香港乳癌資料庫
Hong Kong Breast Cancer Registry
香港乳癌基金會策動 A Hong Kong Breast Cancer Foundation Initiative

香港乳癌資料庫簡報
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香港乳癌患者的前哨淋巴結切片

前言

前哨淋巴結切片是指摘除前幾個前哨淋巴結，這些淋巴結是最先接收源自受癌細胞影響的乳房區域排出的淋巴液。對前哨淋巴結進行組織病理學評估，可以預測到在同一淋巴區域有否出現其他癌細胞轉移。研究結果顯示如果在這些前哨淋巴結內沒有癌細胞，其餘淋巴結也將不會受到癌細胞影響。因此，美國臨床腫瘤學會及美國國家綜合癌症網絡把前哨淋巴結切片訂為是治療臨床淋巴結呈陰性的早期乳癌患者的一個標準治療方法，用以斷定癌症的擴散情況[1,2]。前哨淋巴結切片在美國，英國和加拿大都廣被應用[3-5]。辨認前哨淋巴結的方法是使用低水平的放射性物質（同位素）或一種藍色染料，甚或兩者並用。外科醫生可以憑藉染料和放射性物質來找出前哨淋巴結癌細胞最可能的增殖走向。

用前哨淋巴結切片來取代常規的腋下淋巴切除術，其中一個好處是前者可以免卻不必要地廣泛切除淋巴結的風險，從而大大減低腋下淋巴切除術引發術後併發症的風險，例如淋巴水腫、手臂不適、手術位置感覺減退和肩膀外展困難等[6-12]。前哨淋巴的連續切片更可以偵測到常規的腋下淋巴切除術可能檢查不到的癌細胞微轉移，為病理學提供更多數據。過去 20 年來，前哨淋巴結切片在提高乳癌患者的生活質素上，都被視為在外科技術上一項重要的進步。香港的公營及私營醫療機構自 2002 年起亦已採用前哨淋巴結切片。這是香港首個探討本地乳癌患者使用前哨淋巴結切片情況變化的研究。

研究對象及方法

今次研究的對象是「香港乳癌資料庫第七號報告」所涵蓋的患者群組當中的一個子集。以下為研究對象的篩選準則：

1. 患有單邊入侵性乳癌的女性患者
2. 於 2006 至 2012 年間在香港確診乳癌和進行外科手術
3. 有淋巴結手術的數據
4. 患者沒有接受手術前的前置治療

根據患者的臨床淋巴結狀況（陰性或陽性）、病理學腫瘤大小（分類為 T1 – 4）及癌症期數（「腫瘤大小－淋巴轉移－遠端轉移」TNM 分期）分組，利用卡方檢定測試（Chi-square test）來比較不同組別在使用前哨淋巴結切片的差異。使用病理學腫瘤大小進行分析的原因是我們的患者群組中大部份患者都欠缺臨床腫瘤大小的數據，而且我們相信臨床和病理學的腫瘤大小差別並不顯著。我們利用卡方檢定趨勢測試來比較不同組別患者隨時間過去接受前哨淋巴結切片的變化，同時亦探討隨時間過去接受了不必要的腋下淋巴切除術（亦即接受腋下淋巴切除術但淋巴結並沒有受癌細胞影響）的患者比例。概率值 (p-value) 低於 0.05 的代表在統計學上有明顯的差異，而所有統計分析均使用 SPSS 軟件版本 19.0 進行 (SPSS Inc., Chicago, IL, USA)。

研究結果

本研究涵蓋 6,769 名患者。患者群組在確診乳癌時的年齡中位數是 51.1 歲。大約一半患者（53.8％）在私營醫療機構接受乳房手術。3,853 名患者（56.9％）在首次淋巴結外科手術中接受前哨淋巴結切片，43.1% 只接受了腋下淋巴結切除術而沒有接受前哨淋巴結切片。首次淋巴結外科手術中接受前哨淋巴結切片的患者中，70.6％前哨淋巴結切片顯示淋巴結沒有受癌細胞影響；1.3％顯示有零星癌細胞；28.2％前哨淋巴結切片顯示淋巴結受到癌細胞影響。表 1 顯示患者無論前哨淋巴結切片有沒有顯示癌細胞下，也曾進一步接受腋下淋巴切除術的比例。共有 31.7% 曾接受前哨淋巴結切片的患者進一步接受腋下淋巴切除術。

表 1 接受前哨淋巴結切片患者的前哨淋巴結狀況和進一步接受腋下淋巴切除術的患者比例

前哨淋巴結狀況	人數（%）	進一步接受腋下淋巴切除術的患者人數（%）
N0	2,719 (70.6)	211 (7.8)
N0(i+)	49 (1.3)	8 (16.3)
N1mic	246 (6.4)	197 (80.1)
N1	795 (20.6)	762 (95.8)
N2	43 (1.1)	42 (97.7)
N3	1 (0.0)	1 (100.0)
總計	3,853 (100.0)	1,221 (31.7)

臨床淋巴結狀況

圖 1 顯示臨床淋巴結狀況呈陰性或陽性的患者接受淋巴結手術的類型。5,703 名（62.3%）臨床淋巴結狀況呈陰性的患者當中，62.5% 接受前哨淋巴結切片作為第一個淋巴結外科手術，37.5% 則接受了腋下淋巴切除術。臨床淋巴結呈陰性的患者接受前哨淋巴結切片的比例顯著比呈陽性的患者為高（44.0%比 11.4%；p<0.001）。臨床淋巴結呈陰性的患者接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）的比例在 2006 至 2012 年有正線性上升趨勢（p<0.001），比例從 2006 年的 45.7% 上升到 2012 年的 76.6%（圖 2）。另一方面，臨床淋巴結呈陽性的患者接受前哨淋巴結切片的比例則沒有變化（沒有顯示數據）。

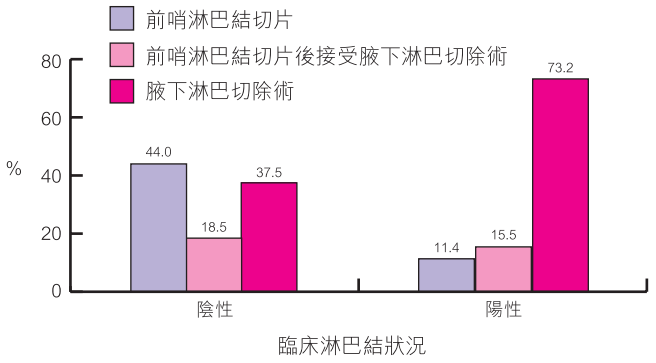

圖 1 臨床淋巴結呈陰性或陽性的患者接受不同種類的淋巴結手術（人數 = 6,769）

不同組別之間的差異顯著 p<0.001

在患者群組中，2,136 名（37.5%）臨床淋巴結呈陰性患者接受腋下淋巴切除術之前並沒有接受前哨淋巴結切片，這些患者當中，40.4% 在私營醫療機構接受外科手術。她們的確診年齡、教育程度、職業、手術地點、手術年份、確診癌症期數和病理學淋巴結狀況列於表 2。

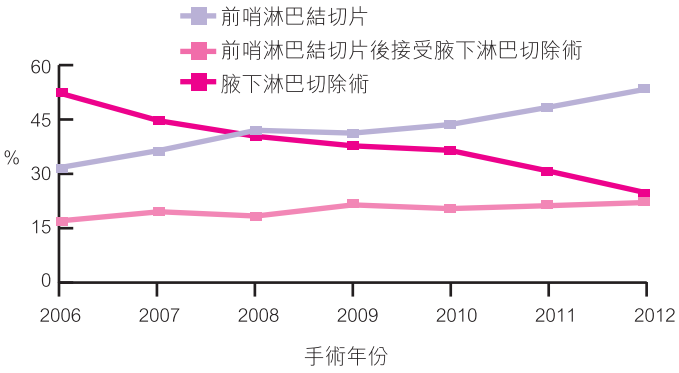

圖 2 臨床淋巴結呈陰性患者接受淋巴結手術的種類，2006 至 2012 年（人數 = 5,703）

p- 值線性趨勢 <0.001

表 2 臨床淋巴結呈陰性但接受腋下淋巴切除術作為第一個淋巴結手術的 2,136 名患者的社會人口統計學和癌症特徵

	患者人數	%
年齡組別		
20-29	13	0.6
30-39	172	8.0
40-49	748	35.0
50-59	730	34.3
60-69	331	15.4
70+	120	5.7
不詳	22	1.0
教育程度		
小學或以下	874	40.9
中學	1,058	49.5
預科或以上	177	8.2
不詳	27	1.3
職業		
專業 / 文職	427	20.0
非文職 / 勞工	695	32.5
自僱人士	30	1.4
主婦	757	35.4
退休 / 失業	198	9.3
不詳	29	1.3
手術地點		
私營	863	40.4
公營	1,273	59.6
手術年份		
2006	336	15.7
2007	317	14.8
2008	335	15.7
2009	334	15.6
2010	333	15.6
2011	278	13.0
2012	203	9.5
確診癌症期數		
I	626	29.3
IIA	762	35.7
IIB	377	17.6
III	357	16.7
IV	14	0.7
病理學淋巴結狀況		
N0	1,214	56.8
N1mic	69	3.2
N1	534	25.0
N2	207	9.7
N3	112	5.2

病理學腫瘤大小

相比腫瘤較大（T3 或 T4）的患者，腫瘤較小（T1）的患者較普遍接受了前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）（T1: 69.0 % 比 T3: 27.6 % 和 T4: 4.7%； p<0.001）（圖 3）。腫瘤屬於 T1 和 T2 的患者，接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）的比例在 2006 至 2012 年有正線性上升趨勢（p<0.001），比例從 2006 年的 50.2% 上升至 2012 年的 80.6%（T1 腫瘤患者），以及從 2006 年的 34.2% 上升至 2012 年的 54.2%（T2 腫瘤患者）（圖 4）。

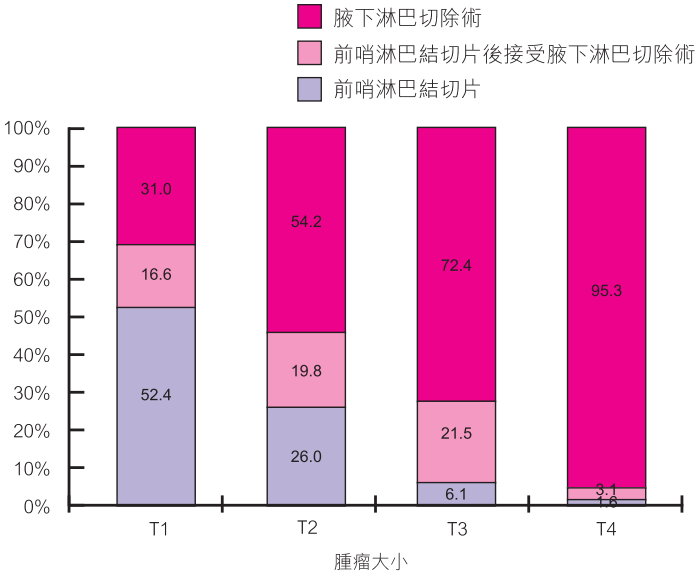

圖 3 腫瘤屬於 T1 到 T4 患者接受不同種類的淋巴結手術（人數 = 6,769）

四個組別之間的差異顯著 p<0.001

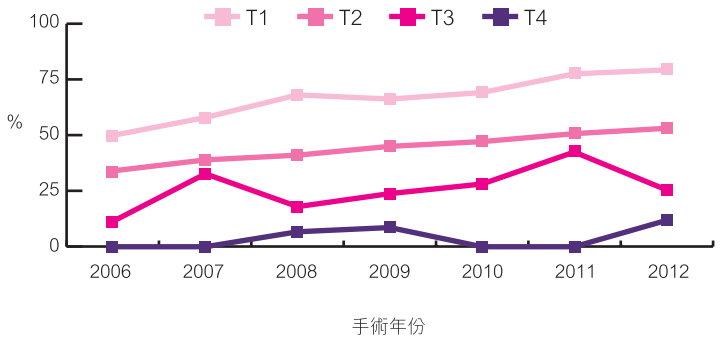

圖 4 腫瘤屬於 T1 至 T4 患者接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）的比例，2006 至 2012 年（人數 = 6,769）

T1：p- 值線性趨勢 <0.001，T2：p- 值線性趨勢 <0.001，T3：p- 值線性趨勢 = 0.102；T4：沒有 p- 值線性趨勢，因為患者人數在某些年份太少。

癌症期數（TNM 分期）

超過 40.0% 的早期乳癌患者（包括 T1N0M0，T1N1M0，T2N0M0 和 T2N1M0）（p<0.001）（圖 5）接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術），情況比第 III 或 IV 期患者較為普遍。出乎意料地，有 2.3 至 28.7% 的第 III 或 IV 期癌症患者曾接受前哨淋巴結切片，但是大部分（97.4%）隨後有接受腋下淋巴切除術。前哨淋巴結切片傾向用於臨床淋巴結呈陰性的癌症，不過有些患者的情況不能在手術前得知，只可透過手術治療後從病理學中確定，她們就如確診較前期癌症的患者般，接受了前哨淋巴結切片作為首次淋巴結手術，這些不能在手術前確定的情況包括術後正電子掃描發現遠端器官擴散，有 4 粒或以上淋巴結呈陽性或有最少 1 粒淋巴結呈陽性的 T3 患者。

在研究時段內，第 III 期和第 IV 期癌症患者接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）的情況沒有顯著差異（沒有顯示數據）。此外，早期癌症患者當中（第 I 期到 IIB 期），T1N0M0，T1N1M0 或 T2N0M0 患者接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片後接受腋下淋巴切除術）均有所增加（圖 6）。

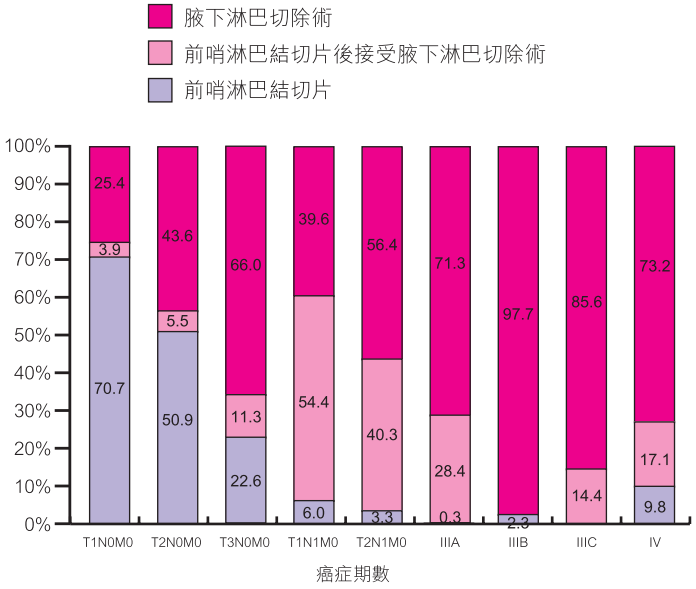

圖 5 不同癌症期數患者接受不同種類的淋巴結手術（人數 = 6,769）

各組別之間的差異顯著 p<0.001

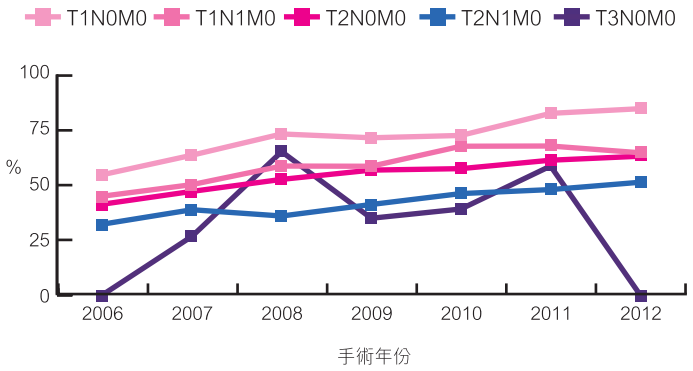

圖 6 不同癌症期數（TNM 分期）患者接受前哨淋巴結切片（包括只接受前哨淋巴結切片和接受前哨淋巴結切片之後接受腋下淋巴切除術）情況（人數 = 5,790）

T1N0M0：p- 值線性趨勢 <0.001，T1N1M0：p- 值線性趨勢 <0.001，T2N0M0 ：p- 值線性趨勢 <0.001，T2N1M0：p- 值線性趨勢 =0.063，T3N0M0：p- 值線性趨勢 =0.169

接受不必要腋下淋巴切除術患者比例隨時間的變化

在研究時段內，接受不必要腋下淋巴切除術（無論有沒有接受前哨淋巴結切片）的患者比例不斷減少，從 2006 年的 44.8% 下降到 2012 年的 28.9%（p<0.001）（圖 7）。

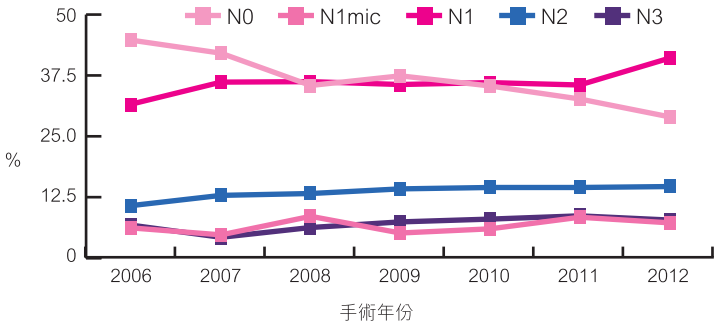

圖 7 接受腋下淋巴切除術（無論有沒有接受前哨淋巴結切片）患者的病理學淋巴結狀況，2006 至 2012 年（人數 = 4,137）

p- 值線性趨勢 <0.001

結論

研究結果顯示前哨淋巴結切片在研究時段內越來越得到外科醫生和患者的接納，尤見於對臨床淋巴結呈陰性的患者或早期癌症的患者。是否採用前哨淋巴結切片來取代腋下淋巴切除術作為斷定癌症的擴散程度，外科醫生的臨床決定和患者的個人決定都具有影響力。外科醫生有責任向患者解釋前哨淋巴結切片以及其用於斷定早期癌症的淋巴結狀況的公認可靠性。同時，香港乳癌基金會將盡更大努力教育乳癌患者有關以前哨淋巴結切片檢查取代腋下淋巴切除術的好處，並為接受大範圍腋下淋巴切除術而造成淋巴水腫的患者提供支援服務。

編者的話

本簡報是「香港乳癌資料庫第七號報告」的補充報告，提供 2006 到 2012 年間香港乳癌患者接受前哨淋巴結切片情況。前哨淋巴結切片比腋下淋巴切除術較少出現副作用，因此是對改善乳癌患者生活質素的一大進步。我們的研究結果顯示，在研究時段內越來越多外科醫生和患者接納前哨淋巴結切片，特別是用於臨床淋巴結呈陰性的患者或早期癌症的患者。我們希望有關研究能為乳癌的治療方法提供獨到見解，以鼓勵更多有助改變政策的研究和討論，符合我們減輕乳癌的威脅和後遺症的使命。

參考資料

請參閱英文版參考資料

鳴謝

香港乳癌資料庫督導委員會成員陳志梅醫生編審本簡報。

建議引用：「香港乳癌資料庫簡報第六期：香港乳癌患者的前哨淋巴結切片。香港乳癌基金會 2015 年 9 月出版。」

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Sentinel Node Biopsy in Hong Kong Breast Cancer Patients

Introduction

Sentinel node biopsy (SNB) is the removal of the first few lymph nodes that drain the lymphatic fluid from the area of the breast affected by tumour. Histopathological evaluation of the sentinel lymph nodes can serve as a predictor of other metastases in the same lymph node basin. Studies have shown that if there is no cancer in these sentinel lymph nodes, the remaining lymph nodes will not have cancer. Therefore, SNB has been regarded as a standard of care for patients with early-stage clinically node negative breast cancer to determine the spread of the disease by the American Society of Clinical Oncology and National Comprehensive Cancer Network[1,2] and has been widely used in the United States, United Kingdom and Canada[3-5]. Sentinel lymph nodes are identified by using a low-grade radioactive substance (isotope) or a blue dye or a combination of both. The dye and radioactive substance will direct the surgeon to which lymph node(s) breast cancer cells are most likely to travel.

One of the benefits for using SNB to replace routine axillary dissection (AD) is that it removes the risk of unnecessary extensive lymph node removal, and thereby significantly decreases the risks of post-surgical complications of AD, such as lymphoedema, arm morbidity, sensory loss, and shoulder abduction deficits[6-12]. It also provides information on enhanced pathology by serial sectioning which detects micrometastasis not otherwise picked up on routine AD. SNB has been regarded as an important surgical advancement in improving the quality of life of breast cancer patients in the past two decades. In Hong Kong, SNB has been used in private and public medical facilities since 2002. This is the first local study looking at the changes in the pattern of SNB usage over time in Hong Kong.

Subjects & Methods

The patients in this study were a subset of our patient cohort covered by the "Hong Kong Breast Cancer Registry Report No.7". The inclusion criteria of this study were as follows:

1. Female patients with unilateral invasive breast cancers.
2. Disease was diagnosed and treated by surgery in Hong Kong from year 2006 to 2012.
3. Data about the nodal surgery must be available.
4. Patients without neoadjuvant therapy.

The use of SNB in different groups of patients specified by their clinical nodal status (negative or positive), pathological tumour size (classified as T1-4) and disease stage (TNM stage) were tested using Chi-square test. Pathological tumour size was used for data analyses as data on clinical tumour size were not available for many of our patients in this cohort, and we believed that the clinical and pathological tumour size did not deviate significantly. Changes in the use of SNB over time in different groups of patients were tested using the Chi-square test for trend. We also looked into the changes in the proportions of patients with unnecessary AD (i.e. patients who received AD but with no lymph nodes affected by cancer) over the study period. A p-value <0.05 was considered to be statistically significant and all statistical analyses were performed using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA).

Results

6,769 patients were included in the study. The median age of the patient cohort at the time of breast cancer diagnosis was 51.1 years old. Around half (53.8%) of the patients received breast surgery in private medical facilities. 3,853 (56.9%) patients received SNB as their first nodal surgeries and 43.1% received AD without SNB. Among the patients who received SNB as their first nodal surgeries, 70.6% showed no cancer on SNB, 1.3% showed isolated tumour cells, while 28.2% showed cancer on SNB. The proportions of these patients, with or without cancer on SNB, who received further AD were shown in Table 1. In total, 31.7% of the patients with SNB received further AD.

Table 1 Sentinel lymph nodes status of patients who received SNB and proportions of patients receiving further AD

Sentinel lymph nodes status	Number (%)	Number (%) patients who received further AD
N0	2,719 (70.6)	211 (7.8)
N0(i+)	49 (1.3)	8 (16.3)
N1mic	246 (6.4)	197 (80.1)
N1	795 (20.6)	762 (95.8)
N2	43 (1.1)	42 (97.7)
N3	1 (0.0)	1 (100.0)
Total	3,853 (100.0)	1,221 (31.7)

Clinical nodal status

Figure 1 shows the types of nodal surgery performed on patients with negative or positive clinical nodal status. Of the 5,703 (62.3%) patients with negative clinical nodal status, 62.5% received SNB and 37.5% received AD as their first nodal surgeries. Significantly, more patients with negative clinical nodal status received SNB alone than their counterparts with positive clinical nodal status (44.0% vs. 11.4%; p<0.001). The proportion of clinically node negative patients receiving SNB (including both SNB alone and SNB followed by AD) showed a positive linear trend over the study period (p<0.001) and the proportion increased from 45.7% in 2006 to 76.6% in 2012 (Figure 2). On the other hand, the use of SNB in patients with positive clinical nodal status did not change over the study period (data not shown).

In the patient cohort, 2,136 (37.5%) patients with negative clinical nodal status received AD without prior SNB. Among them, 40.4% received surgery at private medical facilities. The age of diagnosis, education level, occupation, surgery location, year of surgery, cancer stage and pathological nodal status of these patients were shown in Table 2.

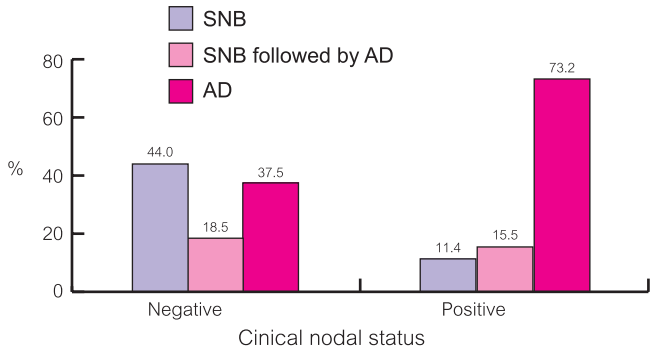

Figure 1 Types of nodal surgery in patients with negative or positive clinical nodal status (N=6,769)

The difference between the groups was significant at p<0.001

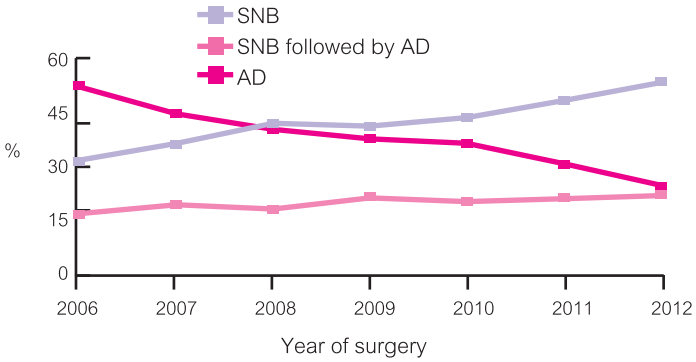

Figure 2 Types of nodal surgery in patients with negative clinical nodal status, 2006-2012 (N=5,703)

p-value for linear trend <0.001

Table 2 Sociodemographic and cancer characteristics of 2,136 patients who had clinically node negative cancers but received AD as their first nodal surgeries

	Number of patients	%
Age group		
20-29	13	0.6
30-39	172	8.0
40-49	748	35.0
50-59	730	34.3
60-69	331	15.4
70+	120	5.7
Not known	22	1.0
Education level		
Primary school or below	874	40.9
Secondary school	1,058	49.5
Matriculation or above	177	8.2
Not known	27	1.3
Occupation		
Professional / clerical	427	20.0
Non-clerical / labour	695	32.5
Self-employed	30	1.4
Housewife	757	35.4
Retired / unemployed	198	9.3
Not known	29	1.3
Surgery location		
Private	863	40.4
Public	1,273	59.6
Year of surgery		
2006	336	15.7
2007	317	14.8
2008	335	15.7
2009	334	15.6
2010	333	15.6
2011	278	13.0
2012	203	9.5
Cancer stage		
I	626	29.3
IIA	762	35.7
IIB	377	17.6
III	357	16.7
IV	14	0.7
Pathological nodal status		
N0	1,214	56.8
N1mic	69	3.2
N1	534	25.0
N2	207	9.7
N3	112	5.2

Pathological tumour size

SNB (including both SNB alone and SNB followed by AD) was more commonly used in patients with smaller tumours (T1) than patients with larger tumours (T3 or T4) (69.0% for T1 vs. 27.6% for T3 and 4.7% for T4; p<0.001) (Figure 3). For T1 and T2 tumours, the use of SNB (including both SNB alone and SNB followed by AD) showed a positive linear trend over the study period (p<0.001) and the proportion increased from 50.2% in 2006 to 80.6% in 2012 (for T1 tumours) and from 34.2% in 2006 to 54.2% in 2012 (for T2 tumours) (Figure 4).

Disease stage (TNM stage)

SNB (including both SNB alone and SNB followed by AD) was more commonly used by over 40.0% of patients with early-stage breast cancer (including T1N0M0, T1N1M0, T2N0M0, and T2N1M0) (p<0.001) (Figure 5). Unexpectedly, SNB was also used in 2.3-28.7% of patients with stage III or IV disease but most of them (97.4%) received AD after SNB. Sentinel node biopsy was intended for clinically node negative cancers. However some patients were found to have conditions that may not have been known before surgery and therefore they received SNB as their first nodal surgeries, similar to their counterparts who had earlier cancer stage. These conditions included having distant organ oligometastasis detected by post operative PET scan, or having four or more positive lymph nodes, or having at least one positive lymph node while having a T3 tumour, which were only confirmed by pathology after cancer surgery.

The use of SNB (including both SNB alone and SNB followed by AD) in stage III or IV cancer was not significantly different over the study period (data not shown). While for early-stage cancers (stage I to IIB), increased use of SNB (including both SNB alone and SNB followed by AD) was observed for patients with T1N0M0, T1N1M0, or T2N0M0 disease over the study period (Figure 6).

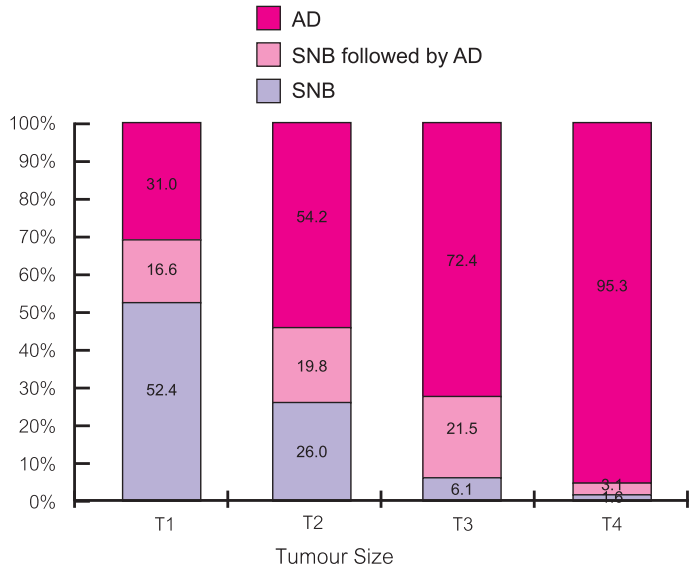

Figure 3 Types of nodal surgery in patients with T1 to T4 tumours (N=6,769)

The difference between the four groups was significant at p<0.001

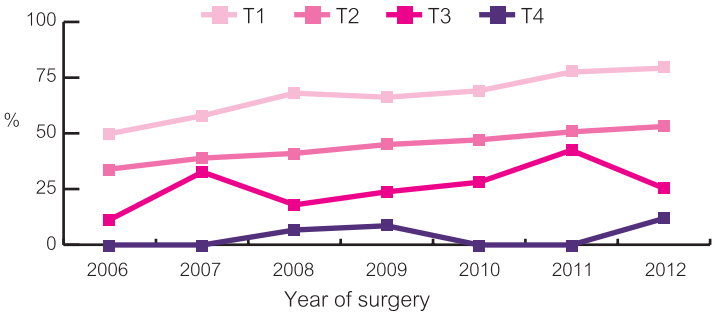

Figure 4 Proportions of patients, with T1 to T4 tumours, who received SNB (including both SNB alone and SNB followed by AD), 2006-2012. (N=6,769)

T1: p-value for linear trend <0.001, T2: p-value for linear trend <0.001, T3: p-value for linear trend = 0.102; T4: p-value for linear trend not available as the sample size were too small in some of the years.

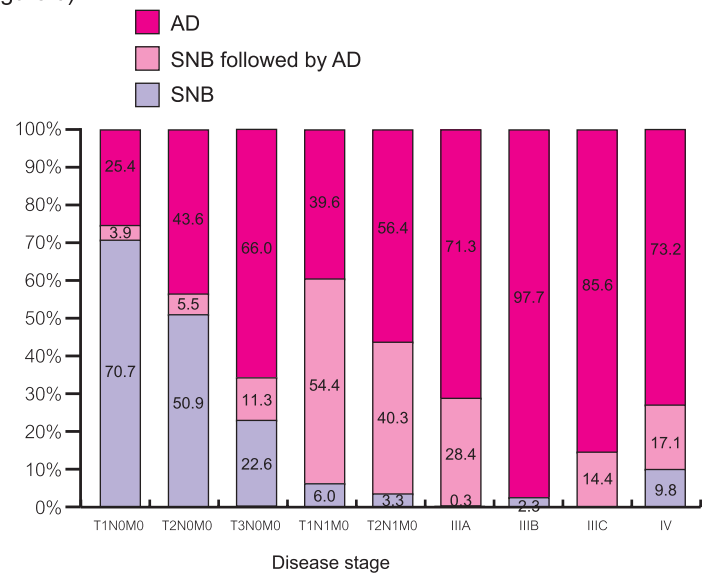

Figure 5 Types of nodal surgery in patients with different disease stage (N=6,769)

The difference between the groups was significant at p<0.001

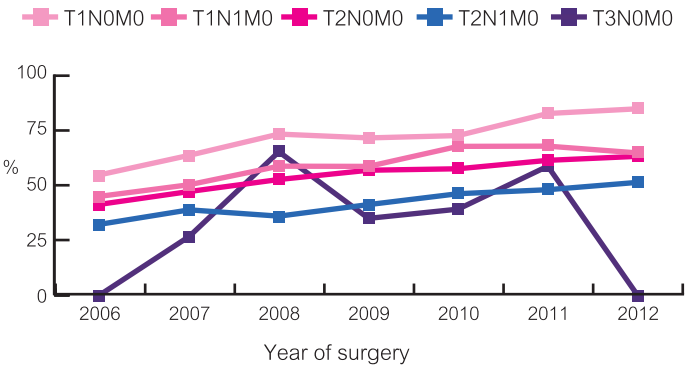

Figure 6 The use of SNB (including both SNB alone and SNB followed by AD) in patients with different disease stage (TNM stage) (N=5,790)

T1N0M0: p-value for linear trend <0.001, T1N1M0: p-value for linear trend <0.001, T2N0M0: p-value for linear trend <0.001, T2N1M0: p-value for linear trend =0.063, T3N0M0: p-value for linear trend =0.169

Changes in the proportions of patients with unnecessary AD over time

The proportions of patients who received unnecessary AD (with or without SNB) decreased over the study period, from 44.8% in 2006 to 28.9% in 2012 (p<0.001) (Figure 7).

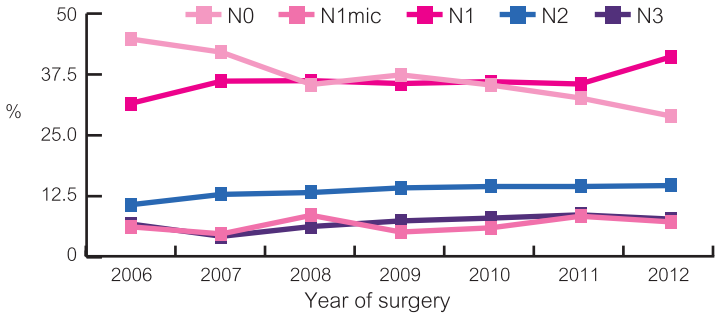

Figure 7 Pathological nodal status of patients who have received AD (with or without SNB) in our patient cohort, 2006-2012 (N=4,137)

p-value for linear trend <0.001

Conclusion

Study results suggested that sentinel node biopsy became more accepted by surgeons and patients over the study period, specifically, for patients presented with negative clinical nodal status or patients with early-stage diseases. Both surgeons' clinical and patients' personal decisions affect the use of SNB to replace AD as the first nodal surgery in determining the extent of diseases. Surgeons have responsibilities to explain to their patients about SNB and its well-established reliability for determining the nodal status in early stage breast cancer. Meanwhile, the Hong Kong Breast Cancer Foundation would put more efforts into educating breast cancer patients about the benefits of SNB over AD as well as providing support service to patients who have developed lymphoedema due to extensive removal of axillary lymph nodes.

Editor's message

This issue intends to complement the "Hong Kong Breast Cancer Registry Report No. 7" on the use of sentinel node biopsy in Hong Kong breast cancer patients for the years 2006-2012. Sentinel node biopsy causes side effects less common than axillary dissection, and therefore it has been an important advancement in improving the quality of life of breast cancer patients. Our findings suggested that sentinel node biopsy became more accepted by surgeons and patients over the study period, specifically, for patients presented with negative clinical nodal status or patients with early-stage diseases. Our study aims to provide insights into breast cancer management to encourage more research and discussion conducive to policy change in synch with our mission to mitigate the threat and sequelae of breast cancer.

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