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Implementation of sentinel node biopsy in breast cancer patients in the Netherlands

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ABSTRACT

Background: This population-based study describes the implementation of the sentinel node biopsy (SNB) in breast cancer patients in the Netherlands. We examined the extent of use over time of SNB in women who were considered eligible for SNB on the basis of their clinical status.

Methods: The study included a total of 35,465 breast cancer patients who were diagnosed with T1–2 tumours (⩽5.0 cm), negative axillary lymph node status and no distant metastases upon clinical examination between 1st January 1998 and 31st December 2003 in six Comprehensive Cancer Centre regions in the Netherlands. Information on axillary surgery was classified as SNB alone, SNB+axillary lymph node dissection (ALND), ALND alone or none. Patterns of use of axillary surgery were summarised as the proportion of patients receiving each surgery type.

Results: Overall, 25.7% of patients underwent SNB alone, 19.1% underwent SNB+ALND, 50.0% had ALND alone and 5.2% did not have axillary surgery. SNB was more common in women who had breast-conserving surgery: 50.5% of patients who received breast-conserving surgery underwent SNB compared to 40.7% of patients who had mastectomy ($p < 0.0001$). Amongst patients receiving breast-conserving treatment, 31.7% had SNB as final axillary surgery, whilst 20.5% of patients who had mastectomy had SNB alone ($p < 0.0001$). The proportion of women who underwent a SNB alone or in combination with ALND increased over the period 1998–2003, from 2.1% to 45.8% and from 6.7% to 24.8%, respectively. There were marked differences in the patterns of dissemination of the use

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of SNB between regions: by 2003, the difference between the regions with the highest and lowest proportion of use was 25%.

Conclusions: SNB has become the standard-of-care for the treatment of breast cancer patients clinically diagnosed with T1–2 tumours, clinically negative lymph nodes and without distant metastases. In 2003, 70.6% of patients with early breast cancer in the Netherlands received SNB, and within this group, 64.9% of patients had SNB as the final axillary treatment. Implementation of SNB may depend on factors associated with regional organisation of care.

1. Introduction

The sentinel node biopsy (SNB) was introduced almost 15 years ago as an intraoperative lymph node staging method for breast cancer patients.[1,2] The SNB had already been described as a staging method for patients with penile cancer in 1977,[3] and the procedure was then further developed for the detection of non-palpable lymph node metastases of melanoma.[4] SNB may also be applied in other solid malignancies.[5]

Axillary lymph node status is the most important prognostic factor for breast cancer, and it affects the choice of adjuvant systemic therapy and radiotherapy. Histopathologic examination of lymph nodes requires axillary-specific surgery as a critical component of breast cancer care. Until recently, axillary surgery consisted of axillary lymph node dissection (ALND). Although ALND is considered a safe procedure resulting in optimal regional control after local treatment and additional prognostic information, dissection of all lymph nodes lacks clinical value if the nodes are tumour negative, as is the case in about 70% of breast cancer patients in countries with mammographic screening programmes. Moreover, post-ALND morbidity, which include upper arm paresthesias, shoulder and arm pain, restriction of shoulder mobility and permanent and potentially disabling lymph oedema, has a significant impact on the patients' quality of life.[6–11] The technique of SNB allows for a selective method of staging, thus enabling lymph node assessment without the use of ALND: as a result, the use of ALND should be restricted to patients with lymph node metastases. Indeed, the risks of short-term morbidity and lymph oedema are markedly lower with SNB.[12–14] Also, SNB shows a similar sensitivity for detecting patients with positive lymph nodes.[15]

SNB is based on the by-now confirmed hypothesis of an orderly pattern of lymphogenic tumour cell dissemination. Sentinel lymph nodes should be at the greatest risk of bearing cancer metastases, and if these nodes prove to be negative, the remaining axillary lymph nodes are also likely to be negative. The sentinel nodes are located by lymphatic mapping with preoperative lymphoscintigraphy alone or the most frequently used combined technique, lymphoscintigraphy with ^{99m}technetium-labelled nanocolloid and patent blue dye. As the colloidal material accumulates in the draining sentinel lymph nodes, the nodes may be identified at surgery, visually and by gamma probe if required, and removed for histopathologic examination. Ideally, sentinel nodes are examined during breast surgery, and if the pathologist then identifies cancer metastases, e.g. by frozen section analysis,[16] ALND may be performed in the same surgery. SNBs require adequate cooperation between the departments of surgery, nuclear medicine and pathology. Since community hospitals may not be equipped with a pathology laboratory, SNBs often require cooperation between hospitals as well.

SNBs are suitable for breast cancer patients with primary tumours with a maximum size of 5 cm or less (T1–2), with no multiple lesions, no previous breast surgery or axillary surgery and no signs of malignancy in axillary lymph nodes.[17] The reliability of the procedure in these patients is considered adequately tested after several studies of SNB with concomitant ALND: experienced surgeons are able to locate sentinel nodes in more than 90% of cases, whilst the prediction of lymph node status assessed by SNB is accurate in 95% (range 84–100%) of cases.[18,19] The false-negative rate has been estimated at 3.2% (range 0–15%), but the follow-up of patients with a negative sentinel lymph node seldom detected axillary metastases.[20–23] A recent study showed a false-negative rate of 9.8%, with higher percentages for patients who had excisional biopsy and patients with a tumour in the upper outer quadrant of the breast.[24]

In the Netherlands, the procedure for SNB was first described in Dutch national guidelines for the staging of breast cancer in 1999,[25] but regional implementation had by then already started. This study examines the implementation of SNB in the Netherlands from 1998 to 2003, a time period during which SNB entered clinical practice.

2. Patients and methods

2.1. Data sources

Information on women with newly diagnosed breast cancer was extracted from the regional cancer registries of six out of nine Dutch Comprehensive Cancer Centres (CCCs, Fig. 1). These six registries cover around 10,350,000 inhabitants in 2006, or approximately 60% of the total Dutch population. The CCCs form a network of health care professionals and institutions for cancer care and palliative care in the Netherlands. The CCC regions cover between 5 and 20 hospitals. The CCCs do not treat patients, but foster expertise and multidisciplinary cohesion in (regional) cancer care. Amongst other activities, they host the Netherlands Cancer Registry (NCR), a nationwide population-based cancer registry established in 1989.

Fig. 1 – The regions of six Dutch Comprehensive Cancer Centres (in dark grey).

The NCR provides incidence data on a national level. It is composed of the Regional Cancer Registries (RCRs) of the nine CCCs in the Netherlands. PALGA, the Dutch network and registry of histo- and cytopathology, notifies the RCRs of all newly diagnosed malignancies. Following this notification, trained registry personnel from the RCRs collect data on diagnosis, staging and treatment from hospital records, including pathology and surgery reports. Primary treatment is coded in sequence of administration, and patients are staged according to the TNM system of the International Union Against Cancer (UICC).[26,27] Case ascertainment is provided by the national hospital discharge database, which receives discharge diagnoses of patients admitted from all hospitals in the Netherlands. The study design, data abstraction process and storage protocols have been approved by the national supervisory committee of the NCR.

2.2. *Study population and eligibility criteria*

The data of the NCR distinguish clinical tumour stages (cTNM) from pathologic stages (pTNM), which enabled us to accurately identify the larger part of patients who should have undergone SNB on the basis of their clinical tumour status (cTNM) according to the Dutch guideline for the treatment of breast cancer.[17] The clinical status of patients was based on physical examination, biopsies, imaging techniques and other diagnostic information retrieved prior to therapeutic intervention; this information was supplemented with post-surgical histopathological examination to determine the pathological tumour status (pTNM). In case the clinical extent of the primary tumour was unknown (cTX), patient information was supplemented by the pathologic extent of the tumour (pT); this was the case for 19.2% of the population. Patients were eligible for this study if they were clinically diagnosed with T1–2 tumours ($\leqslant$ 5.0 cm), negative axillary lymph node status and no (signs of) distant metastases.

Patients had to be presented in one of the six regions participating in the study between 1st January 1998 and 31st December 2003. For the study period, the data from the remaining three CCCs could not be used to identify SNB implementation patterns as these centres only register the most extensive axillary surgery for each patient. In these regions, SNB was not registered if the procedure was followed by ALND.

2.3. *Classification of axillary and definitive breast surgery*

The type of axillary surgery was classified into one of four categories for each patient: no axillary surgery (none); SNB without further axillary surgery (SNB alone); SNB followed by complete ALND (SNB+ALND); or ALND without SNB (ALND alone). Patients were considered as lymph node positive if any axillary lymph node contained histologically proven metastases (whether assessed by SNB or otherwise). Axillary surgery was coded as SNB alone if SNB was performed and the patient had no other axillary surgery at any time during initial treatment of the primary cancer. Axillary surgery was classified as ALND alone if axillary dissection was performed and the patient had no prior or concomitant SNB.

The type of definitive breast surgery was classified into one of three categories for each patient: no breast surgery (none); breast-conserving surgery and mastectomy. Patients who were initially treated with breast-conserving surgery but had subsequent mastectomy were included in the latter category.

2.4. *Statistical analysis*

Descriptive statistics were used to describe the patient population. We summarised the patterns of the use of definitive breast surgery as the proportion of patients receiving each surgery type (i.e. none, breast-conserving surgery or mastectomy). The same was done for the patterns of the use of axillary surgery (i.e. none, SNB alone, SNB+ALND or ALND alone). The type of axillary surgery was also linked with the type of definitive breast surgery. Since our study population consisted mainly of breast cancer patients with small primary tumours, we expected to observe a large group of women who underwent breast-conserving therapy, especially when a SNB had indicated a negative axillary lymph node status in these patients. The χ^2 test was applied to test the associations of axillary surgery with the type of breast surgery. The type of axillary surgery was also analysed according to patient age, clinical and pathological tumour size and pathological tumour stage. A p-value below 0.05 (two-sided) was considered statistically significant.

To describe the implementation of SNB during the study period, we examined the time trends of axillary surgery amongst women who may be considered eligible for SNB on the basis of their clinical status from January 1998 through to December 2003. Time trends were also studied for the separate regions.

3. Results

3.1. Patient characteristics

Between 1st January 1998 and 31st December 2003, 35,904 women were diagnosed with clinically small breast tumours (⩽5.0 cm), clinically negative axillary lymph node status and no signs of distant metastases in the six CCC regions under study. Of these patients, we excluded 439 (1.2%) for the lack of reliable and unambiguous information on definitive breast surgery, leaving 35,465 women (98.8%) in our study. 4825 (13.6%) patients were diagnosed or treated in the region of CCC East (Fig. 1A); 3141 (8.9%) in CCC Limburg (B); 4122 (11.6%) in CCC Middle Netherlands (C); 7888 (22.2%) in CCC North Netherlands (D); 7652 (21.6%) in CCC Rotterdam (E) and 7837 (22.1%) in CCC South (F).

The median age of patients was 59 years (Table 1); 27.1% of all patients was aged 50 years or younger. The clinical tumour size was 2 cm or less for 68.6% of patients, and 52.7% of these patients received breast-conserving surgery. Overall, 48.8% of patients underwent breast-conserving surgery, 49.1% had mastectomy and 2.1% did not have definitive breast surgery. With respect to axillary surgery, 25.7% of all patients had SNB alone, 19.1% had SNB with concomitant ALND and 50.0% had ALND alone; 5.2% of the patients did not have axillary surgery performed.

Table 1 – Patient characteristics for 35,465 patients with breast cancer who presented with a clinical T1–2 tumour (tumour size ⩽5.0 cm), clinically negative lymph nodes and without distant metastases in six Dutch Comprehensive Cancer Centre regions in 1998–2003

Patient characteristics	No. of patients	(%)
Age at diagnosis, years		
<40	2043	(5.8)
40–49	6375	(18.0)
50–59	9332	(26.3)
60–69	7769	(21.9)
70–79	6815	(19.2)
⩾80	3131	(8.8)
Median (interquartile range)	59	(50–71)
Tumour size (cT), cm		
0–2.0	24,326	(68.6)
> 2.0–5.0	11,139	(31.4)
Type of definitive surgery		
None	757	(2.1)
Breast-conserving surgery	17,303	(48.8)
Mastectomy	17,405	(49.1)
Breast-conserving surgery within tumour size, cm		
0–2.0 (n = 24,326)	12,827	(52.7)
>2.0–5.0 (n = 11,139)	4,476	(40.2)
Type of axillary surgery		
None	1847	(5.2)
SNB alone	9111	(25.7)
SNB+ALND	6780	(19.1)
ALND alone	17,727	(50.0)

SNB: sentinel node biopsy; ALND: axillary lymph node dissection.

The patient selection concerns a population which would be considered eligible for SNB on the basis of clinical tumour status (cTNM). As for the pathological staging of patients (pTNM), which is determined post-operatively and therefore does not affect the indication for SNB, 48.5% of patients were diagnosed with stage I breast cancer, 33.9% with stage IIA and 14.5% with IIB. Furthermore, 2.9% of the patients were diagnosed with stage III and 0.2% with stage IV breast cancer. Four (<0.0%) patients had unknown stage, and five (<0.0%) patients were pathologically diagnosed with in situ breast malignancy.

3.2. Patterns of axillary surgery according to definitive surgery type

The use of SNB (SNB alone or with concomitant ALND) was statistically significantly associated with breast-conserving surgery (Table 2). Amongst patients who received breast-conserving surgical treatment 50.6% had SNB, whilst this proportion was 40.7% for patients who underwent mastectomy ($p < 0.0001$). Also, SNB was more often the only axillary surgery in women who were treated with breast-conserving surgery than in women who had mastectomy: 31.7% versus 20.5%, respectively ($p < 0.0001$).

3.3. Patterns of axillary surgery according to patient and tumour characteristics

Overall, the proportion of patients who received SNB alone was 26%, whilst 20% had SNB with concomitant ALND and 50% had ALND alone (Table 3). For women in age groups under 80, the type of axillary surgery was not associated with age. Women aged 80 years or over were most likely not to undergo axillary surgery, and they had the highest proportion of ALND alone when patients who did not undergo axillary surgery are excluded.

SNB alone was more common in patients with smaller tumours, i.e. clinically assessed tumour sizes of 2.0 cm or less (cT1): 29.3% of these patients had SNB as the final axillary treatment, whilst this was the case for 17.7% of patients with a tumour between 2 and 5 cm (cT2). The same pattern was observed in lower tumour stages compared to higher stages.

ALND was most commonly used in almost all pathological tumour sizes and tumour stages.

3.4. Time trends of axillary surgery amongst patients who were eligible for SNB on the basis of their clinical tumour status

Overall, the use of SNB increased from 8.8% in 1998 to 70.6% in 2003. The proportion of women who received SNB as the final axillary treatment (=SNB alone) increased from 2.1% to 45.8% (Fig. 2). In the study period, the proportion of patients who had SNB followed by ALND (SNB+ALND) also shows a temporal trend, with an overall increase from 6.7% to 24.8%. In 2001, the proportion of patients treated with SNB alone exceeded

Table 2 – Definitive breast surgery stratified by the type of axillary surgery for 35,465 breast cancer patients

Type of definitive breast surgery	Type of axillary surgery			
	None, no. (%)	SNB alone, no. (%)	SNB + ALND, no. (%)	ALND alone, no. (%)
	n = 1847 (5.2)	*n* = 9111 (25.7)	*n* = 6780 (19.1)	*n* = 17,727 (50.0)
None	684 (90.4)	47 (6.2)	11 (1.5)	15 (2.0)
Breast-conserving surgery	639 (3.7)	5490 (31.7)	3258 (18.8)	7916 (45.7)
Mastectomy	524 (3.0)	3574 (20.5)	3511(20.2)	9796 (56.3)

SNB: sentinel node biopsy; ALND: axillary lymph node dissection.

Table 3 – Type of axillary surgery by clinical tumour size, pathological tumour stage and age groups for 35,465 breast cancer patients

Patient and tumor characteristics	Type of axillary surgery			
	None, no. (%)	SNB alone, no. (%)	SNB + ALND, no. (%)	ALND alone, no. (%)
	n = 1847 (5.2)	*n* = 9111 (25.7)	*n* = 6780 (19.1)	*n* = 17,727 (50.0)
Age, years				
<40 (*n* = 2043)	33 (1.6)	491 (24.0)	498 (24.4)	1021 (50.0)
40–49 (*n* = 6375)	141 (2.2)	1624 (25.5)	1507 (23.6)	3103 (48.7)
50–59 (*n* = 9332)	233 (2.5)	2631 (28.2)	2007 (21.5)	4461 (47.8)
60–69 (*n* = 7769)	206 (2.7)	2241 (28.8)	1432 (18.4)	3890 (50.1)
70–79 (*n* = 6815)	382 (5.6)	1635 (24.0)	1023 (15.0)	3775 (55.4)
⩾80 (*n* = 3131)	852 (27.2)	489 (15.6)	313 (10.0)	1477 (47.2)
Tumour size (cT), cm				
cT1: 0–2.0 (*n* = 24,326)	1106 (4.5)	7137 (29.3)	4511 (18.5)	11,572 (47.6)
cT2: >2.0–5.0 (*n* = 11,139)	741 (6.7)	1974 (17.7)	2269 (20.4)	6155 (55.3)
Tumour size (pT), cm				
pTis: in situ (*n* = 5)	1 (20.0)	3 (60.0)	1 (20.0)	0 (0.0)
pT1: 0–2.0 (*n* = 22,527)	1086 (4.8)	6703 (29.8)	3913 (17.4)	10,825 (48.1)
pT2: >2.0–5.0 (*n* = 12,169)	726 (6.0)	2333 (19.2)	2707 (22.2)	6403 (52.6)
>pT2: >5.0 (*n* = 764)	34 (4.5)	72 (9.4)	159 (20.8)	499 (65.3)
Tumour stage				
In situ (*n* = 5)	1 (20.0)	3 (60.0)	1 (20.0)	0 (0.0)
I (*n* = 17,193)	1042 (6.1)	6102 (35.5)	1573 (9.1)	8476 (49.3)
IIA (*n* = 12,009)	713 (5.9)	2453 (20.4)	2923 (24.3)	5920 (49.3)
IIB (*n* = 5151)	56 (1.1)	434 (8.4)	1925 (37.4)	2736 (53.1)
IIIA (*n* = 599)	7 (1.2)	62 (10.4)	233 (38.9)	297 (49.6)
IIIB (*n* = 290)	20 (6.9)	30 (10.3)	48 (16.6)	192 (66.2)
IIIC (*n* = 146)	4 (2.7)	26 (17.8)	67 (45.9)	49 (33.6)
IV (*n* = 68)	4 (5.9)	0 (0.0)	10 (14.7)	54 (79.4)
Unknown (*n* = 4)	0 (0.0)	1 (25.0)	0 (0.0)	3 (75.0)

SNB: sentinel node biopsy; ALND: axillary lymph node dissection.

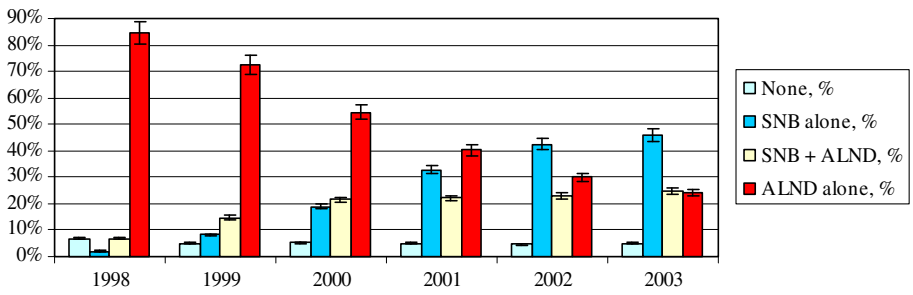

Fig. 2 – Type of axillary surgery for 35,465 breast cancer patients in 1998–2003. SNB: sentinel node biopsy; ALND: axillary lymph node dissection.

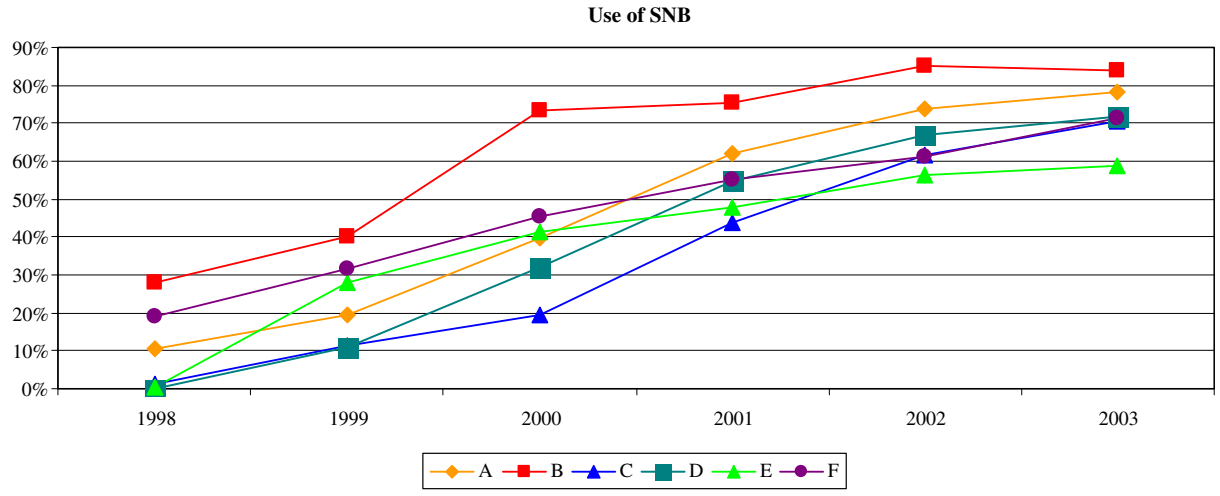

Fig. 3 – Use of SNB in the regions of six Dutch Comprehensive Cancer Centres. SNB: sentinel node biopsy.

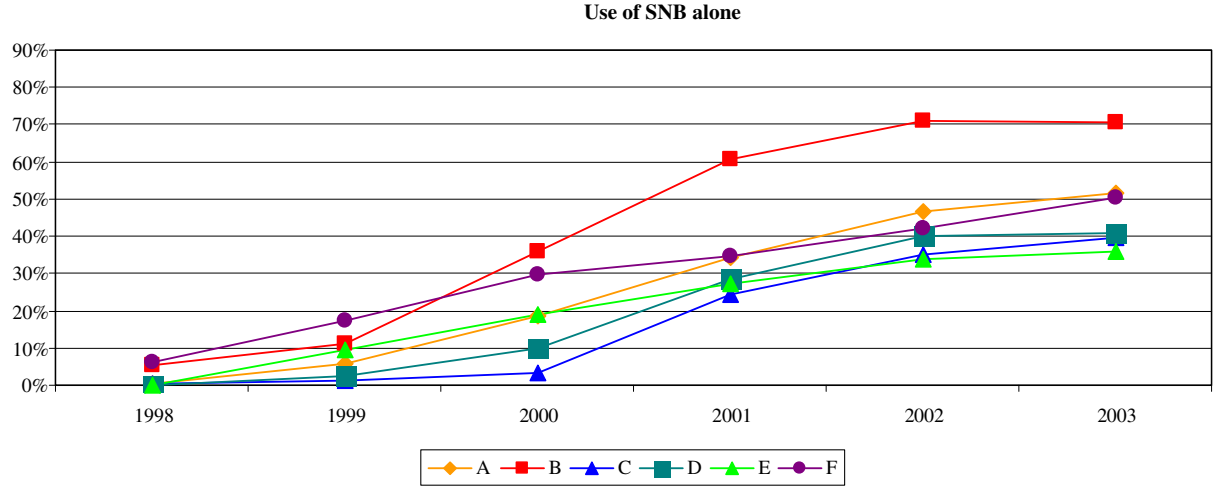

Fig. 4 – Use of SNB alone in the regions of six Dutch Comprehensive Cancer Centres. SNB: sentinel node biopsy.

the proportion of patients treated with SNB and concomitant ALND for the first time. The use of ALND alone gradually decreased from 84.5% in 1998 to 24.3% in 2003.

3.5. *Region-specific patterns in the types of axillary surgery*

In all six regions, we observed an increase in the use of SNB over the period 1998–2003 (Fig. 3). Patients in several regions already received SNB in 1998 (A, B and F), whilst the procedure was still minimally applied in other regions (C, D and E). Over the whole study period, the proportion of women who received SNB was highest in region B (the smallest region): here, the proportion rose from 28.0% in 1998 to 84.0% in 2003, with a sharp increase in 1999–2000 (40.0–73.4%). The difference between the regions with the highest (B: 84.0%) and lowest (E: 58.8%) proportion of the use of SNB at the end of the study period was still 25.2% and statistically significant ($p < 0.0001$).

The increase in the use of SNB alone was also most profound in region (B): from 5.5% in 1998 to 70.7% in 2003 (Fig. 4). The difference between the regions with the highest (B: 70.7%) and lowest (E: 35.9%) proportion of the use of SNB alone in 2003 was also statistically significant ($p < 0.0001$). Two regions (C and D) showed a clear increase during the period 2000–2002.

The use of ALND alone steadily declined in all regions, with region B having the lowest levels of use over the whole study period.

4. Discussion

In the period 1998–2003, 44.8% of breast cancer patients clinically diagnosed with T1–2 tumours, negative axillary lymph node status and no signs of distant metastases received SNB as axillary staging method. The proportion increased from 8.8% in 1998 to 70.6% in 2003. SNB was the final axillary treatment for 25.7% of patients, 2.1% in 1998 to 45.8% in 2003.

Overall, SNB was most common in women who had breast-conserving surgery. The CCC regions show different patterns of the use of SNB, with or without concomitant ALND.

The database of the NCR allowed for a unique population-based study, entailing a large number of patients. As the data of the NCR distinguish between clinical (cTNM) and pathological tumour stages (pTNM), we were able to include women on the basis of clinical eligibility. This provided insight in the patients' upstaging after surgical treatment (even to stage III and IV breast cancer), as the pathological tumour stage is determined through histopathological examination. Patients with higher pathological tumour stages would generally be excluded from other studies.[28]

Apparently, despite their clinical tumour size (cT1–2), approximately half of all patients underwent mastectomy as definitive surgery. By 2003, 24.3% of women still had ALND alone, even though SNB was indicated given their clinical tumour status. Of course, this is in part explained by the relatively high proportion of elderly patients undergoing ALND alone. The pathological presentation of the cancer during breast surgery may also represent a partial explanation, as is indicated by the higher tumour stages (IIB and over) in our patient population. However, we lacked further information to determine patient eligibility more accurately: patients may have had multiple lesions, or they may have had previous breast surgery or axillary surgery. Furthermore, some women may well have preferred one surgery type over another, and the same may be true for their physicians.

The implementation of SNB showed different time trends in the separate regions of the CCCs. Each region's relative proportion of community hospitals, university hospitals and teaching hospitals may explain these trends. Differences in the availability of nuclear medicine departments and pathology laboratories may in addition influence the introduction. Also, the region-specific time trends show that some regions adopted SNB earlier than others. Overall, region B, the smallest in size and covering approximately 5.2% of the total Dutch population, was able to achieve the highest proportion of SNB use. The high proportion of use was maintained during the study period, and by 2003 the difference between this region (83.9%) and the region with the lowest proportion of SNB use (58.8%) was still 25%. The region's relative small geographic size may form an explanation, as new surgical procedures would be able to have spread more rapidly from one hospital to another. In fact, one community hospital had been actively adopting the SNB as the standard-of-care prior to and during the study period.[29]

The difference between the regions with the highest (B: 70.7%) and lowest (E: 35.9%) proportion of the use of SNB alone in 2003 was also statistically significant ($p < 0.0001$). The low proportion of use in region E may be partly explained by incomplete registration in some hospitals at the start of the study period. More importantly, two large medical centres in this region just implemented the SNB in the course of 2003. Two regions (C and D) showed a clear increase during the period 2000–2002.

Like any new surgical procedure, SNB is associated with a learning curve. During the learning curve, surgeons are trained in locating sentinel nodes, and lymph node status is affirmed by concomitant ALND. Hence, SNB would often be followed by ALND in the first years of introduction, after which a negative SNB result would not be followed by ALND due to sufficient training and increased confidence in the procedure.

Limitations of our study include the fact that our data do not permit the description of the learning curve associated with the introduction of the SNB. Hence, we are not able to identify a shift from an early learning phase during which the results of SNB were confirmed by ALND, towards a later stage in which ALND was performed only if the sentinel lymph node was found to be positive. Although our study provides information on the patterns of axillary surgery in only six regions of the CCCs, we consider the data representative for the Dutch population.

The study results show that the implementation of SNB in the Netherlands did not necessarily start with the description and recommendation of the procedure in national clinical practice guidelines in 1999. The study period does coincide with the publication of the literature supporting the use of SNB, and this may well have stimulated the acceptance of SNB by physicians. Acceptance was not hampered by the absence of definitive data from clinical trials addressing the accuracy and safety of the new procedure. Some have pointed out that the widespread use of SNB in the routine care setting may affect accrual and generalisability of the ongoing trials.[28]

Preliminary results of the current clinical trials show that the use of SNB alone resulted in fewer complications (wound infections, axillary seromas and paresthesias) compared to the use of SNB+ALND.[30] Pending definitive trial results, application of SNB already allowed for a selective approach to ALND.[31,32] Some have suggested that ALND may be omitted even in the presence of metastasised tumour cells in the sentinel lymph node, since a relatively high proportion of patients with positive sentinel nodes does not show metastases in the remaining axillary lymph nodes. A wait-and-see policy may be acceptable in women who have a low expected risk of positive lymph nodes.[33,34] The low risk appears to be associated with particular tumour characteristics,[35–37] but additional research is needed. The optimal timing of SNB in relation to neoadjuvant chemotherapy also requires further investigation.[38]

With SNB, sentinel lymph nodes are subjected to extensive examination including serial sectioning and immunohistochemistry. Improved survival of breast cancer patients with a negative lymph node status assessed by SNB as compared to node negative patients determined by ALND has been cautiously attributed to this examination,[39,40] but long-term survival data are still lacking. Concurrently, SNB is held responsible by some for the phenomenon of stage migration in breast cancer patients.[41] Sentinel node examination would leave these patients more often diagnosed with small axillary metastases where they would previously have been classified as node negative. The present study does not examine stage migration or changes in therapy due to the introduction of the SNB, although we reported stage migration in the region of Middle Netherlands (region C) for the incidence years 1997–2002.[42] Since the update of the TNM staging system in 2002, a distinction is made between isolated tumour cells (ITCs) for metastases not exceeding 0.2 mm (pN0(i+)) and micrometastases for metastases between 0.2 mm and

2.0 mm in size (pN1mi). In a study in 360 patients, we observed that the introduction of SNB led to the detection of more ITCs due to the intensified work-up of the sentinel node by the pathologist, but stage migration did not occur when ITCs were categorised as node negative disease, in agreement with the 2002 TNM classification (data not shown). Overall, the prognostic value and clinical significance of both types of minimal metastases have been the subject for debate, and their implications have remained unclear. Some have argued that micrometastases do not affect the survival of patients when compared to node negative women,[43–46] whilst others stated that their survival is worse.[47–49]

In conclusion, Dutch physicians have accepted SNB as the standard-of-care for the treatment of breast cancer patients who are clinically diagnosed with T1–2 tumours, clinically negative lymph nodes and who do not show signs of distant metastases. Approximately 70% of patients received SNB as the first axillary procedure in 2003, and for 46% of patients SNB was the final axillary treatment.

Conflict of interest statement

None declared.

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