is of less importance for these patients as adjuvant chemotherapy would be recommended irrespective of nodal status. The present results suggest that, when the St Gallen 2019 criteria for omitting cALND are applied, approximately one-fifth of patients with ILC and 1 in 30 with NST having one or two confirmed SLN macrometastases will not be offered adjuvant chemotherapy due to understaging of the axilla. Essentially the same results were seen in the Z0011 cohort.

Previous breast cancer studies exploring the impact of nodal staging on adjuvant treatment decision did not specify the histological subtypes and were based on smaller cohorts. Aigner and colleagues included 132 patients and found that 17 per cent of those with Z0011-eligible breast cancer would have been offered more extensive adjuvant treatment based on the information retrieved by cALND. Stenmark Tullberg et al. reported on 238 patients with clinically N0 breast cancers and one or more SLN metastases (at least 1 macrometastasis), in 18 per cent of those with luminal A-like tumours, four or more ALN metastases were detected on cALND.

In the population-based unselected cohort study, patients eligible for omission of cALND according to the St Gallen 2019 recommendation and Z0011 trial had a prognostically more unfavourable ALN status than those originally included in the Z0011, International Breast Cancer Study Group 23-01, and AMAROS trials. Study inclusion was restricted to patients with one or two SLN metastases (at least 1 macrometastasis), and patients with isolated tumour cells in the SLN were excluded. In the seminal trials, a majority of patients had micrometastases only in SLNs, isolated tumour cells were classified as micrometastasis, and at least 90 per cent received adjuvant systemic treatment. These conditions could have affected the outcome data and, with a follow-up time restricted to 10 years, there is still a risk of late recurrences, especially for ILC.

Additionally, only a small number of included patients had ILC (approximately 8 per cent), and in none of the trials were subgroup analyses of ILC versus NST reported.
Fig. 3 Forest plot visualization of multivariable logistic regression model for at least four axillary lymph node metastases in patients fulfilling the St Gallen 2019 criteria for omission of completion axillary lymph node dissection
Odds ratios are shown with 95% confidence intervals. ILC, invasive lobular cancer; NST, invasive ductal cancer of no special type; macro, macrometastasis; micro, micrometastasis; LumB, luminal B-like; LumA, luminal A-like; HER2+, human epidermal growth factor receptor 2-positive; TNBC, triple-negative breast cancer.

Discussion regarding omission of cALND is encouraged for all patients with ILC.

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Supplementary material
Supplementary material is available at BJS online.

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The data set used during this study is available from the corresponding author on reasonable request.

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