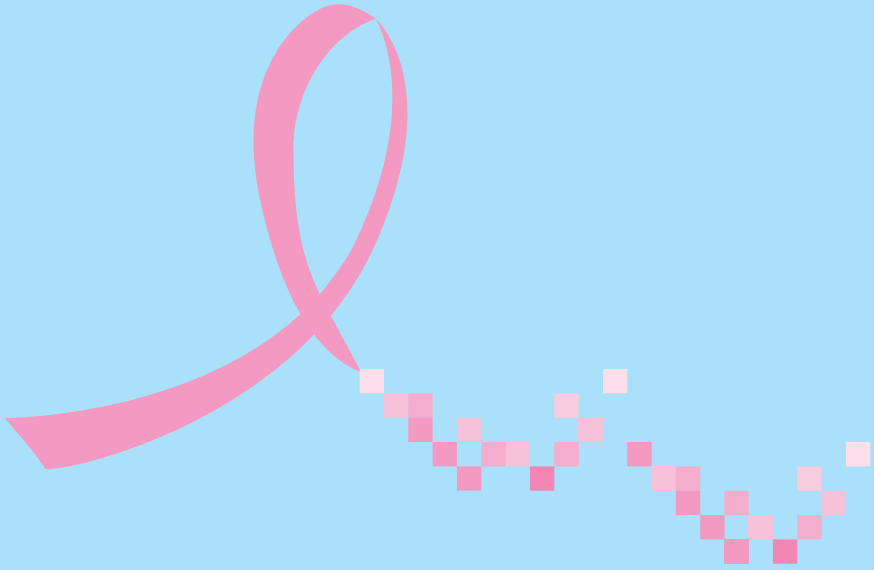

CHAPTER 2

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

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This chapter reviews the data collected from 14,990 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 the local context can be 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 (83.2%). More stage 0 or 1 cancers (34.6% and 13.4% respectively) were detected by mammography screening than stage III or IV cancers (3.0% and 2.1% respectively).
- Most (91.8%) 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 7.0% of our patients felt pain in their breast(s) at initial presentation. Some patients (9.0%) experienced changes in nipple (such as nipple discharge, nipple retraction, redness, scaliness or thickening of nipple).
- After the onset of symptoms, a quarter (25.4%) of our patients who self-detected their cancers by chance waited three or more months before seeking first medical consultation.
- Majority (91.7%) of our patients had unilateral breast cancer, while 370 patients had synchronous bilateral breast cancer at first diagnosis. 340 patients developed a contralateral breast cancer subsequently after diagnosis of an initial primary breast cancer.
- Around half (45.3%) 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 positron emission tomography scan (PET scan) (46.0%), and chest x-ray plus ultrasound of abdomen (44.0%).
- The most common cancer stage at diagnosis was stage II (37.3%). Around 16.4% 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: ±1.5 cm). Tumours larger than 2.0 cm in size were found in 47.2% of our patients. In our patient cohort, screen-detected cancers were significantly smaller than cancers that were self-detected by chance (mean: 1.5 cm vs. 2.5 cm; $p<0.001$). 59.3% 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 (86.2%). 80.2% of invasive breast cancers were either estrogen receptor (ER) or progesterone receptor (PR) positive. 21.1% were c-erbB2/HER2 positive. 11.6% of the invasive breast cancers were triple 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 35.3% of our patients. Of the in situ breast cancers where mammogram (MMG) was performed, 74.5% showed microcalcification on MMG. Ductal cancers were found to be the most common type of in situ breast cancer (93.2%). 82.1% of in situ breast cancers were either ER or PR positive. 27.1% of in situ breast cancers in our cohort were c-erbB2/HER2 positive.

Treatment methods

- Of our 14,990 patients, 14.7% solely received care at private medical service, while 49.9% solely received care at public medical service. Around one-third (35.4%) of patients received care at both private and public medical services.
- Surgery
  - Majority (98.0%) 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.
  - Less than half (47.7%) of our patients with in situ tumours had mastectomy, and among them, 22.1% had reconstruction. Among those who received nodal surgery, 84.2% of them had sentinel node biopsy (SNB) alone and 11.9% received axillary dissection (AD) without SNB.
  - For patients with invasive tumours, two-thirds (64.8%) of them had mastectomy and among them, only 11.7% of them had reconstruction. Less than half (41.3%) of our invasive patients received SNB alone, while 41.0% 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 (53.6% vs. 15.5%).
  - The use of AD was positively correlated with increasing cancer stage.
- Radiotherapy
  - 61.8% of our patients had radiotherapy as one of their treatment. 88.1% of our patients had radiotherapy at public medical facilities, while 11.9% had radiotherapy at private medical facilities.
  - Of our patients with in situ cancer who had breast-conserving surgery, majority (94.0%) of them received radiotherapy afterwards, while only 3.3% of our patients with in situ cancer who had mastectomy received radiotherapy.
  - Over 84% 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.
- Chemotherapy
  - Two-thirds (67.9%) of patients with invasive cancer in the cohort underwent chemotherapy. Among them, 11.2% had neoadjuvant chemotherapy.
  - 86.5% of our patients received chemotherapy in public medical facilities, while 13.5% 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.

- Endocrine therapy
  - 67.4% of our patients received endocrine therapy. 90.5% of our patients received endocrine therapy at public medical facilities, while 9.5% received endocrine therapy at private medical facilities.
  - Endocrine therapy was used in 11.7% of our patients with in situ breast cancer, but was used in over 73.0% of our patients with invasive breast cancer.
- Anti-HER2 targeted therapy
  - Of the patients with invasive HER2-positive breast cancers in our cohort, 58.3% underwent anti-HER2 targeted therapy. 88.7% of our patients received anti-HER2 targeted therapy at public medical facilities, while 11.3% received anti-HER2 targeted therapy at private medical facilities.
  - The use of anti-HER2 targeted therapy was positively correlated with increasing cancer stage.
- Combinations of treatments are usually used for treating breast cancer effectively. In general, the number of treatments increased with increasing cancer stage.
- Complementary and alternative therapies
  - 39.3% of our patients in the cohort received complementary and alternative therapies. Among them, 66.1% used traditional Chinese medicines.

Patient status

- The mean and median follow-up periods were 3.9 and 3.4 years, respectively.
- 596 (4.5%) of patients in our cohort experienced recurrence, where 1.3% of our patients experienced locoregional recurrence (LR) solely, 2.1% experienced distant recurrence (DR) solely, and 1.1% experienced both locoregional and distant recurrence.
- The common sites for locoregional recurrence were chest wall (36.4%) and breast (30.5%) and the common organs involved in distant recurrence were bone (55.2%), lung (46.5%), and liver (39.0%).

2.1 Clinical presentation

The primary method of first breast cancer detection in the patient cohort was self-detection by chance (83.2%) (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 reported that 43% of the breast cancer cases were detected through mammography screening[31], which is significantly higher than the 10.5% observed in Hong Kong within the patient cohort.

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. In contrast, 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[32]. In our patient cohort, the proportion of invasive breast cancers detected by mammography screening (6.9%) were much lower than that of in situ breast cancers (35.2%) (Table 2.2). In addition, more stage 0 or I cancers (34.6% and 13.4% respectively) were detected by mammography screening than stage III or IV cancers (3.0% and 2.1% respectively). Over 90% of patients with stage IIB, III or IV cancers self-detected their cancer by chance (Table 2.3).

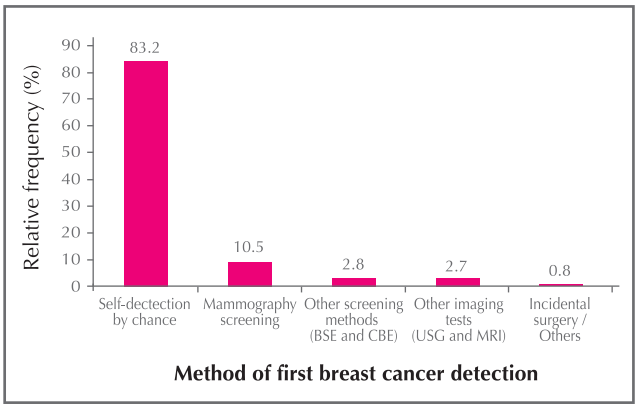

Figure 2.1 The method of first breast cancer detection in our patient cohort (N=14,161)

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=14,028)

	Private medical service users (N=2,055)		Public medical service users (N=6,988)		Mixed private / public medical service users (N=4,985)	
Mode of first breast cancer detection	**Number**	**(%)**	**Number**	**(%)**	**Number**	**(%)**
Self-detection by chance	1,520	(74.0)	5,868	(84.0)	4,290	(86.1)
Mammography screening	304	(14.8)	792	(11.3)	376	(7.5)
Other screening methods (BSE and CBE)	71	(3.5)	171	(2.4)	146	(2.9)
Other imaging tests (USG and MRI)	134	(6.5)	101	(1.4)	141	(2.8)
Incidental surgery / Others	26	(1.3)	56	(0.8)	32	(0.6)

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=14,126)

Method of first breast cancer detection	Type of cancer, Number (%)	
	In situ (N=1,824)	Invasive (N=12,302)
Self-detection by chance	1,002 (54.9)	10,753 (87.4)
Mammography screening	642 (35.2)	845 (6.9)
Other screening methods (BSE and CBE)	56 (3.1)	332 (2.7)
Other imaging tests (USG and MRI)	101 (5.5)	279 (2.3)
Incidental surgery / Others	23 (1.3)	93 (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=13,725)

Method of first breast cancer detection	Cancer stage, Number (%)					
	0 (N=1,695)	I (N=4,406)	IIA (N=3,497)	IIB (N=1,781)	III (N=2,011)	IV (N=335)
Self-detection by chance	959 (56.6)	3,446 (78.2)	3,127 (89.4)	1,665 (93.5)	1,885 (93.7)	311 (92.8)
Mammography screening	586 (34.6)	589 (13.4)	184 (5.3)	43 (2.4)	61 (3.0)	7 (2.1)
Other screening methods (BSE and CBE)	54 (3.2)	158 (3.6)	91 (2.6)	40 (2.2)	29 (1.4)	10 (3.0)
Other imaging tests (USG and MRI)	81 (4.8)	174 (3.9)	71 (2.0)	26 (1.5)	18 (0.9)	5 (1.5)
Incidental surgery / Others	15 (0.9)	39 (0.9)	24 (0.7)	7 (0.4)	18 (0.9)	2 (0.6)

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

Most (91.8%) 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 7.0% of patients felt pain in their breast(s) at initial presentation. Some patients (9.0%) experienced changes in nipple (such as nipple discharge, nipple retraction, redness, scaliness or thickening of nipple) (Figure 2.2).

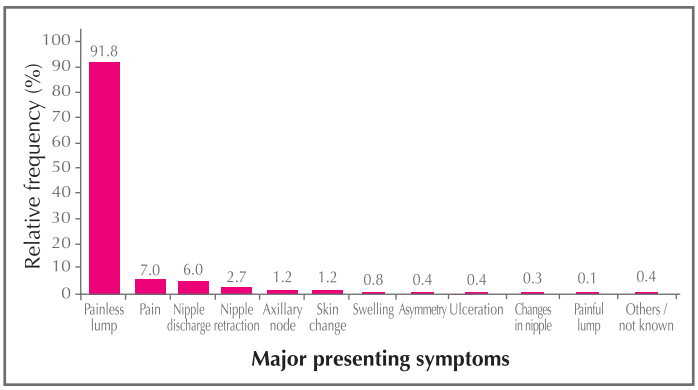

Figure 2.2 Major presenting symptoms of self-detected* breast cancers in our patient cohort (N=11,781)

*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[33]. After the onset of symptoms, only one-third (35.6%) of the patients who self-detected their cancers by chance sought first medical consultation in less than one month (Table 2.4) while a quarter (25.4%) of them waited three or more months before seeking first medical consultation.

The proportion of our patients who sought first medical consultation in less than one month was higher in private medical service users (42.2%) than in public medical service users (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=3,143)

	Number	(%)
Less than 1 month	1,118	(35.6)
1-3 months	1,228	(39.1)
4-12 months	464	(14.8)
More than 12 months	333	(10.6)

*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=3,143)

	Type of medical service users, Number (%)					
	Private (N=654)		Public (N=1,419)		Mixed private / public (N=1,070)	
Less than 1 month	277	(42.4)	397	(28.0)	444	(41.5)
1-3 months	241	(36.9)	562	(39.6)	425	(39.7)
4-12 months	80	(12.2)	266	(18.7)	118	(11.0)
More than 12 months	56	(8.6)	194	(13.7)	83	(7.8)

*Self-detection by chance only

A much higher proportion (11.8%) of patients who sought first medical consultation after 12 months of symptom onset was diagnosed with stage IV disease than those who sought first medical consultation in less than 12 months (Table 2.6).

Table 2.6 Cancer stage at diagnosis among self-detected* patients with different time interval between the onset of symptoms and first medical consultation (N=2,770)

	Time interval between the onset of symptoms and first medical consultation, Number (%)			
Cancer stage at diagnosis	Less than 1 month (N=997)	1 – 3 months (N=1,091)	4 – 12 months (N=403)	More than 12 months (N=279)
Stage I	367 (36.8)	333 (30.5)	112 (27.8)	70 (25.1)
Stage IIA	336 (33.7)	359 (32.9)	122 (30.3)	66 (23.7)
Stage IIB	146 (14.6)	181 (16.6)	68 (16.9)	49 (17.6)
Stage III	135 (13.5)	185 (17.0)	85 (21.1)	61 (21.9)
Stage IV	13 (1.3)	33 (3.0)	16 (4.0)	33 (11.8)

*Self-detection by chance only

2.2 Cancer characteristics

Breast cancer can occur in one (unilateral) or both breasts (bilateral). Majority (91.7%) of our patients had unilateral breast cancer, while 4.9% (n=370) had synchronous bilateral breast cancer at first diagnosis (Figure 2.3). 147 patients (2.0%) developed a contralateral breast cancer within, a median of 2.8 years (range: 0.5– 8.8 years) after diagnosis of an initial primary breast cancer (Figure 2.3). An additional 193 patients had contralateral breast cancer, however as they were diagnosed with their initial primary breast cancer before 2006, only data from second diagnosis occuring after 2006 was included in this report.

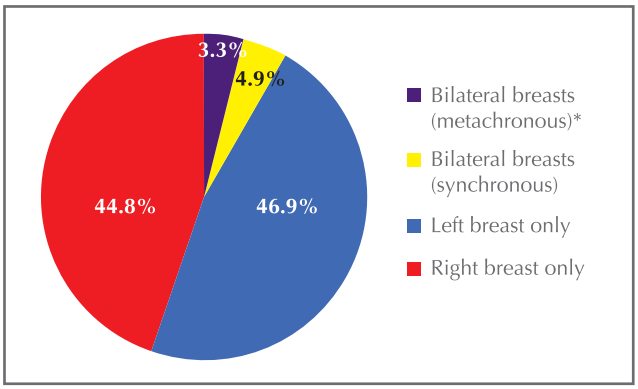

Figure 2.3 Laterality of 14,990 breast cancer cases

* Includes 193 patients who were diagnosed with initial primary breast cancer before 2006 and they developed a contralateral breast cancer after 2006 (only data from second diagnosis was included in this report).

Figure 2.4 shows the proportion of malignant breast tumours occuring in each breast quadrant within the patient cohort. Around half of the breast cancers in either the right or the left breast were detected in the upper outer quadrant (50.3% and 47.1% respectively).

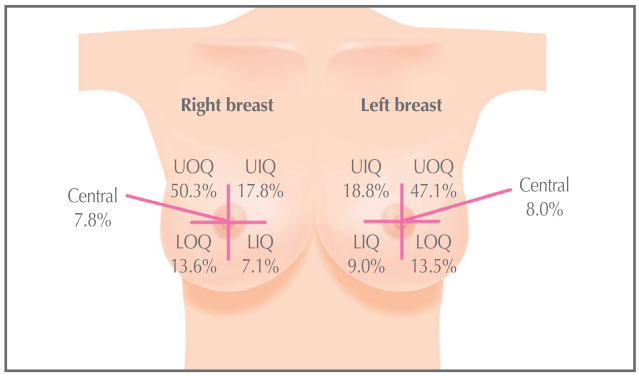

Figure 2.4 Locations of malignant breast tumour on the breasts within our patient cohort (N=14,990)

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 85.4% of our patients MMG was used, while USG was used on 79.7% and MRI was used on only 9.3% 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=14,990)

	Mammography (N=12,804)		Breast ultrasound (N=11,951)		MRI (N=1,392)	
Proportion of patients using the diagnostic test	85.4%		79.7%		9.3%	
Overall sensitivity*	82.6%		90.7%		96.5%	
BIRADS category						
Diagnostic / malignant (BIRADS 5)	4,192	(32.7%)	4,549	(38.1%)	1,108	(79.6%)
Suspicious abnormality (BIRADS 4)	6,381	(49.8%)	6,289	(52.6%)	235	(16.9%)
Probably benign (BIRADS 3)	707	(5.5%)	673	(5.6%)	23	(1.7%)
Benign (BIRADS 2)	537	(4.2%)	197	(1.6%)	11	(0.8%)
Normal (BIRADS 1)	903	(7.1%)	236	(2.0%)	14	(1.0%)
Incomplete (BIRADS 0)	84	(0.7%)	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 62.8% of patients in the cohort with BIRADS 4 or 5 mammograms, while microcalcification was observed in 50.6% (Table 2.8). The mammographic density of a woman's breasts affects the sensitivity of mammography. Heterogeneously dense breast may obscure small masses, while extremely dense breast lowers the sensitivity of mammography. In our patient cohort, two-thirds (69.1%) had heterogeneously dense breasts, while 6.4% had extremely dense breasts (Figure 2.5). Mammographic density of a woman's breasts declines with increasing age. The proportion of patients with extremely dense breast decreases significantly from 12.8% in patients aged 20-29 to 1.0% in patients aged 70 and above (Table 2.9).

Table 2.8 Mammographic findings of patients in our cohort who were diagnosed through mammography (N=10,573)

	Number	(%)
Opacity	6,644	(62.8)
Microcalcification	5,355	(50.6)
Architectural distortion	1,533	(14.5)
Asymmetric density	944	(8.9)
Unclassified	442	(4.2)

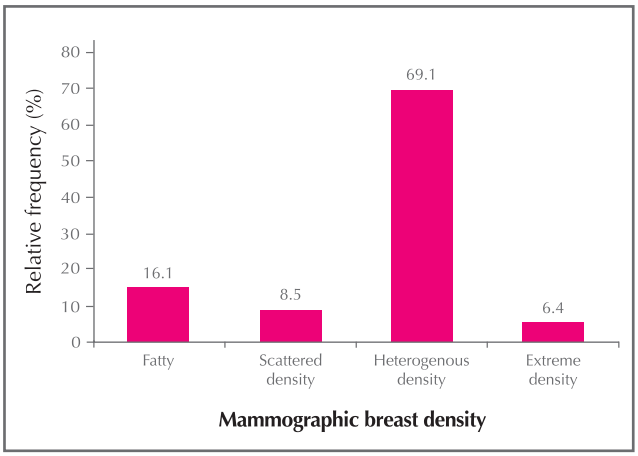

Figure 2.5 Mammographic density of breasts of our patients who were diagnosed through mammography (N=7,661)

Table 2.9 Mammographic density of breasts of our patients who were diagnosed through mammography by age group (N=7,300)

Mammographic density	Age group, Number (%)					
	20-29 (N=47)	30-39 (N=636)	40-49 (N=2,409)	50-59 (N=2,457)	60-69 (N=1,269)	70+ (N=482)
Fatty	3 (6.4)	41 (6.4)	214 (8.9)	396 (16.1)	310 (24.4)	187 (38.8)
Scattered density	2 (4.3)	23 (3.6)	135 (5.6)	225 (9.2)	154 (12.1)	67 (13.9)
Heterogeneous density	36 (76.6)	497 (78.1)	1,851 (76.8)	1,704 (69.4)	758 (59.7)	223 (46.3)
Extreme density	6 (12.8)	75 (11.8)	209 (8.7)	132 (5.4)	47 (3.7)	5 (1.0)

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 86.0% of our patients and among them, 3,427 (26.6%) received FNA solely, 6,543 (50.7%) received CNB solely, and 2,927 (22.7%) received both FNA and CNB. Excisional biopsy was performed in 11.3% of our patients. Excisional biopsy had the highest overall sensitivity of 100%, followed by CNB (98.8%) and FNA (91.7%) (Table 2.10).

Table 2.10 Sensitivity and diagnostic results of breast tissue biopsies (N=14,990)

	FNA (N=6,196)	CNB (N=9,405)	Excisional biopsy (N=1,688)
Proportion of patients using the diagnostic test	41.3%	62.8%	11.3%
Overall sensitivity*	91.7%	98.8%	100.0%
Class			
Diagnostic / malignant (Class V)	3,925 (63.3%)	8,976 (95.4%)	1,688 (100.0%)
Suspicious (Class IV)	1,009 (16.3%)	154 (1.6%)	—
Atypical (Class III)	747 (12.1%)	163 (1.7%)	—
Benign (Class II)	264 (4.3%)	81 (0.9%)	—
Scanty benign (Class I)	251 (4.1%)	31 (0.3%)	—
Incomplete (Class 0)	0 (0.0%)	0 (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 pre-operatively after diagnosis of breast cancer. It is usually conducted in patients with clinically node positive or locally advanced disease. Patients who had only chest x-ray is not considered as having adequate work up and is not included.

Almost half (45.3%) of patients with invasive breast cancer did not have any cancer staging as part of their diagnosis and treatment. Among those who had cancer staging as part of their treatment, the most commonly used method was Positron emission tomography scan (PET scan) (46.0%). A combination of chest x-ray and ultrasound of abdomen was used by 44.0% of our patients (Table 2.11). PET scan was not recommended for patients with early breast cancer, including stage I, stage II, or operable stage III breast cancer, to determine the extent of disease[34]. However, among those who had cancer staging, 18.4% and 36.4% of patients with stages I and IIA diseases, respectively, had PET scan to determine the extent of their disease (Table 2.12).

Table 2.11 Method of clinical staging in 6,178 invasive breast cancer patients

Type of cancer staging method	Number	(%)
Positron emission tomography scan (PET scan)	2,844	(46.0)
Chest X-Ray (CXR) and ultrasound abdomen (USG Abd)	2,716	(44.0)
Computed tomography of body parts*	374	(6.1)
Bone scan	202	(3.3)
Magnetic resonance imaging whole body (MRI whole body)	81	(1.3)
Others (e.g. bone x-ray)	25	(0.4)
Not known	898	(14.5)

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

Table 2.12 The use of PET scan as a form of staging methods in patients with different cancer stages (N=8,908)

	Cancer stage, Number (%)						
	I	IIA	IIB	III	IV	Unstaged	Total
Patients who used PET scan	304 (18.4%)	545 (36.4%)	507 (51.3%)	1,025 (68.5%)	288 (87.3%)	175 (82.2%)	2,844 (46.0%)

Using the American Joint Committee on Cancer (AJCC) Breast Cancer Staging (7th edition)[35] to determine cancer staging in our patient cohort, it was found that the most common cancer stage at diagnosis was stage II (37.3%). 16.4% 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).

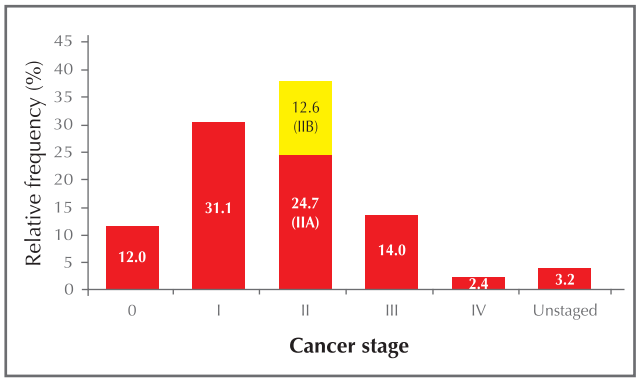

Figure 2.6 Cancer stage at diagnosis in breast cancer patients (N=14,990)

Out of the 14,990 breast cancer cases, data from 13,855 cases with available pathology data was used for the subsequent analyses on cancer characteristics. 11,916 patients (86.0%) were diagnosed with invasive cancers and 1,929 (13.9%) were diagnosed with in situ cancers. 10 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 – 23.0 cm; standard deviation: ±1.5 cm). Tumours of 1 cm or less in size were found in 15.9% 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: 1.5±1.2 cm vs. 2.5±1.8 cm; p<0.001).

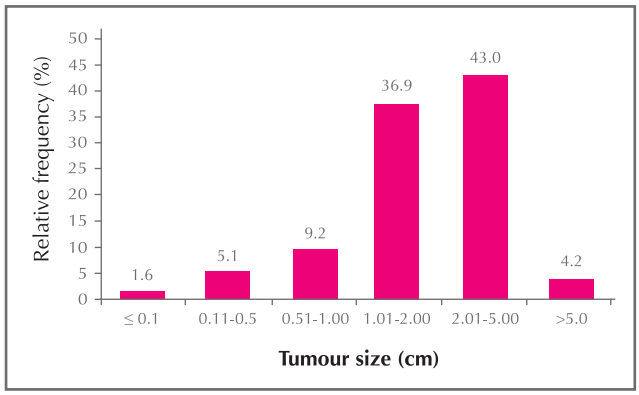

Figure 2.7 Distribution of tumour size (cm) of invasive breast cancers in our cohort (N=11,254)

Lymph node status is one of the factors used to determine breast cancer stage. Multiple affected lymph nodes signify a higher disease stage. Of our patients with invasive breast cancers, 59.3% had no positive lymph nodes, 1.7% had isolated tumour cells, 3.4% had micrometastasis (metastasis size > 0.2 mm to ≤ 2 mm), while 35.6% had at least one positive lymph node with metastasis size greater than 2 mm (Figure 2.8).

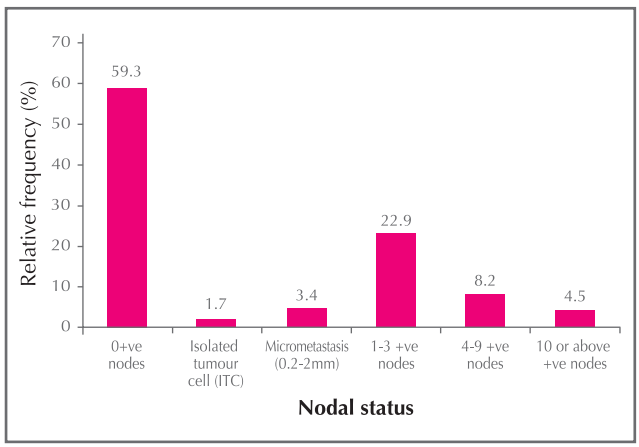

Figure 2.8 Nodal status among our patients with invasive breast cancers (N=11,591)

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 35.0% of our patients while tumours of 2-5 cm in size were found in 30.7% of our patients (Figure 2.9). A small proportion (4.6%) of our patients had in situ tumours greater than 5.0 cm. Of the in situ breast cancers where MMG was performed, 74.5% showed microcalcification on MMG.

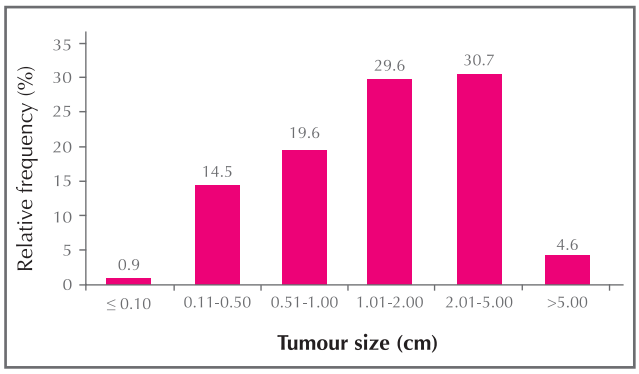

Figure 2.9 Distribution of tumour size (cm) of in situ breast cancers in our cohort (N=1,624)

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 human epidermal growth factor receptor 2 (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 histological type was invasive carcinoma of no specific type (86.2%).

Table 2.13 Histological type, grading, multifocality and multicentricity of invasive breast cancers (N=11,916)

Histological type	Number	(%)
Invasive carcinoma of no specific type	10,272	(86.2)
Lobular	438	(3.7)
Mucinous (colloid)	422	(3.5)
Papillary	124	(1.0)
Tubular	89	(0.7)
Carcinoma with medullary features	72	(0.6)
Mixed ductal and lobular	50	(0.4)
Borderline/ malignant phyllodes	47	(0.4)
Micropapillary	47	(0.4)
Metaplastic carcinoma	44	(0.4)
Carcinoma with neuroendocrine features	24	(0.2)
Carcinoma with apocrine features	16	(0.1)
Adenoid cystic carcinoma	15	(0.1)
Tubulo-lobular carcinoma	6	(0.1)
Paget's disease of nipple	5	(<0.01)
Cribriform carcinoma	4	(<0.01)
Squamous cell carcinoma	3	(<0.01)
Inflammatory	2	(<0.01)
Secretory carcinoma	2	(<0.01)
Lipid rich carcinoma	1	(<0.01)
Sarcoma	1	(<0.01)
Others (e.g. mixed types)	79	(0.7)
Not known	153	(1.3)

	Number	(%)
Grade		
Grade 1	2,080	(17.5)
Grade 2	4,949	(41.5)
Grade 3	3,890	(32.6)
Not known	997	(8.4)
Lymphovascular invasion	**3,365**	**(28.2)**
Multifocality	**1,164**	**(9.8)**
Number of foci		
2	619	(53.2)
3-4	198	(17.0)
≥5	119	(10.2)
Not known	228	(19.6)
Multicentricity	**348**	**(2.9)**
Number of quadrants		
2	299	(85.9)
3	18	(5.2)
4	13	(3.7)
Not known	18	(5.2)

The biological characteristics of invasive breast cancers in the patient cohort are shown in Table 2.14. Among patients with invasive breast cancers who were tested for estrogen or progesterone receptor status, more than three quarters (80.2%) were either estrogen receptor (ER) or progesterone receptor (PR) positive. Amplification or over-expression of the human epidermal growth factor receptor 2 (HER2) oncogene is associated with certain types of breast cancer. A patient with immunohistochemistry (IHC) score 3 is considered as HER2 positive, where score 0 or 1 is considered as negative. For patients with IHC score 2, In Situ Hybridization test will be further performed. Patients who had positive results in ISH test are also considered as HER2 positive. In the patient cohort, 2,424 (21.1%) invasive breast cancers were c-erbB2/HER2 positive.

Table 2.14 Biological characteristics of invasive breast cancers (N=11,916)

	Number	(%)
Estrogen receptor (ER) (97.2% of the patients had the test)		
Positive	9,092	(78.5)
Negative	2,494	(21.5)
Progesterone receptor (PR) (97.0% of the patients had the test)		
Positive	7,673	(66.4)
Negative	3,890	(33.6)
c-erbB2/ HER2 (96.6% of the patients had the test)		
Positive (IHC score 3)	2,183	(19.0)
Equivocal (IHC Score 2) ISH positive	241	(2.1)
Equivocal (IHC Score 2) ISH equivocal	82	(0.7)
Equivocal (IHC Score 2) ISH negative	1,939	(16.8)
Equivocal (IHC Score 2) ISH not done	1,442	(12.5)
Negative (IHC Score 0 / 1)	5,624	(48.9)
Ki-67 index (54.3% of the patients had the test)		
<14%	2,594	(40.1)
≧14%	3,882	(59.9)

HER2: Human epidermal growth factor receptor 2
IHC: Immunohistochemistry
ISH: In Situ Hybridization

Breast cancer is not considered as a single disease and can be further classified into several biological subtypes[36], determined by immunohistochemical staining of several biological markers described in Table 2.14. By combining these biological markers rather than assessing them independently, further prognostic and predictive information can be obtained. The surrogate definitions of these intrinsic biological subtypes and their relative frequencies by cancer stage in the patient cohort are shown in Table 2.15.

Table 2.15 Biological subtypes of invasive tumours by cancer stage (N=11,319)

	Cancer Stage, N (%)											
Biological subtypes	**I**		**IIA**		**IIB**		**III**		**IV**		**Total**	
Luminal A*	1,202	(27.0)	596	(17.2)	269	(16.3)	198	(13.2)	31	(12.3)	2,296	(20.3)
Luminal B (HER2 negative)#	726	(16.3)	709	(20.5)	351	(21.3)	346	(23.0)	42	(16.7)	2,174	(19.2)
Luminal A/B (HER2 negative)†	1,252	(28.1)	915	(26.4)	486	(29.5)	417	(27.8)	81	(32.1)	3,151	(27.8)
Luminal B (HER2 positive)^	504	(11.3)	439	(12.7)	216	(13.1)	245	(16.3)	48	(19.0)	1,452	(12.8)
HER2-positive❊	335	(7.5)	298	(8.6)	130	(7.9)	151	(10.1)	23	(9.1)	937	(8.3)
TND§	438	(9.8)	504	(14.6)	195	(11.8)	145	(9.7)	27	(10.7)	1,309	(11.6)
Total	**4,457**	**(39.4)**	**3,461**	**(30.6)**	**1,647**	**(14.6)**	**1,502**	**(13.3)**	**252**	**(2.2)**	**11,319**	**(100.0)**

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

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

† Luminal A/B (HER2 negative): ER and/or PR+, HER2-, and Ki-67 index 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 and 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 cancers (93.2%).

Table 2.16 Histological type, grading, multifocality and multicentricity of in situ breast cancers (N=1,929)

	Number	(%)
Histological type		
Ductal	1,802	(93.2)
Mixed	53	(2.9)
Papillary	34	(1.6)
Intracystic papillary	14	(0.8)
Encapsulated papillary	8	(0.4)
Apocrine	6	(0.3)
Neuroendocrine	2	(0.1)
Micropapillary	1	(0.1)
Not known	9	(0.5)
Necrosis	**673**	**(34.9)**
Nuclear Grade		
Low	485	(25.1)
Intermediate	630	(32.7)
High	721	(37.4)
Not known	93	(4.8)
Multifocality	**235**	**(12.2)**
Number of foci		
2	107	(45.5)
3	21	(8.9)
4 or more	8	(3.4)
Not known	99	(42.1)
Multicentricity	**49**	**(2.5)**
Number of quadrants		
2	41	(83.7)
3	3	(6.1)
Not known	5	(10.2)

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 estrogen or progesterone receptor status, 82.1% were either estrogen receptor (ER) or progesterone receptor (PR) positive. Among the 452 patients who had HER2 IHC score 2, two showed positive results in ISH test, therefore 347 (27.1%) in situ breast cancers in our patient cohort were c-erbB2/HER2 positive.

Table 2.17 Biological characteristics of in situ breast cancers (N=1,929)

	Number	(%)
Estrogen receptor (ER) (73.2% of the patients had the test)		
Positive	1,144	(81.0)
Negative	268	(19.0)
Progesterone receptor (PR) (71.9% of the patients had the test)		
Positive	1,002	(72.3)
Negative	384	(27.7)
c-erbB2/HER2 (66.4% of the patients had the test)		
Positive (IHC score 3)	345	(27.0)
Equivocal (IHC score 2)	452	(35.3)
Negative (IHC score 0/1)	483	(37.7)
Ki-67 index (40.9% of the patients had the test)		
<14%	517	(65.6)
≧14%	271	(34.4)

HER2: Human epidermal growth factor receptor 2
IHC: Immunohistochemistry

2.4 Treatment methods

Of our 14,990 patients, 14.7% solely received care at private medical services, while 49.9% solely received care at public medical services. Around one-third (35.4%) 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, anti-HER2 targeted therapy, endocrine therapy, and radiotherapy; while patients with in situ tumour require less aggressive treatments including surgery, endocrine therapy, and radiotherapy. Chemotherapy and anti-HER2 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 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 unnecessary lymphoedema which may occur when a large number of lymph nodes are removed by surgery.

In our patient cohort, 51.6% of our patients had surgery at private medical facilities, while 48.4% had surgery at public medical facilities.

For patients with in situ tumour, almost all (99.3%) of them underwent surgery. Around half (51.4%) of them had breast-conserving surgery. Among patients who had mastectomy, 204 patients (22.1%) had reconstruction after mastectomy. One-third (33.3%) of them did not receive nodal surgery, while among those who received nodal surgery, majority (84.2%) of them had SNB alone and 11.9% received axillary dissection without SNB.

For patients with invasive tumour, majority (97.9%) of them underwent surgery as part of their treatment. Two-thirds (64.8%) of patients had mastectomy, while 32.9% had breast-conserving surgery. Among the patients who had mastectomy, 11.7% had either immediate or delayed reconstruction. The most common type of reconstruction was TRAM flap (70.5%) (Table 2.18). Almost all (96.6%) of the patients with invasive tumours received nodal surgery and among them, more than half (57.7%) of patients with invasive tumour required AD, while 41.3% required SNB only.

Table 2.18 Types of surgical operations in the patient cohort (N=14,948)

	Patients with invasive cancer (N=13,008)		Patients with in situ cancer (N=1,940)	
	Number	(%)	Number	(%)
No surgery	233	(1.8)	13	(0.7)
Breast-conserving surgery	4,274	(32.9)	998	(51.4)
Mastectomy	8,431	(64.8)	925	(47.7)
Nodal surgery only	11	(0.1)	0	(0.0)
Type of surgery not known	24	(0.2)	4	(0.2)
Not known if surgery done	35	(0.3)	0	(0.0)
Mastectomy (N=9,356)				
Total mastectomy	7,942	(94.2)	797	(86.2)
Skin sparing	362	(4.3)	99	(10.7)
Areolar sparing	13	(0.2)	4	(0.4)
Nipple sparing	94	(1.1)	24	(2.6)
Not known type of mastectomy	20	(0.2)	1	(0.1)
Reconstruction (N=1,190)				
TRAM flap	695	(70.5)	125	(61.3)
Implant	146	(14.8)	56	(27.5)
LD flap	79	(8.0)	12	(5.9)
LD flap & implant	48	(4.9)	10	(4.9)
Not known type of reconstruction	18	(1.8)	1	(0.5)
Nodal surgery (N=13,855)				
Sentinel node biopsy	5,186	(41.3)	1,090	(84.2)
Axillary dissection	5,149	(41.0)	154	(11.9)
Sentinel node biopsy & axillary dissection	2,096	(16.7)	35	(2.7)
Not known type of nodal surgery	130	(1.0)	15	(1.2)

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

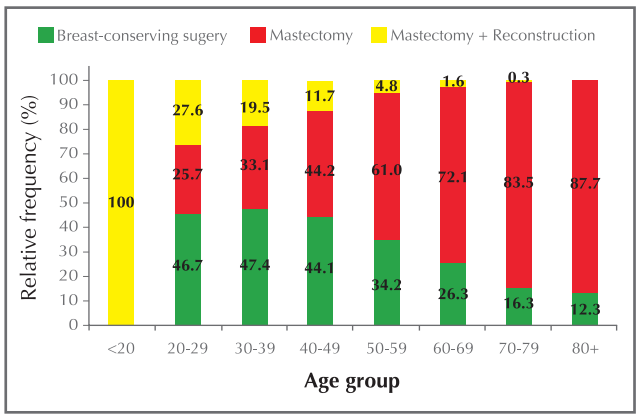

Figure 2.10 Type of surgery by age group (N=13,703)

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).

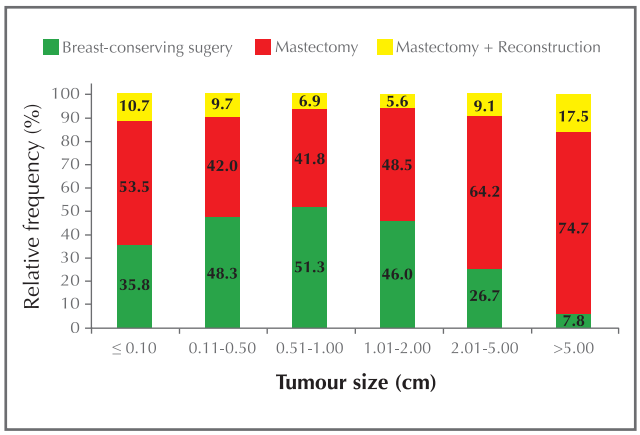

Figure 2.11 Type of surgery by tumour size (N=13,542)

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

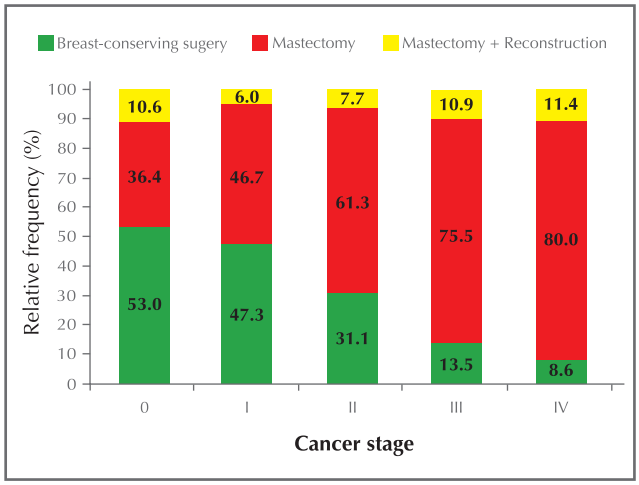

Figure 2.12 Type of surgery by cancer stage (N=14,280)

A higher proportion (45.1%) of patients who had surgery at private medical facilities underwent breast-conserving surgery, compared with 27.0% of those who had surgery at public medical facilities (Figure 2.13).

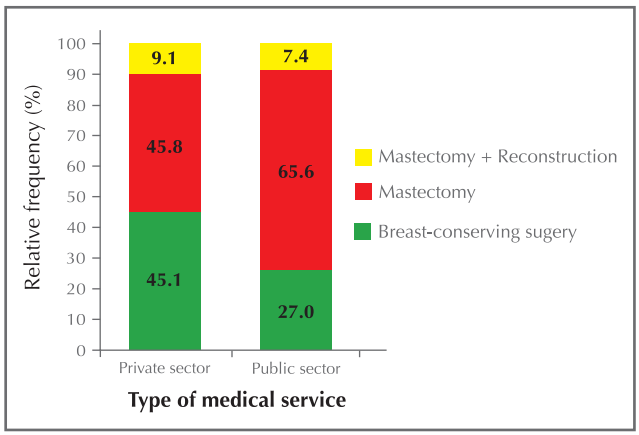

Figure 2.13 Type of surgery by type of medical service (N=14,149)

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 (53.6% vs 15.5%). 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 (71.8% vs 30.2%).

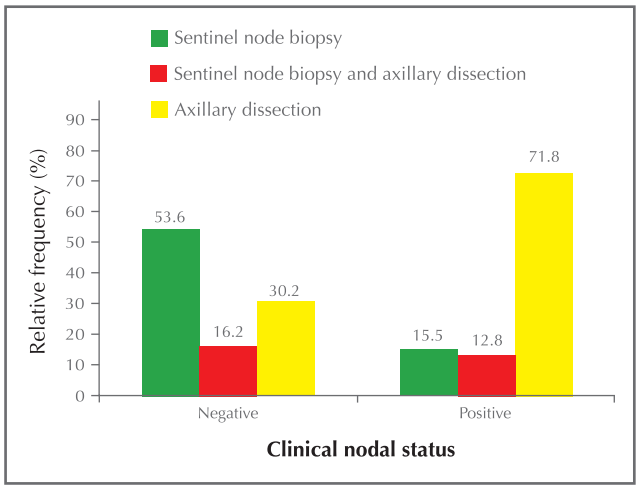

Figure 2.14 Type of nodal surgery by clinical nodal status (N=13,723)

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 received AD as their first nodal surgery (Figure 2.15).

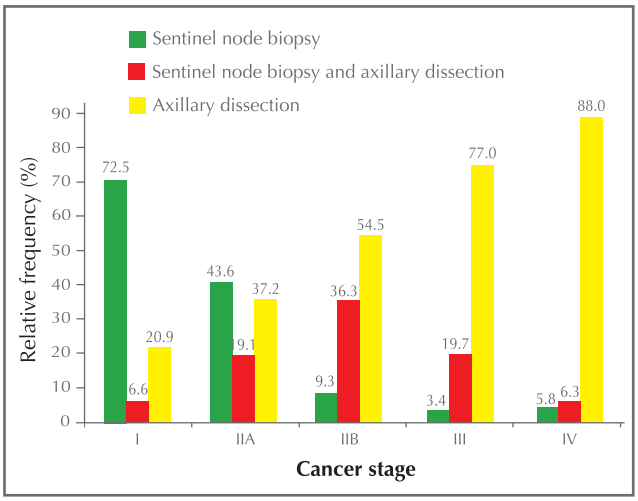

Figure 2.15 Type of nodal surgery in invasive cancer by cancer stage (N=12,180)

Around half (55.4%) of our patients with node positive invasive cancer had tumours of 2 to 5 cm in size, while 9.5% 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 (61.7% vs. 35.2%) (Figure 2.16).

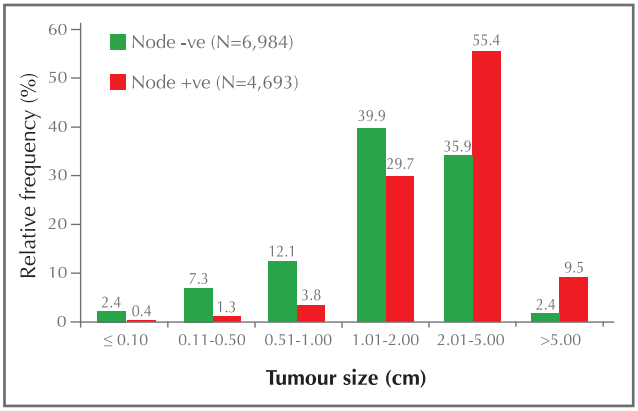

Figure 2.16 Distribution of tumour size in invasive cancer with negative or positive nodal status (N=11,677)

95.8% of patients who underwent SNB alone had no positive lymph node, while almost half (44.7%) of our patients who underwent AD and 16.7% of our patients who underwent AD after SNB had no positive lymph node (Figure 2.17).

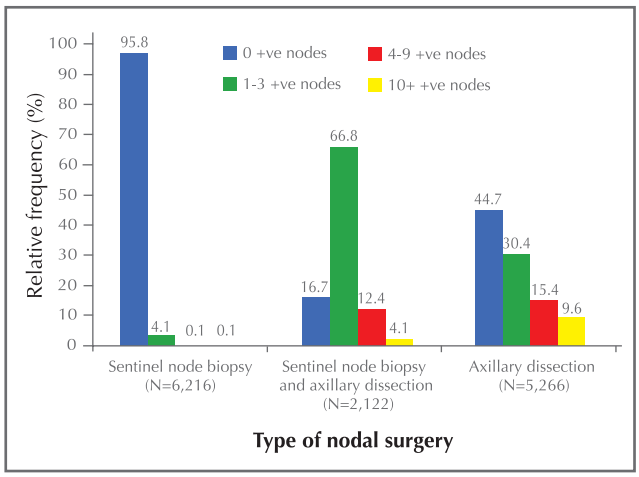

Figure 2.17 Number of positive nodes by type of nodal surgery (N=13,604)

2.4.2 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 affected lymph nodes, or where cancer cells are found in the lymphatic or blood vessels.

In our patient cohort, 9,262 (61.8%) patients had radiotherapy as one of their treatment, among which 97.9% were adjuvant, 0.2% were neoadjuvant, and 1.9% were palliative. 88.1% of our patients were treated with radiotherapy at public medical facilities, while 11.9% had radiotherapy at private medical facilities.

Of our patients with in situ cancer who had breast-conserving surgery, majority (94.0%) of them were treated with radiotherapy afterwards (Figure 2.18), while only 3.3% of our patients with in situ cancer who had mastectomy underwent radiotherapy (Figure 2.19).

The use of radiotherapy in our patients receiving breast-conserving surgery and mastectomy, respectively, are shown in Figures 2.18 and 2.19. Over 94% of invasive breast cancer patients with breast-conserving surgery underwent radiotherapy, while the use of radiotherapy in invasive breast cancer patients with mastectomy increased with progressing cancer stages, with the exception of stage IV disease.

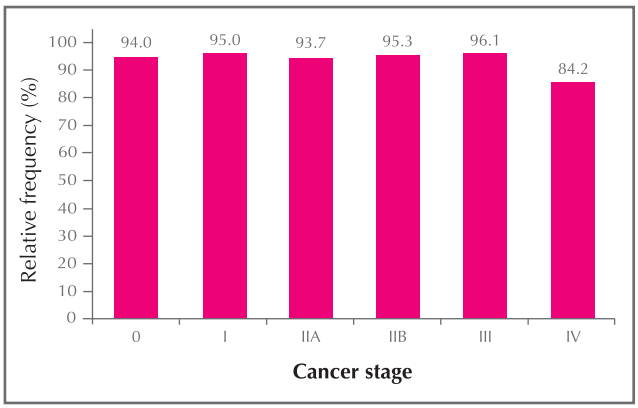

Figure 2.18 The use of radiotherapy in our patients receiving breast-conserving surgery at different cancer stages (N=5,177)

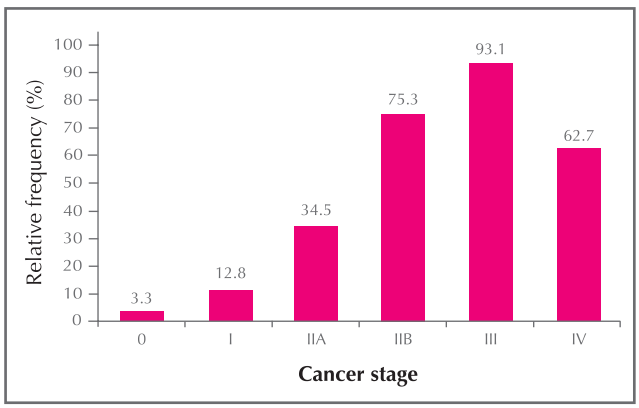

Figure 2.19 The use of radiotherapy in our patients receiving mastectomy at different cancer stages (N=9,113)

Radiotherapy for breast cancer involves localized irradiation of regions such as breast/chest wall, with or without regional nodes. Table 2.19 shows the irradiated regions among our patients receiving radiotherapy by the type of surgery received.

Table 2.19 Irradiated regions among our patients with different types of surgery (N=6,067)

	Total# (N=6,067)		Breast-conserving surgery (N=3,116)		Mastectomy (N=2,888)	
Target volume	**Number**	**(%)**	**Number**	**(%)**	**Number**	**(%)**
Breast	2,632	(43.4)	2,611	(83.8)	0	(0.0)
Breast + regional*	540	(8.9)	505	(16.2)	0	(0.0)
Chest wall	750	(12.4)	0	(0.0)	744	(25.8)
Chest wall + regional*	2,145	(35.4)	0	(0.0)	2,144	(74.2)

* regional nodes: includes supraclavicular fossa and/or axilla and/or internal mammary chain
# Total number of patients includes 63 patients with radiotherapy details not known

2.4.3 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 for stage IV metastatic disease (palliative).

8,838 (67.9%) patients with invasive cancer in the cohort underwent chemotherapy. 85.2% of our patients had adjuvant chemotherapy, 11.2% had neoadjuvant chemotherapy, and 3.6% had palliative chemotherapy. 86.5% of our patients received chemotherapy in public medical facilities, while 13.5% received in private medical facilities.

In our patient cohort, the use of chemotherapy with curative intent was positively correlated to progressing cancer stage for early stage disease (stage I to III). Not all, but 85.1% of the patients with stage IV cancers underwent palliative chemotherapy (Figure 2.20).

Table 2.20 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, stage IIA, or stage IIB disease, the use of chemotherapy decreased with increasing age group.

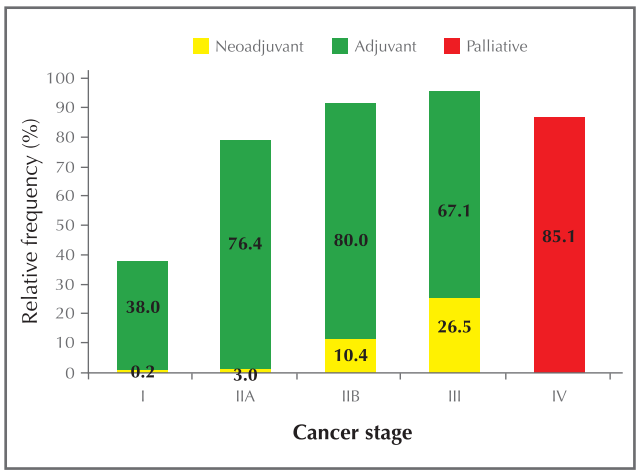

Figure 2.20 The use of chemotherapy in our patients at different cancer stages (N=12,556)

Table 2.20 Use of chemotherapy by age group and cancer stage at diagnosis (N=11,779)

	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	21	(67.7)	23	(92.0)	18	(100.0)	14	(100.0)	3	(100.0)
30-39	239	(58.2)	333	(91.5)	171	(99.4)	187	(98.9)	26	(92.9)
40-49	714	(45.9)	994	(90.0)	558	(97.4)	676	(98.8)	103	(96.3)
50-59	541	(39.9)	975	(88.4)	581	(96.8)	634	(97.7)	102	(87.9)
60-69	170	(24.7)	420	(69.5)	266	(89.9)	302	(93.8)	34	(87.2)
70-79	6	(2.8)	23	(11.9)	17	(18.3)	35	(40.2)	9	(42.9)
80+	0	(0.0)	1	(2.2)	0	(0.0)	2	(12.5)	2	(33.3)

2.4.3.1 Neoadjuvant chemotherapy

Out of 8,838 patients who underwent chemotherapy, 986 patients received it as neoadjuvant treatment. The use of neoadjuvant chemotherapy increased substantially with progressing cancer stage, from 0.2% of stage I patients to 26.5% of stage III patients (Figure 2.20). The regimens used by patients with different biological subtypes are shown in Figure 2.21.

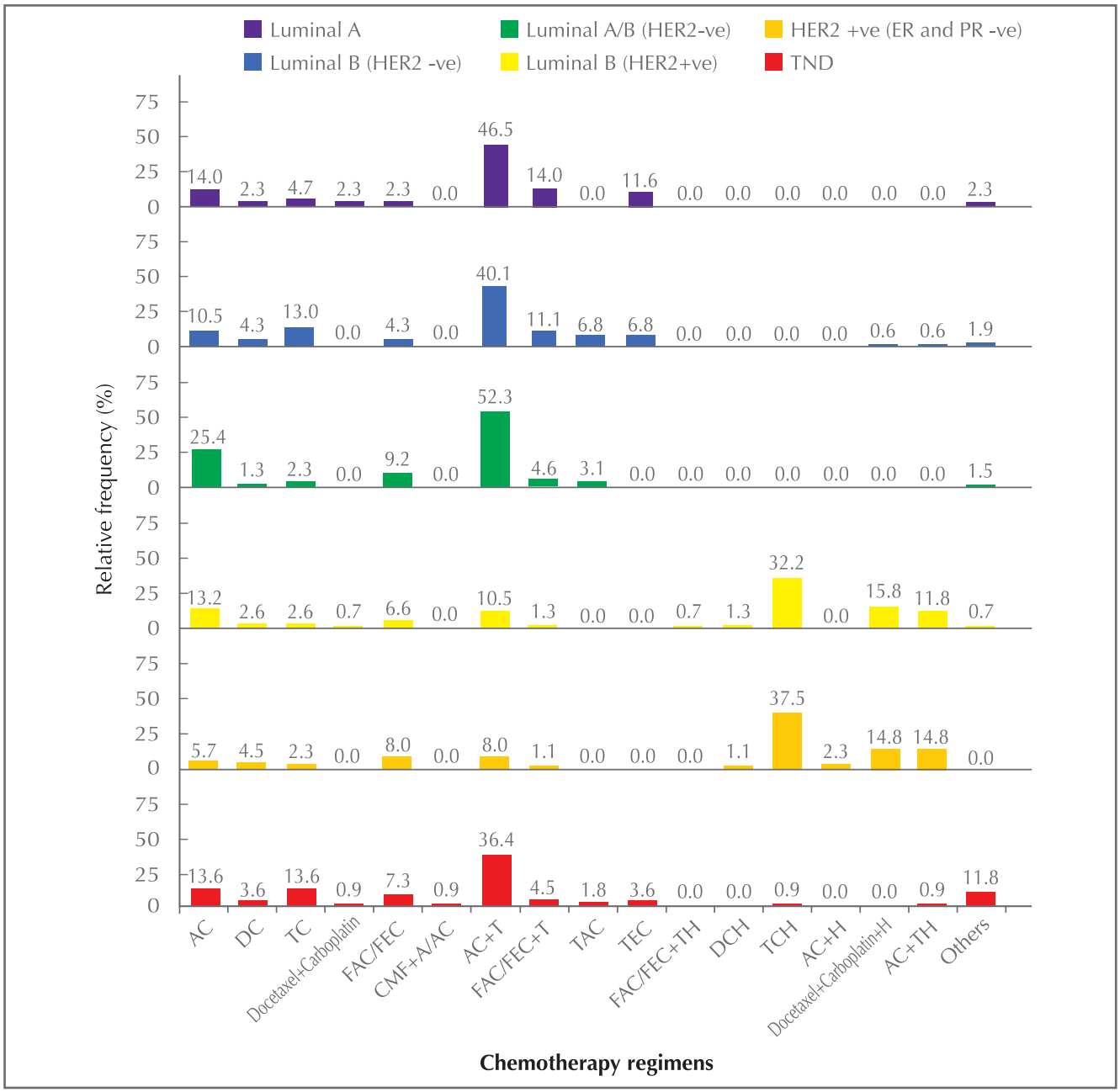

Figure 2.21 Type of chemotherapy regimens in neoadjuvant setting in patients by biological subtype (N=685)

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

2.4.3.2 Adjuvant chemotherapy

Of the 8,838 patients who underwent chemotherapy, 7,531 (85.2%) received it as adjuvant (Stage I-III) treatment. Figures 2.22 and 2.23 show the relative frequency for different types of chemotherapy regimen used by patients with different biological subtypes and cancer stages, respectively, in our patient cohort.

2.4.3.3 Palliative chemotherapy

Of the 8,838 patients who underwent chemotherapy, 321 (3.6%) received it as palliative (Stage IV) treatment. Figure 2.24 shows the relative frequency for different types of chemotherapy regimen used by patients with different biological subtypes in our patient cohort.

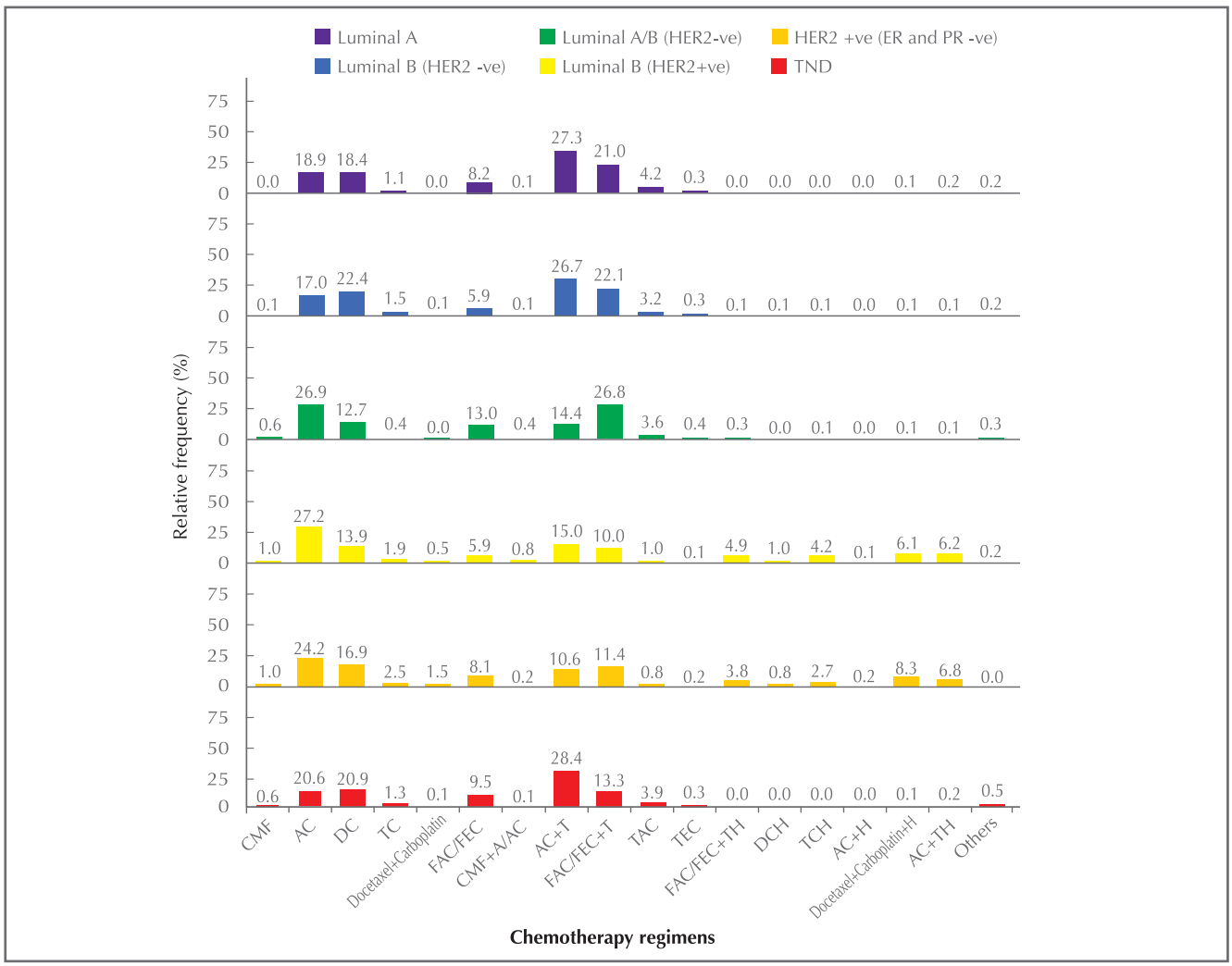

Figure 2.22 Type of chemotherapy regimens in adjuvant setting in patients by biological subtype (N=6,259)

C: Cyclophosphamide;
M: Methotrexate;
F: Fluorouracil (5FU);
A: Adriamycin / Doxorubicin;
E: Epirubicin;
T: Paclitaxel / Docetaxel;
H: Trastuzumab;
DC: Docetaxel + Cyclophosphamide;
DCH: Docetaxel + Cyclophosphamide + Trastuzumab
TC: Paclitaxel + Carboplatin;
TCH: Paclitaxel + Carboplatin + Trastuzumab
Others: Capecitabine, Gemcitabine, or Vinorelbin

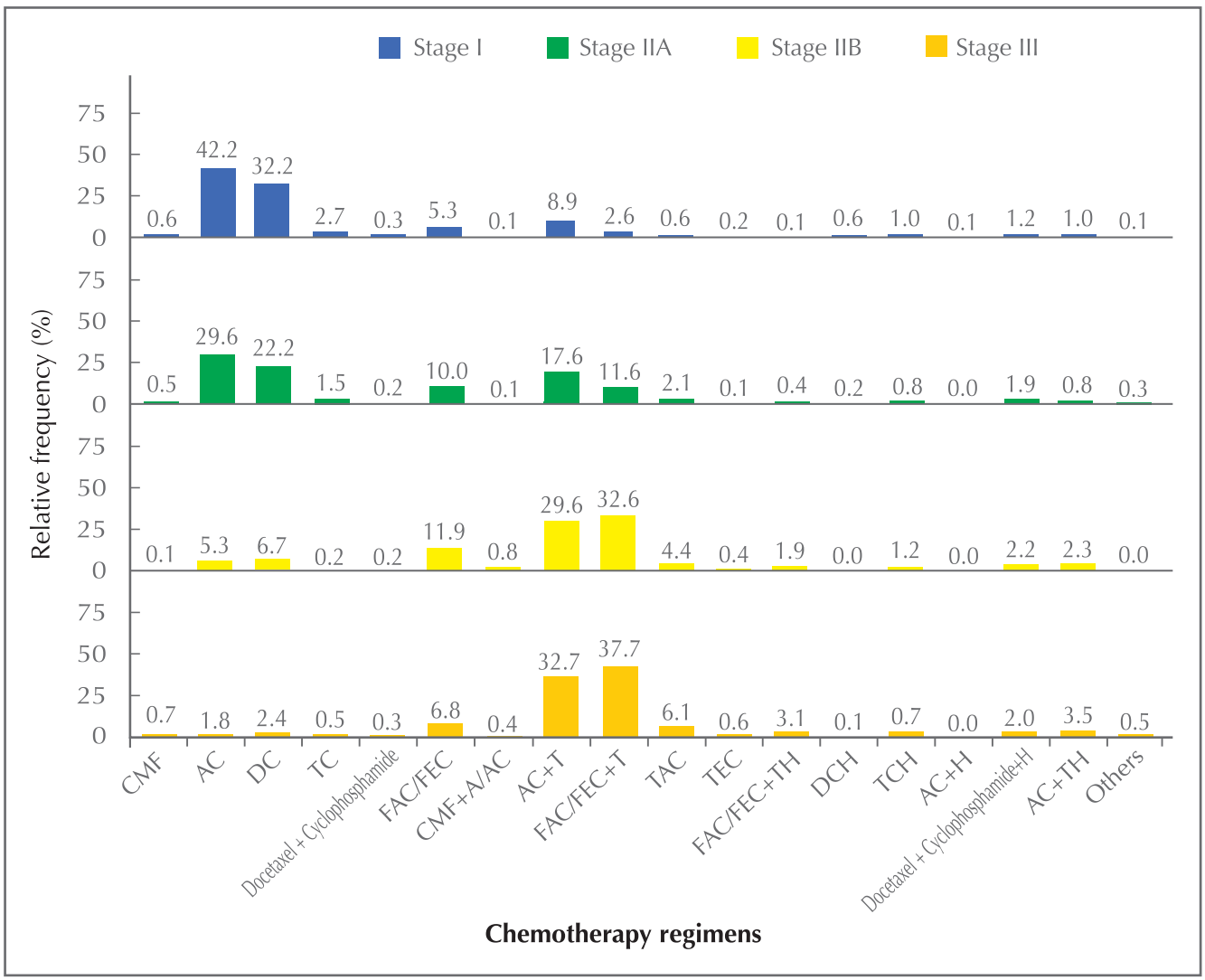

Figure 2.23 Type of chemotherapy regimens in adjuvant setting in patients by cancer stage (N=6,356)

C: Cyclophosphamide;
M: Methotrexate;
F: Fluorouracil (5FU);
A: Adriamycin / Doxorubicin;
E: Epirubicin;
T: Paclitaxel / Docetaxel;
H: Trastuzumab;
DC: Docetaxel + Cyclophosphamide;
DCH: Docetaxel + Cyclophosphamide + Trastuzumab
TC: Paclitaxel + Carboplatin;
TCH: Paclitaxel + Carboplatin + Trastuzumab
Others: Capecitabine, Gemcitabine, or Vinorelbin

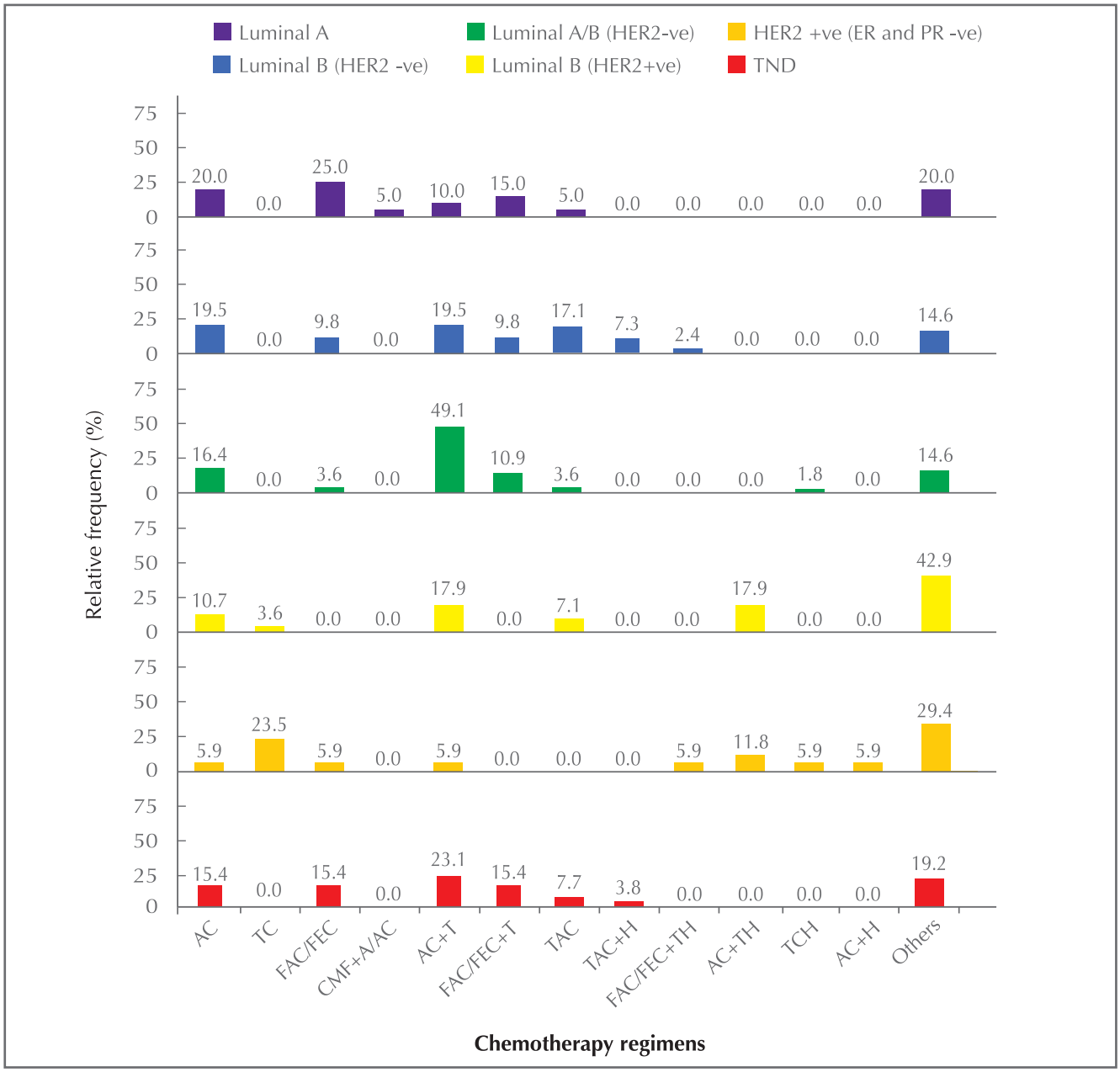

Figure 2.24 Type of chemotherapy regimens in palliative setting in patients by biological subtype (N=187)

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

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, 10,097 (67.4%) patients were treated with endocrine therapy. Among them, 96.8% were adjuvant, 0.5% were neoadjuvant, and 2.8% were palliative. 90.5% of our patients received endocrine therapy at public medical facilities, while 9.5% received at private medical facilities.

Endocrine therapy was used in 11.7% of our patients with in situ breast cancer, but was used in over 73% of our patients with stages I-IV breast cancer (Figure 2.25).

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 attaching and blocking 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 2.26 shows the use of Tamoxifen and Aromatase inhibitors by our patient cohort in three age groups.

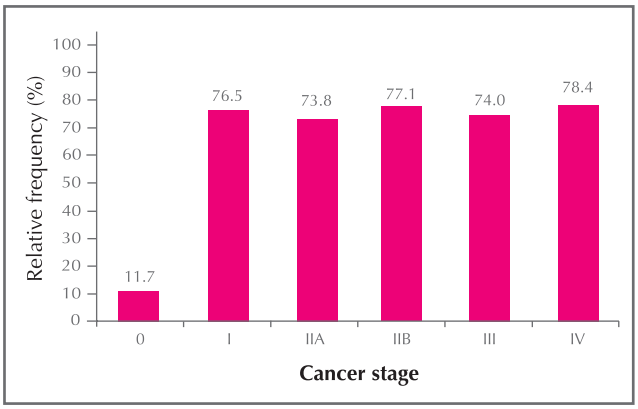

Figure 2.25 The use of endocrine therapy in our patients by cancer stage (N=14,504)

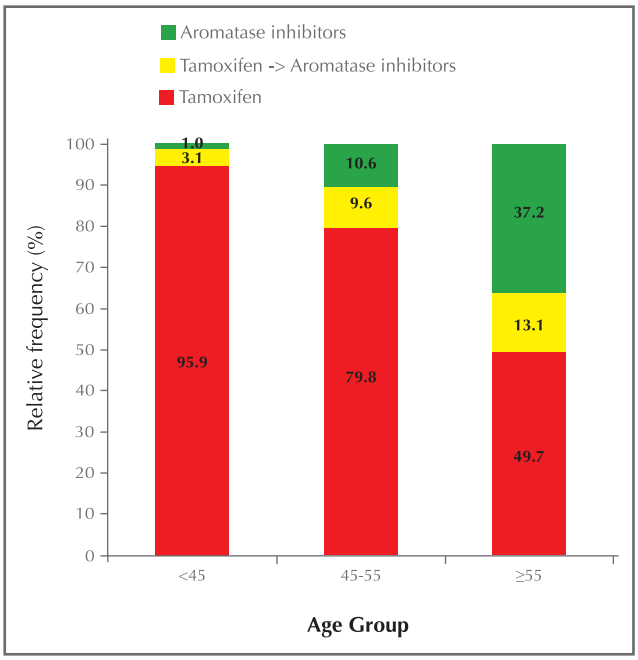

Figure 2.26 Forms of endocrine therapy used in our patient cohort by age group (N=8,903)

2.4.5 Anti-HER2 targeted therapy

Anti-HER2 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 oncogene (HER2-positive breast cancer).

Of the 2,844 patients with invasive HER2-positive breast cancers in our cohort, 1,657 (58.3%) underwent anti-HER2 targeted therapy. Among them, 92.1% were adjuvant, 4.5% were neoadjuvant, and 3.4% were palliative. Majority (88.7%) of our patients received anti-HER2 targeted therapy at public medical facilities, while 11.3% received at private medical facilities. The use of anti-HER2 targeted therapy was positively correlated with increasing cancer stage (Figure 2.27).

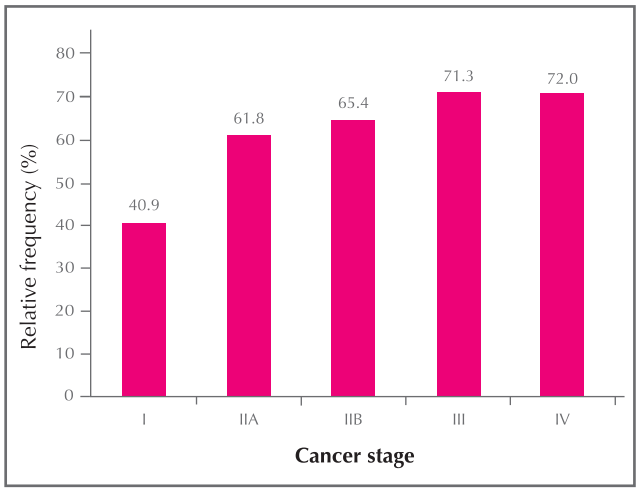

Figure 2.27 The use of anti-HER2 targeted therapy in HER2 positive patients by cancer stage in our cohort (N=2,777)

2.4.6 Multimodality treatment

Combinations of treatments, including surgery, chemotherapy, radiotherapy, endocrine therapy, and anti-HER2 targeted therapy are usually used for treating breast cancer effectively. Table 2.21 shows the multimodality treatment pattern of our patients. In general, the number of treatments increased with increasing cancer stage. In our patient cohort, majority (93.9%) of patients with stage 0 disease received two or less treatments, while 61.0% 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=14,051)

No. of treatment	Cancer Stage, Number (%) 0 (N=1,752)	I (N=4,526)	IIA (N=3,585)	IIB (N=1,834)	III (N=2,028)	IV (N=326)	Total (N=14,051)
0	3 (0.2)	1 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	2 (0.6)	8 (0.1)
1	738 (42.1)	295 (6.5)	68 (1.9)	12 (0.7)	11 (0.5)	26 (8.0)	1,150 (8.2)
2	908 (51.8)	1,468 (32.4)	649 (18.1)	113 (6.2)	46 (2.3)	53 (16.3)	3,237 (23.0)
3	101 (5.8)	1,909 (42.2)	1,338 (37.3)	510 (27.8)	377 (18.6)	108 (33.1)	4,343 (30.9)
4	1 (0.1)	738 (16.3)	1,372 (38.3)	1,029 (56.1)	1,316 (64.9)	111 (34.0)	4,567 (32.5)
5	1 (0.1)	115 (2.5)	158 (4.4)	170 (9.3)	276 (13.6)	26 (8.0)	746 (5.3)

2.4.7 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. 5,897 (39.3%) of the patients in the cohort received complementary and alternative therapies as part of their treatment. Among them, 95.4% were adjuvant, 3.4% were neoadjuvant, and 1.2% were palliative. 66.1% of our patients used traditional Chinese medicines (Figure 2.28).

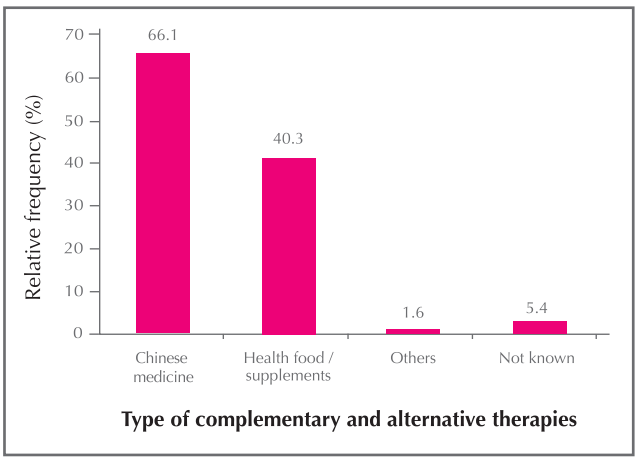

Figure 2.28 Type of complementary and alternative therapies used in 5,897 patients

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

2.5 Patient Status

Once treatment is completed, patients registered with the HKBCR were followed up annually to ascertain the efficacy of the treatment. To date, 13,235 patients in our cohort were followed up and 59.8% of them had the last follow-up within the last two years. About one-third (30.3%) of our patients were followed up for 5 or more years (Table 2.22). The mean and median follow-up period were 3.9 and 3.4 years, respectively.

596 (4.5%) of patients in our cohort experienced recurrence, where 1.3% of our patients experienced locoregional recurrence (LR) solely, 2.1% experienced distant recurrence (DR) solely, and 1.1% experienced both locoregional and distant recurrence concurrently or sequentially. The mean and median time to recurrence are shown in Table 2.22.

Table 2.22 Follow-up of 13,235 patients

Follow-up period	Number	(%)
< 1 year	1,068	(8.1)
1-2 years	2,551	(19.3)
2-5 years	5,609	(42.4)
5-10 years	3,839	(29.0)
10-15 years	168	(1.3)
Mean follow-up period		3.9 years
Median follow-up period		3.4 years
Locoregional recurrence		
No. of locoregional recurrences	170	(1.3)
Mean time to locoregional recurrence		2.8 years
Median time to locoregional recurrence		2.4 years
Distant recurrence		
No. of distant recurrences	275	(2.1)
Mean time to distant recurrence		2.9 years
Median time to distant recurrence		2.7 years
Locoregional and distant recurrence		
No. of locoregional and distant recurrences	151	(1.1)
Mean time to locoregional and distant recurrence		3.1 years
Median time to locoregional and distant recurrence		2.8 years
Mortality		
No. of deaths from breast cancer	130	(1.0)
No. of deaths from unrelated causes	82	(0.6)
No. of deaths with causes not known	31	(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. Of our patient with stage IIA disease, the proportion of patients with LR was higher among patients with breast-conserving surgery than those who received mastectomy. Among our patients with stage I, IIA or IIB disease, the proportions suffered from LR was lower in patients who had undergone BCS followed by radiotherapy than those who underwent BCS without radiotherapy (the number of patients with stage III disease who did not receive radiotherapy might be too low to observe such difference) (Table 2.23). The common sites for locoregional recurrence were chest wall (36.4%) and breast (30.5%) (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 with RT	18/1,820	26/1,056	3/374	10/242	57/3,492
	(1.0)	(2.5)	(0.8)	(4.1)	(1.6)
BCS without RT	5/92	3/61	1/13	0/9	9/175
	(5.4)	(4.9)	(7.7)	(0.0)	(5.1)
MTX	34/2,147	41/2,130	27/1,295	77/1,605	179/7,177
	(1.6)	(1.9)	(2.1)	(4.8)	(2.5)

BCS: Breast-conserving surgery; MTX: Mastectomy

Table 2.24 Sites involved in locoregional recurrence in our patients (N=321)

Sites involved	Number	(%)
Chest wall	117	(36.4)
Breast	98	(30.5)
Axilla	96	(29.9)
Supraclavicular fossa	69	(21.5)
Internal mammary node	27	(8.4)
Infraclavicular fossa	4	(1.2)
Others	20	(6.2)

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

In our patient cohort, 426 (3.2%) patients experienced distant recurrence. Among them, the common organs involved were bone (55.2%), followed by lung (46.5%) (Table 2.25). One-third of the patients experienced distant recurrence that involved liver (39.0%).

Table 2.25 Organs involved in distant recurrence (N=426)

Distant organs affected	Number	(%)	Distant organs affected	Number	(%)
Bone	235	(55.2)	Peritoneal	6	(1.4)
Lung	198	(46.5)	Ovary	4	(0.9)
Liver	166	(39.0)	Spleen	4	(0.9)
Mediastinal nodes	71	(16.7)	Thyroid glands	3	(0.7)
Brain	68	(16.0)	Pancreas	2	(0.5)
Distant lymph nodes	41	(9.6)	Thorax	2	(0.5)
Neck	28	(6.6)	Kidney	1	(0.2)
Contralateral axillary nodes	12	(2.8)	Uterus	1	(0.2)
Adrenal	8	(1.9)	Unspecified	18	(4.2)
Abdomen	6	(1.4)			

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 did not show any associations with cancer stage at diagnosis. However, the proportion of our patients with DR solely increased from 0.8% of stage I patients to 5.3% of stage III patients. The proportion of our patients with LR and DR also showed positive correlation with increasing cancer stage, from 0.3% of stage I patients to 2.9% of stage III patients (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=4,663)	IIA (N=3,700)	IIB (N=1,887)	III (N=2,102)	Total (N=12,352)
LR solely	42 (0.9)	42 (1.1)	8 (0.4)	28 (1.3)	120 (1.0)
DR solely	38 (0.8)	52 (1.4)	46 (2.4)	112 (5.3)	248 (2.0)
LR and DR	15 (0.3)	29 (0.8)	23 (1.2)	60 (2.9)	127 (1.0)

130 (1.0%) patients in the cohort died from breast cancer. More than half (60.5%) of the patients who died from breast cancer were diagnosed with stage III or IV disease at initial diagnosis. Survival time ranged from 0.6 – 11.1 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=130)

	Cancer stage at initial diagnosis						
	0	I	IIA	IIB	III	IV	Unstaged
No. of cases (% of breast cancer death cases)	**1 (0.8)**	**15 (11.5)**	**16 (12.3)**	**9 (6.9)**	**56 (43.1)**	**22 (16.9)**	**11 (8.5)**
Survival time (range in years)	**4.4**	**1.6 – 6.8**	**1.9 – 8.9**	**2.1 – 11.1**	**0.8 – 9.4**	**0.8 – 7.3**	**0.6 – 6.2**
Biological subtypes							
Luminal A*	0	3	2	1	7	0	0
Luminal B (HER2 negative)#	0	3	3	0	8	2	1
Luminal A/B (HER2 negative)†	0	2	3	3	12	9	2
Luminal B (HER2 positive)^	1	2	2	0	9	5	2
HER2 Positive ❊	0	2	1	0	12	3	0
TND§	0	3	4	4	7	1	2
Not known	0	0	1	1	1	2	4

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

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

† Luminal A/B (HER2 negative):ER and/or PR+, HER2-, and Ki67 index not known

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

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

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