Original Article

Eur J Breast Health 2024; 20(4): 270-276
DOI: 10.4274/ejbh.galenos.2024.2024-5-11

# Applying the SOUND Trial for Omitting Axillary Surgery in Patients With Early Breast Cancer in Bahrain

Ali Hasan Abdulla[1], Reem Althawadi[1], Ahmed Zuhair Salman[1], Tareq Hamed Altaei[2], Amina Mohamed Mahdi[2], Hussain Adnan Abdulla[1]

[1]Department of Surgery, Salmaniya Medical Complex, Government Hospitals, Manama, Bahrain
[2]Department of Radiology, Salmaniya Medical Complex, Government Hospitals, Manama, Bahrain

## ABSTRACT

**Objective:** The Sentinel Node vs. Observation After Axillary Ultra-Sound (SOUND) trial reported that omission of axillary surgery was not inferior to sentinel lymph node biopsy (SLNB) in those with cT1 breast cancer and negative preoperative axillary ultrasound. The aim of our study was to evaluate the clinical characteristics of early breast cancer patients undergoing breast conserving surgery (BCS) at our institution in order to investigate the exportability of SOUND criteria to our patient population.

**Materials and Methods:** We retrospectively reviewed patients with cT1N0 breast cancer undergoing BCS and adjuvant radiotherapy according to the SOUND trial criteria. Comparison was made between the eligible group of our cohort and the SLNB arm of the SOUND trial.

**Results:** The proportion of younger patients was higher in our eligible cohort (37.7% *vs.* 17.5%, $p = 0.002$). Postmenopausal patients were more prevalent in the SOUND trial (79.4% *vs.* 56.6%, $p = 0.004$). On final pathology, tumours were more likely to be upgraded to T2 in our group (26.4% vs. 4.4%, $p = 0.001$). Patients in our cohort were more likely to receive adjuvant chemotherapy (37.7% *vs.* 20.1%, $p = 0.002$).

**Conclusion:** The clinicopathological differences between our cohort and the SOUND trial population could be attributed to aggressive tumours in Bahrain compared to Western countries. Our study may influence others to investigate the applicability of the SOUND trial in clinical practice. Nevertheless, it is a study that should generate multidisciplinary discussion in the de-escalation of axillary surgery.

**Keywords:** Early breast cancer; sentinel lymph node biopsy; axillary surgery; breast conserving surgery; SOUND trial

**Cite this article as:** Abdulla AH, Althawadi R, Salman AZ, Altaei TH, Mahdi AM, Abdulla HA. Applying the SOUND Trial for Omitting Axillary Surgery in Patients With Early Breast Cancer in Bahrain. Eur J Breast Health. 2024; 20(4): 270-276

### Key Points

- Sentinel lymph node biopsy (SLNB) is the standard of care in clinically node-negative breast cancer for axillary staging and locoregional control.
- The Sentinel Node vs. Observation After Axillary Ultra-Sound (SOUND) trial concluded that patients with small breast cancer and sonographically normal appearing lymph nodes can be safely spared any axillary surgery, as lack of pathological information does not influence adjuvant therapy.
- Compared to the SOUND trial, early breast cancer patients in Bahrain tend to be of younger age, premenopausal, have larger tumours on final pathology and are more likely to receive adjuvant chemotherapy.
- Given the difference between our population and the SOUND trial patients, our findings still support a role for SLNB to guide adjuvant therapy decisions.
- This study evaluates the applicability of the SOUND trial in a real-world patient population.

## Introduction

The management of the axilla in breast cancer has changed considerably in the past few decades. In early breast cancer, sentinel lymph node biopsy (SLNB) has replaced axillary dissection as the standard of care for axillary staging and locoregional control (1, 2). The landmark American College of Surgeons Oncology Group Z0011 (ACOSOG Z0011) trial (3) has revolutionised axillary management in women undergoing breast conserving surgery (BCS) followed by adjuvant radiotherapy and systemic therapy, sparing patients axillary dissection even when 1–2 sentinel nodes are positive for macrometastasis. The findings from the ACOSOG Z0011 trial were supported by other randomised controlled trials and became the standard for axillary management in early breast cancer, showing reduced patient morbidity without compromised oncological outcomes (4, 5). Despite presentation of ACOSOG Z0011 data in 2010, the trial was debated and has not yet been incorporated into practice (6). It was only between 2016 and 2017 when we started to adopt the ACOSOG Z0011 criteria in Bahrain, after an updated clinical practice guideline was recommended by

Corresponding Author:
Hussain Adnan Abdulla; hussainaabdulla@yahoo.com

Received: 28.05.2024
Accepted: 27.07.2024
Available Online Date: 26.09.2024

the National Comprehensive Cancer Network (7), representing a milestone in surgical de-escalation.

There are several prospective randomised trials evaluating the omission of SLNB in clinically node-negative early breast cancer patients undergoing upfront surgery (8). The Sentinel Node vs. Observation After Axillary Ultra-Sound (SOUND) trial (9) was the earliest to open in 2012 and it was published recently. It reported that omission of axillary surgery was not inferior to SLNB in those with cT1 breast cancer and negative preoperative axillary ultrasound, meaning that these patients can be safely spared axillary surgery when the lack of pathological nodal status does not influence the adjuvant treatment decisions (10). They found no difference in baseline characteristics, in five-year distant disease-free survival and the rate of axillary recurrences between those that underwent SLNB and patients that did not. Although this trial is unlikely to change clinical practice immediately, it is a study that will likely influence multidisciplinary discussion. The aim of this study was to review the clinical characteristics of early breast cancer patients undergoing BCS and SLNB in Bahrain at a single centre in order to evaluate the external generalisability of SOUND criteria to our patient population.

## Materials and Methods

This study was approved by the Ethical Committee of Government Hospitals Bahrain (approval number: 116051223, date: 05.12.2023). We conducted a retrospective review from a prospectively maintained database, from October 2021 to September 2023. Patients were included if they had cT1-T2 breast cancer without palpable adenopathy before surgery, underwent SLNB with no prior neoadjuvant systemic therapy. Patients were excluded if they had failure of localisation of sentinel lymph nodes, multiple suspicious lymph nodes, extensive multifocality or multicentricity, bilateral cancers, those with local recurrence and synchronous tumours. The recruited patients were then divided into two groups according to the SOUND trial criteria: Women with invasive breast cancer up to 2 cm in diameter, no axillary lymphadenopathy at clinical evaluation and a plan to undergo BCS and adjuvant radiotherapy. The eligible group comprised patients who met the SOUND trial criteria for omitting axillary surgery, while the ineligible group consisted of patients who did not meet these criteria.

All patients underwent bilateral mammogram and ultrasound of breasts and axillae to define the clinical T and N stage. In case of a suspicious lymph node on ultrasound, a biopsy was performed to rule out the presence of nodal metastases. Patients were excluded if the biopsy confirmed axillary metastasis. At our institution, we do not proceed with SLNB for patients with 1–2 suspicious lymph nodes on ultrasound, due to demand by our oncologists and the tumour board for comprehensive investigation, including axillary biopsy. Patients with a biopsy positive for axillary metastasis undergo upfront axillary dissection or neoadjuvant therapy, and these patients were excluded from the study. All patients with clinically node-negative invasive cancer or a node biopsy negative for metastasis had SLNB to stage the axilla. SLNB was performed using dual technique, comprising radioisotope and patent blue dye. Intraoperative frozen section was carried out in all patients. Completion axillary lymph node dissection (ALND) was performed if >2 nodes contained macrometastases, applying ACOSOG Z0011 criteria.

### Statistical Analysis

The following patient demographics and tumour characteristics were collected and tabulated: age at diagnosis, menopausal status, histological tumour type, tumour grade, pathological tumour size, pathological nodal status, oestrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 (HER2) status, Ki-67 index, tumour molecular subtype and type of adjuvant therapy received. The eligible group was compared with the ineligible group. Comparison was then made between the eligible group of our cohort and the SLNB arm of the SOUND trial using the chi-squared test. Statistical analysis was performed using SPSS software, version 29.0 (IBM, Armonk, NY, USA). *P*-values less than 0.05 were considered to be significant.

## Results

A total of 147 patients with early breast cancer underwent SLNB at our institution between October 2021 and September 2023. Baseline characteristics of the study population are summarised in Table 1. All patients were female. The median (range) number of sentinel nodes removed was 3 (1–5), while the median number of histologically pathological sentinel nodes was 2 (1–4). Approximately one-quarter of patients had macrometastases (23.1%), with only 5.4% of cases undergoing axillary dissection. Out of the 147 patients, only 53 patients who met the SOUND criteria for omitting SLNB were included in the eligible group, while 94 patients who did not meet the criteria were labelled as ineligible and excluded from the analysis, having cT2 tumours or a mastectomy (Figure 1).

Table 2 compares the eligible patients in our study and those in the SOUND trial SLNB arm. The factors showing significant differences between the two groups were age, menopausal status, tumour size on final pathology and adjuvant chemotherapy. In particular, even though the majority of patients in both cohorts were 50 years or older, the proportion of younger (<50 years) patients in our eligible group was approximately twice a large than that in the SOUND trial (37.7% *vs.* 17.5%, $p = 0.002$). Similarly, a higher percentage of premenopausal patients were observed in our eligible group compared with the no axillary surgery arm in the SOUND trial (43.4% *vs.* 20.6%, $p = 0.004$). On final pathology, over a quarter of our patients were upgraded to T2 tumours, compared to only 4.4% in the SOUND trial cohort ($p = 0.001$). The patients in our eligible group were more likely to receive adjuvant chemotherapy than those in the SOUND trial population (37.7% *vs.* 20.1%, $p = 0.002$). Otherwise, there were no significant differences between the two cohorts in terms of histological subtype, tumour grade, pathological nodal status, hormone receptor

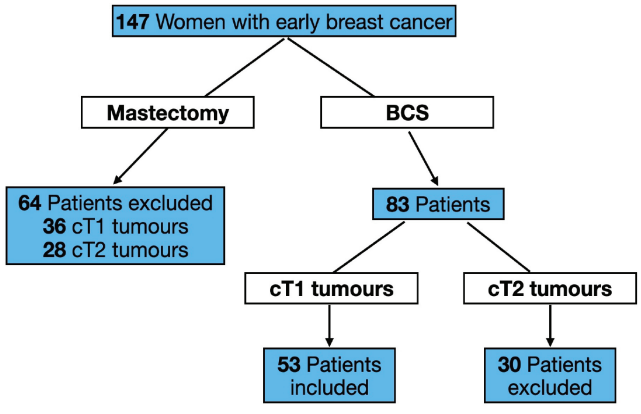


**Figure 1.** Flow chart representing inclusion of patients in the study analysis

*BCS: Breast conserving surgery*

Table 1. Clinicopathological characteristics of early breast cancer patients undergoing SLNB at our institution

| | |
|---|---|
| **Age** | |
| Mean | 56.3 (±12.3) |
| Median | 57 |
| Range | 26–92 |
| **Menopausal status** | |
| Premenopausal | 54 (36.7%) |
| Postmenopausal | 93 (63.3%) |
| **Histology** | |
| Ductal | 121 (82.3%) |
| Lobular | 16 (10.9%) |
| Other | 10 (6.8%) |
| **cT stage** | |
| T1mi or T1a | 2 (1.36%) |
| T1b | 18 (12.2%) |
| T1c | 69 (46.9%) |
| T2 | 58 (39.4%) |
| **pT stage** | |
| T1mi or T1a | 10 (6.8%) |
| T1b | 17 (11.6%) |
| T1c | 50 (34.0%) |
| T2 | 70 (47.6%) |
| **pN status** | |
| N0 | 108 (73.4%) |
| N1mi | 5 (3.4%) |
| N1 | 29 (19.7%) |
| N2 | 5 (3.4%) |
| **Tumor grade** | |
| 1 | 34 (23.1%) |
| 2 | 91 (61.9%) |
| 3 | 22 (14.9%) |
| **ER status** | |
| Negative | 133 (90.5%) |
| Positive | 14 (9.5%) |
| **PR status** | |
| Negative | 121 (82.3%) |
| Positive | 26 (17.6%) |
| **HER2 status** | |
| Positive | 14 (9.5%) |
| Negative | 133 (90.5%) |
| **Ki-67 index** | |
| <20 | 91(61.9%) |
| ≥20 | 56 (38.1%) |
| **Hormonal therapy** | |
| Yes | 132 (89.8%) |
| No | 15 (10.2%) |
| **Chemotherapy** | |
| No | 45 (30.6%) |
| Yes | 102 (69.4%) |
| **Radiotherapy** | |
| Yes | 104 (70.7%) |
| No | 43 (29.3%) |
| **Trastuzumab** | |
| Yes | 14 (9.5%) |
| No | 133 (90.5%) |
| **Surgery** | |
| Breast conserving surgery | 83 (56.5%) |
| Mastectomy | 64 (43.5%) |

SLNB: Sentinel lymph node biopsy; ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth factor receptor 2

and HER2 status, Ki-67 proliferation index and other modalities of adjuvant therapies.

## Discussion and Conclusion

The present study retrospectively evaluated feasibility of applying the SOUND trial strategy for omission of SLNB to a cohort of breast cancer patients in Bahrain. To the best of our knowledge, this is the first study in literature investigating the exportability of SOUND trial findings to avoid axillary surgery in other breast cancer populations.

Our results demonstrate some differences between our group of patients who were potentially eligible for omitting SLNB according to the SOUND criteria and the SLNB population in the SOUND trial. Of note, the percentages of younger and premenopausal patients in our study were significantly higher than those of patients in the SOUND trial. This difference could be related to social, economic and population differences in the age of diagnosis between Arab and Western populations (11). Another explanation could be attributed to the fact that Arab countries generally have a younger population compared to Western countries (12). This reflects the relatively higher proportion of breast cancer patients in Bahrain with more aggressive disease compared to Western populations (11). Specifically, our patients tend to be of younger age and have larger and higher grade tumours, and these are likely to be risk factors for the significant proportion of axillary lymph node metastasis in Bahrain (13). There was a higher proportion of pathological T2 tumours in our eligible group compared with the SOUND cohort. This could be linked to underestimation of tumour size by preoperative imaging, as ultrasound and mammogram have been reported to underestimate the size of clinically T1 tumours (up to 20 mm) (14), with radiological and pathological concordance influenced by various factors, including tumour histology, molecular subtypes and breast density (15).

Data from the SOUND trial indicated that adjuvant treatments were not significantly different between the SLNB group and the no axillary surgery group (10). However, a relatively higher percentage of patients who underwent adjuvant chemotherapy were observed in our cohort compared to those in the SOUND trial, indicating the

Table 2. Comparison of patients in the current study and the SLNB arm in the SOUND trial

| | Patients, No. (%) | | |
|---|---|---|---|
| **Characteristic** | **Current study (*n* = 53)** | **SOUND trial (*n* = 708)** | ***p*-value** |
| **Age** | | | |
| <50 | 20 (37.7) | 124 (17.5) | 0.002 |
| ≥50 | 33 (62.3) | 584 (82.5) | |
| **Menopausal status** | | | |
| Premenopausal | 23 (43.4) | 145 (20.6) | 0.004 |
| Postmenopausal | 30 (56.6) | 558 (79.4) | |
| **Histology** | | | |
| Ductal | 45 (84.9) | 551 (77.8) | 0.419 |
| Lobular | 4 (7.5) | 61 (8.6) | |
| Other | 4 (7.5) | 96 (13.5) | |
| **pT stage** | | | |
| T1mi or T1a | 4 (7.5) | 71 (10.0) | |
| T1b | 10 (18.9) | 251 (35.5) | 0.001 |
| T1c | 25 (47.2) | 355 (50.1) | |
| T2 | 14 (26.4) | 31 (4.4) | |
| **pN status** | | | |
| Nx | 0 | 12 (1.7) | |
| N0 or N0 (i+) | 42 (79.2) | 599 (84.6) | 0.098 |
| N1mi | 2 (3.8) | 36 (5.1) | |
| N1 | 8 (15.1) | 57 (8.1) | |
| N2 | 1 (1.9) | 4 (0.6) | |
| **Tumor grade** | | | |
| 1 | 10 (18.9) | 194 (27.7) | 0.233 |
| 2 | 32 (60.3) | 377 (53.8) | |
| 3 | 11 (20.8) | 130 (18.5) | |
| **ER status** | | | |
| Negative | 6 (11.3) | 56 (7.9) | 0.158 |
| Positive | 47 (88.7) | 652 (92.1) | |
| **PR status** | | | |
| Negative | 11 (20.8) | 108 (15.3) | 0.151 |
| Positive | 42 (79.2) | 600 (84.7) | |
| **Ki-67 index** | | | |
| <20 | 29 (54.7) | 455 (64.4) | 0.220 |
| ≥20 | 24 (45.3) | 252 (35.6) | |
| **HER2 status** | | | |
| Negative | 47 (88.7) | 660 (93.2) | 0.096 |
| Positive | 6 (11.3) | 48 (6.8) | |
| **Molecular subtype** | | | |
| Luminal HER2-negative | 44 (83) | 617 (87.1) | 0.423 |
| HER2-enriched | 6 (11.3) | 48 (6.8) | |
| Triple-negative | 3 (5.7) | 33 (6.1) | |

Table 2. Continued

| | Patients, No. (%) | | |
|---|---|---|---|
| **Characteristic** | **Current study (*n* = 53)** | **SOUND trial (*n* = 708)** | ***p*-value** |
| **Hormonal therapy** | | | |
| No | 6 (11.3) | 66 (9.3) | 0.248 |
| Yes | 47 (88.7) | 642 (90.7) | |
| **Chemotherapy** | | | |
| No | 33 (62.3) | 566 (79.9) | 0.002 |
| Yes | 20 (37.7) | 142 (20.1) | |
| **Radiotherapy** | | | |
| No | 2 (3.7) | 14 (2.0) | 0.551 |
| Yes | 51 (96.3) | 694 (98.0) | |
| **Trastuzumab** | | | |
| No | 47 (88.7) | 661 (93.4) | 0.192 |
| Yes | 6 (11.3) | 47 (6.6) | |

SLNB: Sentinel lymph node biopsy; ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth factor receptor 2; SOUND: The Sentinel Node vs. Observation After Axillary Ultra-Sound

SLNB still has a role in Bahraini patients for axillary staging in order to guide adjuvant therapy decisions. As outlined in the RxPONDER (A Clinical Trial RX for Positive Node, Endocrine Responsive Breast Cancer) trial, chemotherapy is associated with a survival benefit in younger patients with node-positive disease (16). Furthermore, identification of nodal disease in ER-positive breast cancer influences treatment options in terms of cyclin-dependent kinase 4 and 6 inhibitor eligibility as well as extended hormonal therapy (up to 10 years) (17-19). In addition, the absence of pathological nodal disease may allow for de-escalation of hormonal therapy, both in terms of choice of medication and duration of treatment (10). On the other hand, in patients with other molecular tumour subtypes undergoing upfront surgery, nodal status might be important to properly tailor adjuvant systemic therapy. In particular, adjuvant treatment in node-negative patients with HER2-positive disease might only be limited to paclitaxel and trastuzumab (20).

The data from the SOUND trial support the Society of Surgical Oncology Choosing Wisely guideline recommendation against routine SLNB in patients aged over 70 years with small hormone receptor-positive and HER2-negative breast cancer, as axillary surgery does not influence adjuvant therapy decisions in these patients (21). A previous study from our institution also reported findings consistent with the Choosing Wisely campaign, suggesting the safety of omitting SLNB in this subset of patients (13). In terms of adjuvant radiation therapy, nodal radiation fields are usually included for patients with nodal involvement as a complement to whole-breast radiation after BCS (10). On the contrary, select patients aged 65 years and older with node-negative disease would be candidates for omission of radiation therapy (22).

The findings from the SOUND trial evaluated the reliability of ultrasound to detect nodal involvement and implied whether it might replace axillary surgery for staging in the future (23). The sensitivity of axillary ultrasound to detect lymph node involvement ranges from 24–94% (24). Although the presence of axillary metastases was relatively higher in our group compared to that of the SOUND trial (20.8% *vs.* 15.9%), the difference was not statistically significant. Given the very limited number of patients with extensive nodal involvement in our group (1.9%) and the extremely low incidence of axillary recurrence in the no axillary surgery group of the SOUND trial (0.4% at 5 years), the use of ultrasound can be clinically meaningful to rule out nodal involvement (10). Even though the SOUND trial is unlikely to be incorporated into the guidelines immediately, multidisciplinary discussions are important before applying changes in clinical practice while we look forward to future data from other trials, including the Intergroup Sentinel Mamma trial, similarly investigating omission of axillary surgery in patients with tumours up to 5 cm undergoing BCS (25).

The SOUND trial is limited by enrolment of a cohort comprising of low-risk patients, including older women and those with very small tumours, which might not be representative of real-world data. In addition, the SOUND trial, which mandated ALND for a positive sentinel node, was ongoing at the time ACOSOG Z0011 was published, when the same patients with low axillary disease burden could omit ALND. This further confirms the selection bias in the SOUND trial. Limitations of our study include its retrospective nature and small sample size. There is probable selection bias for included patients with good prognosis, as we applied a very strict criteria for performing SLNB. With lack of data on recurrence, mortality and follow-up from our cohort, there might be cases that have loco-regional recurrence and long-term follow-up is needed to confirm the validity of our data. Despite these limitations, to the best of our knowledge, this is the first published study evaluating the SOUND trial criteria in Bahraini patients with early breast cancer.

Before applying the SOUND trial to clinical practice, it is important to determine whether the trial population is representative of a real-world patient population. This study did not demonstrate external generalisability of the SOUND trial criteria to Bahraini patients with early breast cancer undergoing BCS. The differences could

be attributed to aggressive tumour characteristics in our patients compared to Western groups. Nevertheless, the SOUND trial is a landmark study in the de-escalation of axillary surgery that will influence multidisciplinary discussion. Axillary ultrasound and the use of genomic assays may obviate the need for axillary surgery to inform adjuvant systemic therapy decisions in cT1-2N0 patients with breast cancer in the future. Our study may influence other researchers to investigate the applicability of SOUND criteria to their own populations and ensure how to implement these data into their local guidelines and clinical practice.

---

**Ethics Committee Approval:** This study was approved by the Ethical Committee of Government Hospitals Bahrain (approval number: 116051223, date: 05.12.2023).

**Informed Consent:** We conducted a retrospective review from a prospectively maintained database, from October 2021 to September 2023.

### Authorship Contributions

Surgical and Medical Practices: A.H.A., R.A., A.Z.S., T.H.A., A.M.M., H.A.A.; Concept A.M.M., H.A.A.; Design: A.M.M., H.A.A.; Data Collection and/or Processing: A.H.A., R.A., A.Z.S., T.H.A.; Analysis and/or Interpretation: A.H.A., A.Z.S., H.A.A.; Literature Search: A.H.A., R.A., A.Z.S.; Writing: A.H.A., R.A., A.Z.S., T.H.A., A.M.M., H.A.A.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## References

1. Krag DN, Anderson SJ, Julian TB, Brown AN, Harlow SP, Costantino JP, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010; 11: 927-933. (PMID: 20863759) [Crossref]
2. Galimberti V, Cole BF, Zurrida S, Viale G, Luini A, Veronesi P, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. 2013; 14: 297-305. (PMID: 23491275) [Crossref]
3. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011; 305: 569-575. (PMID: 21304082) [Crossref]
4. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJH, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014; 15: 1303-1310. (PMID: 25439688) [Crossref]
5. Tinterri C, Gentile D, Gatzemeier W, Sagona A, Barbieri E, Testori A, et al. Preservation of Axillary Lymph Nodes Compared with Complete Dissection in T1-2 Breast Cancer Patients Presenting One or Two Metastatic Sentinel Lymph Nodes: The SINODAR-ONE Multicenter Randomized Clinical Trial. Ann Surg Oncol. 2022; 29: 5732-5744. (PMID: 35552930) [Crossref]
6. Reimer T. Omission of axillary sentinel lymph node biopsy in early invasive breast cancer. Breast. 2023; 67: 124-128. (PMID: 36658052) [Crossref]
7. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, Cyr A, et al. NCCN Guidelines Insights: Breast Cancer, Version 1.2017. J Natl Compr Canc Netw. 2017; 15: 433-451. (PMID: 28404755) [Crossref]
8. Hersh EH, King TA. De-escalating axillary surgery in early-stage breast cancer. Breast. 2022; 62: S43-S49. (PMID: 34949533) [Crossref]
9. Gentilini O, Veronesi U. Abandoning sentinel lymph node biopsy in early breast cancer? A new trial in progress at the European Institute of Oncology of Milan (SOUND: sentinel node vs Observation after axillary UltraSouND). Breast. 2012; 21: 678-681. (PMID: 22835916) [Crossref]
10. Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al. Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes: The SOUND Randomized Clinical Trial. JAMA Oncol. 2023; 9: 1557-1564. (PMID: 37733364) [Crossref]
11. Hamadeh RR, Abulfatih NM, Fekri MA, Al-Mehza HE. Epidemiology of Breast Cancer among Bahraini Women: Data from the Bahrain Cancer Registry. Sultan Qaboos Univ Med J. 2014; 14: e176-e182. (PMID: 24790739)
12. Najjar H, Easson A. Age at diagnosis of breast cancer in Arab nations. Int J Surg. 2010; 8: 448-452. (PMID: 20601253) [Crossref]
13. Abdulla HA, Salman AZ, Alaraibi SJ, Nazzal K, Ahmed SA, Almahari SA, et al. Risk factors associated with sentinel lymph node metastasis in clinically node-negative breast cancer. Eur J Breast Health. 2023; 19: 229-234. (PMID: 37415656) [Crossref]
14. Kapur H, Bazzarelli A, Warburton R, Pao JS, Dingee C, Chen L, et al. Accuracy of preoperative imaging estimates: opportunities to de-escalate surgery for early invasive breast cancer. Am J Surg. 2022; 24: 722-727. (PMID: 35422328) [Crossref]
15. Azhdeh S, Kaviani A, Sadighi N, Rahmani M. Accurate estimation of breast tumor size: a comprison between ultrasonography, mammography, magnetic resonance imaging, and associated contributing factors. Eur J Breast Health. 2021; 17: 53-61. (PMID: 33796831) [Crossref]
16. Kalinsky K, Barlow WE, Gralow JR, Meric-Bernstam F, Albain KS, Hayes DF, et al. 21-gene assay to inform chemotherapy benefit in node-positive breast cancer. N Engl J Med. 2021; 385: 2336-2347. (PMID: 34914339) [Crossref]
17. Davies C, Pan H, Godwin J, Gray R, Arriagada R, Raina V, et al. Adjuvant tamoxifen: longer against shorter (ATLAS) collaborative group. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet. 2013; 381: 805-816. (PMID: 23219286) [Crossref]
18. Goss PE, Ingle JN, Pritchard KI, Robert NJ, Muss H, Gralow J, et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. N Engl J Med. 2016; 375: 209-219. (PMID: 27264120) [Crossref]
19. Johnston SRD, Toi M, O'Shaughnessy J, Rastogi P, Campone M, Neven P, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. Lancet Oncol. 2023; 24: 77-90. (PMID: 36493792) [Crossref]
20. Tolaney SM, Barry WT, Dang CT, Yardley DA, Moy B, Marcom PK, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. N Engl J Med. 2015; 372: 134-141. (PMID: 25564897) [Crossref]
21. Choosing Wisely. Society of Surgical Oncology: Don't routinely use sentinel node biopsy in clinically node negative women ≥70 years of age with early stage hormone receptor positive, HER2 negative invasive breast cancer; 2019. [cited 21 January 2024] [Crossref]

22. Kunkler IH, Williams LJ, Jack WJL, Cameron DA, Dixon JM. Breast-conserving surgery with or without irradiation in early breast cancer. N Engl J Med. 2023; 388: 585-594. (PMID: 36791159) [Crossref]

23. Gentilini OD. Lessons from the SOUND trial and future perspectives on axillary staging in breast cancer. Br J Surg. 2024; 111: znad391. (PMID: 38059555) [Crossref]

24. Le Boulc'h M, Gilhodes J, Steinmeyer Z, Molière S, Mathelin C. Pretherapeutic imaging for axillary staging in breast cancer: a systematic review and meta-analysis of ultrasonography, MRI and FDG PET. J Clin Med. 2021; 10: 1543. (PMID: 33917590) [Crossref]

25. Reimer T, Stachs A, Veselinovic K, Polata S, Müller T, Kühn T, et al. Patient-reported outcomes for the Intergroup Sentinel Mamma study (INSEMA): A randomised trial with persistent impact of axillary surgery on arm and breast symptoms in patients with early breast cancer. EClinicalMedicine. 2022; 55: 101756. (PMID: 36457648) [Crossref]