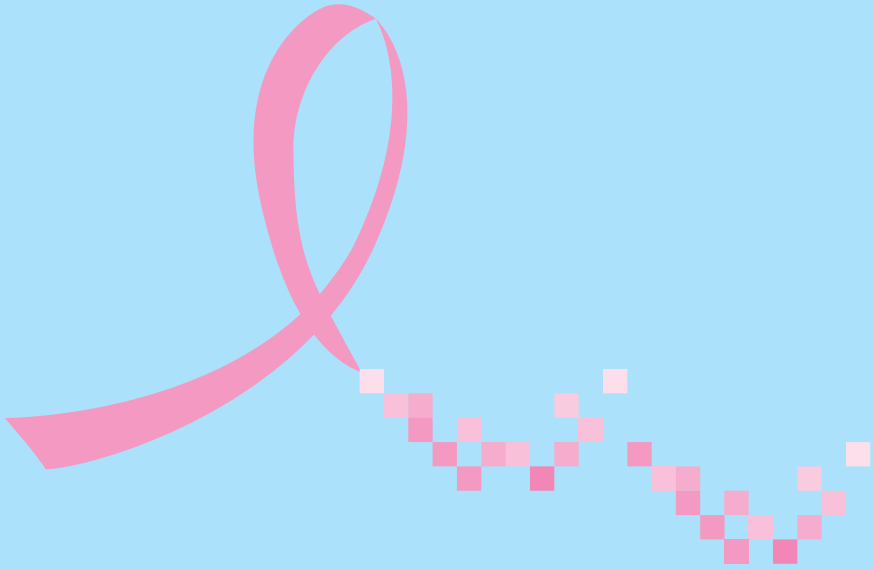

CHAPTER 2

DISEASE PATTERN, TREATMENT TREND AND CLINICAL OUTCOME OF BREAST CANCER IN HONG KONG

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This chapter reviews the clinical presentation, cancer characteristics of breast cancer in Hong Kong and treatment methods used from data on 14,064 breast cancer patients. The objectives of this chapter are to look into the clinical management of breast cancer, and to identify disease and treatment trends in a local context in order to develop and improve the standard of care for breast cancer patients in Hong Kong.

KEY FINDINGS

Clinical presentations

- Self-detection by chance was the primarily method of first breast cancer detection among our patient cohort (84.5%). More invasive breast cancers were self-detected by chance (88.2%) than in situ breast cancers (58.0%).
- Most (92.2%) patients who self-detected their cancers by chance found a painless lump on their breast(s). Pain is not usually a symptom of breast cancer; only 6.0% of our patients felt pain in their breast(s) at initial presentation.
- Of the self-detected breast cancers in our patient cohort, after the onset of symptoms, only one-third (36.9%) of the patients sought first medical consultation in less than one month.
- Majority (91.4%) of our patients had unilateral breast cancer, while 4.5% (n=314) had synchronous bilateral breast cancer at first diagnosis. 295 (4.2%) patients developed a contralateral breast cancer subsequently after diagnosis of an initial primary breast cancer.
- A quarter (24.5%) of our invasive breast cancer patients did not conduct cancer staging, while among those who conducted cancer staging, the most commonly used method was chest x-ray and ultrasound of abdomen (35.2%). Positron emission tomography scan (PET scan) was used by 25.2% of our patients.
- The most common cancer stage at diagnosis was stage II (38.1%). 14.6% of our patients were diagnosed with stages III-IV diseases while 11.7% of our patients were diagnosed with in situ cancers.

Cancer characteristics

- The mean size of invasive breast cancers for our patient cohort was 2.2 cm (standard deviation: ±1.4 cm). Tumours larger than 2.0 cm in size were found in 46.7% of our patients. In our patient cohort, screen-detected cancers were significantly smaller than cancers that were self-detected by chance (mean: 1.3 cm vs. 2.3 cm; $p<0.001$). 59.5% of our patients with invasive breast cancers had no positive lymph nodes. Most common type was invasive carcinoma of no specific type (86.0%). Over three quarters (79.5%) of invasive breast cancers were either estrogen receptor (ER) or progesterone receptor (PR) positive, and 21.7% were c-erbB2/HER2 positive. 12.0% were triple negative diseases.
- The mean size of in situ cancers for our patient cohort was 2.0 cm (standard deviation: ±1.5 cm). Tumours larger than 2.0 cm were found in 37.2% of our patients. Of the in situ breast cancers where mammogram (MMG) was performed, 62.8% showed microcalcification on MMG. Ductal carcinoma in situ was found to be a major type

of in situ breast cancers (93.8%). 80.9% of in situ breast cancers were either ER or PR positive, and 29.0% were c-erbB2/HER2 positive.

Treatment methods

- 14.8% of our patients received care solely at private medical facilities, 49.8% received care solely at public medical facilities, and 35.4% received are at both private and public medical facilities.
- Surgery
  - Majority (98.2%) of our patients underwent surgery as part of their treatment.
  - 51.6% of our patients had surgery at private medical facilities, while 48.4% had surgery at public medical facilities.
  - Two-thirds (63.6%) of our patients had mastectomy, while 34.3% had breast-conserving surgery.
  - The percentage of our patients who underwent mastectomy was both positively correlated with increasing age and increasing cancer stage.
  - A higher proportion of patients who had surgery at private medical facilities underwent breast-conserving surgery than those who had surgery at public medical facilities (44.5% vs 25.9%).
  - Sentinel node biopsy (SNB) was more commonly used by our patients with negative clinical nodal statuses than those with positive clinical nodal statuses (41.2% vs 11.1%).
  - The use of axillary dissection was positively correlated with progressing cancer stage.
- Chemotherapy
  - 60.3% of patients in our cohort underwent chemotherapy, and among them, 9.4% had neoadjuvant chemotherapy.
  - 85.3% of our patients received chemotherapy in public medical facilities, while 14.7% received in private medical facilities.
  - In general for all cancer stages, the use of chemotherapy among our patients aged over 70 was much lower than that among patients aged below 70.
- Radiotherapy
  - 62.1% of our patients had radiotherapy as one of their treatment.
  - 86.2% of our patients received radiotherapy at public medical facilities, while 13.8% received at private medical facilities.
  - Over 90% of our patients with breast-conserving surgery received radiotherapy, while the use of radiotherapy in patients with mastectomy increased with increasing cancer stages, with the exception of stage IV disease.
- Endocrine therapy
  - 66.7% of our patients received endocrine therapy.
  - 97.5% of our patients received endocrine therapy at public medical facilities, while 2.5% received at private medical facilities.
  - Endocrine therapy was used over 74.0% of our patients with stages I-IV breast cancer, but was only used in 15.9% of our patients with stage 0 breast cancer.
- Targeted therapy
  - 41.1% of our patients with c-erbB2/HER2 positive cancers underwent targeted therapy.
  - 87.2% of our patients received targeted therapy at public medical facilities, while 12.8% received at private medical facilities.
  - The most commonly used targeted therapy drug was Trastuzumab (96.0%).

- Complementary and alternative therapies
  - 39.8% of our patients in the cohort received complementary and alternative therapies as part of their treatment.
  - 66.8% of our patients used traditional Chinese medicines.
- Combinations of treatments are usually used for treating breast cancer effectively. In general, the number of treatments increased with increasing cancer stage.

Patient status

- The mean follow-up period was 5.2 years and median follow-up period was 4.1 years.
- 834 (6.6%) of patients in our cohort experienced recurrence, where 2.8% of our patients experienced locoregional recurrence (LR) solely, 2.7% experienced distant recurrence (DR) solely, and 1.1% experienced both locoregional and distant recurrence at the same time.
- The common sites for locoregional recurrence were breast (36.6%) and chest wall (31.2%) and the common organs involved in distant recurrence were bone (54.4%) and lung (44.3%).

2.1 Clinical presentation

Self-detection by chance was the primary method of first breast cancer detection among our patient cohort (84.5%) (Figure 2.1). Relatively small proportions of breast cancers in our cohort were detected through healthcare service-assisted screening methods, including clinical breast examination (CBE), mammography screening (MMG), and ultrasound screening (USG). A study in the United States[27], where there are population-based breast cancer screening programmes for women, found that 43% of the breast cancer cases in the US are detected through mammography screening, which is much higher than the 9.7% observed in our patient cohort in Hong Kong.

When comparing the method of first breast cancer detection by types of medical service received, the proportion of our patients who self-detected their breast cancer by chance was higher in public medical service users or mixed private/public medical service users than in private medical service users. Additionally, the proportion of our patients whose breast cancer was first detected through mammography screening was higher for private medical service users than either public medical service users or mixed private / public medical service users (Table 2.1).

Studies have shown that mammography screening is effective in detecting early cancers when there are neither signs nor symptoms that can be observed by patients or medical professionals[28]. In our patient cohort, the proportion of invasive breast cancers detected by mammography screening (6.4%) were much lower than that of in situ breast cancers (33.3%) (Table 2.2). In

addition, more stage 0 or I cancers (32.7% and 11.8% respectively) were detected by mammography screening than stage III or IV cancers (3.0% and 1.6% respectively). Over 90% of our patients with stage IIB, III or IV cancers self-detected their cancer by chance (Table 2.3).

These findings highlight the importance of increased awareness of breast self-examination (BSE), and the need for increased mammography screening in public health care facilities.

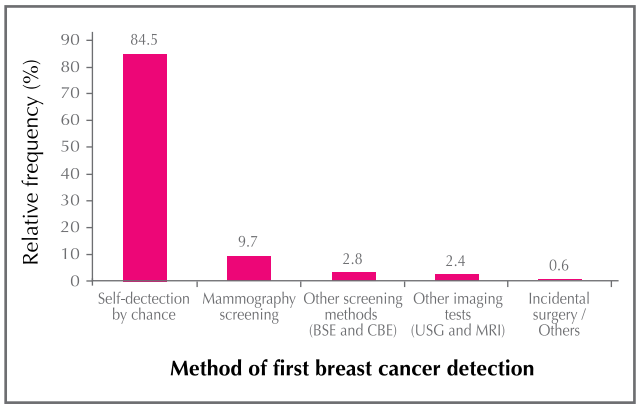

Figure 2.1 Method of first breast cancer detection in our patient cohort (N=13,054)

BSE: Breast self-examination; CBE: Clinical breast examination; USG: Ultrasound screening; MRI: Magnetic resonance imaging

Table 2.1 Method of first breast cancer detection by types of medical service received for cancer diagnosis and treatment (N=13,053)

	Private medical service users (N=1,907)		Public medical service users (N=6,475)		Mixed private / public medical service users (N=4,671)	
Method of first breast cancer detection	**Number**	**(%)**	**Number**	**(%)**	**Number**	**(%)**
Self-detection by chance	1,446	(75.8)	5,547	(85.7)	4,035	(86.4)
Mammography screening	259	(13.6)	656	(10.1)	349	(7.5)
Other screening methods (BSE and CBE)	73	(3.8)	144	(2.2)	154	(3.3)
Other imaging tests (USG and MRI)	112	(5.9)	89	(1.4)	112	(2.4)
Incidental surgery / Others	17	(0.9)	39	(0.6)	21	(0.4)

BSE: Breast self-examination; CBE: Clinical breast examination; USG: Ultrasound screening; MRI: Magnetic resonance imaging

Table 2.2 Method of first breast cancer detection by type of cancer (N=12,668)

Method of first breast cancer detection	Type of cancer, Number (%)	
	In situ (N=1,645)	Invasive (N=11,023)
Self-detection by chance	954 (58.0)	9,720 (88.2)
Mammography screening	548 (33.3)	703 (6.4)
Other screening methods (BSE and CBE)	53 (3.2)	311 (2.8)
Other imaging tests (USG and MRI)	79 (4.8)	230 (2.1)
Incidental surgery / Others	11 (0.7)	59 (0.5)

BSE: Breast self-examination; CBE: Clinical breast examination; USG: Ultrasound screening; MRI: Magnetic resonance imaging

Table 2.3 Method of first breast cancer detection by cancer stage (N=12,511)

Method of first breast cancer detection	Cancer stage, Number (%)					
	0 (N=1,529)	I (N=4,053)	IIA (N=3,328)	IIB (N=1,674)	III (N=1,672)	IV (N=255)
Self-detection by chance	910 (59.5)	3,259 (80.4)	2,988 (89.8)	1,565 (93.5)	1,576 (94.3)	235 (92.2)
Mammography screening	500 (32.7)	480 (11.8)	162 (4.9)	45 (2.7)	50 (3.0)	4 (1.6)
Other screening methods (BSE and CBE)	49 (3.2)	139 (3.4)	103 (3.1)	34 (2.0)	27 (1.6)	10 (3.9)
Other imaging tests (USG and MRI)	61 (4.0)	150 (3.7)	57 (1.7)	24 (1.4)	12 (0.7)	4 (1.6)
Incidental surgery / Others	9 (0.6)	25 (0.6)	18 (0.5)	6 (0.4)	7 (0.4)	2 (0.8)

BSE: Breast self-examination; CBE: Clinical breast examination; USG: Ultrasound screening; MRI: Magnetic resonance imaging

Most (92.2%) patients who self-detected their cancers by chance found a painless lump on their breast(s). Pain is not usually a symptom of breast cancer; only 6.0% of our patients felt pain in their breast(s) at initial presentation. Some patients (8.3%) experienced changes in nipple (such as nipple discharge, nipple retraction, redness, scaliness or thickening of nipple) (Figure 2.2).

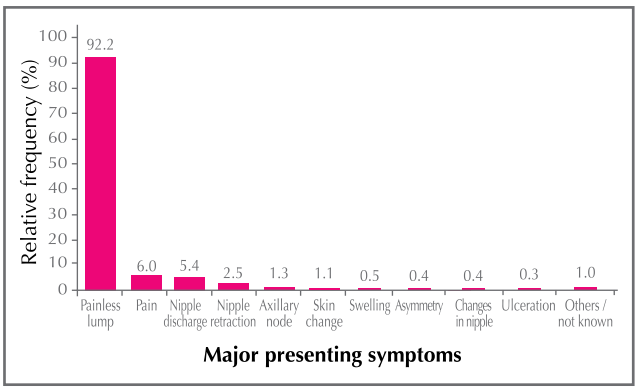

Figure 2.2 Major presenting symptoms of self-detected* breast cancers in our patient cohort (N=11,028)

*self-detection by chance only

2.1.1 Time interval between the onset of symptoms and first medical consultation

Longer delay in seeking medical consultation was associated with higher probability of local cancer spread or distant metastasis, and poorer prognosis[29]. Of the self-detected breast cancers in our patient cohort, after the onset of symptoms, only one-third (36.9%) of the patients sought first medical consultation in less than one month (Table 2.4).

A higher proportion (44.4%) of our patients who were treated in private medical facilities sought first medical consultation in less than one month, than patients that attended in public medical facilities (28.0%) (Table 2.5).

Table 2.4 Time interval between the onset of symptoms and first medical consultation for our patients who self-detected* their cancers (N=2,984)

	Number	(%)
Less than 1 month	1,101	(36.9)
1-3 months	1,134	(38.0)
4-12 months	420	(14.1)
More than 12 months	329	(11.0)

*Self-detection by chance only

Table 2.5 Time interval between the onset of symptoms and first medical consultation for our patients who self-detected* their cancers by types of medical service (N=2,984)

	Private medical service users (N=728)		Public medical service users (N=1,234)		Mixed private / public medical service users (N=1,022)	
	Number	(%)	Number	(%)	Number	(%)
Less than 1 month	323	(44.4)	345	(28.0)	433	(42.4)
1-3 months	255	(35.0)	485	(39.3)	394	(38.6)
4-12 months	92	(12.6)	219	(17.7)	109	(10.7)
More than 12 months	58	(8.0)	185	(15.0)	86	(8.4)

*Self-detection by chance only

A larger proportion (38.4%) of our patients with stage IV disease took more than 12 months to seek first medical consultation than those with early stage cancer (stage I or IIA or IIB) (Table 2.6).

Table 2.6 Time interval between the onset of symptoms and first medical consultation for our patients who self-detected* their cancers by cancer stage at diagnosis (N=2,704)

	Cancer stage, Number (%)				
	I (N=868)	IIA (N=822)	IIB (N=422)	III (N=411)	IV (N=73)
Less than 1 month	368 (42.4)	325 (39.5)	143 (33.9)	120 (29.2)	12 (16.4)
1-3 months	315 (36.3)	327 (39.8)	175 (41.5)	163 (39.7)	20 (27.4)
4-12 months	113 (13.0)	107 (13.0)	53 (12.6)	70 (17.0)	13 (17.8)
More than 12 months	72 (8.3)	63 (7.7)	51 (12.1)	58 (14.1)	28 (38.4)

*Self-detection by chance only

2.2 Cancer characteristics

Breast cancer can occur in one (unilateral) or both breasts (bilateral). Majority (91.4%) of our patients had unilateral breast cancer, while 4.5% (n=314) had synchronous bilateral breast cancer at first diagnosis (Figure 2.3). 295 (4.2%) patients developed a contralateral breast cancer within, on average, 7.9 years (range: 0.5 – 36.1 years, median: 6.0 years) after diagnosis of an initial primary breast cancer (Figure 2.3).

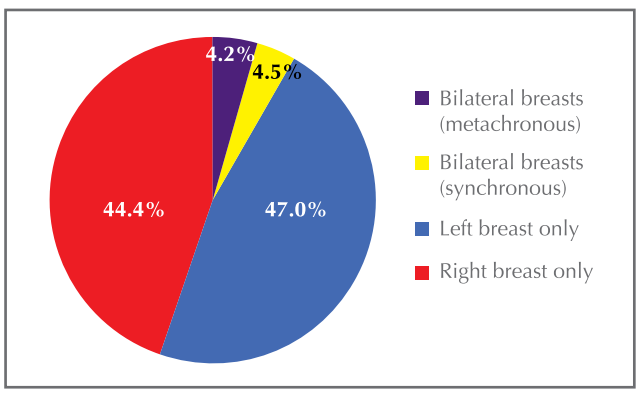

Figure 2.3 Laterality of 14,064 breast cancer cases

Figure 2.4 shows the locations of breast cancer occurrence on the breasts within our patient cohort. In our patient cohort, around half of the breast cancers in either the left or right breast were detected in the upper outer quadrant (46.3% and 49.7% respectively).

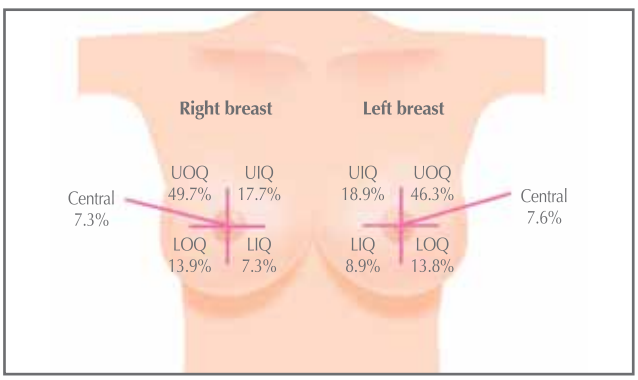

Figure 2.4 Locations of breast cancer occurrence on the breasts within our patient cohort (N=14,064)

UOQ: Upper outer quadrant UIQ: Upper inner quadrant
LOQ: Lower outer quadrant LIQ: Lower inner quadrant
*Figures include multicentric cancers

2.2.1 Diagnostic tests for breast cancer

There are two types of breast cancer diagnostic tests: imaging tests and biopsies. Imaging tests include diagnostic mammography (MMG), ultrasound (USG) and magnetic resonance imaging (MRI). Diagnostic mammography is a common procedure for breast cancer diagnosis particularly to detect non-palpable microcalcifications before breast-conserving surgery, and ultrasound is used to distinguish a solid mass, which may be cancer, from a fluid-filled cyst, which is usually not cancer. Breast MRI is usually performed on women who have been diagnosed with breast cancer to check the other breast for cancer or to find out the extent of their disease. For around 80.8% of our patients MMG was used, while USG was used on 74.3% and MRI was used on only 7.0% of our patients in cancer diagnosis (Table 2.7). Results of imaging tests are classified into categories using a system called the Breast Imaging Reporting and Data System (BIRADS). The system suggests that women with BIRADS 4 or 5 mammograms are suspicious for cancer and should be checked by further surgical tests such as biopsies.

Table 2.7 Sensitivity and diagnostic results of breast imaging tests (N=14,064)

	Mammography (N=11,358)	Breast ultrasound (N=10,453)	MRI (N=983)
Proportion of patients using the diagnostic test	80.8%	74.3%	7.0%
Overall sensitivity*	81.1%	89.4%	95.9%
BIRADS category			
Diagnostic / malignant (BIRADS 5)	3,503 (30.8%)	3,824 (36.5%)	762 (77.5%)
Suspicious abnormality (BIRADS 4)	5,712 (50.3%)	5,517 (52.8%)	181 (18.4%)
Probably benign (BIRADS 3)	687 (6.0%)	643 (6.2%)	14 (1.4%)
Benign (BIRADS 2)	493 (4.3%)	213 (2.0%)	9 (0.9%
Normal (BIRADS 1)	899 (7.9%)	247 (2.4%)	16 (1.6%)
Incomplete (BIRADS 0)	64 (0.6%)	9 (0.1%)	1 (0.1%)

MRI: Magnetic resonance imaging; BIRADS: Breast Imaging Reporting and Data System

*Sensitivity: Number of true positives (BIRADS 4-5) divided by total number of patients who had the test

Opacity was observed in 59.9% of our patients with BIRADS 4 or 5 mammograms, while microcalcification was observed in 50.4% (Table 2.8). The sensitivity of mammography is affected by the mammographic density of a woman's breasts. Heterogeneously dense breast may disguise small masses, while extremely dense breast lowers the sensitivity of mammography. In our patient cohort, two-thirds (68.1%) had heterogeneously dense breasts, while 6.1% had extremely dense breasts (Figure 2.5). Table 2.9 shows the mammographic density of breasts of our patients in different age groups.

Table 2.8 Mammographic findings of patients in our cohort who were diagnosed through mammography (N=9,215)

	Number	(%)
Opacity	5,521	(59.9)
Microcalcification	4,647	(50.4)
Architectural distortion	1,240	(13.5)
Asymmetric density	896	(9.7)
Unclassified	465	(5.0)

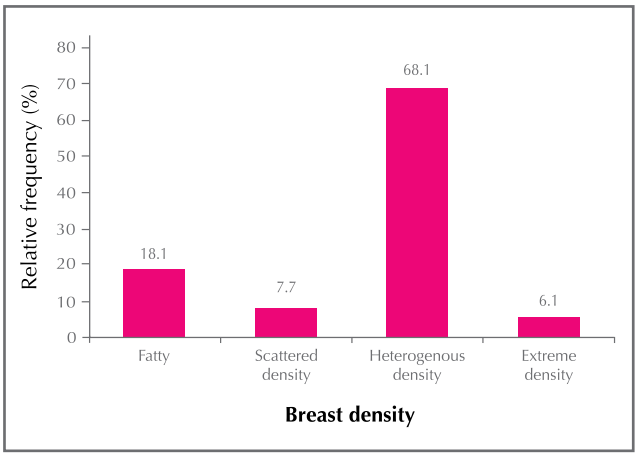

Figure 2.5 Mammographic density of breasts of our patients who were diagnosed through mammography (N=6,574)

Table 2.9 Mammographic density of breasts of our patients who were diagnosed through mammography by age group (N=6,388)

	Age group, Number (%)													
Mammographic density	**<20**		**20-29**		**30-39**		**40-49**		**50-59**		**60-69**		**70+**	
Fatty	0	(0.0)	4	(10.8)	46	(8.1)	253	(11.4)	407	(19.1)	293	(28.8)	163	(40.1)
Scattered density	0	(0.0)	1	(2.7)	20	(3.5)	131	(5.9)	182	(8.6)	103	(10.1)	54	(13.3)
Heterogeneous density	1	(100.0)	29	(78.4)	450	(78.8)	1,661	(74.6)	1,426	(67.0)	583	(57.3)	184	(45.3)
Extreme density	0	(0.0)	3	(8.1)	55	(9.6)	183	(8.2)	112	(5.3)	39	(3.8)	5	(1.2)

Biopsies (samplings of breast cells or tissues for examination) for breast cancer diagnosis include fine needle aspiration (FNA), core needle biopsy (CNB), and excisional biopsy. As a standard of care, these biopsies are used to confirm before surgery if the breast lesion is malignant. FNA and CNB are less invasive sampling methods and are more often used, but sometimes excisional biopsy, which removes the largest amount of breast tissue, is conducted. FNA and / or CNB were performed in 80.9% of our patients and among them, 3,916 (34.4%) received FNA solely, 5,120 (45.0%) received CNB solely, and 2,336 (20.5%) received both FNA and CNB. Excisional biopsy was performed in 14.2% of our patients. Excisional biopsy had the highest overall sensitivity of 100%, followed by CNB (98.7%) and FNA (90.0%) (Table 2.10).

Table 2.10 Sensitivity and diagnostic results of breast tissue biopsies (N=14,064)

	FNA (N=6,252)	CNB (N=7,456)	Excisional biopsy (N=1,998)
Proportion of patients using the diagnostic test	44.5%	53.0%	14.2%
Overall sensitivity*	90.0%	98.7%	100.0%
Class			
Diagnostic / malignant (Class V)	3,835 (61.4%)	7,076 (94.9%)	1,998 (100.0%)
Suspicious (Class IV)	1,109 (17.7%)	157 (2.1%)	—
Atypical (Class III)	684 (10.9%)	124 (1.7%)	—
Benign (Class II)	297 (4.8%)	67 (0.9%)	—
Scanty benign (Class I)	220 (3.5%)	30 (0.4%)	—
Incomplete (Class 0)	107 (1.7%)	2 (0.0%)	—

FNA: Fine needle aspiration; CNB: Core needle biopsy;
*Sensitivity: Number of true positives (Class III-V) divided by total number of patients who had the test

2.2.2 Methods of cancer staging

Cancer staging is the process of finding out the extent of the disease in the body after diagnosis of breast cancer. A quarter (24.5%) of our invasive breast cancer patients did not conduct cancer staging, while among those who conducted cancer staging, the most commonly used method was chest x-ray and ultrasound of abdomen (35.2%). Positron emission tomography scan (PET scan) was used by 25.2% of our patients (Table 2.11). According to the 2010 practice guidelines of the National Comprehensive Cancer Network (NCCN), patients with early breast cancer, including stage I, stage II, or operable stage III breast cancer, are not recommended to use PET scan to determine the extent of disease[30]. However, 9.6% and 18.6% of our stages I and IIA patients, respectively, used PET scan to determine the extent of their disease (Table 2.12).

Table 2.11 Cancer staging in 10,548 invasive breast cancer patients

Type of cancer staging method	Number	(%)
No cancer staging	2,579	(24.5)
Chest X-Ray (CXR)	5,822	(73.1)
Ultrasound abdomen (USG Abd)	3,066	(38.5)
Positron emission tomography scan (PET scan)	2,010	(25.2)
Bone scan	309	(3.9)
Computed tomography of body parts*	278	(3.5)
Magnetic resonance imaging whole body (MRI whole body)	38	(0.5)
Unspecified	525	(6.6)

* Body parts include abdomen, thorax, pelvis, brain, or whole body

Table 2.12 The use of PET scan as a form of staging methods by cancer stage (N=7,969)

	Cancer stage						
	I	IIA	IIB	III	IV	Unstaged	Total
No. (%) of patients used PET scan	259 (9.6)	435 (18.6)	366 (30.1)	710 (51.8)	203 (80.9)	37 (44.6)	2,010 (25.2)

Using the American Joint Committee on Cancer (AJCC) Breast Cancer Staging (7th edition)[31] to study cancer staging in our patient cohort, it was found that the most common cancer stage at diagnosis was stage II (38.1%). Around 14.6% of our patients were diagnosed with stages III-IV diseases while 11.7% of our patients were diagnosed with in situ cancers (Figure 2.6).

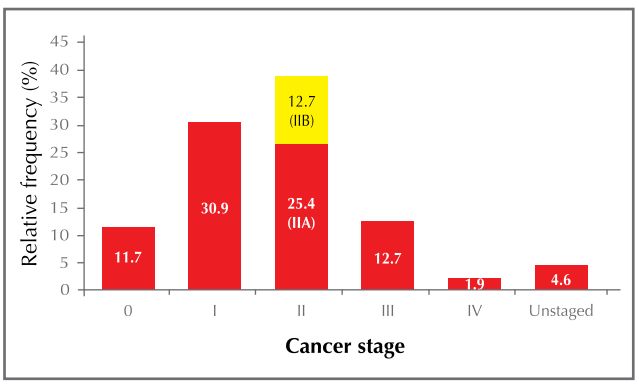

Figure 2.6 Cancer stage at diagnosis in our breast cancer patients (N=14,064)

Out of our 14,064 cancer cases, data from 12,973 cases with available pathology data was used for the following analyses on cancer characteristics. 11,203 patients (86.2%) were diagnosed with invasive cancers and 1,761 (13.7%) were diagnosed with in situ cancers. 9 cases (0.1%) were diagnosed with occult primary breast cancers.

2.2.3 Characteristics of invasive breast cancer

The mean size of invasive breast cancers for our patient cohort was 2.2 cm (range: 0.01 – 22.0 cm; standard deviation: ±1.4 cm). Tumours of 1 cm or less in size were found in 16.0% of our patients and tumours of 2-5 cm in size were found in 43.3% of our patients (Figure 2.7). In our patient cohort, screen-detected cancers were significantly smaller than cancers that were self-detected by chance (mean: 1.3±1.0 cm vs. 2.3±1.4 cm; p<0.001).

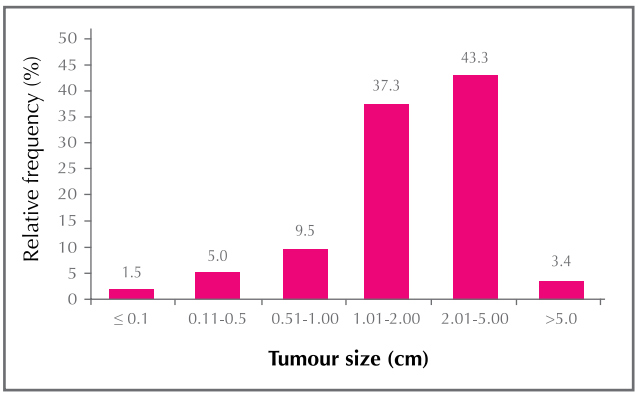

Figure 2.7 Distribution of tumour size (cm) of invasive breast cancers in our patient cohort (N=10,587)

Lymph node status is one of the factors used to determine disease stage. Multiple affected lymph nodes signify a higher disease stage. Of our patients with invasive breast cancers, 59.5% had no positive lymph nodes, 0.9% had isolated tumour cells, 4.5% had micrometastasis (metastasis size > 0.2 mm to ≤ 2 mm), while 35.1% had at least one positive lymph node with metastasis size greater than 2 mm (Figure 2.8).

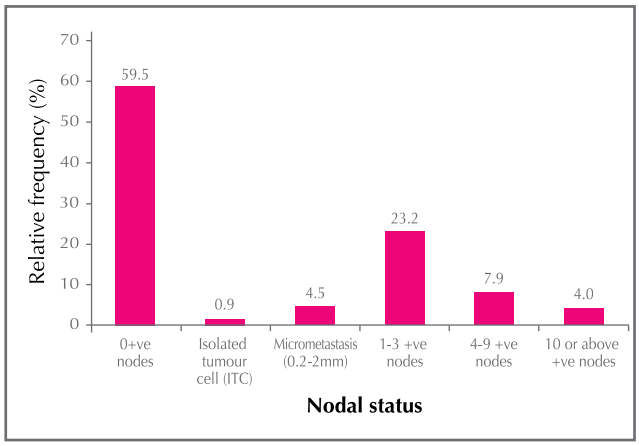

Figure 2.8 Number of positive lymph nodes among our patients with invasive breast cancers (N=11,030)

2.2.4 Characteristics of in situ breast cancer

The mean size of in situ breast cancers for our patient cohort was 2.0 cm (range: 0.02 – 10.0 cm; standard deviation: ±1.5 cm). Tumours of 1 cm or less in size were found in 32.7% of our patients while tumours of 2-5 cm in size were found in 32.8% of our patients (Figure 2.9). A small proportion (4.4%) of our patients had in situ tumours greater than 5.0 cm. Of the in situ breast cancers where MMG was performed, 62.8% showed microcalcification on MMG.

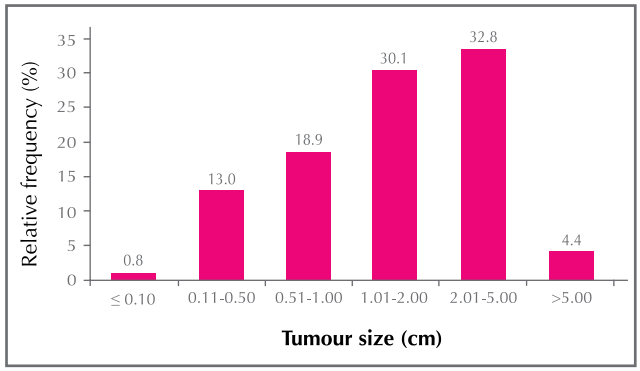

Figure 2.9 Distribution of tumour size (cm) of in situ breast cancers in our cohort (N=1,504)

2.3 Histological and biological characteristics

Breast cancer is a heterogeneous group of tumours, consisting of different histologic subtypes with diverse microscopic appearances. The histological data of breast carcinomas provides valuable prognostic information. It complements other independent parameters including size, grade, nodal status, hormonal receptor status and HER2 oncogene status to help predict the likelihood of recurrence and response to treatment.

2.3.1 Invasive breast cancer

Table 2.13 shows the histological characteristics, grading, multifocality and multicentricity of invasive breast cancers in our patient cohort. The most common type was invasive carcinoma of no specific type (86.0%).

The biological characteristics of invasive breast cancers in our patient cohort are shown in Table 2.14. Among our patients with invasive breast cancers who were tested for either estrogen or progesterone receptor status, 79.5% were either estrogen receptor (ER) or progesterone receptor (PR) positive. 2,263 (21.7%) invasive breast cancers in our patient cohort were c-erbB2/HER2 positive.

Table 2.13 Histological type, grading, multifocality and multicentricity of invasive breast cancers (N=11,203)

Histological type	Number	(%)
Invasive carcinoma of no specific type	9,636	(86.0)
Lobular	417	(3.7)
Mucinous (colloid)	413	(3.7)
Papillary	107	(1.0)
Tubular	97	(0.9)
Carcinoma with medullary features	71	(0.6)
Mixed ductal and lobular	59	(0.5)
Borderline / malignant phyllodes	47	(0.4)
Micropapillary	39	(0.3)
Metaplastic carcinoma	34	(0.3)
Carcinoma with apocrine features	19	(0.2)
Carcinoma with neuroendocrine features	18	(0.2)
Adenoid cystic carcinoma	14	(0.1)
Cribriform carcinoma	10	(0.1)
Paget's disease of nipple	6	(0.1)
Inflammatory	3	(0.0)
Secretory carcinoma	2	(0.0)
Lipid rich carcinoma	1	(0.0)
Sarcoma	1	(0.0)
Others	82	(0.7)
Not known	127	(1.1)

Grade	Number	(%)
Grade 1	1,917	(17.1)
Grade 2	4,599	(41.1)
Grade 3	3,686	(32.9)
Not known	1,001	(8.9)
Lymphovascular invasion	**3,146**	**(28.1)**
Multifocality	**1,096**	**(9.8)**
Number of foci		
2	585	(53.4)
3-4	202	(18.4)
≥5	113	(10.3)
Not known	196	(17.9)
Multicentricity	**325**	**(2.9)**
Number of quadrants		
2	276	(84.9)
3	22	(6.8)
4	10	(3.1)
Not known	17	(5.2)

Table 2.14 Biological characteristics of invasive breast cancers (N=11,203)

	Number	(%)
Estrogen receptor (ER) (96.4% of the patients had the test)		
Positive	8,318	(77.0)
Negative	2,485	(23.0)
Progesterone receptor (PR) (96.1% of the patients had the test)		
Positive	7,011	(65.1)
Negative	3,752	(34.9)
c-erbB2 / HER2 (92.9% of the patients had the test)		
Positive (IHC score 3)	2,107	(20.2)
Equivocal (IHC Score 2)	3,153	(30.3)
FISH / CISH +ve	*156*	*(4.9)*
Negative (IHC score 0/1)	5,151	(49.5)
Ki-67 index (47.7% of the patients had the test)		
<14%	2,291	(42.9)
≧14%	3,051	(57.1)

HER2: Human epidermal growth factor receptor 2

Breast cancer is not considered as a single disease. It can be further classified into several biological subtypes, determined by immunohistochemical staining of several biological markers described in Table 2.14 . By combining these biological markers rather than assessing them separately, further prognostic and predictive information can be achieved. The biological subtypes include luminal A, luminal B (HER2 negative), luminal B (HER2 positive), HER2-positive, and triple negative[32]. Their relative frequencies by cancer stage in our patient cohort are shown in Table 2.15.

Table 2.15 Biological subtypes of invasive tumors by cancer stage (N=10, 299)

	Cancer Stage, N (%)											
Biological subtypes[32]	**I**		**IIA**		**IIB**		**III**		**IV**		**Total**	
Luminal A*	1,020	(25.7)	563	(17.4)	250	(15.8)	166	(11.8)	11	(9.4)	2,010	(19.5)
Luminal B (HER2 negative)#	523	(13.2)	556	(17.2)	274	(17.3)	269	(19.2)	18	(15.4)	1,640	(15.9)
Luminal A/B (HER2 negative)†	1,227	(31.0)	929	(28.8)	519	(32.7)	442	(31.5)	51	(43.6)	3,168	(30.8)
Luminal B (HER2 positive)^	478	(12.1)	417	(12.9)	214	(13.5)	241	(17.2)	20	(17.1)	1,370	(13.3)
HER2-positive❊	298	(7.5)	273	(8.5)	140	(8.8)	149	(10.6)	11	(9.4)	871	(8.5)
TND§	418	(10.5)	491	(15.2)	188	(11.9)	137	(9.8)	6	(5.1)	1,240	(12.0)
Total	**3,964**	**(38.5)**	**3,229**	**(31.4)**	**1,585**	**(15.4)**	**1,404**	**(13.6)**	**117**	**(1.1)**	**10,299**	**(100.0)**

* Luminal A: ER and/or PR+, HER2-, and Ki-67 low (<14%)

\# Luminal B (HER2 negative): ER and/or PR+, HER2-, and Ki-67 high (≧14%)

† Luminal A/B (HER2 negative): ER and/or PR+, HER2-, and Ki-67 not known

^ Luminal B (HER2 positive): ER and/or PR+, HER2+, and any Ki-67

❊ HER2-positive: ER and PR-, HER2+, and any Ki-67

§ TND (Triple Negative Disease): ER-, PR-, HER2-, and any Ki-67

2.3.2 *In situ breast cancer*

Table 2.16 shows the histological characteristics, grading, multifocality and multicentricity of in situ breast cancers in our patient cohort. Ductal cancers were found to be a major type of in situ breast cancers (93.8%).

Table 2.16 Histological type, grading, multifocality and multicentricity of in situ breast cancers (N=1,761)

	Number	(%)
Histological type		
Ductal	1,652	(93.8)
Mixed	51	(2.9)
Papillary	27	(1.5)
Intracystic papillary	12	(0.7)
Encapsulated papillary	5	(0.3)
Apocrine	3	(0.2)
Neuroendocrine	2	(0.1)
Not known	9	(0.5)
Necrosis	**645**	**(36.6)**
Nuclear Grade		
Low	413	(23.5)
Intermediate	581	(33.0)
High	664	(37.7)
Not known	103	(5.8)
Multifocality	**212**	**(12.0)**
Number of foci		
2	93	(43.9)
3	17	(8.0)
4 or more	9	(4.2)
Not known	93	(43.9)
Multicentricity	**33**	**(1.9)**
Number of quadrants		
2	25	(75.8)
3	2	(6.1)
Not known	6	(18.2)

The biological characteristics of in situ breast cancers in our patient cohort are shown in Table 2.17. Among our patients with in situ breast cancers who were tested for either estrogen or progesterone receptor status, 80.9% were either estrogen receptor (ER) or progesterone receptor (PR) positive. 344 (29.0%) in situ breast cancers in our patient cohort were c-erbB2/HER2 positive.

Table 2.17 Biological characteristics of in situ breast cancers (N=1,761)

	Number	(%)
Estrogen receptor (ER) (72.8% of the patients had the test)		
Positive	1,017	(79.3)
Negative	265	(20.7)
Progesterone receptor (PR) (71.8% of the patients had the test)		
Positive	899	(71.1)
Negative	366	(28.9)
c-erbB2/HER2 (67.4% of the patients had the test)		
Positive (IHC score 3)	342	(28.8)
Equivocal (IHC score 2)	389	(32.8)
FISH / CISH +ve	*2*	*(0.5)*
Negative (IHC Score 0 / 1)	456	(38.4)
Ki-67 index (42.8% of the patients had the test)		
<14%	529	(70.3)
≧14%	224	(29.8)

2.4 Treatment methods

Of our 14,064 patients, 14.8% solely received care at private medical facilities, while 49.8% solely received care at public medical facilities. Around one-third (35.4%) of our patients received care at both private and public medical facilities.

2.4.1 Surgical treatment

Surgery is an important consideration in the effective treatment of breast cancer. With the continuing developments in breast cancer treatment, surgery is less disfiguring today. Options for local treatment include breast-conserving surgery or total mastectomy. Breast-conserving surgery followed by radiotherapy gives equivalent survival rates compared with mastectomy. Women who have a mastectomy may also decide to have breast reconstruction, either at the same time or at a later stage.

Nodal surgery is usually conducted together with breast surgery to ascertain the extent of disease. Lymph node surgery includes sentinel lymph node biopsy (SNB) or axillary dissection (AD). For patients with negative clinical nodal status, SNB can be conducted before AD to determine whether any lymph node is affected. This is to prevent lymphoedema which may occur when a large number of lymph nodes are removed by surgery.

Majority (98.2%) of our patients underwent surgery as part of their treatment. 51.6% of our patients had surgery at private medical facilities, while 48.4% had surgery at public medical facilities. Two-thirds (63.6%) of our patients had mastectomy, while 34.3% had breast-conserving surgery. Of our patients who had mastectomy, 13.5% had either immediate or delayed reconstruction. The most common type of reconstruction was TRAM flap (66.2%) (Table 2.18).

One-third (35.7%) of our patients received SNB only, while 47.5% received AD without SNB. 15.9% of our patients received AD after SNB (Table 2.18).

Table 2.18 Types of surgical operations in our patient cohort (N=14,064)

	Number	(%)
No surgery	221	(1.6)
Breast-conserving surgery	4,827	(34.3)
Mastectomy	8,942	(63.6)
Nodal surgery only	12	(0.1)
Type of surgery not known	36	(0.3)
Not known if surgery is done	26	(0.2)
Mastectomy (N=8,942)		
Total mastectomy	8,361	(93.5)
Skin sparing	470	(5.3)
Nipple sparing	75	(0.8)
Areolar sparing	15	(0.2)
Not known	21	(0.2)
Reconstruction (N=1,203)		
TRAM flap	796	(66.2)
Implant	226	(18.8)
LD flap	92	(7.6)
LD flap & implant	69	(5.7)
Not known	20	(1.7)
Nodal surgery (N=12,925)		
Sentinel node biopsy	4,614	(35.7)
Sentinel node biopsy & axillary dissection	2,054	(15.9)
Axillary dissection	6,141	(47.5)
Not known	116	(0.9)

The percentage of our patients who underwent mastectomy was positively correlated with increasing age, while the percentage of our patients who underwent mastectomy and reconstruction was negatively correlated with increasing age (Figure 2.10).

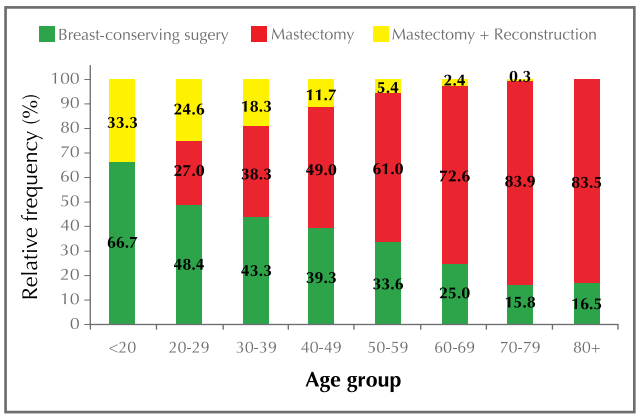

Figure 2.10 Type of surgery by age group (N=13,346)

For our patients with tumours larger than 1 cm in size, the percentage of patients that had breast-conserving surgery was negatively correlated with increasing tumour size (Figure 2.11).

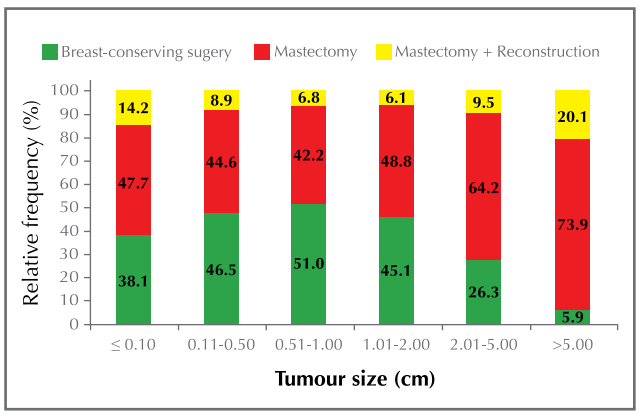

Figure 2.11 Type of surgery by tumour size (N=12,069)

The proportion of our patients receiving breast-conserving surgery was negatively correlated with increasing cancer stage. Mastectomy and reconstruction did not show any correlation with increasing cancer stage (Figure 2.12).

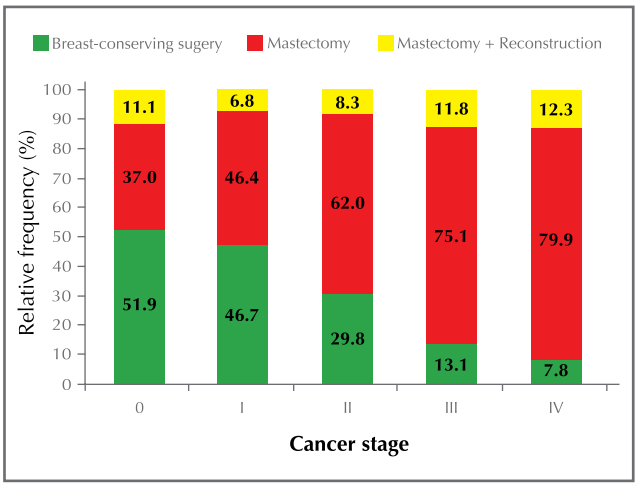

Figure 2.12 Type of surgery by cancer stage (N=13,219)

A higher proportion of patients who had surgery at private medical facilities underwent breast-conserving surgery than those who had surgery at public medical facilities (Figure 2.13).

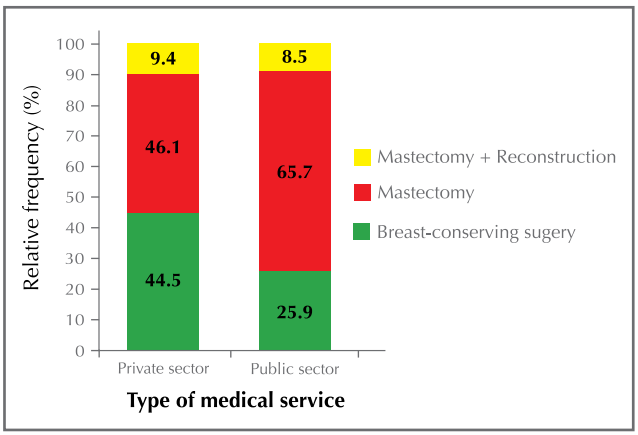

Figure 2.13 Type of surgery by type of medical service (N=13,222)

Figure 2.14 shows the type of nodal surgery received by our patients with positive or negative clinical nodal status. SNB alone was more commonly used by our patients with negative clinical nodal statuses than those with positive clinical nodal statuses (41.2% vs 11.1%). On the other hand, AD without SNB was more commonly used on our patients with positive clinical nodal statuses than those with negative clinical nodal statuses (76.4 vs 42.0%).

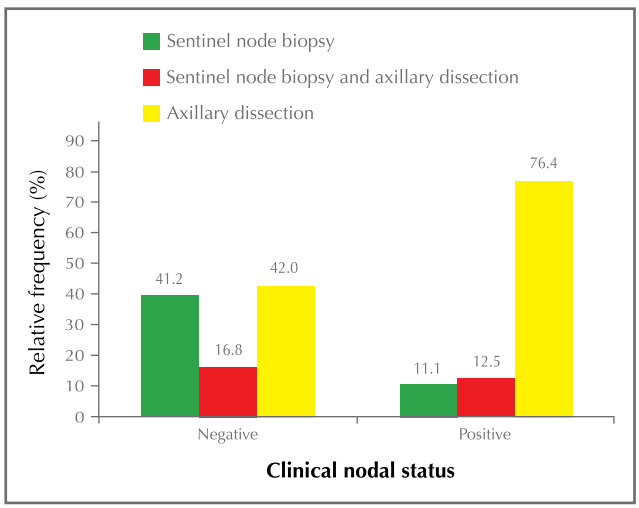

Figure 2.14 Type of nodal surgery by clinical nodal status (N=12,810)

The use of AD was positively correlated with progressing cancer stage. In our patient cohort, the use of AD after SNB increased from stage I to II patients, but then decreased for stage III or IV patients. This trend is likely due to the fact that most of our patients with stage III or IV disease went for AD as their first nodal surgery (Figure 2.15).

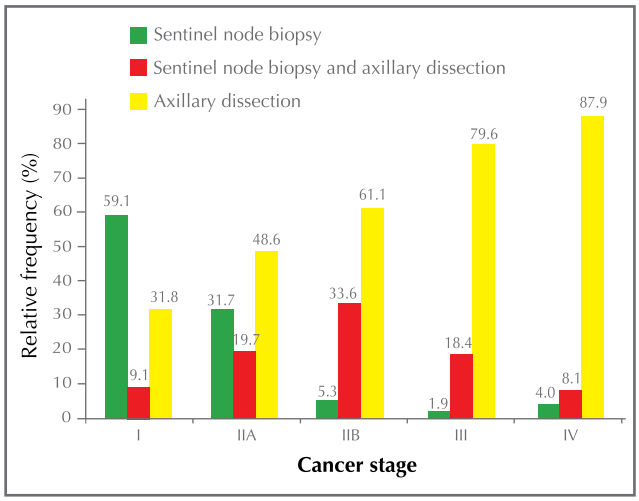

Figure 2.15 Type of nodal surgery in invasive cancers by cancer stage (N=11,292)

Around half (56.0%) of our patients with node positive invasive cancer had tumours of 2 to 5 cm in size, while 6.2% had tumours greater than 5 cm. In our patient cohort, more patients with node negative invasive cancer had tumours less than 2 cm when compared to patients with node positive invasive cancer (63.6% vs. 37.8%) (Figure 2.16).

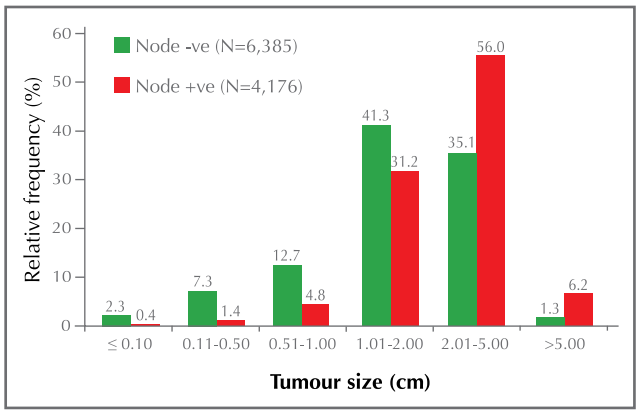

Figure 2.16 Distribution of tumour size in invasive cancer with negative or positive nodal status (N=10,561)

A small proportion of our patients (3.9%) who underwent SNB alone had at least one positive lymph node, while half (48.7%) of our patients who underwent AD and a quarter (23.8%) of our patients who underwent AD after SNB had no positive lymph node (Figure 2.17).

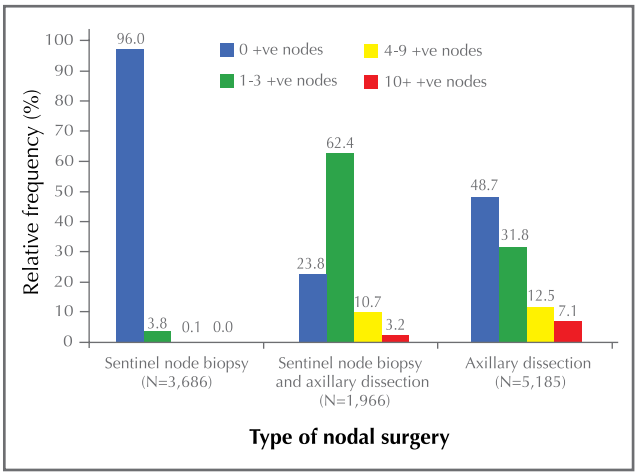

Figure 2.17 Number of positive nodes by type of nodal surgery (N=10,837)

In our patient cohort, the use of chemotherapy was positively correlated to progressing cancer stage, with the exception of stage IV disease (Figure 2.18). The lower use of chemotherapy observed in our stage IV patients might be due to the fact that for patients with ER positive stage IV disease, the usual clinical practice consists of palliative treatments including endocrine therapy +/- radiotherapy; not chemotherapy.

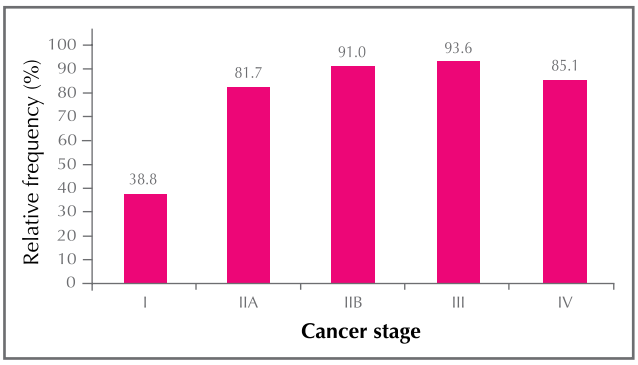

Figure 2.18 Chemotherapy treatment in our patients at different cancer stages (N=11,669)

2.4.2 Chemotherapy

Chemotherapy is a form of systemic treatment using one or more cytotoxic drugs to kill or control cancer cell growth. The drugs destroy breast cancer cells by interfering with their ability to grow and split. 8,476 (60.3%) patients in our cohort underwent chemotherapy. 88.3% of our patients had adjuvant chemotherapy, 9.4% had neoadjuvant chemotherapy, and 2.3% had palliative chemotherapy. 85.3% of our patients received chemotherapy in public medical facilities, while 14.7% received in private medical facilities.

Table 2.19 shows the percentage of patients in our cohort who received chemotherapy by age group and cancer stage. In general for all cancer stages, the use of chemotherapy among our patients aged over 70 was much lower than that among patients aged below 70. For our patients with stage I or stage IIB disease, the use of chemotherapy decreased with increasing age group.

Table 2.19 Use of chemotherapy by age group and cancer stage at diagnosis (N=11,334)

	Number of patients received chemotherapy (% of patients in the same age group and cancer stage)									
Age group	I		IIA		IIB		III		IV	
<20	2	(100.0)	–*		–*		–*		–*	
20-29	25	(62.5)	26	(96.3)	20	(100.0)	11	(91.7)	3	(100.0)
30-39	236	(52.7)	355	(89.0)	177	(99.4)	168	(99.4)	18	(90.0)
40-49	729	(44.7)	1,125	(90.7)	620	(97.6)	646	(98.9)	89	(94.7)
50-59	489	(38.9)	961	(87.7)	527	(95.3)	518	(96.8)	83	(87.4)
60-69	132	(23.8)	334	(68.7)	226	(88.6)	251	(93.3)	21	(80.8)
70-79	6	(3.1)	17	(10.4)	10	(12.5)	27	(36.5)	7	(43.8)
80+	0	(0.0)	1	(2.9)	0	(0.0)	1	(4.8)	1	(16.7)

*No patient diagnosed with Stages IIA, IIB, III and IV was aged <20.

For chemotherapy, several drugs are given in combination and each drug damages the cells at some point in their reproductive cycle. Figure 2.19 shows the relative frequency of different types of chemotherapy regimen used by our patients at different cancer stages. Around half (48.6%) of our patients with stage I disease and one-third (34.9%) of our patients with stage IIA disease used Adriamycin / Doxorubicin and Cyclophosphamide (AC), while AC and Taxane (AC+T) or a combination of Fluorouracail, Adriamycin / Doxorubicin (or Epirubicin), and Cyclophosphamide followed by Taxotere (FAC/FEC+T) was more widely used for our patients with stage IIB or III disease. In our patient cohort, 28.9% of patients with stage IV disease used Capecitabine, or Gemcitabine, or Vinorelbine, more often than our patients with less advance diseases (stages I to III).

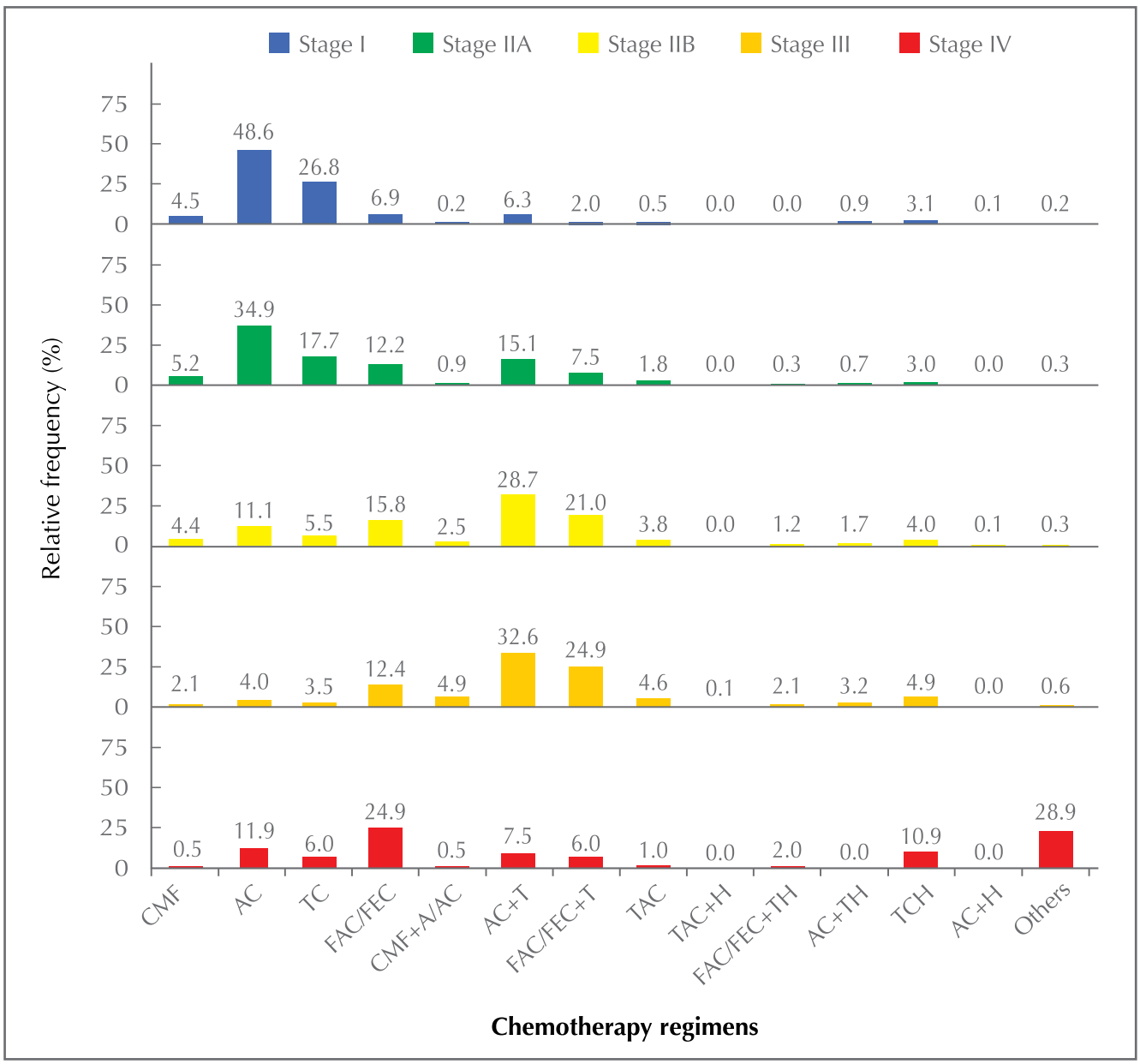

Figure 2.19 Type of chemotherapy regimens in patients by cancer stage (N=7,269)

C: Cyclophosphamide;
M: Methotrexate;
F: Fluorouracil (5FU);
A: Adriamycin / Doxorubicin;
E: Epirubicin;
T: Taxane (Docetaxel in TC and TAC, Paclitaxel or Docetaxel in AC+T);
H: Trastuzumab;
TCH: Docetaxel / Carboplatin / Trastuzumab or Paclitaxel / Carboplatin / Trastuzumab
Others: Capecitabine, Gemcitabine or Vinorelbine

2.4.3 Radiotherapy

Radiotherapy is a treatment to kill cancer cells using ionizing radiation. Radiation is capable of inflicting damage at the DNA level of a cell and can stop cells from reproducing. In our patient cohort, 8,738 (62.1%) patients had radiotherapy as one of their treatment, among which 98.1% were adjuvant, 0.1% were neoadjuvant, and 1.8% were palliative. 86.2% of our patients received radiotherapy at public medical facilities, while 13.8% received at private medical facilities.

Radiotherapy to the breast following breast-conserving surgery is an integral part of breast-conserving therapy for breast cancer in order to achieve equivalent outcome as mastectomy. This applies to all patients with invasive breast cancer and most patients with in situ cancer. Radiotherapy is also needed by some patients who have mastectomy, if the tumour is locally advanced; for example large tumour size or with multiple lymph nodes showing cancer, or where cancer cells are formed in the lymphatic or blood vessels. Of our patients who had breast-conserving surgery, 93.5% received radiotherapy, while 45.6% of our patients who had mastectomy received radiotherapy.

Figures 2.20 and 2.21 show the percentage of our patients with breast-conserving surgery or mastectomy, respectively, who received radiotherapy as part of their treatment at different cancer stages. Over 90% of our patients with breast-conserving surgery received radiotherapy (Figure 2.20), while the use of radiotherapy in patients with mastectomy increased with increasing cancer stages, with the exception of stage IV disease (Figure 2.21).

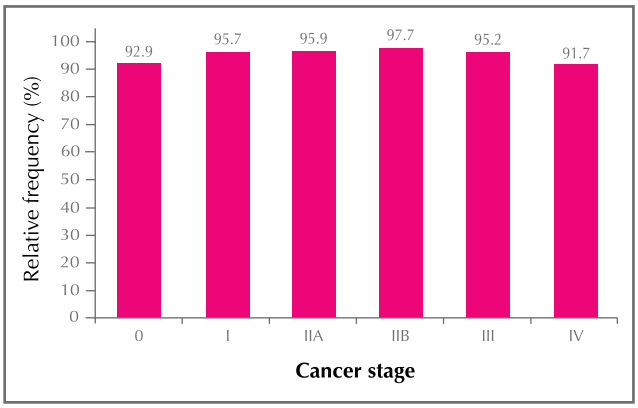

Figure 2.20 The use of radiotherapy in our patients receiving breast-conserving surgery at different cancer stages (N=4,648)

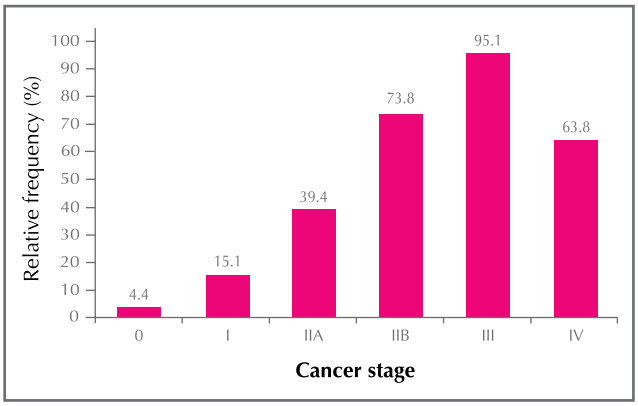

Figure 2.21 The use of radiotherapy in our patients receiving mastectomy at different cancer stages (N=8,388)

Radiotherapy for breast cancer involves localized irradiation of regions such as breast/chest wall, with or without regional nodes. Table 2.20 shows the irradiated regions among our patients receiving radiotherapy by the type of surgery received.

Table 2.20 Irradiated regions among our patients with different types of surgery (N=5,913)

	Total (N=5,913)	Breast-conserving Surgery (N=2,911)	Mastectomy (N=2,937)
Target volume	**Number (%)**	**Number (%)**	**Number (%)**
Breast	2,459 (41.6)	2,429 (83.4)	0 (0.0)
Breast + regional*	512 (8.7)	482 (16.6)	0 (0.0)
Chest wall	891 (15.1)	0 (0.0)	888 (30.2)
Chest wall + regional*	2,051 (34.7)	0 (0.0)	2,049 (69.8)

SCF: Supraclavicular fossa; IMC: Internal mammary chain;
*regional nodes: includes SCF and/or axilla and/or IMC
#Total number of patients includes 65 patients with surgical data not known

2.4.4 Endocrine therapy

Endocrine therapy has played an important role in all stages of the treatment and prevention strategy for hormone receptor-positive breast cancer. Breast cancers all develop from abnormal breast cells which are often sensitive to sex hormones, such as estrogen and progesterone. Endocrine therapy acts on hormone receptors of the cancer cells. In our patient cohort, 9,381 (66.7%) patients received endocrine therapy. Among them, 97.0% were adjuvant, 0.3% were neoadjuvant, and 2.6% were palliative. 97.5% of our patients received endocrine therapy at public medical facilities, while 2.5% received at private medical facilities. Endocrine therapy was used over 74.0% of our patients with stages I-IV breast cancer, but was only used in 15.9% of our patients with stage 0 breast cancer (Figure 2.22).

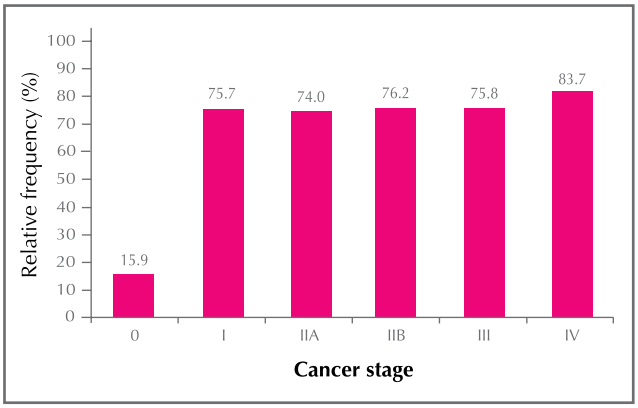

Figure 2.22 Proportions of our patients who received endocrine therapy by cancer stage (N=13,224)

Two types of drugs are commonly used to reduce the level of female hormones: anti-estrogens and aromatase inhibitors. Anti-estrogen drugs slow down breast cancer growth by sticking to estrogen receptors on the breast cancer cells. The most common anti-estrogen is Tamoxifen which is used in both pre-menopausal and post-menopausal women. Aromatase inhibitors decreases the level of estrogen in the body. Aromatase inhibitors, including Anastrozole, Letrozole and Exemestane, are only effective for women who are post-menopausal. Figure 2.23 shows the use of Tamoxifen and Aromatase inhibitors by our patient cohort in three age groups.

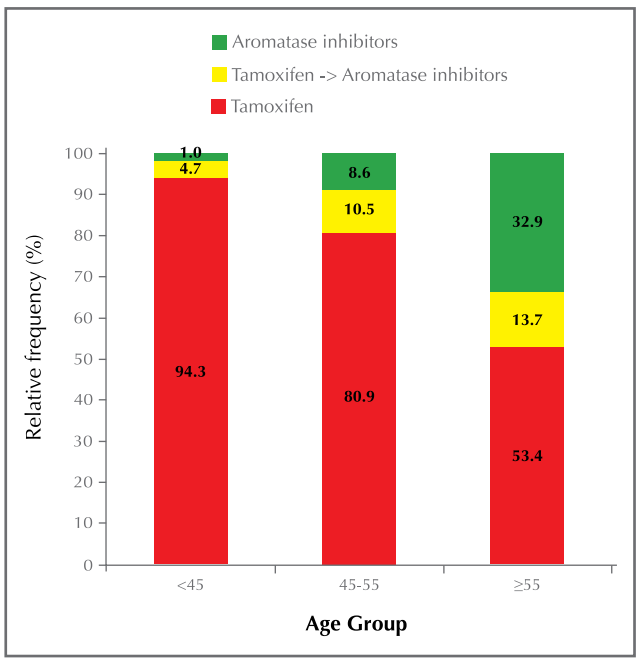

Figure 2.23 Forms of endocrine therapy used in our patient cohort by age group (N=8,672)

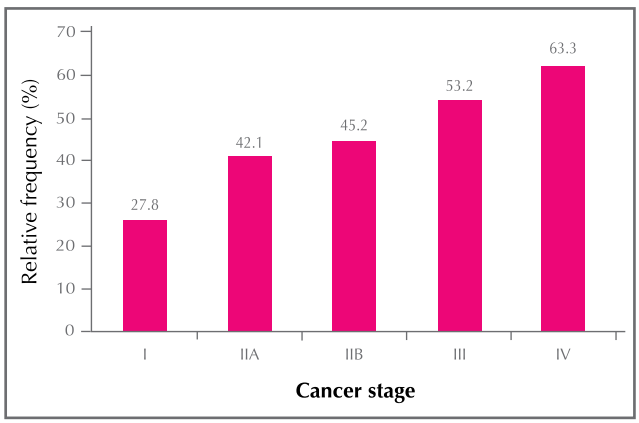

Figure 2.24 Targeted therapy rate in the HER2 positive patients by cancer stage in our cohort (N=2,050)

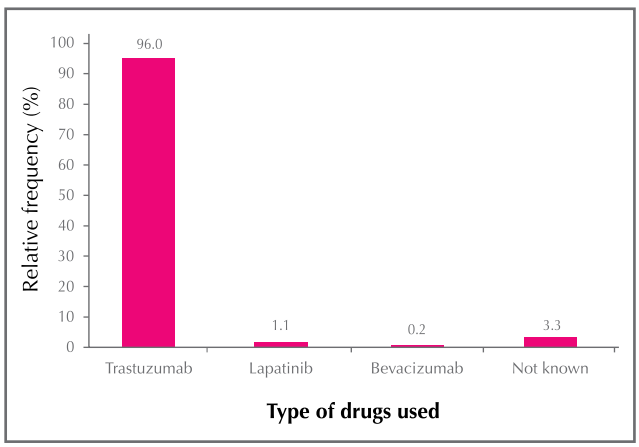

Figure 2.25 Type of drugs used for targeted therapy in our patient cohort (N=930)

2.4.5 Targeted therapy

Targeted therapy uses a drug that specifically attacks the abnormal growth pathway of cancer cells by blocking specific molecules required for tumour growth or carcinogenesis. It is used for treating patients with breast cancer cells that over-express HER2 (HER2-positive breast cancer). Of the 2,265 patients with HER2-positive breast cancers in our cohort, 930 (41.1%) underwent targeted therapy. Among them, 97.3% were adjuvant, 0.4% were neoadjuvant, and 2.3% were palliative. 87.2% of our patients received targeted therapy at public medical facilities, while 12.8% received at public medical facilities.

The use of targeted therapy was positively correlated with increasing cancer stage (Figure 2.24). The most commonly used targeted therapy drug was Trastuzumab (96.0%) (Figure 2.25).

2.4.6 Complementary and alternative therapies

Apart from the standard medical care of breast cancer that was described in previous sections of this chapter, patients may go for different kinds of complementary and alternative therapies, such as taking traditional Chinese medicines, health foods/supplements etc. 5,602 (39.8%) of the patients in the cohort received complementary and alternative therapies as part of their treatment. Among them, 95.4% were adjuvant, 3.8% were neoadjuvant, and 0.9% were palliative. 66.8% of our patients used traditional Chinese medicines (Figure 2.26).

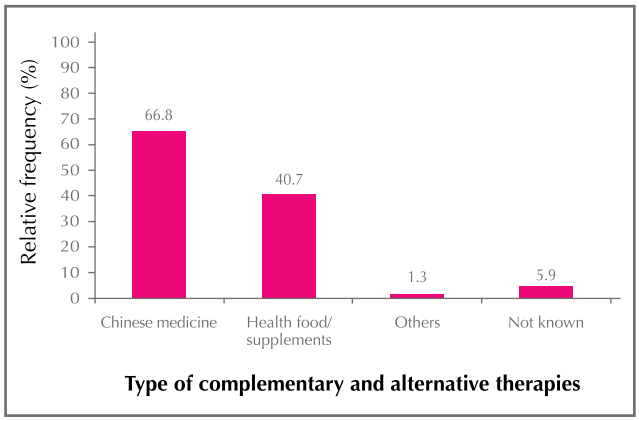

Figure 2.26 Type of complementary and alternative therapies used in 5,602 patients

Others include: Tai Chi, Qigong, Naturopathy, acupuncture and moxibustion, massage and yoga

2.4.7 Multimodality treatment

Combinations of treatments are usually used for treating breast cancer effectively. Table 2.21 shows the multimodality treatment pattern of our patients. As complementary and alternative therapies are not part of standard medical care, these therapies are excluded from this part of analysis. In general, the number of treatments increased with increasing cancer stage. In our patient cohort, most patients with stage 0 disease received one (42.6%) or two (49.5%) treatment(s), while 58.9% of our patients with stage I disease received three or more treatments. More than 80% of our patients with stage IIA, IIB, or III received three or more treatments.

Table 2.21 Number of treatment combinations received by patients by cancer stages (N=13,409)

	Cancer stage, Number (%)						
No. of treatment	0 (N=1,643)	I (N=4,346)	IIA (N=3,578)	IIB (N=1,792)	III (N=1,785)	IV (N=265)	Total (N=13,409)
0	2 (0.1)	1 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	3 (1.1)	8 (0.1)
1	700 (42.6)	319 (7.3)	94 (2.6)	21 (1.2)	25 (1.4)	27 (10.2)	1,186 (8.8)
2	814 (49.5)	1,464 (33.7)	620 (17.3)	137 (7.6)	62 (3.5)	42 (15.8)	3,139 (23.4)
3	127 (7.7)	1,801 (41.4)	1,418 (39.6)	574 (32.0)	384 (21.5)	91 (34.3)	4,395 (32.8)
4	0 (0.0)	687 (15.8)	1,345 (37.6)	958 (53.5)	1,133 (63.5)	85 (32.1)	4,208 (31.4)
5	0 (0.0)	74 (1.7)	101 (2.8)	102 (5.7)	179 (10.0)	17 (6.4)	473 (3.5)

2.5 Patient Status

Once treatment is completed, annual follow-ups are conducted to ascertain the efficacy of the treatment. To date, 62.1% of our patient in the cohort had the last follow-up within the last 2 years. Around one-third (35.9%) of our patients were followed up for 2-5 years, while 40.8% were followed up for 5 or more years (Table 2.22). The mean follow-up period was 5.2 years and median follow-up period was 4.1 years.

834 (6.6%) of patients in our cohort experienced recurrence, where 2.8% of our patients experienced locoregional recurrence (LR) solely, 2.7% experienced distant recurrence (DR) solely, and 1.1% experienced both locoregional and distant recurrence at the same time. The mean and median time to recurrence are shown in Table 2.22.

Table 2.22 Follow-up of 12,573 patients

Follow-up period	Number	(%)
< 1 year	922	(7.3)
1-2 years	2,013	(16.0)
2-5 years	4,510	(35.9)
5-10 years	3,672	(29.2)
10-15 years	1,051	(8.4)
>15 years	405	(3.2)
Mean follow-up period		5.2 years
Median follow-up period		4.1 years
Locoregional recurrence		
No. of locoregional recurrences	349	(2.8)
Mean time to locoregional recurrence		5.5 years
Median time to locoregional recurrence		3.7 years
Distant recurrence		
No. of distant recurrences	340	(2.7)
Mean time to distant recurrence		4.3 years
Median time to distant recurrence		3.3 years
Locoregional and distant recurrence		
No. of locoregional and distant recurrences	145	(1.1)
Mean time to locoregional and distant recurrence		5.2 years
Median time to locoregional and distant recurrence		4.3 years
Mortality		
No. of deaths from breast cancer	119	(0.9)
No. of deaths from unrelated causes	77	(0.6)

Table 2.23 shows the number of invasive breast cancer patients with LR in different subgroups specified by surgery type and cancer stage in our patient cohort. The overall proportions of our patients with LR were similar in patients receiving either breast-conserving surgery or mastectomy (3.0% vs. 3.4%). However, for stage IIA patients in our patient cohort, the proportion of patients with LR was higher among patients with breast-conserving surgery than those who received mastectomy. On the other hand, for our stage IIB and III patients, the proportion of patients with LR was higher among patients with mastectomy than those who received breast-conserving surgery. In our patient cohort, regardless of the types of surgery received, patients with stage III disease had a higher proportion of patients with LR than their counterparts with early stage of disease. The common sites for locoregional recurrence were breast (36.6%) and chest wall (31.2%) (Table 2.24).

Table 2.23 Number of cases with locoregional recurrence by type of surgery and cancer stage

	Cancer stage, Number (% in the overall patient cohort with surgeries)				
	I	IIA	IIB	III	Total
BCS	45/1,839 (2.4)	42/1,070 (3.9)	8/352 (2.3)	10/217 (4.6)	105/3,478 (3.0)
MTX	57/2,138 (2.7)	67/2,220 (3.0)	44/1,323 (3.3)	75/1,418 (5.3)	243/7,099 (3.4)

BCS: Breast-conserving surgery; MTX: Mastectomy

Table 2.24 Sites involved in locoregional recurrence in our patients (N=494)

Sites involved	Number	(%)
Breast	181	(36.6)
Chest wall	154	(31.2)
Axilla	115	(23.3)
Supraclavicular	90	(18.2)
Internal mammary node	27	(5.5)
Others	31	(6.3)

Note: Recurrence may involve multiple sites simultaneously, so the total percentages for recurrence sites may exceed 100.

In our patient cohort, 485 (3.9%) patients experienced distant recurrence. Among them, the common organs involved were bone (54.4%), followed by lung (44.3%) (Table 2.25).

Table 2.25 Organs involved in distant recurrence (N=485)

Distant organs affected	Number	(%)	Distant organs affected	Number	(%)
Bone	264	(54.4)	Thyroid glands	6	(1.2)
Lung	215	(44.3)	Pancreas	5	(1.0)
Liver	165	(34.0)	Ovary	4	(0.8)
Mediastinal nodes	89	(18.4)	Thorax	4	(0.8)
Brain	71	(14.6)	Uterus	4	(0.8)
Neck	42	(8.7)	Spleen	3	(0.6)
Contralateral nodal metatases	18	(3.7)	Kidney	1	(0.2)
Abdomen	14	(2.9)	Unspecified	25	(5.2)
Adrenal	8	(1.6)			

Note: Recurrence may involve multiple sites simultaneously, so the total percentages for recurrence sites may exceed 100.

Among patients with invasive breast cancer in our cohort, the proportion of patients with LR solely was quite static (around 2%) for all cancer stages, while the proportion of our patients with DR solely or LR and DR at the same time showed positive correlation with increasing cancer stage (Table 2.26).

Table 2.26 Proportions of our invasive breast cancer patients with locoregional and distant recurrence by cancer stage

	Cancer stage, Number (%)				
Recurrence	I (N=3,939)	IIA (N=3,268)	IIB (N=1,663)	III (N=1,639)	Total (N=10,509)
LR solely	86 (2.2)	76 (2.3)	27 (1.6)	42 (2.6)	231 (2.2)
DR solely	57 (1.4)	69 (2.1)	64 (3.8)	109 (6.6)	299 (2.8)
LR and DR	16 (0.4)	34 (1.0)	25 (1.5)	44 (2.7)	119 (1.1)

LR: Locoregional recurrence; DR: Distant recurrence

119 (0.9%) patients in the cohort died from breast cancer. The proportion of our patients who died from breast cancer was highest in stage IV (8.3%). Survival time ranged from 0.8 – 21.9 years. Information on biological subtypes of these patients can be found in Table 2.27.

Table 2.27 Characteristics of breast cancer-specific deaths (N=119)

	Cancer stage						
	0	I	IIA	IIB	III	IV	Unstaged
No. of cases (% of all breast cancer cases in that cancer stage)	**1 (0.1)**	**15 (0.3)**	**19 (0.6)**	**8 (0.5)**	**45 (2.7)**	**19 (8.3)**	**12 (2.1)**
Survival time (range in years)	**4.5**	**1.8 – 10.4**	**1.9 – 20.6**	**4.7 – 16.2**	**0.8 – 9.3**	**1.2 – 10.3**	**1.4 – 21.9**
Biological subtypes[32]							
Luminal A*	0	1	1	1	5	0	2
Luminal B (HER2 negative)#	0	3	3	1	5	2	0
Luminal A/B (HER2 negative)†	0	4	4	3	12	10	1
Luminal B (HER2 positive)^	1	2	2	1	8	2	2
HER2-positive ❉	0	3	2	0	7	3	2
TND§	0	2	4	1	7	1	1
Not known	0	0	3	1	1	1	4

* Luminal A: ER and/or PR+, HER2-, and Ki-67 low (<14%)

\# Luminal B (HER2 negative): ER and/or PR+, HER2-, and Ki-67 high (≧14%)

† Luminal A/B (HER2 negative):ER and/or PR+, HER2-, and Ki-67 not known

^ Luminal B (HER2 positive): ER and/or PR+, HER2+, and any Ki-67

❉ HER2-positive: ER and PR-, HER2+, and any Ki-67

§ TND (Triple Negative Disease): ER-, PR-, HER2-, and any Ki-67