CHAPTER 2

DISEASE PATTERN, TREATMENT TREND AND CLINICAL OUTCOME OF BREAST CANCER

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Apart from demographics and risk factors, the clinical management of breast cancer with different cancer characteristics provide important information which can be useful in understanding the current status of breast cancer in Hong Kong. In this chapter, clinical presentation, cancer characteristics, histological and biological characteristics as well as treatment methods of the patient cohort are studied.

KEY FINDINGS

I. Clinical presentations

► In the cohort of 6,848 patients, 87.1% self-discovered their breast cancer by chance.

► 82.1% of the patients were diagnosed at early stages (stages 0-II); 14.1% were diagnosed at advanced stages (stages III-IV) and 3.8% were unstaged. Of them, 5,822 (85%) had invasive breast cancer.

► 1,589 patients (23.2%) were diagnosed and treated at private medical facilities; 2,797 (40.8%) had their treatment at public medical facilities; 2,462 (36.0%) used both private and public medical service.

► 30.8% of the patients sought medical consultation within one month of the onset of symptoms. 27.6% of the patients took more than 12 months to seek their first medical consultation.

► Mammography was used in the diagnosis of 80.5% of the patients, while ultrasound screening was used in 74.5% and magnetic resonance imaging was used in only 6.1% of the patients.

► Malignancy was confirmed by fine needle aspiration in 49.3% of the patients, while core needle biopsy was used in 44.5% of patients and excisional biopsy was used in 14.8% of the patients.

► The tests most commonly used in cancer staging in the patient cohort were chest X-rays / abdominal ultrasound (64.5%), PET scan (17.7%) and bone scan (3.8%).

► Tumour size ranged from 0.01-22cm. The mean tumour size of invasive breast cancer in self-detected cases vs screen-detected cases: 2.3cm vs. 1.9cm. Nearly half (48.1%) of the patients had tumours larger than 2cm.

► The most common biological subtype was ER+PR+HER2- (47.3%), while ER-PR+HER2+ (1.1%) was the least common. 12.6% of the cases were triple negative (ER-PR-HER2-); 11.4% were ER+PR+HER2+; 4.7% were ER+PR-HER2+; 1.1% were ER-PR+HER2+ and 10.5% were ER-PR-HER2+.

► Of the patients, 12.1% (829) had in situ breast cancer with mean tumour size of 2.14cm and a size range of 0.02-9cm. 42.3% of patients had in situ tumour larger than 2cm.

► 77.2% of in situ breast cancer cases were ER positive; 67.2% were PR positive; 30.9% were HER2 positive.

II. Treatment

► Within the patient cohort, the most common combination of treatments was surgery, chemotherapy, endocrine therapy and radiotherapy (30.0%).

► The most common combination used for stage 0 cases was surgery and radiotherapy (42.3%).

► The most common treatment combination used by patients of stage I disease was surgery, endocrine therapy and radiotherapy (24.8%).

	Total %	Treatment in private sector %	Treatment in public sector %	Stage					
				0 %	I %	IIA %	IIB %	III %	IV %
Surgery	98.4	60.5	39.5	99.2	99.9	99.8	99.9	99.6	61.9
Breast conserving surgery	37.7	46.3	25.3	55.4	49.6	37.8	24.3	14.9	7.1
Mastectomy	62.3	53.7	74.7	44.6	50.4	62.2	75.7	85.1	92.9
Chemotherapy	62.1	20.0	80.0	--	41.3	83.8	91.6	93.8	89.9
Radiotherapy	62.3	21.8	78.2	54.8	55.4	59.7	78.4	93.7	67.0
Endocrine therapy	65.9	21.1	78.9	21.8	73.1	73.5	74.6	75.3	82.9
Targeted therapy	6.4	24.9	75.1	--	3.1	7.7	8.2	14.8	13.8

2.1 Clinical presentation

Most patients (87.1%) self-detected their cancers by chance (Figure 2.1), highlighting low awareness of regular screening for breast cancer when no symptoms are present. The low breast cancer screening rate could be a major contributing factor for the delayed diagnosis in Hong Kong.

The rate of detecting breast cancer through mammography and other screening methods was higher in private healthcare patients (20.5%) than in public healthcare patients (9.2%).

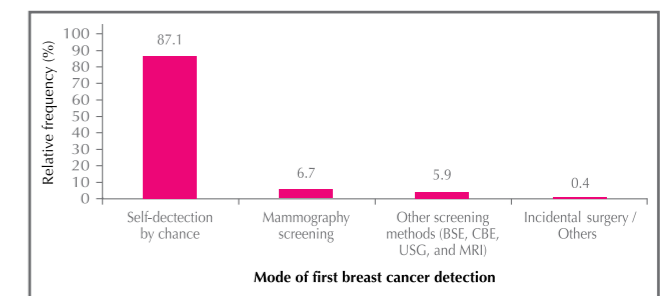The most common symptom in self-detected cases was a painless lump (92.7%) (Figure 2.2).

Figure 2.1 Mode of first breast cancer detection in the patient cohort (N=6,140)

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

Table 2.1 Mode of first breast cancer detection by type of medical service received at diagnosis (N=6,140)

Mode of first breast cancer detection	Private sector (N=833) Number (%)	Public sector (N=1,335) Number (%)	Mixed private/public sector (N=1,299) Number (%)
Self-detection by chance	1,109 (78.9)	2,254 (90.4)	1,982 (88.4)
Mammography screening	158 (11.2)	131 (5.3)	121 (5.4)
Other screening methods (BSE, CBE, USG, and MRI)	131 (9.3)	97 (3.9)	132 (5.9)
Incidental surgery / Others	8 (0.6)	11 (0.4)	6 (0.3)

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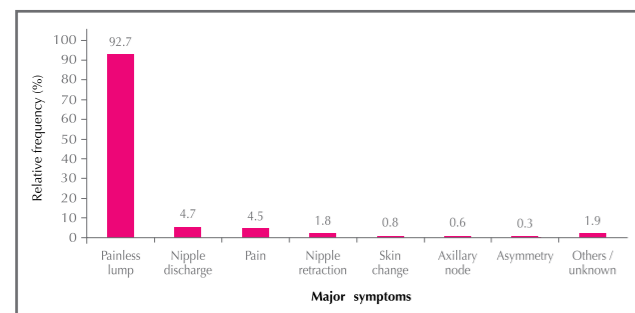

Figure 2.2 Major symptoms of self-detected breast cancer (N=5,361)

Table 2.2 Duration from onset of symptoms to first medical consultation for patients who self-detected their cancers (N=2,545)

	Number	(%)
Less than 1 month	784	(30.8)
1-3 months	743	(29.2)
4-12 months	315	(12.4)
More than 12 months	703	(27.6)

2.1.1 Duration from onset of symptoms to first medical consultation

After self-detection, only 30.8% of the patients sought their medical consultation within one month of the onset of symptoms (Table 2.2). Alarmingly 27.6% of the patients took more than 12 months to seek their first medical consultation. A qualitative study in 2009 on Hong Kong Chinese women found that patients with painless lump and atypical symptoms delayed their medical consultation until symptoms intensified or until they discussed with someone who has experience with breast cancer. The barriers to timely medical consultation included financial difficulties, lack of access and time and embarrassment[22].

More private (37.4%) and mixed healthcare patients (32.5%) sought their first medical consultation in less than one month from the onset of symptoms, compared with the public healthcare patients (22.1%). Additionally, more public healthcare patients (30.1%) delayed their first medical consultation for more than 12 months after the onset of symptoms than private (24.6%) and mixed (28.1%) healthcare patients.

Table 2.3 Duration from onset of symptoms to first medical consultation for patients who self-detected their cancers by type of medical service (N=2,545)

	Private sector (N=833) Number (%)	Public sector (N=1,335) Number (%)	Mixed private/public medical service users (N=1,299) Number (%)
Less than 1 month	305 (37.4)	175 (22.1)	304 (32.5)
1-3 months	216 (26.5)	245 (30.9)	282 (30.1)
4-12 months	94 (11.5)	134 (16.9)	87 (9.3)
More than 12 months	201 (24.6)	239 (30.1)	263 (28.1)

Among the patients diagnosed at stage IV, 40.8 % took more than 12 months before seeking first consultation after symptom onset, and 77.5% took more than one month to seek first medical consultation, suggesting the majority of stage IV cancer could potentially have been caught at earlier stages.

Table 2.4 Duration from onset of symptoms to first medical consultation for patients who self-detected their cancers by cancer stage at diagnosis (N=2,472)

	Stage 0 (N=255) Number (%)	Stage I (N=763) Number (%)	Stage IIA (N=746) Number (%)	Stage IIB (N=328) Number (%)	Stage III (N=331) Number (%)	Stage IV (N=49) Number (%)
Less than 1 month	77 (30.3)	261 (34.2)	248 (33.2)	90 (27.4)	84 (25.4)	11 (22.4)
1-3 months	65 (25.5)	207 (27.1)	235 (31.5)	108 (32.9)	101 (30.5)	10 (20.4)
4-12 months	33 (12.9)	87 (11.4)	78 (10.5)	36 (11.0)	60 (18.1)	8 (16.3)
More than 12 months	80 (31.4)	208 (27.3)	185 (24.8)	94 (28.7)	86 (26.0)	20 (40.8)

2.2 Cancer characteristics

In the patient cohort, 47.4% of patients had breast cancer in their left breast; 45.3% had breast cancer in their right breast, and 7.3% had cancer in both breasts (Figure 2.3).
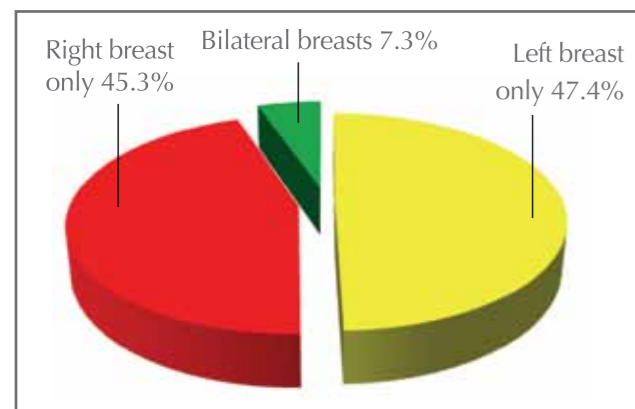

Figure 2.3 Laterality of 6,848 breast cancer cases

In both left and right breasts, the most common location of breast cancer was the upper outer quadrant (44.1-48.3%), while breast cancer was less likely to occur in the lower inner quadrant (7.6-9.4%) (Figure 2.4).
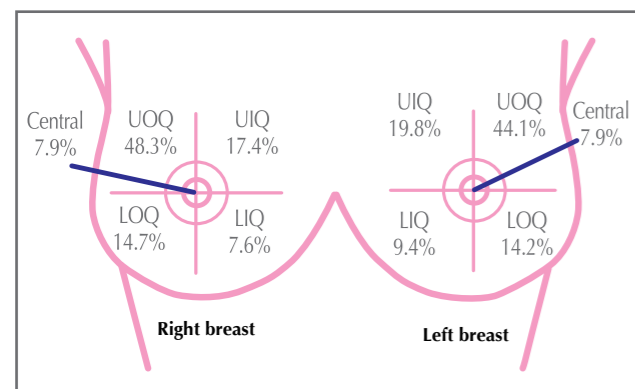

Figure 2.4 Locations of breast cancer (N=6,848)

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

After a lump or other sign of breast cancer is detected, several tests are performed to diagnose breast cancer. Mammography (MMG) is currently recognised to be the "gold standard" of breast imaging test, while breast ultrasound imaging (USG) and magnetic resonance imaging (MRI) are used for further investigation. Fine needle aspiration (FNA) and core needle biopsy (CNB) are used to confirm malignancy of breast lesion.

MMG was used in the diagnosis of 80.5% of patients, while USG was used in 74.5% and MRI was used in only 6.1% of patients (Table 2.3).

BIRADS (Breast Imaging Reporting and Data System) is a classification used by radiologists to determine the likelihood of diagnosing malignancy in breast images. BIRADS classification of the patient cohort demonstrated that sensitivity of USG (86.4%) is higher than that of MMG (77.5%). MRI had the best sensitivity, however due to the low number of MRI conducted in the patients, a comparison of MRI with other techniques cannot be made.

To confirm malignancy, FNA was used in 49.3% of the patients, while CNB and excisional biopsy were used in 44.5% and 14.8% of the patients respectively. The overall sensitivity of CNB was higher than FNA, and excisional biopsy had 100% sensitivity (Table 2.5).

Table 2.5 Sensitivity and diagnostic results of breast imaging tests

	Mammography (N=5,512)	Breast ultrasound (N=5,100)	MRI (N=419)
Proportion of subjects using the diagnostic test	80.5%	74.5%	6.1%
Overall sensitivity*	77.5%	86.4%	95.0%
BIRADS category			
Diagnostic/ malignant (BIRADS 5)	1,600 (29.0%)	1,774 (34.8%)	280 (66.8%)
Suspicious abnormality (BIRADS 4)	2,673 (48.5%)	2,630 (51.6%)	118 (28.2%)
Probably benign (BIRADS 3)	421 (7.6%)	401 (7.9%)	8 (1.9%)
Benign (BIRADS 2)	340 (6.2%)	154 (3.0%)	4 (1.0%)
Normal (BIRADS 1)	459 (8.3%)	133 (2.6%)	9 (2.1%)
Incomplete (BIRADS 0)	19 (0.3%)	8 (0.2%)	0 (0.0%)

MRI: Magnetic resonance imaging; BIRADS: Breast Imaging Reporting and Data System
*Sensitivity: Number of true positives divided by total number of patients who have taken the test

Table 2.6 Sensitivity and diagnostic results of breast tissue biopsies

	FNA (N=3,374)	CNB (N=3,048)	Excisional biopsy (N=1,014)
Proportion of subjects using the diagnostic test	49.3%	44.5%	14.8%
Overall sensitivity*	89.3%	98.6%	100.0%
Class			
Diagnostic/ malignant (Class V)	1,979 (58.7%)	2,863 (93.9%)	1,014 (100.0%)
Suspicious (Class IV)	668 (19.8%)	92 (3.0%)	—
Atypical (Class III)	367 (10.9%)	51 (1.7%)	—
Benign (Class II)	192 (5.7%)	25 (0.8%)	—
Scanty benign (Class I)	115 (3.4%)	15 (0.5%)	—
Incomplete (Class 0)	53 (1.6%)	2 (0.1%)	—

FNA: Fine needle aspiration;   CNB: Core needle biopsy;
*Sensitivity: Number of true positives divided by total number of patients who have taken the test

Of the 4,273 patients diagnosed through MMG, the most common finding was opacity (52.7%), closely followed by microcalcification (49.6%) (Table 2.7).

Table 2.7 Mammographic findings of the patients diagnosed through mammography (N=4,273)

	Number	(%)
Opacity	2,250	(52.7)
Microcalcifications	2,121	(49.6)
Architectural distortion	511	(12.0)
Asymmetric density	429	(10.0)
Others	50	(1.2)

Asian women are known to have denser breasts than western women. Indeed, 76% of the patient cohort had either heterogeneous or extreme density (Figure 2.5).
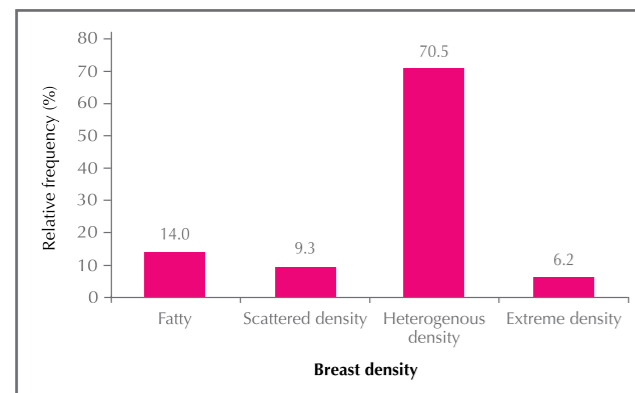

Figure 2.5 Mammographic density of breasts of the patients (N=3,852)

2.2.2 Methods of cancer staging

After diagnosis, cancer staging is conducted to detect any distant metastasis. The commonly used tests include chest X-rays, abdominal ultrasound, PET scans, MRIs, bone scans and CT scans. Around 15% of the patients did not have any tests for cancer staging. The most commonly used cancer staging tests were chest X-rays / abdominal ulstrasound (64.5%), PET scan (17.7%) and bone scan (3.8%) (Table 2.8).

Table 2.8 Cancer staging in 5,798 breast cancer patients

Type of cancer staging method	Number	(%)
No cancer staging	901	(15.5)
Chest X-rays (CXR) /Abdominal ultrasound (USG Abd)	3,739	(64.5)
Positron emission tomography scan (PET scan)	1,027	(17.7)
Bone scan	223	(3.8)
Computed tomography of body parts*	151	(2.6)
Magnetic resonance imaging whole body (MRI whole body)	36	(0.6)
Unspecified	616	(10.6)

* Body parts include abdomen, thorax, pelvis, brain

Of the 6,848 breast cancer cases, 82% were diagnosed at early stages (stages 0-II); 14% were found to be at advanced stages (stages III-IV) (Figure 2.6).
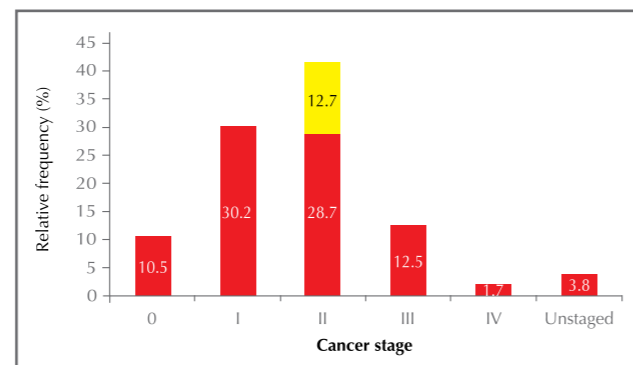

Figure 2.6 Cancer stage at diagnosis in breast cancer patients (N=6,848)

2.2.3 Characteristics of invasive breast cancer

Of the 5,822 patients (85%) diagnosed with invasive breast cancer, majority were diagnosed at stage I (35.1%) and stage II (48.5%). Tumour size ranged from 0.01-22cm. The mean tumour size of invasive breast cancer in self-detected cases vs. screen-detected cancers: 2.3cm vs. 1.9cm. Around half (48.1%) of the patients had tumours larger than 2cm.
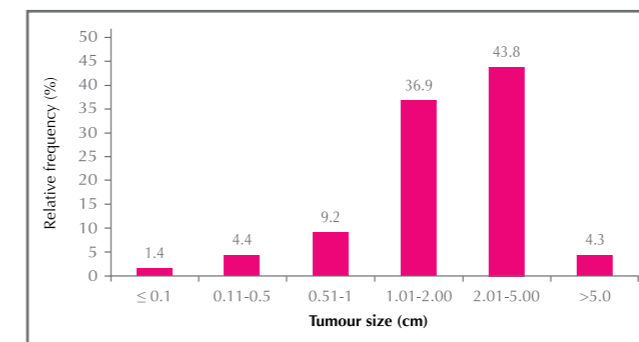

Figure 2.7 Distribution of tumour size of invasive breast cancer (N=5,822)

Of the invasive breast cancer cases, 56.3% had no lymph node involvement. 22.2% had 1-3 positive nodes, and 13.8% had 4 or more positive lymph nodes. 4.9% of patients had nodal micrometastasis with size between 0.2-2mm. 2.8% had isolated tumour cells (ITC) (Figure 2.8).
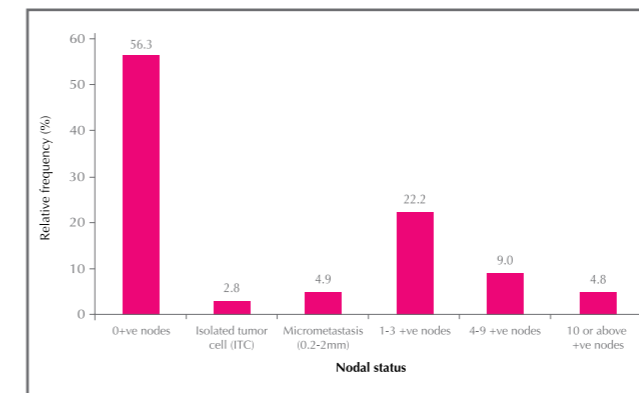

Figure 2.8 Number of positive lymph nodes in invasive breast cancer (N=4,044)

2.2.4 Characteristics of in situ breast cancer

Of the breast cancer patients, 12.1% (829) had in situ breast cancer, with mean tumour size of 2.14cm and a size range of 0.02-9cm. 42.3% of patients had in situ tumours larger than 2cm (Figure 2.9).
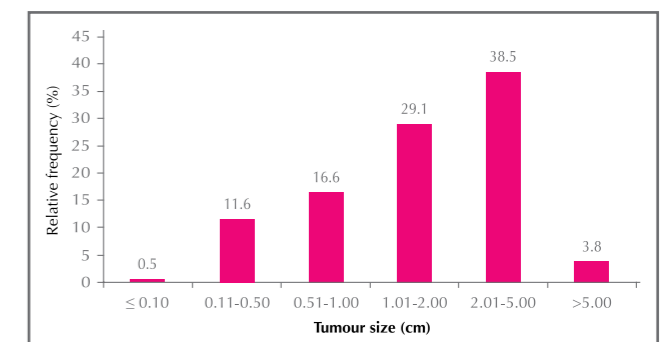

Figure 2.9 Distribution of tumour size of in situ breast cancer (N=743)

2.3 Histological and biological characteristics

2.3.1 Invasive breast cancer

After diagnosis and staging of invasive breast cancer, histological analysis is conducted. Histological characteristics, grading, multifocality and multicentricity of invasive breast cancer cases can be found in Table 2.9.

Table 2.9 Histological type, grading, multifocality and multicentricity of invasive breast cancer (N=5,822)

	Number	(%)
Histological type		
Ductal	4,953	(85.0)
Lobular	241	(4.1)
Mucinous (colloid)	227	(3.9)
Papillary	58	(1.0)
Tubular	55	(0.9)
Medullary	41	(0.7)
Mixed ductal and lobular	37	(0.6)
Borderline/ malignant phyllodes	24	(0.4)
Micropapillary	20	(0.3)
Metaplastic carcinoma	16	(0.3)
Apocrine carcinoma	11	(0.2)
Cribriform carcinoma	7	(0.1)
Adenoid cystic carcinoma	6	(0.1)

	Number	(%)
Neuroendocrine carcinoma	5	(0.1)
Paget's disease of the nipple	3	(0.1)
Inflammatory	2	(0.0)
Secretory carcinoma	2	(0.0)
Lipid rich carcinoma	1	(0.0)
Sarcoma	1	(0.0)
Others	19	(0.3)
Unknown	93	(1.6)
Grade		
Grade 1	951	(16.3)
Grade 2	2,360	(40.5)
Grade 3	1,976	(33.9)
Unknown	535	(9.2)
Lymphovascular invasion	**1,732**	**(29.7)**
Multifocality	**641**	**(11.0)**
Number of foci		
2	327	(51.0)
3-4	137	(21.4)
≥5	80	(12.5)
Unknown	97	(15.1)
Multicentricity	**170**	**(2.9)**
Number of quadrants		
2	140	(82.4)
3	13	(7.6)
4	13	(7.6)
Unknown	4	(2.4)

Biologically, breast cancer can be classified into four subtypes: luminal A, luminal B, c-erbB2/HER2 positive and triple negative.

Of the invasive breast cancer cases, 75.5% were ER positive while 63% were PR positive, and 22.3% were HER2 positive. Of the 26.9% found to be weakly HER2 positive by immunohistochemistry, only 3.5% were found to be positive by FISH/CISH test (Table 2.10).

Table 2.10 Biological characteristics of invasive breast cancer (N=5,822)

	Number	(%)
Oestrogen receptor (ER) (N=5,616, 96.5%)		
Positive	4,241	(75.5)
Negative	1,375	(24.5)
Progesterone receptor (PR) (N=5,593, 96.1%)		
Positive	3,523	(63.0)
Negative	2,070	(37.0)
c-erbB2/ HER2 (N=5,421, 93.1%)		
Positive (IHC Score 3)	1,209	(22.3)
Weakly positive (IHC Score 2)	1,459	(26.9)
FISH / CISH +ve	*50*	*(3.4)*
Negative (IHC Score 0 / 1)	2,753	(50.8)
Ki-67 index (N=3,184, 54.7%)		
<14%	1,445	(45.4)
14-49%	1,349	(42.4)
≥50%	390	(12.2)

HER2: Human epidermal growth factor receptor 2

The most common biological subtype in the cohort was ER+PR+HER2- (47.3%), while ER-PR+HER2+ (1.1%) was the least common. 12.6% of cases were triple negative (ER-PR-HER2-) (Table 2.11).

Table 2.11 Biological subtypes of oestrogen receptors, progesterone receptors and HER2 receptors in 5,822 invasive breast cancer cases

	Number	(%)
ER+PR+HER2+	517	(11.4)
ER+PR+HER2-	2,141	(47.3)
ER+PR-HER2+	212	(4.7)
ER+PR-HER2-	471	(10.4)
ER-PR+HER2+	51	(1.1)
ER-PR+HER2-	89	(2.0)
ER-PR-HER2+	474	(10.5)
ER-PR-HER2-	571	(12.6)

ER+: Oestrogen receptor positive   ER-: Oestrogen receptor negative
PR+: Progesterone receptor positive PR-: Progesterone receptor negative
HER2+: Human epidermal growth factor receptor 2 positive
HER2-: Human epidermal growth factor receptor 2 negative

2.3.2 In situ breast cancer

Histological characteristics, grading, multifocality and multicentricity of in situ breast cancer cases can be found in Table 2.12. Microcalcification was found on the mammograms of 51.3% of the in situ breast cancer cases.

Table 2.12 Histological type, grade, multifocality and multicentricity of in situ breast cancer (N=829)

	Number	(%)
Histological type		
Ductal	760	(91.7)
Lobular	12	(1.4)
Mixed	23	(2.8)
Others	22	(2.7)
Unknown	12	(1.4)
Necrosis	**370**	**(44.6)**
Nuclear Grade		
Low	178	(21.5)
Intermediate	264	(31.8)
High	326	(39.3)
Unknown	61	(7.4)
Multifocality	**100**	**(12.1)**
Number of foci		
2	51	(51.0)
3	8	(8.0)
4 or more	5	(5.0)
Unknown	36	(36.0)
Multicentricity	**13**	**(1.6)**
Number of quadrants		
2	9	(69.2)
3	2	(15.4)
Unknown	2	(15.4)

77.2% of in situ breast cancer were ER positive while 67.2% were PR positive. 32.7% were HER2 positive (Table 2.13).

Table 2.13 Biological characteristics of in situ breast cancer (N=829)

	Number	(%)
Oestrogen receptor (ER) (N=623, 75.2%)		
Positive	481	(77.2)
Negative	142	(22.8)
Progesterone receptor (PR) (N=616, 74.3%)		
Positive	414	(67.2)
Negative	202	(32.8)
c-erbB2/ HER2 (N=589, 71.0%)		
Positive (IHC score 3)	182	(30.9)
Weakly positive (IHC score 2)	163	(27.7)
FISH / CISH +ve	*3*	*(1.8)*
Negative (IHC score 0/1)	244	(41.4)
Ki-67 index (N=495, 59.7%)		
<14%	344	(69.5)
14-49%	135	(27.3)
≥50%	16	(3.2)

2.4 Treatment methods

Treatment is the most important part of a patient's recovery from breast cancer, and the success of treatment is strongly dependent on the cancer stage at diagnosis, timely medical consultation, and tumour characteristics.

Out of the 6,848 patients, 1,589 (23.2%) were diagnosed and treated at private medical facilities; 2,797 (40.8%) had their treatment at public medical facilities and 2,462 (36.0%) used both private and public medical facilities.

2.4.1 Surgical treatment

Almost all patients underwent surgery as part of their treatment for breast cancer. 60.5% of the patients received surgery in private healthcare facilities while 39.5% of patients underwent surgery at public healthcare facilities.

Of the patients, 37% underwent breast conserving surgery while 61.2% underwent mastectomy. The most common type of mastectomy was total mastectomy (92.8%), followed by skin sparing (6%) and nipple or areolar sparing (1%). Only 15.3% underwent some form of reconstruction surgery (Table 2.14).

Sentinal node biopsy has been shown to reduce morbidity such as lymphoedema during recovery from breast cancer. Of the 49.2% of patients who underwent sentinel node biopsy, only 16.6% had received axillary dissection as well. However, 50.5% of the patients were treated with axillary dissection only.

Table 2.14 Types of surgical operations in the patient cohort (N=6,837)

	Number	(%)
No surgery	111	(1.6)
Breast conserving surgery	2,533	(37.0)
Mastectomy	4,184	(61.2)
Unknown	9	(0.1)
Mastectomy (N=4,184)		
Total mastectomy	3,884	(92.8)
Skin sparing	249	(6.0)
Areolar sparing	9	(0.2)
Nipple sparing	32	(0.8)
Unknown	10	(0.2)
Reconstruction (N=641)		
TRAM flap	385	(60.1)
Implant	152	(23.7)
LD flap	46	(7.2)
LD flap & implant	47	(7.3)
Unknown	11	(1.7)
Nodal surgery (N=6,259)		
Sentinel node biopsy	2,039	(32.6)
Axillary dissection	3,162	(50.5)
Sentinel node biopsy & axillary dissection	1,040	(16.6)
Unknown	18	(0.3)

Breast surgery

The only patient aged under 20 underwent breast conserving surgery. While 84.1% of those over 80 underwent mastectomy. A trend of increased mastectomy and reduced breast conserving surgery towards increasing ages was observed (Figure 2.10). Breast reconstruction as expected was more common among younger women, and the percentage of reconstructive surgeries decreased with increasing age.
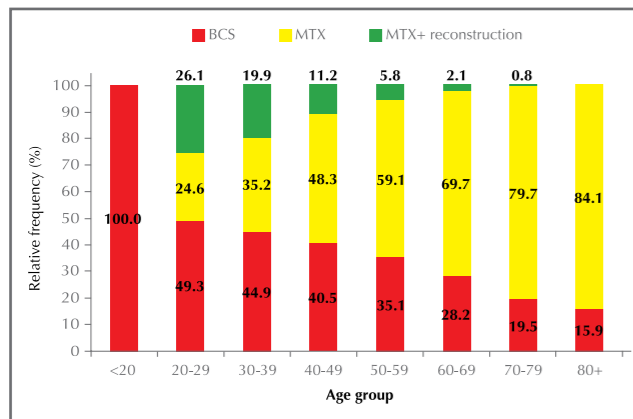
Additionally, it was observed that rate of mastectomy increased and the rate of breast conserving surgery dropped with increasing cancer stage. Surprisingly, 44.6% of the patients with stage 0 disease underwent mastectomy. However, no trend was observed in the relationship between reconstuction rate and cancer stage, suggesting that cancer stage was not an important factor in the decision making process for reconstructive surgery (Figure 2.12).
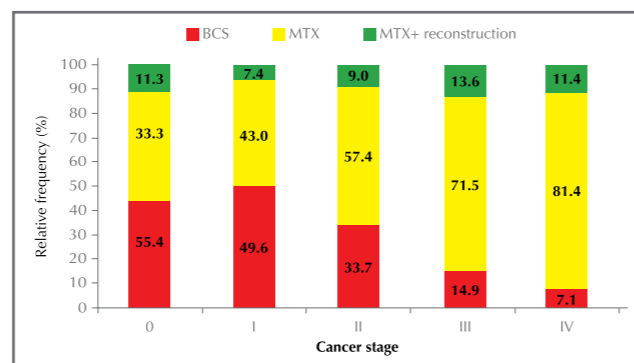

Figure 2.10 Type of surgery by age group (N=6,500)

BCS: Breast conserving surgery; MTX: Mastectomy
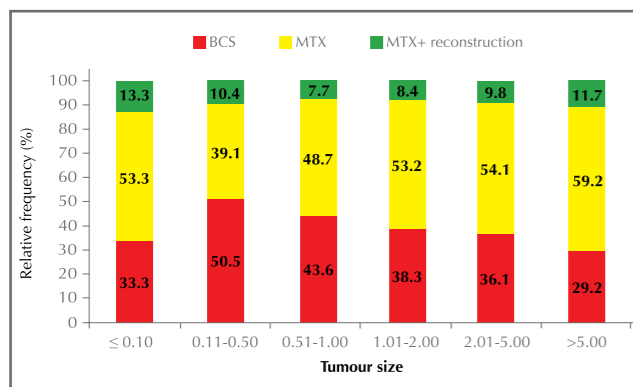
Figure 2.11 Type of surgery by tumour size (N=5,607)

BCS: Breast conserving surgery; MTX: Mastectomy

Figure 2.12 Type of surgery by cancer stage (N=6,507)

BCS: Breast conserving surgery; MTX: Mastectomy

Of the patients who used private health care services, 46.3% underwent breast conserving surgery. Of the patients using public health care services, only 25.3% had breast conserving surgery probably because their tumour sizes were so large that lumpectomy was not an option. Of the patients who had mastectomy, 10.6% in private health care underwent reconstruction surgery while 7.9% underwent reconstruction surgery in public health care (Figure 2.13).
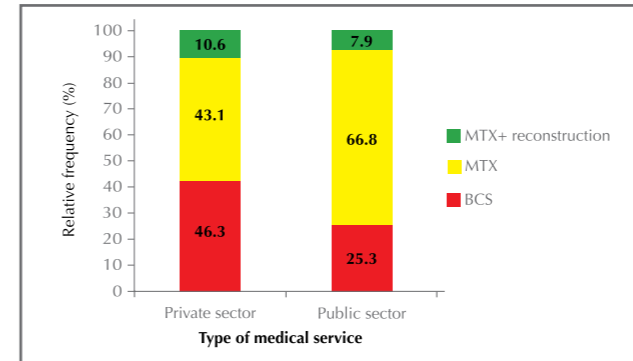

Figure 2.13 Type of surgery by type of medical service (N=6,593)

BCS: Breast conserving surgery; MTX: Mastectomy

Axillary surgery

Sentinel node biopsy was recommended for patients with tumour smaller than 5 cm and clinically node negative disease. Axillary dissection was performed when nodes were positive before cancer surgery or when sentinel node biopsy was positive (Figure 2.14).
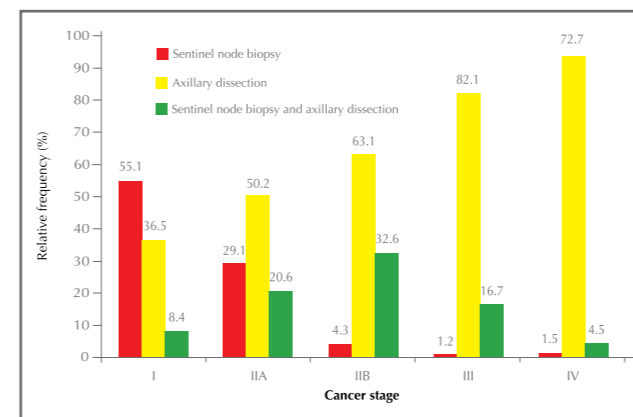

Figure 2.14 Type of nodal surgery in invasive cancer by cancer stage (N=5,550)

Of the invasive and node positive cancer cases, 54.3% had tumour size of 2.01-5cm while 0.7% had tumours smaller than 0.1cm.
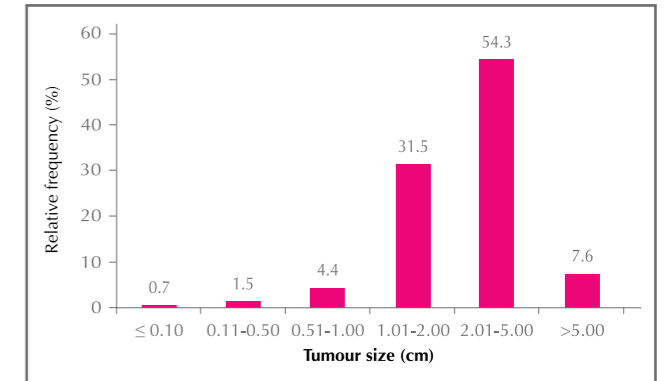

Figure 2.15 Distribution of node positive cancer by tumour size (invasive tumour only)

More node positive tumours than node negative tumours were observed in invasive cancer with tumour size larger than 2 cm.
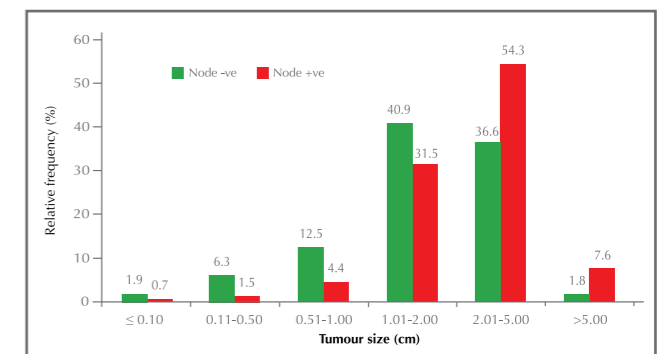

Figure 2.16 Distribution of tumour size in invasive cancer with negative or positive nodal status

Of the in situ and node positive cases, 25% had tumour size of 2.01-5cm. Increasing tumour size did not correlate with more node positive than node negative disease, in fact the proportions varied greatly between the tumour sizes.
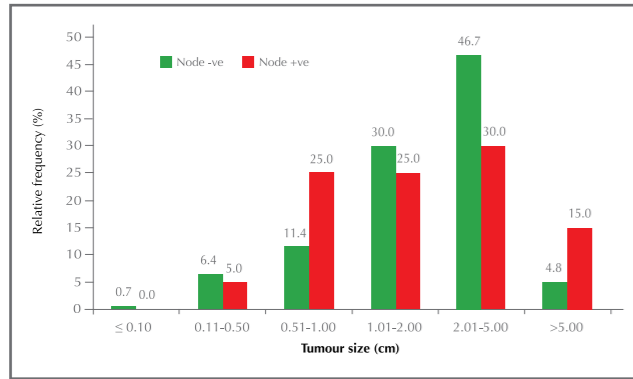
Figure 2.17 Distribution of tumour size in in situ cancer with negative or positive nodal status

Analysis of number of positive nodes by type of nodal surgery revealed that 48.8% of patients who underwent the more morbid axillary dissection had no positive nodes, while 4.8% of patients who had sentinal node biopsy only had 1 or more positive nodes.
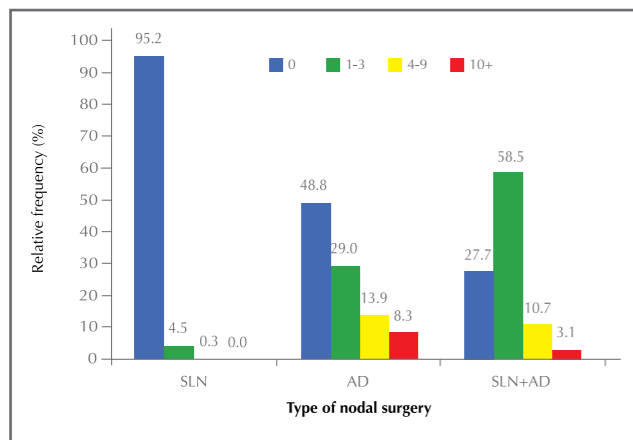

Figure 2.18 Number of positive nodes by type of nodal surgery

AD: Axillary dissection; SLN: Sentinel node biopsy

2.4.2 Chemotherapy

Chemotherapy is an important part of treatment for breast cancer. In the patient cohort, 4,255 (62.1%) patients were treated with chemotherapy. Of them, 3,873 (91.0%) were adjuvant; 313 (7.4%) were neoadjuvant and 69 (1.6%) were palliative.

Majority of the patients (80%) received chemotherapy in public medical facilities while 20% received chemotherapy in private medical facilities. 172 (4.0%) patients received chemotherapy and targeted therapy at the same time.

Less than half (41.3%) of the patients diagnosed at stage I breast cancer underwent chemotherapy, while most (83.8% - 93.8%) of the patients disgnosed at stage II or higher stage underwent chemotherapy (Figure 2.19).
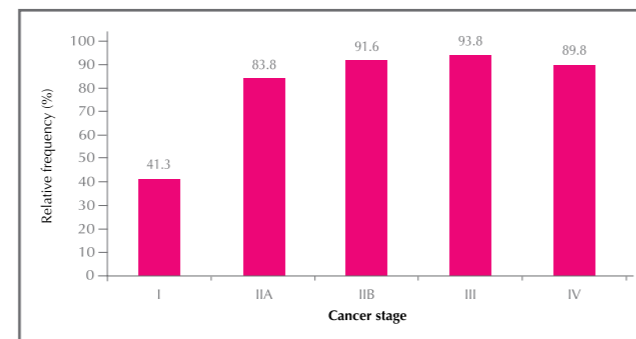

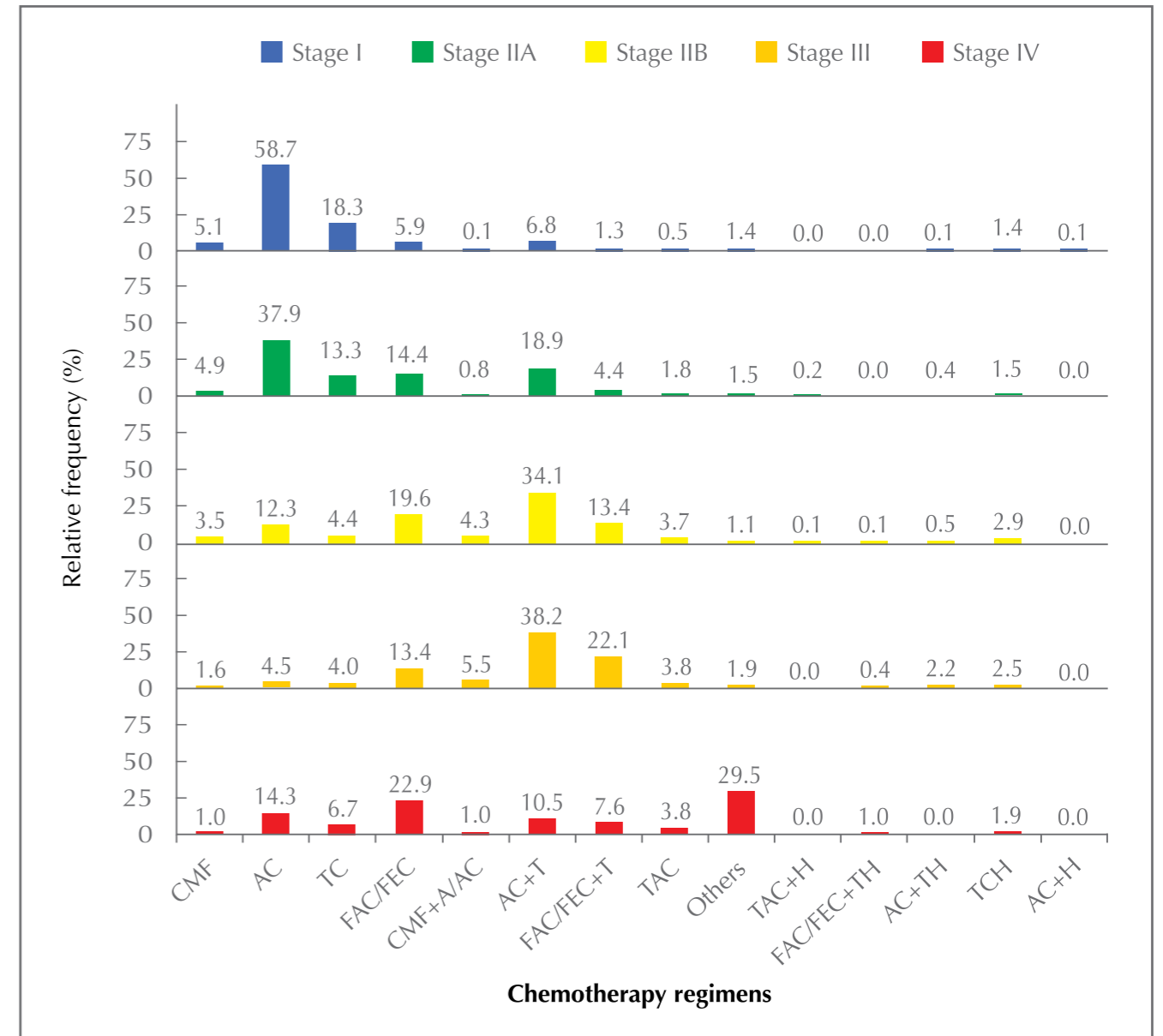**Figure 2.19 Chemotherapy treatment in patients at different cancer stages (N=6,440)**

Figure 2.20 Type of chemotherapy regimens in patients by cancer stage (N=3,868)

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

2.4.3 Radiotherapy

Within the patient cohort, 4,266 (62.3%) patients were treated with radiotherapy. Among them, 4,204 (98.5%) were adjuvant; 7 (0.2%) were neoadjuvant and 55 (1.3%) were palliative. Most patients (78.2%) went to public medical facilities while 21.8% of the patients attended private medical facilities for radiotherapy.

The percentage of patients treated with radiotherapy increased with cancer stage from 54.8% in stage 0 patients to 93.7% in patients at stage III. However, only 67% of the patients with stage IV breast cancer were treated with radiotherapy (Figure 2.21).
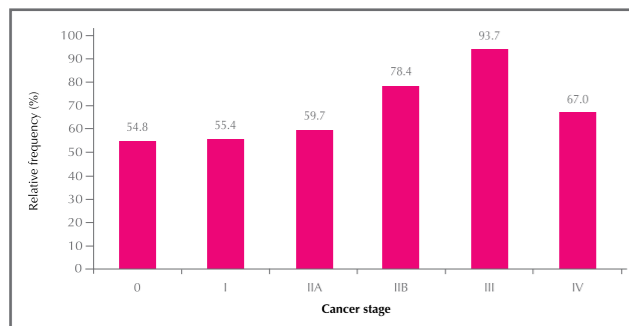

Figure 2.21 Radiotherapy rate in patients at different cancer stages (N=6,371)

Most of the patients who underwent breast conserving surgery had radiotherapy afterwards (94.3%) while around half of the patients who underwent mastectomy had radiotherapy (46.7%). The distribution of cancer stages in patients treated with mastectomy and radiotherapy was shown in Figure 2.22.
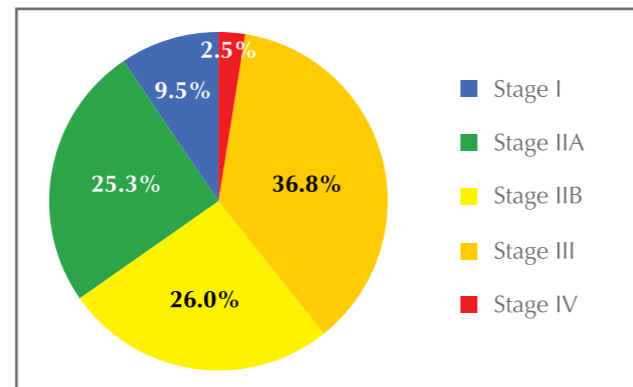

Figure 2.22 Distribution of cancer stages in patients treated with mastectomy and radiotherapy (N=1,774)

The most common target volume for patients who underwent breast conserving surgery was breast only (54.7%). For the patients who underwent mastectomy, it was chest wall and regional lymph node basin (48.8%) (Table 2.15).

Table 2.15 Irradiated regions among the patients receiving radiotherapy (N=4,266)

Target volume	Total (N=4,266) Number (%)	Breast Conserving Surgery (N=2,329) Number (%)	Mastectomy (N=1,896) Number (%)
Breast	1,285 (30.1)	1,274 (54.7)	—
Breast + regional nodes*	216 (5.1)	203 (8.7)	—
Chest wall	451 (10.6)	—	448 (23.6)
Chest wall + regional nodes*	925 (21.7)	—	925 (48.8)
Axilla	6 (0.1)	3 (0.1)	2 (0.1)
SCF	14 (0.3)	3 (0.1)	11 (0.6)
Axilla + SCF	6 (0.1)	1 (0.0)	5 (0.3)
IMC	2 (0.0)	1 (0.0)	1 (0.1)
IMC + SCF	2 (0.0)	0 (0.0)	2 (0.1)
Unspecified	1,344 (31.5)	844 (36.2)	493 (26.0)

* Regional nodes: Axilla;   IMC: Internal mammary chain;   SCF: supraclavicular fossa

2.4.4 Endocrine therapy

4,512 (65.9%) patients were treated with endocrine therapy. Among them, 4,416 (97.9%) were adjuvant; 17 (0.4%) were neoadjuvant and 79 (1.8%) were palliative. 78.9% of patients received endocrine treatment at public health care facilities while 21.1% received endocrine treatment at private health care facilities.

21.8% of patients with stage 0 disease underwent endocrine therapy. The use of endocrine therapy increased with increasing cancer stage. The rate increased from 73.1% in stage I patients to 82.9% in stage IV patients (Figure 2.23).
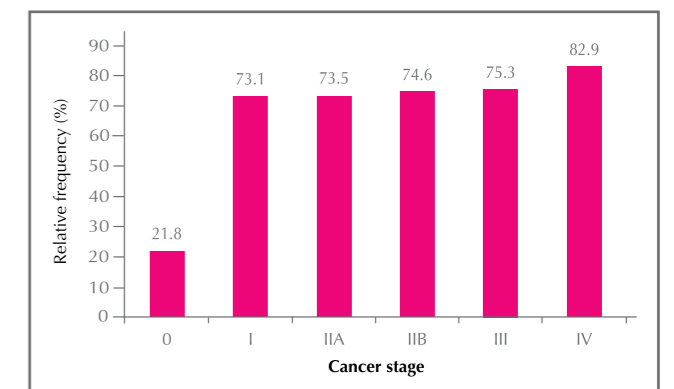

Figure 2.23 Endocrine therapy rates in patients by cancer stage (N=6,403)

94.1% of the patients aged under 45 used Tamoxifen alone, while 33% of women over 55 used Aromatase inhibitors alone. A trend of reduced use of Tamoxifen alone and increased use of Aromatase inhibitors alone or Tamoxifen followed by Aromatase inhibitors was observed with increasing age groups.
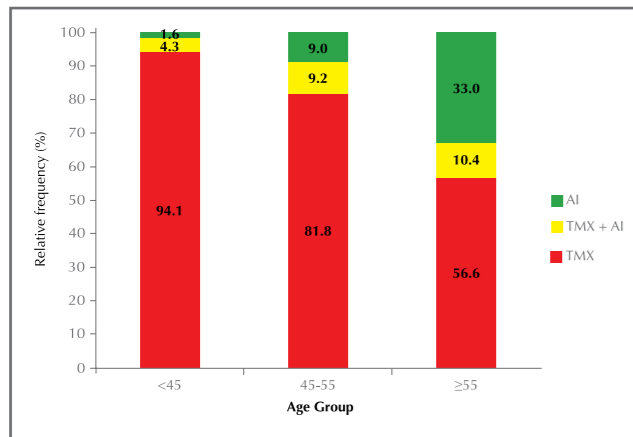

Figure 2.24 Forms of endocrine therapy used in patients by age group (N=4,183)

TMX: Tamoxifen; AI: Aromatase inhibitors

37 (0.9%) patients had ovarian ablation±TMX/AI which is not included in Figure 2.24.

2.4.5 Targeted therapy

Of the patient cohort, 440 (6.4%) patients were treated with targeted therapy. Among them, 396 (90.0%) were adjuvant, 35 (7.9%) were neoadjuvant, and 9 (2.0%) were palliative. 75.1% of patients received targeted therapy at public medical facilities, while 24.9% received targeted therapy in private medical facilities.

Use of targeted treatment increased with increasing cancer stage from 3.1 % for patients diagnosed at stage I to 14.8% for patients diagnosed at stage III. 13.8% of stage IV patients also underwent targeted therapy (Figure 2.25).
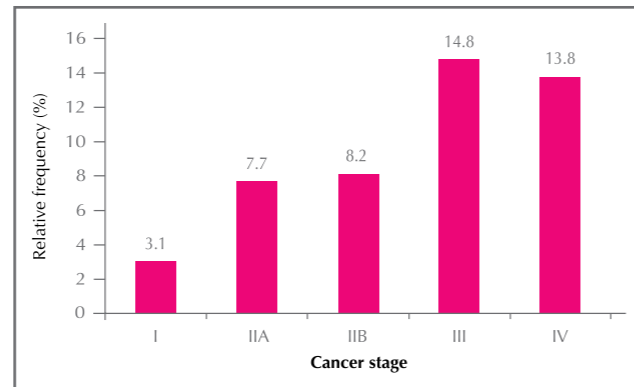

Figure 2.25 Targeted therapy rate in the patients by cancer stage (N=6,449)

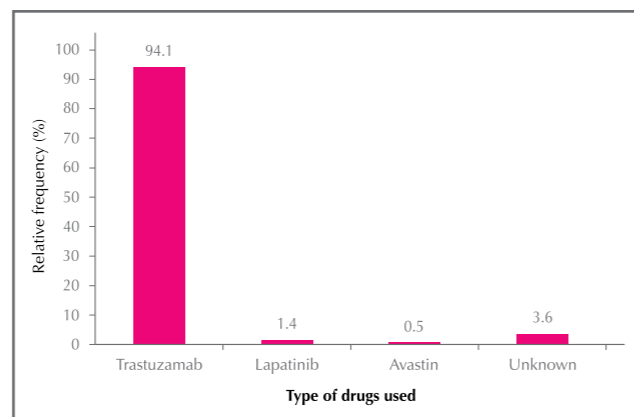The most common drug used for targeted therapy was Trastuzumab (94.1%).

Figure 2.26 Type of drugs used for targeted therapy in patients

2.4.6 Complementary and alternative therapies

Complementary and alternative therapies were used by 33.4% of patients. Among them, 2,169 (94.8%) were adjuvant, 103 (4.5%) were neoadjuvant and 16 (0.7%) were palliative.

72.4% of patients resorted to Chinese medicine, while 35.4% of patients took health food / supplements (Figure 2.27).
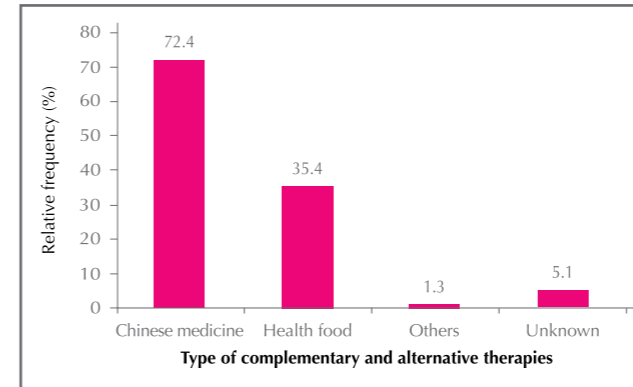

Figure 2.27 Type of complementary and alternative therapies used in 2,288 patients

Others include: Acupuncture, moxibustion, naturopathy, Qigong, Tai Chi, yoga, etc

2.4.7 Multimodality treatment

Within the patient cohort, the most common combination of treatments was surgery, chemotherapy, endocrine therapy and radiotherapy (30.0%), and the least common combination of treatments was chemotherapy, targeted therapy and radiotherapy, which was only used by one patient who was diagnosed at stage IV.

The most common combination used for stage 0 disease was surgery and radiotherapy (42.3%). The most common treatment combination used by patients of stage I disease was surgery, endocrine therapy and radiotherapy (24.8%), while the combination of surgery, chemotherapy, radiotherapy and endocrine therapy was most commonly used by patients of stage II, III and IV disease (Figure 2.16).

Table 2.16 Most common treatment combinations received by patients by cancer stages

| Combination | | | | | Stage (%) | | | | | | |
OT	CT	BT	ET	RT	0	I	IIA	IIB	III	IV	Total
✔	✔		✔	✔	0 (0.0)	299 (15.2)	653 (34.8)	416 (49.9)	478 (59.0)	34 (30.6)	1,880 (30.0)
✔	✔		✔		0 (0.0)	206 (10.5)	395 (21.0)	113 (13.5)	25 (3.1)	10 (9.0)	749 (11.9)
✔			✔	✔	80 (11.7)	487 (24.8)	110 (5.9)	27 (3.2)	26 (3.2)	5 (4.5)	735 (11.7)
✔			✔		63 (9.3)	414 (21.1)	131 (7.0)	25 (3.0)	11 (1.4)	0 (0.0)	644 (10.3)
✔	✔			✔	0 (0.0)	128 (6.5)	241 (12.8)	136 (16.3)	124 (15.3)	5 (4.5)	634 (10.1)
✔				✔	288 (42.3)	119 (6.1)	24 (1.3)	13 (1.6)	10 (1.2)	0 (0.0)	454 (7.2)
✔					242 (35.5)	137 (7.0)	39 (2.1)	7 (0.8)	3 (0.4)	0 (0.0)	428 (6.8)
	✔	✔		✔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	20 (18.0)	20 (0.3)

OT: Surgery;   CT: Chemotherapy;   BT: Targeted therapy;   ET: Endocrine therapy;   RT: Radiotherapy

2.5 Patient Status

Among the patients who had completed their treatment, 71.7% had been followed up for over 2 years; 5.8% had been followed up for less than one year for the purpose of tracking their health status. Locoregional recurrence rate was 3.9%; 3% of patients experienced distant recurrences. Mortality rate from breast cancer was 0.5% (Table 2.17).

The common sites of locoregional recurrence were breast (40.0%) and chest wall (25.2%). The number of cases having recurrence at different locoregional sites by the type of surgery received was shown in Table 2.18.

Table 2.17 Follow-up of 5,958 subjects

Follow-up period (N=5,958)	Number	(%)
< 1 year	344	(5.8)
1-2 years	1,228	(20.6)
2-5 years	2,417	(40.6)
5-10 years	1,524	(25.6)
10-15 years	325	(5.5)
>15 years	120	(2.0)
Mean follow-up period		4.4 years
Median follow-up period		3.5 years
Locoregional recurrence		
No. of locoregional recurrence	230	(3.9)
Mean time to locoregional recurrence		4.9 years
Median time to locoregional recurrence		3.6 years
Distant recurrence		
No. of distant recurrence	178	(3.0)
Mean time to distant recurrence		4.5 years
Median time to distant recurrence		3.7 years
Mortality		
No. of deaths from breast cancer	32	(0.5)
No. of deaths from unrelated causes	19	(0.3)

Table 2.18 Sites involved in locoregional recurrence in patients by type of surgery received

Locoregional recurrence Sites involved	Type of surgery received					
	BCS N (%) (N=75)	MTX N (%) (N=99)	MTX + reconstruction N (%) (N=24)	Not done N (%) (N=2)	Unknown N (%) (N=30)	Total N (%) (N=230)
Breast	64 (85.3)	0 (0.0)	1 (4.2)	0 (0.0)	27 (90.0)	92 (40.0)
Chest wall	0 (0.0)	47 (47.5)	7 (29.2)	0 (0.0)	4 (13.3)	58 (25.2)
Skin	2 (2.7)	5 (5.1)	1 (4.2)	0 (0.0)	1 (3.3)	9 (3.9)
Axilla	7 (9.3)	23 (23.2)	9 (37.5)	0 (0.0)	2 (6.7)	41 (17.8)
Supraclavicular	6 (8.0)	24 (24.2)	4 (16.7)	1 (50.0)	3 (10.0)	38 (16.5)
Internal mammary node	1 (1.3)	9 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	10 (4.3)
Others	0 (0.0)	15 (15.2)	7 (29.2)	1 (50.0)	0 (0.0)	23 (10.0)

BCS: Breast conserving surgery;   MTX: Mastectomy

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

The most common organ involved in distant metastasis was bone (47.2%), followed by lung (36.0%).

65.8% of deaths occurred in patients with stage III and above breast cancer.

Table 2.19 Organs involved in distant metastasis

Distant organs affected	Number	(%)
Mediastinal nodes	25	(14.0)
Cervical nodes	6	(3.4)
Bone	84	(47.2)
Lung	64	(36.0)
Liver	48	(27.0)
Brain	18	(10.1)
Others	27	(15.2)

Table 2.20 Characteristics of breast cancer-specific deaths

Cancer stage	No. of cases (Number, %)	Survival time (years)	Age at diagnosis in years (range)	Biological subtypes, No. of cases		
				ER+HER2-	HER2+	Triple negative ER-PR-HER2-
I	4 (12.5)	3.7 – 10.4	34-57	2	2	0
IIA	5 (15.6)	1.9 - 20.5	36-76	0	1	2
IIIA	6 (18.8)	1.1 – 8.2	40-52	4	1	1
IIIB	3 (9.4)	0.8 – 5.0	45-46	0	2	1
IIIC	6 (18.8)	0.8 – 4.9	36-59	3	0	2
IV	6 (18.8)	1.1 – 3.3	47-76	4	2	0
Unknown	2 (6.3)	3.3 – 21.8	37-45	0	0	0