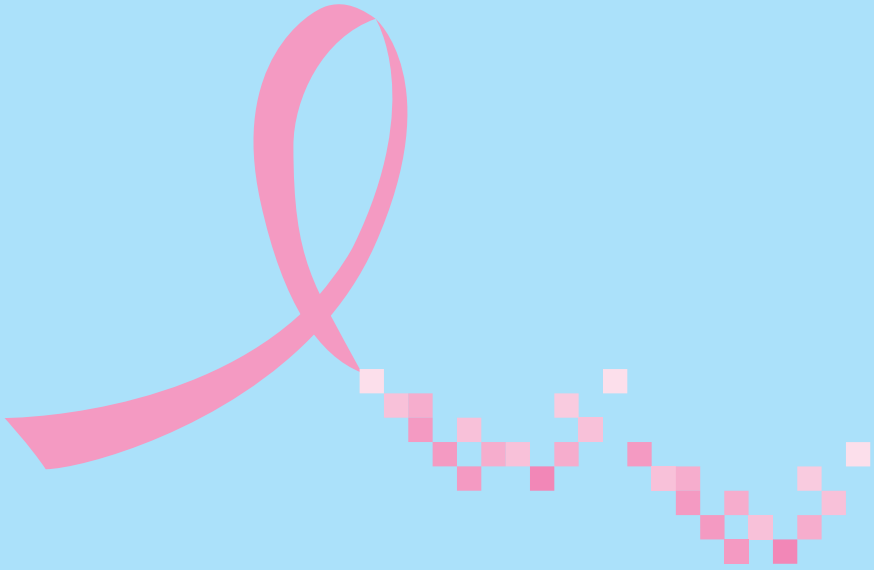

CHAPTER 2

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

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This chapter reviews the data collected from 13,265 breast cancer patients regarding their cancer's clinical presentation, cancer characteristics and treatment methods. Through this, the clinical management of breast cancer is analysed, and trends in disease and treatment in a local context are identified in order to develop and improve the standard of care for breast cancer patients in Hong Kong.

KEY FINDINGS

Clinical presentation

- The primary method of first breast cancer detection in the patient cohort was self-detection by chance (83.0%). More invasive breast cancers were self-detected by chance (87.2%) than in situ breast cancers (54.6%).
- Most (91.7%) patients who self-detected their cancers by chance found a painless lump on their breast(s).
- After the onset of symptoms, a quarter (25.2%) of our patients who self-detected their cancers by chance waited three or more months before seeking first medical consultation.
- Majority (92.0%) of our patients had unilateral breast cancer.
- A quarter (24.0%) of our patients with invasive breast cancer did not have any cancer staging as part of their treatment. Among those who had cancer staging as part of their treatment, the most commonly used method was chest x-ray and ultrasound of abdomen (31.2%), and positron emission tomography scan (PET scan) (31.0%).
- The most common cancer stage at diagnosis was stage II (36.9%). Around 15.2% of our patients were diagnosed with stages III-IV diseases while 12.0% 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 46.6% of our patients with invasive cancer.
- In our patient cohort, screen-detected invasive cancers were significantly smaller than cancers that were self-detected by chance (mean: 1.3 cm vs. 2.3 cm).
- 59.5% of our patients with invasive breast cancers had no positive lymph nodes.
- The most common histological type of invasive cancer was invasive carcinoma of no specific type (86.5%). 80.0% of invasive breast cancers were either estrogen receptor (ER) or progesterone receptor (PR) positive. 21.3% were c-erbB2/HER2 positive. 11.5% of the invasive breast cancers were triple negative (ER, PR, and c-erbB2/HER2 negative).
- The mean size of in situ cancers for our patient cohort was 2.0 cm (standard deviation: ±1.6 cm).
- Tumours larger than 2.0 cm were found in 35.2% of our patients with in situ cancer.

- Of the in situ breast cancers where mammogram (MMG) was performed, 62.2% showed microcalcification on MMG.
- Ductal cancers were found to be the most common type of in situ breast cancer (93.7%). 82.5% of in situ breast cancers were either ER or PR positive. 27.0% of in situ breast cancers in our cohort were c-erbB2/HER2 positive.

Treatment methods

- Of our 13,265 patients, 14.7% solely received care at private medical service, while 51.3% solely received care at public medical service. Around one-third (34.0%) of patients received care at both private and public medical services.
- Surgery
  - Majority (98.3%) of our patients underwent surgery as part of their treatment. 50.3% of our patients had surgery at private medical facilities, while 49.7% had surgery at public medical facilities.
  - Less than half (48.3%) of our patients with in situ tumour had mastectomy, and among them, only 21.8% had reconstruction. Among those who received nodal surgery, 83.4% of them had sentinel node biopsy (SNB) alone and 12.7% received axillary dissection (AD) without SNB.
  - For patients with invasive tumours, two-thirds (64.8%) of them had mastectomy and among them, only 12.2% of them had reconstruction. Less than half (39.5%) of our invasive patients received SNB alone, while 42.5% received AD without SNB.
  - The percentage of our patients who underwent mastectomy was positively correlated with both increasing age and cancer stage.
  - SNB alone was more commonly used on our patients with negative clinical nodal statuses than those with positive clinical nodal statuses (51.4% vs. 14.6%).
  - The use of AD was positively correlated with increasing cancer stage.
- Chemotherapy
  - Two-thirds (68.4%) of patients with invasive cancer in the cohort underwent chemotherapy. Among them, 10.5% had neoadjuvant chemotherapy.
  - 86.2% of our patients received chemotherapy in public medical facilities, while 13.8% received chemotherapy in private medical facilities.
  - In our patient cohort, the use of chemotherapy was positively correlated to progressing cancer stage, with the exception of stage IV disease.
- Radiotherapy
  - 62.0% of our patients had radiotherapy as one of their treatment. 93.0% of our patients had radiotherapy at public medical facilities, while 7.0% had radiotherapy at private medical facilities.
  - Of our patients with in situ cancer who had breast-conserving surgery, majority (94.3%) of them received radiotherapy afterwards, while only 3.0% of our patients with in situ cancer who had mastectomy received radiotherapy.
  - Over 90% of invasive breast cancer patients with breast-conserving surgery received radiotherapy, while the use of radiotherapy in invasive breast cancer patients with mastectomy increased with increasing cancer stages, with the exception of stage IV disease.
- Endocrine therapy
  - 67.3% of our patients received endocrine therapy. 97.1% of our patients received endocrine therapy at public medical facilities, while 2.9% received endocrine therapy at private medical facilities.

- Endocrine therapy was used in 11.9% of our patients with in situ breast cancer, but was used in over 74.0% of our patients with invasive breast cancer.

► Targeted therapy
- Of the patients with invasive HER2-positive breast cancers in our cohort, 53.7% underwent targeted therapy. 95.7% of our patients received targeted therapy at public medical facilities, while 4.3% received targeted therapy at private medical facilities.
- The use of targeted therapy was positively correlated with increasing cancer stage. The most commonly used targeted therapy drug was Trastuzumab (95.3%).

► Complementary and alternative therapies
- 40.0% of our patients in the cohort received complementary and alternative therapies. Among them, 66.5% 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 and median follow-up periods were 3.6 and 3.2 years, respectively.

► 508 (4.3%) of patients in our cohort experienced recurrence, where 1.2% of our patients experienced locoregional recurrence (LR) solely, 2.0% 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 chest wall (39.6%) and axilla lymph nodes (30.0%) and the common organs involved in distant recurrence were bone (53.4%), lung (44.7%), and liver (41.6%).

2.1 Clinical presentation

The primary method of first breast cancer detection in the patient cohort was self-detection by chance (83.0%) (Figure 2.1). Relatively small proportion 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). In the United States, a study[24] reported that 43% of the breast cancer cases detected through mammography screening, which is much higher than the 10.6% 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 in private medical service users than in 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[25]. In the HKBCR patient cohort, the proportion of invasive breast cancers detected by mammography screening (6.8%) was much lower than that of in situ breast cancers (35.7%) (Table 2.2). In addition, more stage 0 or I cancers (35.1% and 13.1% respectively) were detected by mammography screening than stage III or IV cancers (3.2% and 1.7% respectively). Over 90% of our patients with stage IIB, III or IV cancers self-detected their cancer by chance (Table 2.3).

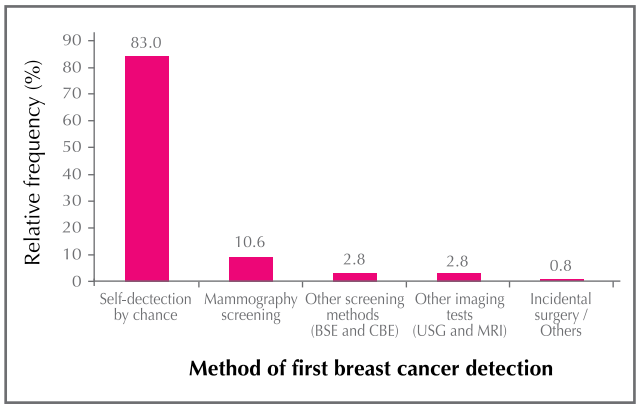

Figure 2.1 The method of first breast cancer detection in our patient cohort (N=12,589)

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

Table 2.1 The method of first breast cancer detection by types of medical service received at cancer diagnosis and treatment (N=12,589)

	Private medical service users (N=1,834)		Public medical service users (N=6,442)		Mixed private / public medical service users (N=4,313)	
Mode of first breast cancer detection	**Number**	**(%)**	**Number**	**(%)**	**Number**	**(%)**
Self-detection by chance	1,351	(73.7)	5,416	(84.1)	3,682	(85.4)
Mammography screening	271	(14.8)	726	(11.3)	334	(7.7)
Other screening methods (BSE and CBE)	68	(3.7)	151	(2.3)	137	(3.2)
Other imaging tests (USG and MRI)	123	(6.7)	99	(1.5)	130	(3.0)
Incidental surgery / Others	21	(1.1)	50	(0.8)	30	(0.7)

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

Table 2.2 The method of first breast cancer detection by type of cancer (N=12,526)

Method of first breast cancer detection	Type of cancer, Number (%)	
	In situ (N=1,623)	Invasive (N=10,903)
Self-detection by chance	886 (54.6)	9,512 (87.2)
Mammography screening	579 (35.7)	746 (6.8)
Other screening methods (BSE and CBE)	50 (3.1)	302 (2.8)
Other imaging tests (USG and MRI)	91 (5.6)	260 (2.4)
Incidental surgery / Others	17 (1.0)	83 (0.8)

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

Table 2.3 The method of first breast cancer detection by cancer stage (N=11,970)

Method of first breast cancer detection	Cancer stage, Number (%)					
	0 (N=1,518)	I (N=3,888)	IIA (N=3,121)	IIB (N=1,523)	III (N=1,634)	IV (N=286)
Self-detection by chance	855 (56.3)	3,045 (78.3)	2,770 (88.8)	1,422 (93.4)	1,529 (93.6)	265 (92.7)
Mammography screening	533 (35.1)	508 (13.1)	172 (5.5)	39 (2.6)	52 (3.2)	5 (1.7)
Other screening methods (BSE and CBE)	47 (3.1)	144 (3.7)	86 (2.8)	31 (2.0)	23 (1.4)	9 (3.1)
Other imaging tests (USG and MRI)	72 (4.7)	159 (4.1)	69 (2.2)	25 (1.6)	16 (1.0)	5 (1.7)
Incidental surgery / Others	11 (0.7)	32 (0.8)	24 (0.8)	6 (0.4)	14 (0.9)	2 (0.7)

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

Most (91.7%) 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 6.6% of our patients felt pain in their breast(s) at initial presentation. Some patients (8.9%) experienced changes in nipple (such as nipple discharge, nipple retraction, redness, scaliness or thickening of nipple) (Figure 2.2).

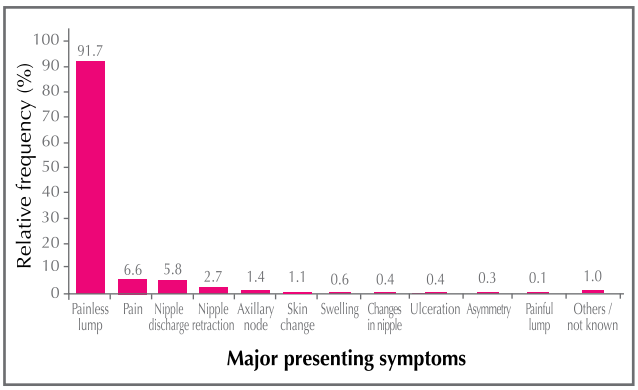

Figure 2.2 Major presenting symptoms of self-detected* breast cancers in our patient cohort (N=10,449)

*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 is associated with higher probability of local cancer spread or distant metastasis, and poorer prognosis[26]. After the onset of symptoms, a quarter (25.2%) of our patients who self-detected their cancers by chance waited three or more months before seeking first medical consultation (Table 2.4).

A higher proportion (32.4%) of our patients who were treated in public medical facilities waited three or more months before seeking first medical consultation, than patients that attended in private medical facilities (21.2%) (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=2,838)

	Number	(%)
Less than 1 month	1,035	(36.5)
1-3 months	1,088	(38.3)
4-12 months	408	(14.4)
More than 12 months	307	(10.8)

*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=2,838)

	Private medical service users (N=619)		Public medical service users (N=1,273)		Mixed private / public medical service users (N=946)	
	Number	(%)	Number	(%)	Number	(%)
Less than 1 month	260	(42.0)	365	(28.7)	410	(43.3)
1-3 months	228	(36.8)	496	(39.0)	364	(38.5)
4-12 months	76	(12.3)	235	(18.5)	97	(10.3)
More than 12 months	55	(8.9)	177	(13.9)	75	(7.9)

*Self-detection by chance only

A larger proportion (36.0%) 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=2,470)

	Cancer stage, Number (%)				
	Stage I (N=791)	Stage IIA (N=795)	Stage IIB (N=389)	Stage III (N=406)	Stage IV (N=89)
Less than 1 month	333 (42.1)	313 (39.4)	136 (35.0)	119 (29.3)	14 (15.7)
1-3 months	292 (36.9)	315 (39.6)	155 (39.8)	163 (40.1)	28 (31.5)
4-12 months	103 (13.0)	106 (13.3)	53 (13.6)	73 (18.0)	15 (16.9)
More than 12 months	63 (8.0)	61 (7.7)	45 (11.6)	51 (12.6)	32 (36.0)

*Self-detection by chance only

2.2 Cancer characteristics

Breast cancer can occur in one (unilateral) or both breasts (bilateral). Majority (92.0%) of our patients had unilateral breast cancer, while 5.0% (n=331) had synchronous bilateral breast cancer at first diagnosis (Figure 2.3). 109 patients (1.6%) developed a contralateral breast cancer within, on average, 3.3 years (range: 0.5 – 8.7 years, median: 2.7 years) after diagnosis of an initial primary breast cancer. Another 179 patients (1.3%) were diagnosed with initial primary breast cancer before 2006 and they developed a contralateral breast cancer after 2006. For these patients, only the second cases diagnosed in or after 2006 were included in this report (Figure 2.3).

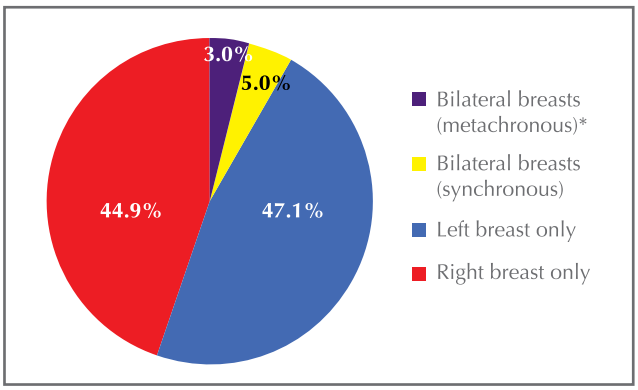

Figure 2.3 Laterality of 13,265 breast cancer cases

* Included 179 patients who were diagnosed with initial primary breast cancer before 2006 and they developed a contralateral breast cancer after 2006. Thus, only the second cases diagnosed in after 2006 were included in this report.

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 (47.4% and 50.7% respectively).

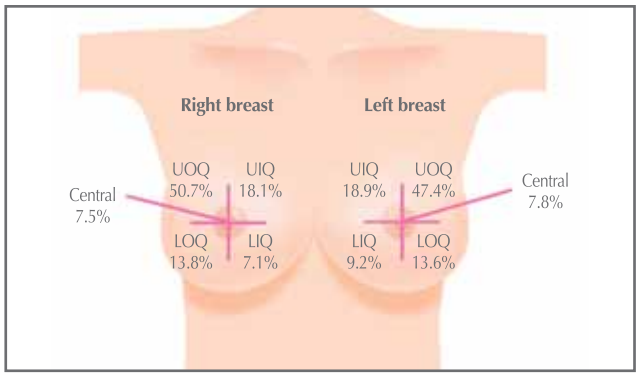

Figure 2.4 Locations of breast cancer occurrence on the breasts within our patient cohort (N=13,265)

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, 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 85.7% of our patients MMG was used, while USG was used on 79.7% and MRI was used on only 8.9% 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), where BIRADS 4 or 5 are suspected breast cancers and should be checked by further surgical tests such as biopsies.

Table 2.7 Sensitivity and diagnostic results of breast imaging tests (N=13,265)

	Mammography (N=11,370)	Breast ultrasound (N=10,573)	MRI (N=1,178)
Proportion of patients using the diagnostic test	85.7%	79.7%	8.9%
Overall sensitivity*	82.2%	90.4%	96.4%
BIRADS category			
Diagnostic / malignant (BIRADS 5)	3,634 (32.0%)	3,974 (37.6%)	928 (78.8%)
Suspicious abnormality (BIRADS 4)	5,715 (50.3%)	5,588 (52.9%)	208 (17.7%)
Probably benign (BIRADS 3)	647 (5.7%)	600 (5.7%)	16 (1.4%)
Benign (BIRADS 2)	474 (4.2%)	179 (1.7%)	10 (0.8%)
Normal (BIRADS 1)	829 (7.3%)	225 (2.1%)	15 (1.3%)
Incomplete (BIRADS 0)	71 (0.6%)	7 (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 62.3% of patients in the cohort 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 breast density. Heterogeneously dense breast may obscure small masses, while extremely dense breast lowers the sensitivity of mammography. In our patient cohort, two-thirds (68.9%) had heterogeneously dense breasts, while 6.3% had extremely dense breasts (Figure 2.5). Table 2.9 shows the mammographic density of breasts of our patients in different age groups. Higher proportions of young patients were found to have denser breasts than their older counterparts.

Table 2.8 Mammographic findings of patients in our cohort who were diagnosed through mammography (N=9,349)

	Number	(%)
Opacity	5,828	(62.3)
Microcalcification	4,712	(50.4)
Architectural distortion	1,328	(14.2)
Asymmetric density	872	(9.3)
Unclassified	408	(4.4)

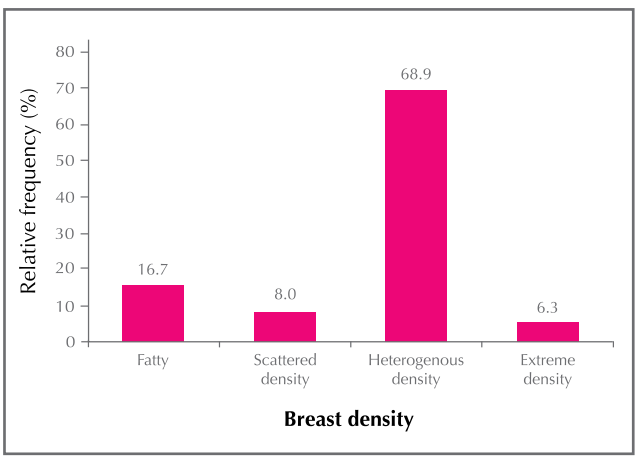

Figure 2.5 Mammographic density of breasts of our patients who were diagnosed through mammography (N=6,827)

Table 2.9 Mammographic density of breasts of our patients who were diagnosed through mammography by age group (N=6,683)

Mammographic density	Age group, Number (%)					
	20-29 (N=34)	30-39 (N=521)	40-49 (N=2,167)	50-59 (N=2,312)	60-69 (N=1,186)	70+ (N=463)
Fatty	3 (8.8)	35 (6.7)	204 (9.4)	393 (17.0)	309 (26.1)	177 (38.2)
Scattered density	1 (2.9)	17 (3.3)	118 (5.4)	205 (8.9)	129 (10.9)	64 (13.8)
Heterogeneous density	25 (73.5)	412 (79.1)	1,658 (76.5)	1,589 (68.7)	705 (59.4)	214 (46.2)
Extreme density	5 (14.7)	57 (10.9)	187 (8.6)	125 (5.4)	43 (3.6)	8 (1.7)

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 used more often, but sometimes excisional biopsy, which removes a relatively larger portion of breast tissue, is conducted. FNA and/or CNB were performed in 85.4% of our patients and among them, 3,149 (27.8%) received FNA solely, 5,688 (50.2%) received CNB solely, and 2,495 (22.0%) received both FNA and CNB. Excisional biopsy was performed in 11.6% of our patients. Excisional biopsy had the highest overall sensitivity of 100%, followed by CNB (98.8%) and FNA (89.9%) (Table 2.10).

Table 2.10 Sensitivity and diagnostic results of breast tissue biopsies (N=13,265)

	FNA (N=5,644)	CNB (N=8,183)	Excisional biopsy (N=1,545)
Proportion of patients using the diagnostic test	42.5%	61.7%	11.6%
Overall sensitivity*	89.9%	98.8%	100.0%
Class			
Diagnostic / malignant (Class V)	3,467 (62.0%)	7,800 (95.3%)	1,545 (100.0%)
Suspicious (Class IV)	917 (16.2%)	137 (1.7%)	—
Atypical (Class III)	659 (11.7%)	145 (1.8%)	—
Benign (Class II)	245 (4.3%)	71 (0.9%)	—
Scanty benign (Class I)	228 (4.0%)	27 (0.3%)	—
Incomplete (Class 0)	98 (1.7%)	3 (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. Less than a quarter (24.0%) of our patients with invasive breast cancer did not have any cancer staging as part of their treatment. Among those who had cancer staging as part of their treatment, the most commonly used method was chest x-ray and ultrasound of abdomen (31.2%), and positron emission tomography scan (PET scan) (31.0%) (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[27]. However, 10.5% and 21.1% of our patients with stages I and IIA diseases, respectively, had PET scan to determine the extent of their disease (Table 2.12).

Table 2.11 Cancer staging in 10,622 invasive breast cancer patients

Type of cancer staging method	Number	(%)
No cancer staging	2,551	(24.0)
Chest X-Ray (CXR) and ultrasound abdomen (USG Abd)	2,517	(31.2)
Positron emission tomography scan (PET scan)	2,505	(31.0)
Bone scan	184	(2.3)
Computed tomography of body parts*	330	(4.1)
Magnetic resonance imaging whole body (MRI whole body)	32	(0.4)
Unspecified	3,095	(38.3)

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

Table 2.12 The use of PET scan by cancer stage (N=8,071)

	Cancer stage, Number (%)						
	I	IIA	IIB	III	IV	Unstaged	Total
Use of PET scan	273 (10.5%)	468 (21.1%)	392 (34.2%)	781 (57.0%)	241 (84.0%)	350 (77.4%)	2,505 (31.0%)

Using the American Joint Committee on Cancer (AJCC) Breast Cancer Staging (7th edition)[28] to determine cancer staging in our patient cohort, it was found that the most common cancer stage at diagnosis was stage II (36.9%). 15.2% of our patients were diagnosed with stages III-IV diseases while 12.0% of our patients were diagnosed with in situ cancers (Figure 2.6).

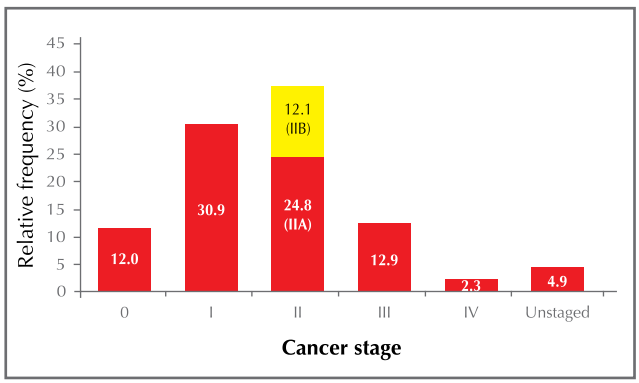

Figure 2.6 Cancer stage at diagnosis in our breast cancer patients (N=13,265)

Out of 13,265 breast cancer cases analysed, data from 12,026 cases with available pathology data was used for the following analyses on cancer characteristics. 10,313 patients (85.8%) were diagnosed with invasive cancers and 1,704 (14.2%) 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 – 19.1 cm; standard deviation: ±1.4 cm). Tumours of 1 cm or less in size were found in 16.1% of our patients and tumours of 2-5 cm in size were found in 43.0% 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).

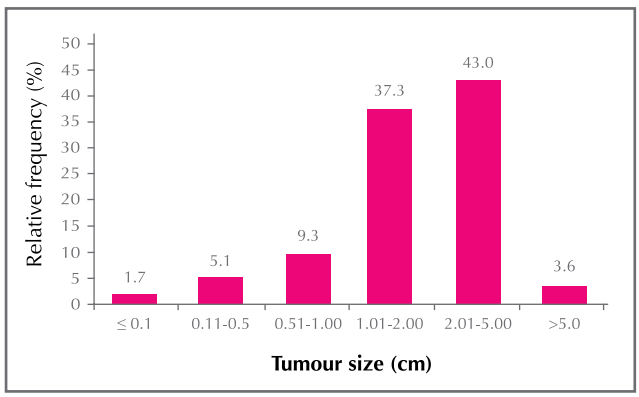

Figure 2.7 Distribution of tumour size (cm) of invasive breast cancers in our patient cohort (N=9,870)

Lymph node status is one of the factors used to determine breast cancer 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, 1.7% had isolated tumour cells, 3.1% had micrometastasis (metastasis size > 0.2 mm to ≤ 2 mm), while 35.7% had at least one positive lymph node with metastasis size greater than 2 mm (Figure 2.8).

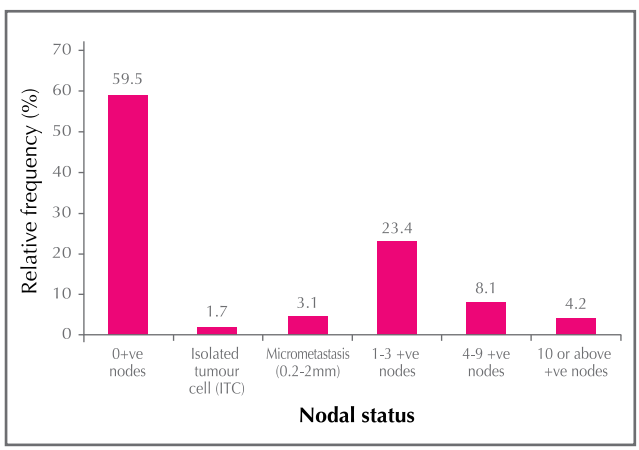

Figure 2.8 Number of positive lymph nodes among our patients with invasive breast cancers (N=10,253)

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: ±1.6 cm). Tumours of 1 cm or less in size were found in 34.8% of our patients while tumours of 2-5 cm in size were found in 30.8% 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, 62.2% showed microcalcification on MMG.

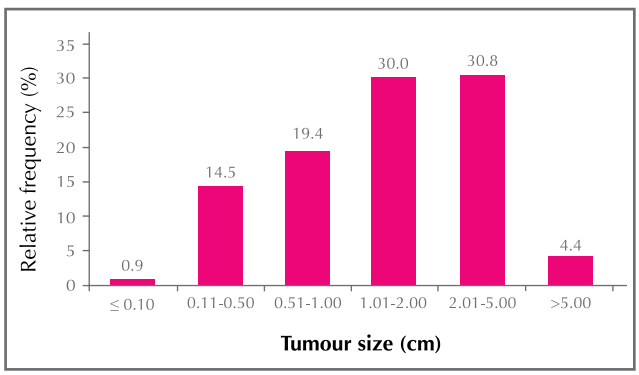

Figure 2.9 Distribution of tumour size (cm) of in situ breast cancers in our cohort (N=1,453)

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 (86.5%).

Table 2.13 Histological type, grading, multifocality and multicentricity of invasive breast cancers (N=10,313)

Histological type	Number	(%)
Invasive carcinoma of no specific type	8,923	(86.5)
Lobular	377	(3.7)
Mucinous (colloid)	370	(3.6)
Papillary	109	(1.1)
Tubular	77	(0.7)
Carcinoma with medullary features	63	(0.6)
Mixed ductal and lobular	48	(0.5)
Borderline / malignant phyllodes	43	(0.4)
Micropapillary	39	(0.4)
Metaplastic carcinoma	38	(0.4)
Carcinoma with neuroendocrine features	19	(0.2)
Carcinoma with apocrine features	15	(0.1)
Adenoid cystic carcinoma	11	(0.1)
Paget's disease of nipple	5	(<0.01)
Cribriform carcinoma	4	(<0.01)
Secretory carcinoma	2	(<0.01)
Inflammatory	1	(<0.01)
Others	90	(0.9)
Not known	79	(0.8)

	Number	(%)
Grade		
Grade 1	1,834	(17.8)
Grade 2	4,328	(42.0)
Grade 3	3,415	(33.1)
Not known	736	(7.1)
Lymphovascular invasion	**2,987**	**(29.0)**
Multifocality	**1,023**	**(9.9)**
Number of foci		
2	554	(54.2)
3-4	175	(17.1)
≥5	109	(10.7)
Not known	185	(18.1)
Multicentricity	**304**	**(2.9)**
Number of quadrants		
2	261	(85.9)
3	17	(5.6)
4	9	(3.0)
Not known	17	(5.6)

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 estrogen or progesterone receptor presence, more than three quarters (80.0%) were either estrogen receptor (ER) or progesterone receptor (PR) positive. 2,137 (21.3%) invasive breast cancers in our patient cohort were c-erbB2/HER2 positive.

Table 2.14 Biological characteristics of invasive breast cancers (N=10,313)

	Number	(%)
Estrogen receptor (ER) (97.9% of the patients had the test)		
Positive	7,881	(78.1)
Negative	2,214	(21.9)
Progesterone receptor (PR) (97.7% of the patients had the test)		
Positive	6,650	(66.0)
Negative	3,424	(34.0)
c-erbB2/ HER2 (97.3% of the patients had the test)		
Positive (IHC score 3)	1,948	(19.4)
Equivocal (IHC Score 2)	3,157	(31.5)
FISH / CISH +ve	*189*	*(6.0)*
Negative (IHC score 0/1)	4,927	(49.1)
Ki-67 index (54.0% of the patients had the test)		
<14%	2,264	(40.6)
≧14%	3,308	(59.4)

HER2: Human epidermal growth factor receptor 2

Breast cancer is not considered 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 surrogate definitions of these intrinsic biological subtypes[29] and 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=9,921)

	Cancer Stage, N (%)											
Biological subtypes	**I**		**IIA**		**IIB**		**III**		**IV**		**Total**	
Luminal A*	1,059	(27.1)	541	(17.3)	243	(16.6)	176	(13.0)	3	(5.0)	2,022	(20.4)
Luminal B (HER2 negative)#	595	(15.2)	630	(20.2)	300	(20.4)	304	(22.4)	11	(18.3)	1,840	(18.5)
Luminal A/B (HER2 negative)†	1,126	(28.8)	831	(26.6)	435	(29.7)	381	(28.0)	22	(36.7)	2,795	(28.2)
Luminal B (HER2 positive)^	444	(11.3)	399	(12.8)	197	(13.4)	226	(16.6)	13	(21.7)	1,279	(12.9)
HER2-positive❊	295	(7.5)	276	(8.8)	120	(8.2)	144	(10.6)	6	(10.0)	841	(8.5)
TND§	393	(10.0)	446	(14.3)	172	(11.7)	128	(9.4)	5	(8.3)	1,144	(11.5)
Total	**3,912**	**(39.4)**	**3,123**	**(31.5)**	**1,467**	**(14.8)**	**1,359**	**(13.7)**	**60**	**(0.6)**	**9,921**	**(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 index

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

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

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 the most common type of in situ breast cancer (93.7%).

Table 2.16 Histological type, grading, multifocality and multicentricity of in situ breast cancers (N=1,704)

	Number	(%)
Histological type		
Ductal	1,597	(93.7)
Mixed	44	(2.6)
Papillary	25	(1.5)
Intracystic papillary	14	(0.8)
Encapsulated papillary	8	(0.5)
Apocrine	5	(0.3)
Neuroendocrine	2	(0.1)
Not known	9	(0.5)
Necrosis	**604**	**(35.4)**
Nuclear Grade		
Low	429	(25.2)
Intermediate	567	(33.3)
High	639	(37.5)
Not known	69	(4.0)
Multifocality	**211**	**(12.4)**
Number of foci		
2	97	(46.0)
3	18	(8.5)
4 or more	8	(3.8)
Not known	88	(41.7)
Multicentricity	**40**	**(2.3)**
Number of quadrants		
2	33	(82.5)
3	2	(5.0)
Not known	5	(12.5)

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 estrogen or progesterone receptor status, 82.5% were either estrogen receptor (ER) or progesterone receptor (PR) positive. 313 (27.0%) in situ breast cancers in our patient cohort were c-erbB2/HER2 positive.

Table 2.17 Biological characteristics of in situ breast cancers (N=1,704)

	Number	(%)
Estrogen receptor (ER) (73.9% of the patients had the test)		
Positive	1,022	(81.2)
Negative	237	(18.8)
Progesterone receptor (PR) (72.6% of the patients had the test)		
Positive	898	(72.6)
Negative	339	(27.4)
c-erbB2/HER2 (68.0% of the patients had the test)		
Positive (IHC score 3)	311	(26.8)
Equivocal (IHC score 2)	410	(35.4)
FISH / CISH +ve	*2*	*(0.5)*
Negative (IHC Score 0 / 1)	438	(37.8)
Ki-67 index (42.5% of the patients had the test)		
< 14%	494	(68.1)
≧ 14%	231	(31.9)

HER2: Human epidermal growth factor receptor 2

2.4 Treatment methods

Of our 13,265 patients, 14.7% solely received care at private medical service, while 51.3% solely received care at public medical service. Around one-third (34.0%) of patients received care at both private and public medical services. Patients with invasive tumour are usually treated with multimodality treatments which may include surgery, chemotherapy, targeted therapy, endocrine therapy, and radiotherapy; while patients with in situ tumour require less aggressive treatments including surgery, endocrine therapy, and radiotherapy. Chemotherapy and targeted therapy are generally not required for patients with in-situ tumour.

2.4.1 Surgical treatment

Surgery is an important consideration in the effective treatment of both in situ and invasive 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.

In our patient cohort, 50.3% of our patients had surgery at private medical facilities, while 49.7% had surgery at public medical facilities.

Almost all (99.5%) of our patients with in situ tumour underwent surgery. Less than half (48.3%) of them had mastectomy and among them, only 21.8% had reconstruction. One-third (32.4%) of them did not receive nodal surgery. Among those who received nodal surgery, 83.4% of them had SNB alone and 12.7% received AD without SNB (Table 2.18).

For patients with invasive tumour, majority (98.1%) of the patients underwent surgery as part of their treatment. Two-thirds (64.8%) of our patients with invasive cancer had mastectomy and among them, only 12.2% of them had reconstruction. Less than half (39.5%) of our invasive patients received SNB alone, while 42.5% received AD without SNB. 17.0% of patients received AD after SNB (Table 2.18).

Table 2.18 Types of surgical operations in our patient cohort (N=13,194)

	Patients with invasive cancer (N=11,480)		Patients with in situ cancer (N=1,714)	
	Number	(%)	Number	(%)
No surgery	186	(1.6)	8	(0.5)
Breast-conserving surgery	3,785	(33.0)	879	(51.3)
Mastectomy	7,447	(64.8)	824	(48.1)
Nodal surgery only	7	(0.1)	0	(0.0)
Type of surgery not known	19	(0.2)	3	(0.2)
Not known if surgery done	36	(0.3)	0	(0.0)
Mastectomy (N=8,271)				
Total mastectomy	7,004	(94.1)	717	(87.0)
Skin sparing	334	(4.5)	86	(10.4)
Areolar sparing	13	(0.2)	4	(0.5)
Nipple sparing	77	(1.0)	16	(1.9)
Not known	19	(0.3)	1	(0.1)
Reconstruction (N=1,087)				
TRAM flap	627	(69.1)	112	(62.2)
Implant	142	(15.7)	50	(27.8)
LD flap	72	(7.9)	8	(4.4)
LD flap & implant	48	(5.3)	9	(5.0)
Not known	18	(2.0)	1	(0.6)
Nodal surgery (N=12,265)				
Sentinel node biopsy	4,391	(39.5)	958	(83.4)
Axillary dissection	4,728	(42.5)	146	(12.7)
Sentinel node biopsy & axillary dissection	1,889	(17.0)	30	(2.6)
Not known	108	(1.0)	15	(1.3)

The percentage of our patients who underwent mastectomy was positively correlated with increasing age (Figure 2.10).

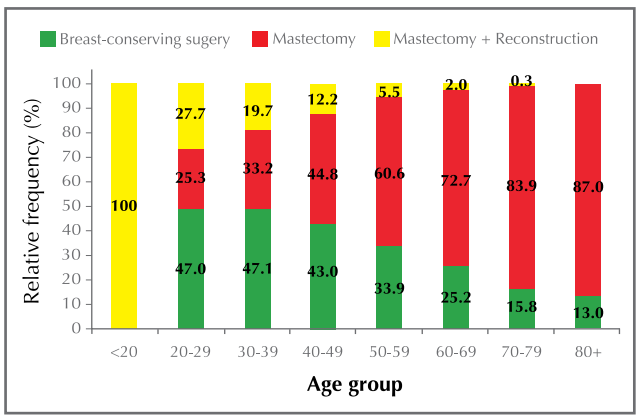

Figure 2.10 Type of surgery by age group (N=12,708)

For our patients with tumours larger than 0.5 cm in size, the percentage of patients that had breast-conserving surgery was negatively correlated with increasing tumour size (Figure 2.11).

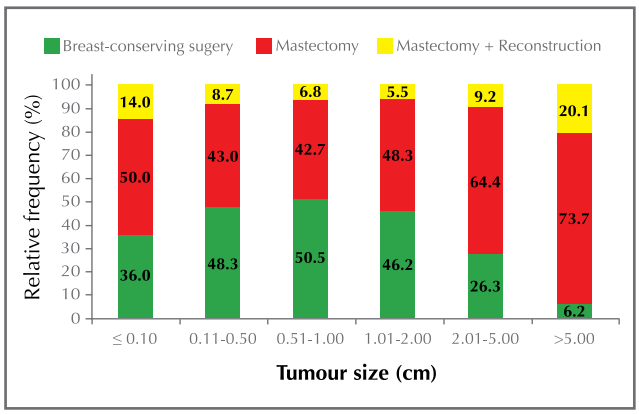

Figure 2.11 Type of surgery by tumour size (N=11,362)

The proportion of 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).

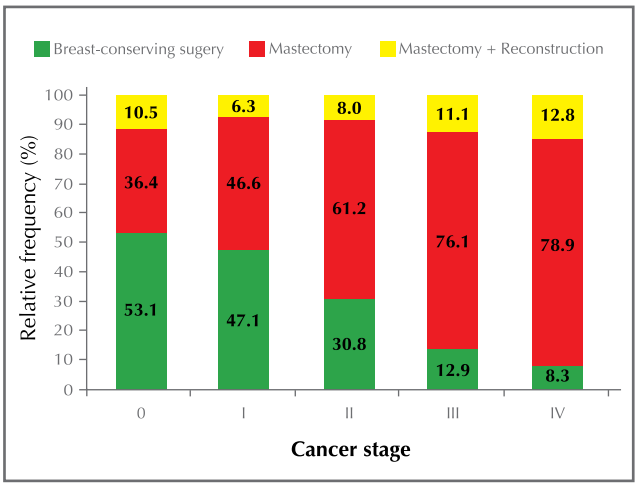

Figure 2.12 Type of surgery by cancer stage (N=12,444)

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).

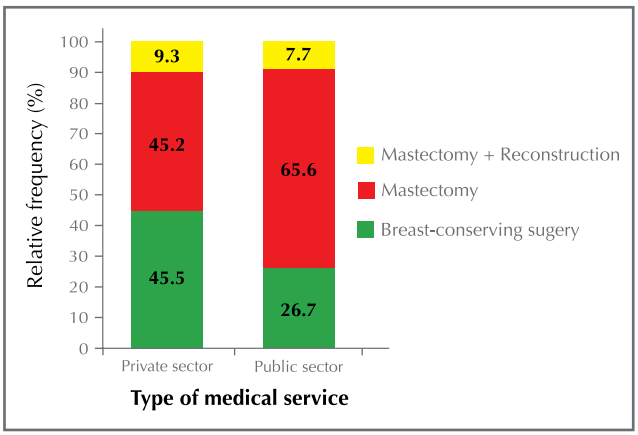

Figure 2.13 Type of surgery by type of medical service (N=12,560)

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 on our patients with negative clinical nodal statuses than those with positive clinical nodal statuses (51.4% vs 14.6%). 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 (72.4 vs 32.2%).

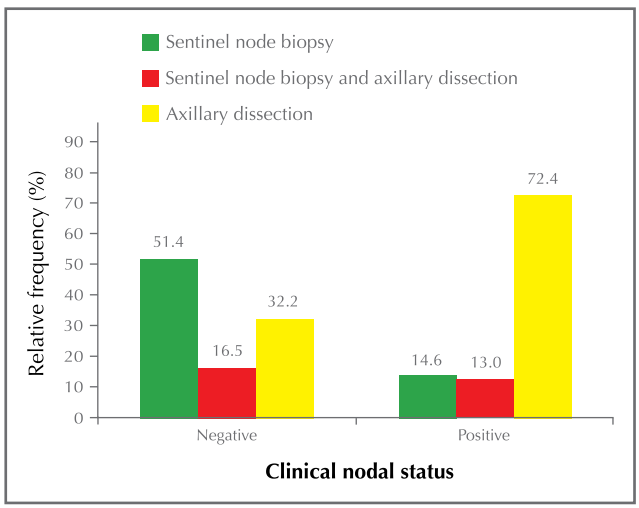

Figure 2.14 Type of nodal surgery by clinical nodal status (N=12,163)

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).

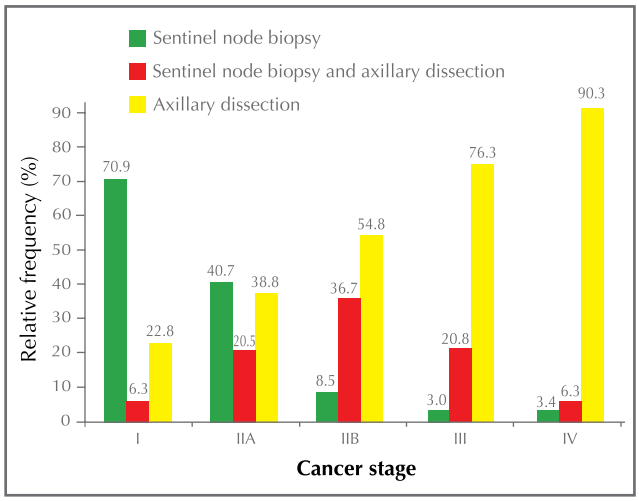

Figure 2.15 Type of nodal surgery in invasive cancer by cancer stage (N=10,648)

Around half (55.9%) of our patients with node positive invasive cancer had tumours of 2 to 5 cm in size, while 6.4% 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 (63.7% vs. 37.7%) (Figure 2.16).

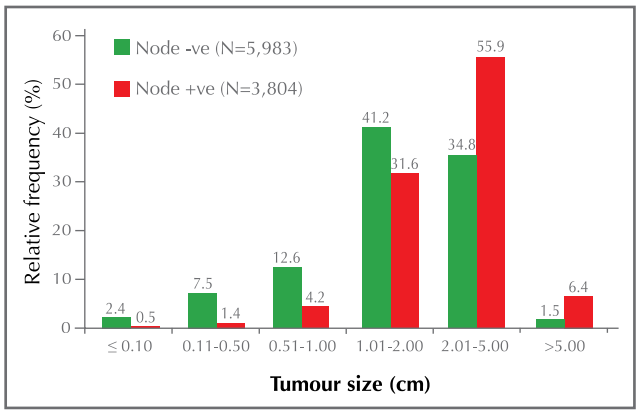

Figure 2.16 Distribution of tumour size in invasive cancer with negative or positive nodal status (N=9,787)

96.4% of patients who underwent SNB alone had no positive lymph node, while almost half (45.6%) of our patients who underwent AD and 17.0% of our patients who underwent AD after SNB had no positive lymph node (Figure 2.17).

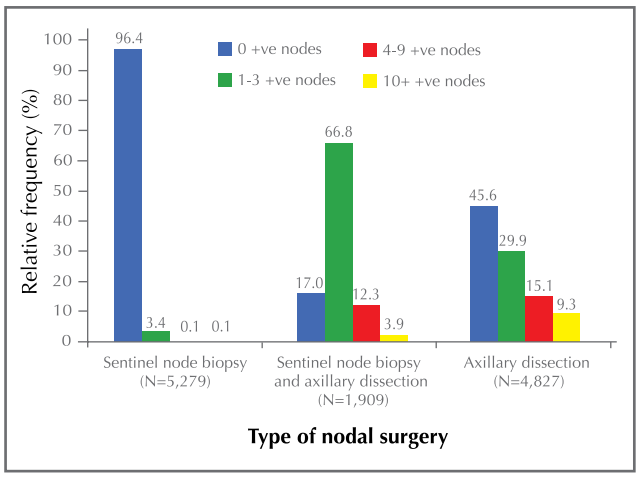

Figure 2.17 Number of positive nodes by type of nodal surgery (N=12,015)

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 multiply. Chemotherapy is generally not required for patients with in-situ tumour. Chemotherapy can be administered before surgery (neoadjuvant chemotherapy) or after surgery (adjuvant or palliative chemotherapy).

7,849 (68.4%) patients with invasive cancer in the cohort underwent chemotherapy. 86.0% of our patients had adjuvant chemotherapy, 10.5% had neoadjuvant chemotherapy, and 3.5% had palliative chemotherapy. 86.2% of our patients received chemotherapy in public medical facilities, while 13.8% received in private medical facilities.

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 stage IV cancer 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 hormonal therapy +/- radiotherapy; not chemotherapy.

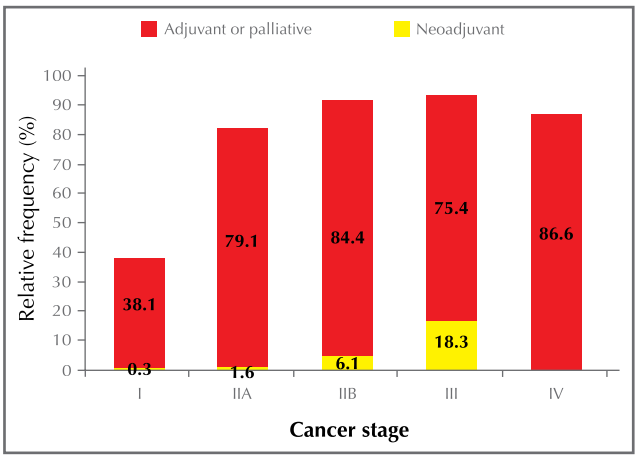

Figure 2.18 Chemotherapy treatment in our patients at different cancer stages (N=10,794)

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 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=10,779)

	Number of patients received chemotherapy (% of patients in the same age group and cancer stage)									
Age group	Stage I		Stage IIA		Stage IIB		Stage III		Stage IV	
20-29	18	(75.0)	18	(94.7)	13	(100.0)	10	(100.0)	3	(100.0)
30-39	201	(56.5)	280	(91.5)	131	(99.2)	135	(99.3)	19	(90.5)
40-49	636	(45.4)	887	(90.2)	498	(97.5)	565	(98.3)	93	(95.9)
50-59	492	(38.3)	952	(87.6)	503	(95.8)	534	(96.9)	97	(87.4)
60-69	159	(24.8)	393	(69.7)	255	(89.2)	276	(93.9)	29	(82.9)
70-79	7	(3.2)	19	(10.9)	10	(12.0)	30	(37.5)	9	(47.4)
80+	1	(2.2)	1	(2.0)	0	(0.0)	2	(10.0)	2	(28.6)

2.4.2.1 Neoadjuvant chemotherapy

Out of 7,849 patients who underwent chemotherapy, 825 patients (10.5%) received it as neoadjuvant treatment. The use of neoadjuvant chemotherapy increased substantially with progressing cancer stage, from 0.3% of stage I patients to 18.3% of stage III patients (Figure 2.18). The regimens used by patients with different cancer stages are shown in Figure 2.19. Around one-third (30.5%) of the patients who have received neoadjuvant chemotherapy received further adjuvant chemotherapy after surgical treatment.

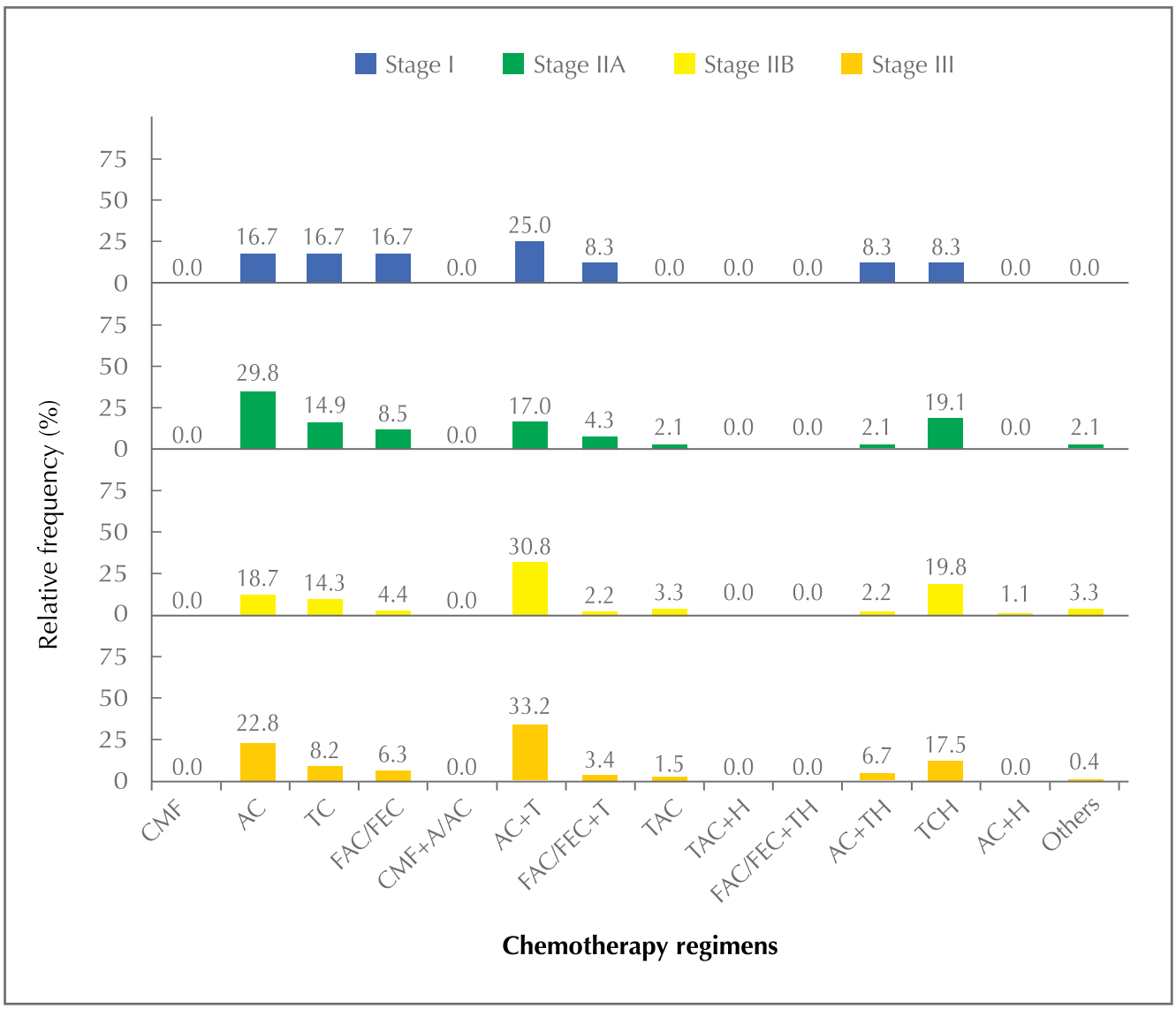

Figure 2.19 Type of chemotherapy regimens in neoadjuvant setting in patients by cancer stage (N=418)

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

2.4.2.2 Adjuvant or palliative chemotherapy

Of the 7,849 patients who underwent chemotherapy, 7,024 (89.5%) received it as adjuvant (Stage I-III) or palliative (Stage IV) treatment. Figure 2.20 shows the relative frequency for different types of chemotherapy regimen used during the different stages of the disease in our patient cohort.

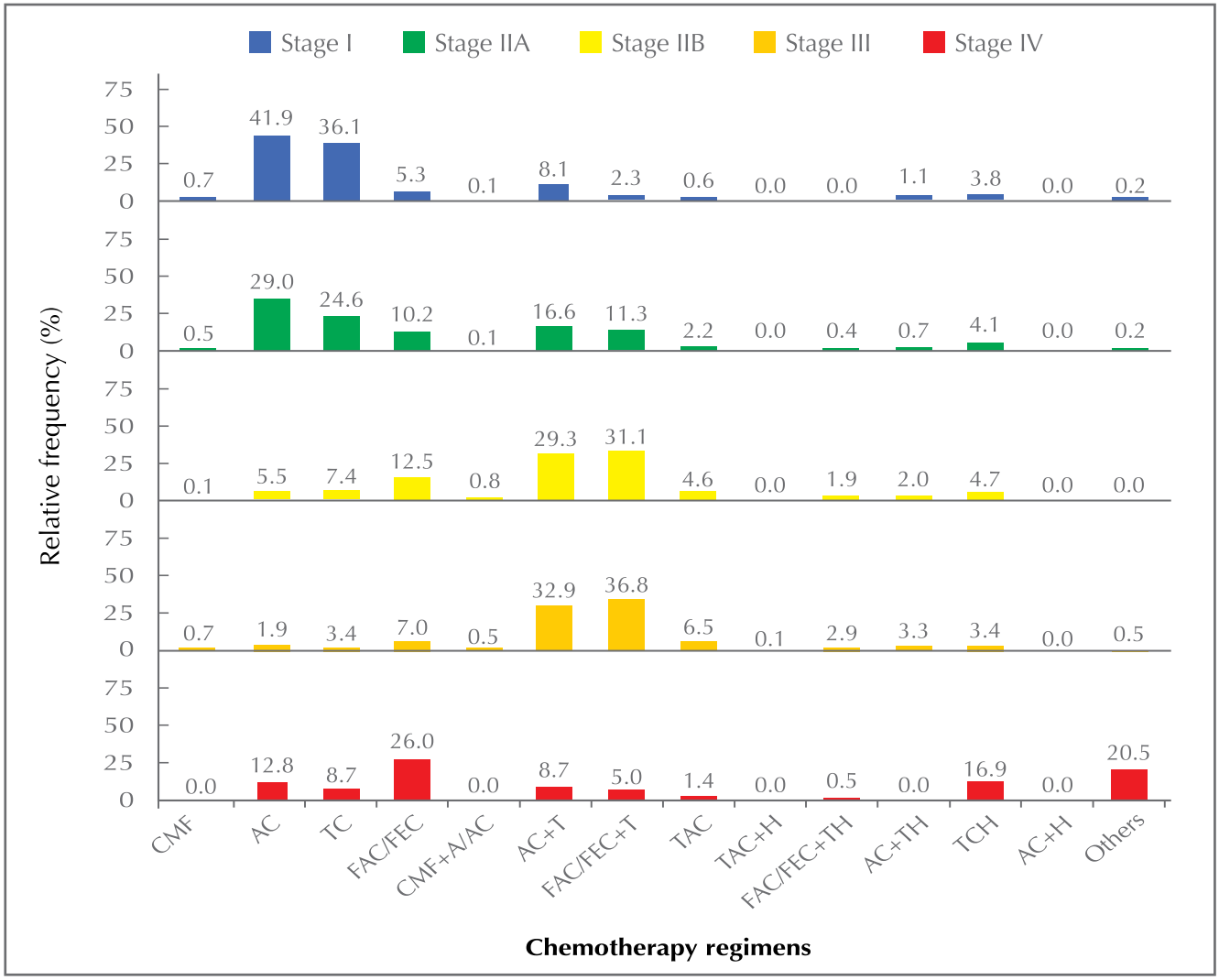

Figure 2.20 Type of chemotherapy regimens in adjuvant or palliative setting in patients by cancer stage (N=6,099)

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.

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.

In our patient cohort, 8,219 (62.0%) patients had radiotherapy as one of their treatment, among which 97.8% were adjuvant, 0.2% were neoadjuvant, and 1.9% were palliative. 93.0% of our patients were treated with radiotherapy at public medical facilities, while 7.0% had radiotherapy at private medical facilities.

Of our patients with in situ cancer who had breast-conserving surgery, majority (94.3%) of them received radiotherapy afterwards (Figures 2.21), while only 3.0% of our patients with in situ cancer who had mastectomy received radiotherapy (Figures 2.22).

The proportions of our invasive breast cancer patients who had breast-conserving surgery or mastectomy, respectively, who received radiotherapy as part of their treatment at different cancer stages are shown in Figures 2.21 and 2.22. Over 90% of invasive breast cancer patients with breast-conserving surgery received radiotherapy, while the use of radiotherapy in invasive breast cancer patients with mastectomy increased with increasing cancer stages, with the exception of stage IV disease.

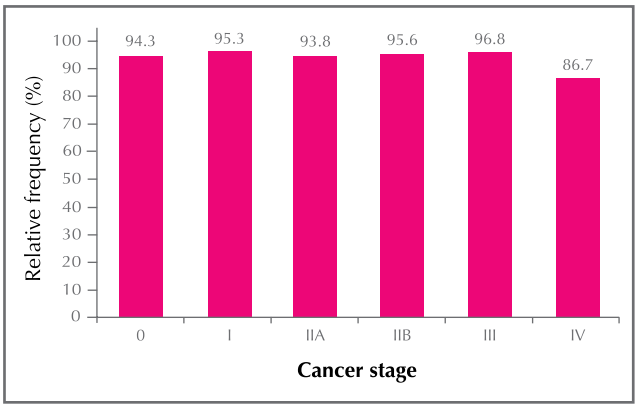

Figure 2.21 The use of radiotherapy in our patients receiving breast-conserving surgery at different cancer stages (N=4,531)

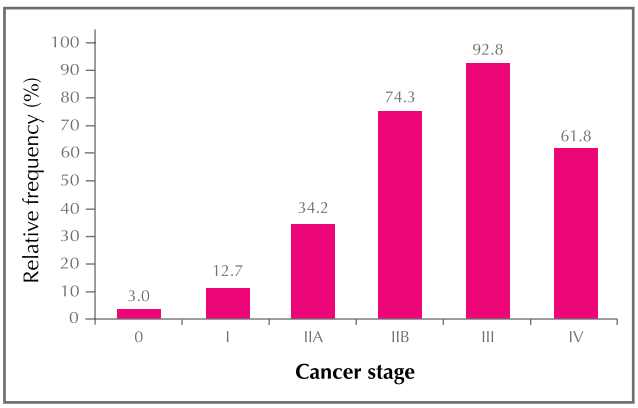

Figure 2.22 The use of radiotherapy in our patients receiving mastectomy at different cancer stages (N=7,913)

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=5,478)

	Total# (N=5,478)		Breast-conserving surgery (N=2,831)		Mastectomy (N=2,591)	
Target volume	**Number**	**(%)**	**Number**	**(%)**	**Number**	**(%)**
Breast	2,381	(43.5)	2,360	(83.4)	0	(0.0)
Breast + regional nodes*	502	(9.2)	471	(16.6)	0	(0.0)
Chest wall	669	(12.2)	0	(0.0)	668	(25.8)
Chest wall + regional nodes*	1,926	(35.2)	0	(0.0)	1,923	(74.2)

SCF: Supraclavicular fossa; IMC: Internal mammary chain;
*regional nodes: includes SCF and/or axilla and/or IMC
#Total number of patients includes 56 patients with surgical data not known

2.4.4 Endocrine therapy

Endocrine therapy plays an important role in all stages of the treatment and prevention strategy for hormone receptor-positive invasive or in-situ 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, 8,922 (67.3%) patients received endocrine therapy. Among them, 96.7% were adjuvant, 0.5% were neoadjuvant, and 2.8% were palliative. 97.1% of our patients received endocrine therapy at public medical facilities, while 2.9% received endocrine therapy at private medical facilities. Endocrine therapy was used in 11.9% of our patients with in situ breast cancer, but was used in over 74.0% of our patients with invasive breast cancer (Figure 2.23).

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 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 2.24 shows the use of Tamoxifen and Aromatase inhibitors by our patient cohort in three age groups.

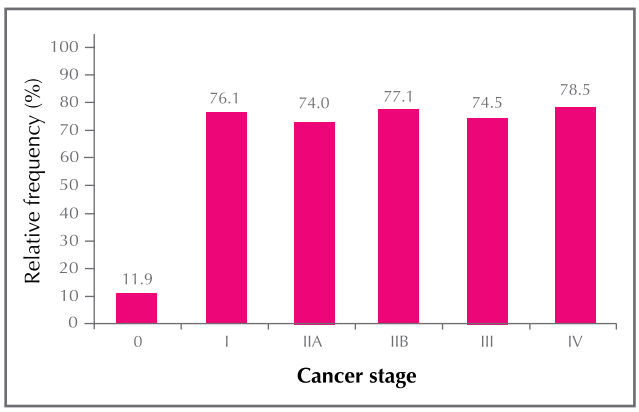

Figure 2.23 Endocrine therapy rates in our patients by cancer stage (N=12,610)

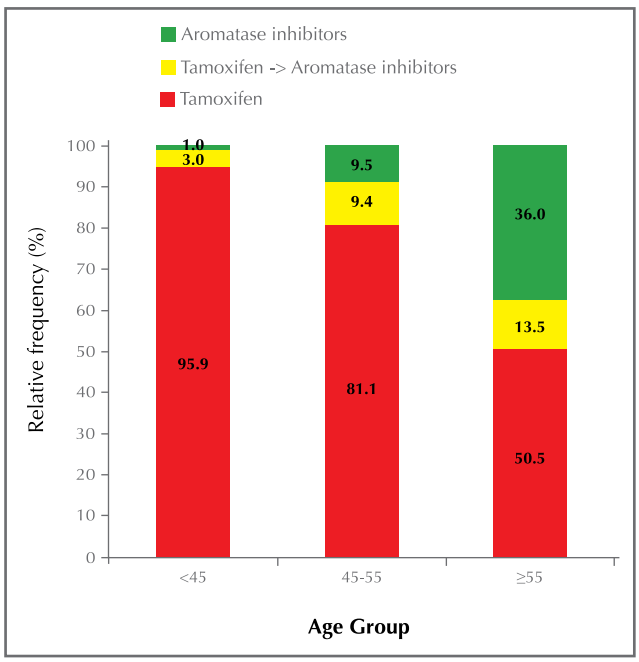

Figure 2.24 Forms of endocrine therapy used in our patient cohort by age group (N=8,222)

The use of targeted therapy was positively correlated with increasing cancer stage (Figure 2.25). The most commonly used targeted therapy drug was Trastuzumab (95.3%) (Figure 2.26).

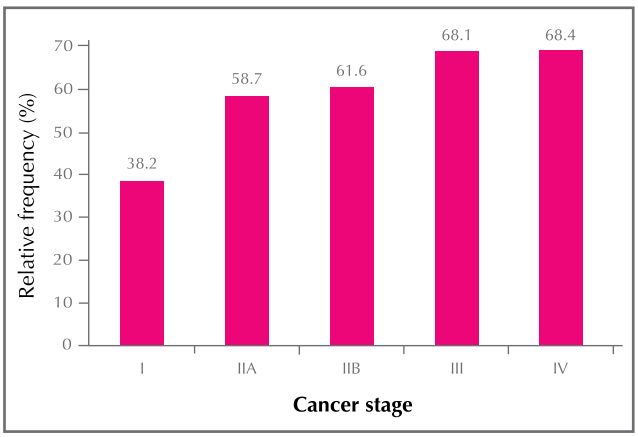

Figure 2.25 Targeted therapy rate in the HER2 positive patients by cancer stage in our cohort (N=2,122)

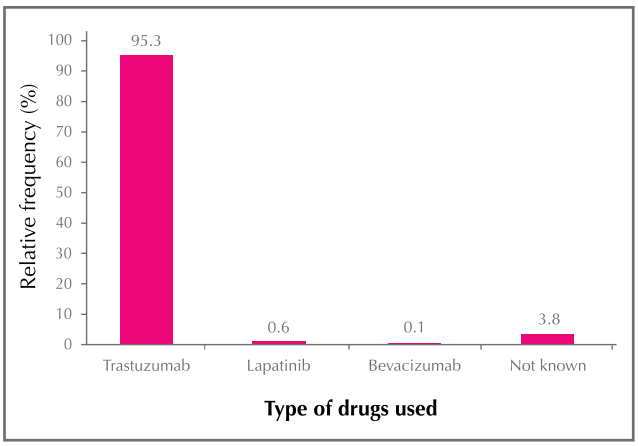

Figure 2.26 Type of drugs used for targeted therapy in our patient cohort (N=1,146)

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 invasive breast cancer cells that over-express HER2 (HER2-positive breast cancer). Of the 2,136 patients with invasive HER2-positive breast cancers in our cohort, 1,146 (53.7%) underwent targeted therapy. Among them, 98.3% were adjuvant, 0.4% were neoadjuvant, and 1.2% were palliative. Majority (95.7%) of our patients received targeted therapy at public medical facilities, while 4.3% received targeted therapy at private medical facilities.

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. 5,310 (40.0%) of the patients in the cohort received complementary and alternative therapies. Among them, 95.2% were adjuvant, 3.9% were neoadjuvant, and 0.9% were palliative. 66.5% of our patients used traditional Chinese medicines (Figure 2.27).

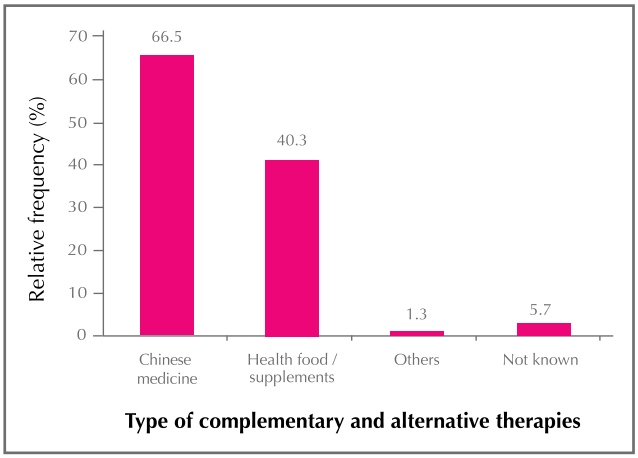

Figure 2.27 Type of complementary and alternative therapies used in 5,310 patients

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, majority (94.4%) of patients with stage 0 disease received two or less treatments, while over half of our patients with stage I or II disease received three or more treatments. Three-quarters (76.0%) of patients with stage III disease received four or more treatments.

Table 2.21 Number of treatment combinations received by patients by cancer stages (N=12,610)

	Stage, Number (%)						
No. of treatment	0 (N=1,597)	I (N=4,102)	IIA (N=3,291)	IIB (N=1,608)	III (N=1,710)	IV (N=302)	Total (N=12,610)
0	3 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.7)	6 (<0.05)
1	674 (42.2)	300 (7.3)	88 (2.7)	18 (1.1)	23 (1.3)	26 (8.6)	1,129 (9.0)
2	831 (52.0)	1,351 (32.9)	594 (18.0)	114 (7.1)	57 (3.3)	54 (17.9)	3,001 (23.8)
3	89 (5.6)	1,702 (41.5)	1,232 (37.4)	465 (28.9)	330 (19.3)	102 (33.8)	3,920 (31.1)
4	0 (0.0)	658 (16.0)	1,244 (37.8)	876 (54.5)	1,086 (63.5)	97 (32.1)	3,961 (31.4)
5	0 (0.0)	91 (2.2)	133 (4.0)	134 (8.3)	214 (12.5)	21 (7.0)	593 (4.7)

2.5 Patient Status

Once treatment is completed, annual follow-ups are conducted to ascertain the efficacy of the treatment. To date, annual follow-ups were conducted on 11,866 patients in our cohort and among them, 64.7% had the last follow-up within the last two years. Around two-thirds (67.3%) of our patients were followed up for at least two years after initial diagnosis (Table 2.22). The mean follow-up period was 3.6 years and median follow-up period was 3.2 years.

508 (4.3%) of patients in our cohort experienced recurrence, where 1.2% of our patients experienced locoregional recurrence (LR) solely, 2.0% 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 11,866 patients

Follow-up period	Number	(%)
< 1 year	1,400	(11.8)
1-2 years	2,472	(20.8)
2-5 years	4,929	(41.5)
5-10 years	3,042	(25.6)
10-15 years	23	(0.2)
Mean follow-up period		3.6 years
Median follow-up period		3.2 years
Locoregional recurrence		
No. of locoregional recurrences	143	(1.2)
Mean time to locoregional recurrence		2.7 years
Median time to locoregional recurrence		2.4 years
Distant recurrence		
No. of distant recurrences	235	(2.0)
Mean time to distant recurrence		2.7 years
Median time to distant recurrence		2.4 years
Locoregional and distant recurrence		
No. of locoregional and distant recurrences	130	(1.1)
Mean time to locoregional and distant recurrence		2.7 years
Median time to locoregional and distant recurrence		2.4 years
Mortality		
No. of deaths from breast cancer	110	(0.9)
No. of deaths from unrelated causes	68	(0.6)
No. of deaths with causes not known	18	(0.2)

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 (1.6% vs. 2.1%). 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 involved in LR were chest wall (39.6%) and axilla (30.0%) (Table 2.24).

Table 2.23 Number of invasive breast cancer 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	19/1,938	28/1,150	4/364	8/219	59/3,671
	(1.0)	(2.4)	(1.1)	(3.7)	(1.6)
MTX	28/2,160	36/2,132	24/1,238	59/1,477	147/7,007
	(1.3)	(1.7)	(1.9)	(4.0)	(2.1)

BCS: Breast-conserving surgery; MTX: Mastectomy

Table 2.24 Sites involved in locoregional recurrence in our patients (N=273)

Sites involved	Number	(%)
Chest wall	108	(39.6)
Axilla	82	(30.0)
Breast	78	(28.6)
Supraclavicular	61	(22.3)
Internal mammary node	22	(8.1)
Infraclavicular	3	(1.1)
Others	27	(9.9)

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

In our patient cohort, 365 (3.1%) patients experienced DR. Among them, the common organs involved were bone (53.4%), followed by lung (44.7%) and liver (41.6%) (Table 2.25).

Table 2.25 Organs involved in distant recurrence (N=365)

Distant organs affected	Number	(%)	Distant organs affected	Number	(%)
Bone	195	(53.4)	Abdomen	4	(1.1)
Lung	163	(44.7)	Ovary	4	(1.1)
Liver	152	(41.6)	Spleen	4	(1.1)
Brain	58	(15.9)	Thyroid glands	3	(0.8)
Mediastinal nodes	57	(15.6)	Thorax	2	(0.5)
Neck	22	(6.0)	Pancreas	2	(0.5)
Distant nodes	16	(4.4)	Uterus	1	(0.3)
Contralateral nodal metatases	12	(3.3)	Kidney	1	(0.3)
Adrenal	5	(1.4)	Unspecified	17	(4.7)

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 1%) 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=4,102)		IIA (N=3,291)		IIB (N=1,608)		III (N=1,710)		Total (N=10,711)	
LR solely	33	(0.8)	38	(1.2)	8	(0.5)	21	(1.2)	100	(0.9)
DR solely	33	(0.8)	48	(1.5)	33	(2.1)	90	(5.3)	204	(1.9)
LR and DR	14	(0.3)	26	(0.8)	20	(1.2)	46	(2.7)	106	(1.0)

LR: Locoregional recurrence; DR: Distant recurrence

110 (0.9%) patients in the cohort died from breast cancer. Around half (55.4%) of the patients who died from breast cancer were diagnosed with stage III or IV disease at initial diagnosis. Survival time ranged from 0.8 – 8.8 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=110)

	Cancer stage at initial diagnosis						
	0	I	IIA	IIB	III	IV	Unstaged
No. of cases (% of breast cancer death cases)	**1 (0.9)**	**14 (12.7)**	**14 (12.7)**	**5 (4.5)**	**45 (40.9)**	**16 (14.5)**	**15 (13.6)**
Survival time (range in years)	**4.4**	**1.8 – 6.8**	**1.9 – 8.8**	**2.1 – 6.6**	**0.8 – 7.6**	**1.1 – 4.8**	**0.6 – 6.2**
Biological subtypes							
Luminal A*	0	2	1	1	3	0	3
Luminal B (HER2 negative)#	0	3	3	0	7	2	2
Luminal A/B (HER2 negative)†	0	2	3	1	12	6	2
Luminal B (HER2 positive)^	1	2	2	0	8	3	2
HER2-positive ❉	0	2	1	0	9	3	0
TND§	0	3	4	2	6	1	2
Not known	0	0	0	1	0	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