World Breast Cancer Report

2012

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Published and distributed by:

International Prevention Research Institute
95 cours Lafayette, 69006 Lyon, France

iPRI Library Cataloguing in Publication Data

Boyle, P (Peter)

World Breast Cancer Report 2012

Edited by Boyle P, Autier P, Adebamowo C, Anderson B, Pinillos Aston L, Badwe RA and Yamaguchi N

(IPRI Publication 2)

1 Breast Cancer

2 Breast Cancer Control

3 Disparities

ISBN : 978-2-9539268-1-1

EAN : 9782953926811

Printed in France

Chapter 25

Breast Cancer in Turkey

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Demographics

Breast cancer is the leading cancer type among women according to the latest report released by the Turkish Ministry of Health (MoH) in 2006. Rough and age-standardised rates of breast cancer in women were 41.7/100,000 and 37.6/100,000. The highest incidence rate (162.7/100,000) was found in women 80-84 years of age. However, incidence of breast cancer in the Turkish population showed two surges through the whole life, one being at an earlier age (60-64 year old; 123/100,000) and another at the age of 80 as given in Table 25.1. Incidence rates showed a steady increase during the previous 3 years although it is not very striking. Overall breast cancer constituted 23.7% of all cancers detected according to the figures in 2006 as being the far leading cancer type in Turkish women. On the other hand, rough mortality rate of breast cancer was 7.1/100,000 (2006) in Turkey (Eser et al, 2011).

Table 25.1: Breast cancer incidence data retrieved from cancer registries in 8 cities in Turkey, 2006 (representing 15% of the Turkish population)

Age	Incidence (case number / 100,000 population)
0-4	0
5-9	0
10-14	0.2
15-19	0
20-24	0.8
25-29	6.5
30-34	18.6
35-39	40.7
40-44	80.9
45-49	100.1
50-54	106
55-59	110
60-64	123.2
65-69	119.3
70-74	109.7
75-79	99.4
80-84	162.7
85+	71.8

Screening

Turkey has a nation-wide full-scale population-based mammography screening programme since 2008. The Turkish MoH established more than 125 cancer screening, early diagnosis and training centres (KETEM; *Kanser Erken Teşhis, Tarama ve Eğitim Merkezi*) all over the country to implement breast, cervix, and colorectal cancer screening. The ultimate goal of MoH is to establish one KETEM per 250.000 inhabitants before the end of 2015 (280 KETEMs totally). Currently, there is at least one KETEM in each city in Turkey and KETEMs are primary centers for population-based cancer screenings, based on a call & recall system, In accordance with national screening guidelines and European Union Quality Assurance Criteria. Each KETEM employs 2 general practioners, 4 nurses and 4 consultants in addition to administrative staff (Figures 25.1, 25.2, 25.3, 25.4) (Cancer Control Department, 2010a). According to the Turkish national screening guidelines which KETEMs currently follow, women biannually undergo a bilateral two-view mammography starting at the age of 50 until they reach the age of 69 (KSBD, 2011; Ozmen et al, 2009). First roll-out of the programme is yet to be completed. However, coverage rate is currently below 20%. MoH plans to involve family physicians in KETEMs by 2013 in order to increase the coverage rate to over 70% before the end of 2015 (Cancer Control Department, 2010a). During 2009-2011, MoH conducted a mass media campaign for breast cancer awareness and KETEM based population-based screening programme. Additionally, MoH collaborates with the World Health Organization (WHO), the European Union IPA Projects, the Union International for Cancer Control, the International Agency for Research on Cancer (IARC), the International Prevention Research Institute (IPRI) and the Asian Pacific Countries in similar campaigns. Also, MoH is the co-founder of Black Sea Countries Breast Cancer Screening Coalition [*personal communication*].

Figure 25.1: KETEM main building

Figure 25.2: KETEM mammography unit

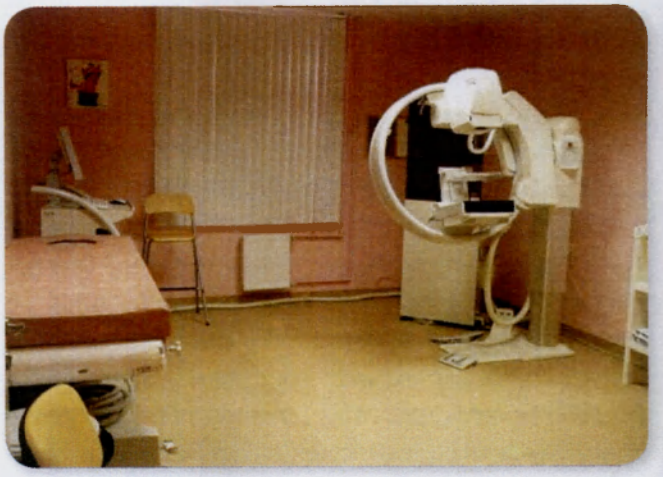


Figure 25.3: KETEM mammography reading & reporting unit

Figure 25.4: KETEM waiting area

More than 85% of all breast cancers discovered at KETEMs were reported to be stage I-II (Cancer Control Department, 2010a). However, in contrast to the Turkish MoH reports, another study from 13 large scale cancer centers in highly populated cities in Turkey revealed that 27% of breast cancer patients over 50 years of age never underwent a breast ultrasound or a mammography examination until their diagnosis. It was found that the initial presentation of breast cancer was a self-detected mass in 85% of cases (Saip et al, 2011).

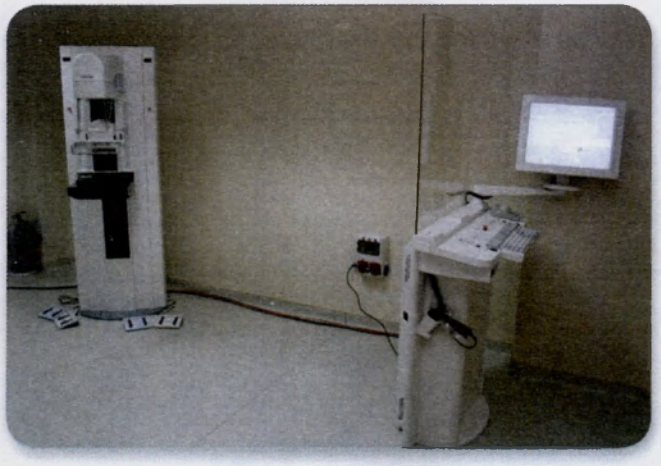
There are also other pilot screening projects undergoing in Turkey. Istanbul Greater City Municipality currently conducts an opportunistic breast cancer screening service in three districts, one at Asian side (Uskudar; population of 530,000) and the other two at European side (Bahcelievler and Bayrampasa; population of 580,000 and 270,000, respectively). In this programme, women between 40-69 years old are screened annually by bilateral two-view digital mammography imaging and breast self-examination training is provided by expert health professionals. The programme started in 2003 and until 2012, nearly 170,000 women were screened. Results of this programme are yet to be reported [*personal communication*].

Bahcesehir Mammograhy Screening Programme which is a privately funded population-based screening project was started in late 2008. Its objective is to biannually screen nearly 5,500 women who are between 40-69 years old with both bilateral two-view digital mammography and clinical examination at Bahcesehir District, Istanbul (Figures 25.5, 25.6, 25.7) (Ozmen et al, 2011; Ozmen, 2011). So far, this project completed its first round with a compliance rate of nearly 80% [*personal communication*]. The very first preliminary report of the first round is expected to be reported soon this year.

Figure 25.5: Bahcesehir Mammograhy Screening Center in Istanbul: Main building

Figure 25.6: Bahcesehir Mammography Screening Center in Istanbul: Main entrance

Figure 25.7: Bahcesehir Mammography Screening Center in Istanbul: Mammography unit



Breast Cancer Registry and Patient Characteristics

Turkish MoH recently established cancer registry centres in 12 regions in Turkey. Of those, two are already accredited by IARC. The population of these 12 regions constitutes for more than 20% of Turkey. Accuracy and completeness of collected data at these centres are audited annually by an independent party. All cancer statistics in Turkey are estimated from data retrieved from these centres, similar to the SEER database in the USA. MoH also collects passive cancer registry data from each city in Turkey. However, reliability of data collected at these centres is questionable (Eser, 2011).

The Turkish Federation of National Breast Societies (TFNBS) also established a separate registration system for breast cancer in 2005. A revised version of this database is used on-line and off-line since 2009. Until late 2011 more than 15,000 breast cancer cases from 39 cancer centres in Turkey were recorded in this database and a first overall report of this registry will be published soon this year.

Briefly, from those data recorded between 2005 and 2011, it was found that overall 1% of all cases was men. Seventeen per cent of breast cancer patients were below 40 years of age and 55% of patients were above 50. Forty-five per cent of cases were pre-menopausal. Locally advanced and metastatic cases constituted 23% of all breast cancer cases. Sixty-six per cent of all cases underwent total mastectomy (Ozmen, 2011). Although breast reconstruction following mastectomy is becoming more popular, it was only applied to 5% of those patients who had a mastectomy. Besides, almost all these patients received delayed instead of immediate reconstruction (Goktas-Baltaci et al, 2011). For those whose receptor expressions were assessed, 66% were oestrogen receptor (ER) positive, 48% were progesteron receptor (PR) positive and 24% were HER-2-neu positive. As adjuvant hormone treatment (HT), 90% of patients received tamoxifen and 10% received one of aromatase inhibitors (Ozmen, 2011). Nearly one third of the Turkish breast cancer patients used at least one type of complementary and/or alternative medicine. Almost all patients used these medications as complementary, not alternative to their regular conventional therapy. Most of them reported that they chose herbal medicines because they think that those support their general health status. Nettle (Urtica diocia/Urtica urens) was the most common consumed herbal medicine (Gulluoglu et al, 2008). A study revealed that a 5-year disease-free survival occurred in 97% of the Turkish patients with pathological stage I disease who were treated at a tertiary university hospital (Basaran et al, 2004).

According to a large questionnaire-based study, it was found that there is a wide variance regarding clinical and pathological stages of breast cancer cases in Turkey. In Marmara region, where Istanbul is the largest city, most of the breast cancer cases were early-stage (stage I; 45%), whereas at East and Middle Anatolian regions advanced or metastatic diseases were relatively more common (stage III and IV; 46.1 and 40%, respectively). Overall 6.6% of patients were reported to be stage 0 (Canturk and Gulluoglu, 2011). However, probable selection bias should be considered when assessing reliability of these findings. Also, these findings were not consistent with MoH data which reveal similar stage distribution at Eastern and Western Turkey (Cancer Control Department, 2010b).

Health care Provision Characteristics

The most common biopsy technique for diagnosis were both core biopsy (41%) and general biopsy, however this also varied according to the geographical area where the practice is done. According to records, in Marmara region core biopsy (48%) was the most common diagnostic technique, whereas in the rest of Turkey excisional biopsy was more common for tissue diagnosis in breast masses (42-70%). Breast conserving surgery (BCS) was the overall most preferred surgical treatment method in 53% of early (stage I-II) cases. Again the rates were different at each geographical region. At Marmara region, BCS rate was found to be 77%, whereas it was 21% and 23% at South East and Mediterranean regions, respectively. It was reported that overall 81% of units perform sentinel lymph node biopsy. Again the rate was lower at South East and Mediterranean regions (16% and 18%, respectively) (Canturk and Gulluoglu, 2011).

Of those university hospitals all over Turkey, 55% have a separate outpatient clinic for breast patients, 26% have a separate breast surgery unit and 17% have a high-risk outpatient clinic. Again at those university hospitals, 91% have mammography and USG equipments, 76% have magnetic resonance imaging (MRI) device and 81% have at least one dedicated radiologist specialized in breast diagnostics. Also, 69% have at least one dedicated pathologist for breast diseases and 41% have a PET-CT device. Again, it was reported that 71% of the university hospitals have at least one plastic & re-constructive surgeon who is experienced in breast reconstruction and oncoplastic surgery is performed in 48% of the hospitals (Canturk and Gulluoglu, 2011).

Regarding adjuvant treatments, 69% of hospitals have at least one medical oncologist and 64% of them have at least one radiation oncologist. However, only 55% of hospitals have a radiation oncology unit. But in 76% of the hospitals, systemic treatments are planned and administered by either medical or radiation oncologists. Also, neoadjuvant treatments are administered in 76% of the university hospitals in Turkey. In 62% of those, regular multidisciplinary tumour board meetings are held. However, only in 14% of the hospitals, patient satisfaction for breast care given by the institution is measured periodically. And, it was found that 21% of the hospitals have a physical rehabilitation and lymphedema unit (Canturk and Gulluoglu, 2011).

Again in another multicentric study, median time between symptom recognition by the patient herself and admission was found to be 10 days. Median time from first admission to tissue diagnosis, from tissue diagnosis to definitive surgery, and from surgery to systemic treatment administration were 19, 10 and 31 days, respectively. However, these intervals varied according to the geographical region where the patients reside and admit to the hospital. Interestingly, those patients who live in small-scale cities in Central Anatolia and in Marmara region had shorter intervals between symptom recognition and admission to the hospital, and also between tissue diagnosis and definitive surgery when compared to those in the three most populated cities such as Istanbul, Ankara, Izmir and cities in the Black Sea region, East and South-East Anatolia (Saip et al, 2011).

As it is obvious from all above studies, there are wide differences in means of breast cancer diagnosis and treatment in different geographic regions in Turkey. Therefore, no homogeneity exists in breast health service even at tertiary university hospitals. Considering this heterogeneity, Turkish MoH developed a national radiotherapy investment plan to be implemented before the end of 2023. Regional population distributions, infrastructure, logistic and human resource issues were taken under consideration for the planning according to the international quality performance indicators (Goksel et al, 2011).

Non-Government Organizations for Breast Care

Professional Organizations

The Turkish Federation of National Breast Societies (TFNBS):

Currently, there are 14 regional breast societies in Turkey. In 2007, TFNBS was established and 13 of regional societies decided to work under its authority. Every odd years, TFNBS organizes national breast congress and every even years the national consensus meeting for breast cancer. It has its own breast cancer registry system. It coordinates large multicentric trials on breast diseases in Turkey, as well as periodic in-service training programs of those professionals working at MoH's KETEM units. TFNBS also publishes the Journal of Breast Health which is a quarterly released, internationally indexed journal (Ozmen, 2011).

SENATURK (Senology Academy):

It was founded in 2010 in Istanbul, Turkey. Its institutional missions include developing teaching materials and programs for integrated education for breast health professionals, constructing infrastructure for learning, providing pre-service and in-training education to medical professionals, nurses, technicians, and society, determining regional quality indicators for training, research, and breast care, maintaining, auditing, and benchmarking terms and performances for providing qualified health care, designing and conducting clinical and translational research and giving face-to-face or distant counselling to individuals or institutions, as well as developing software for all these services. It has 16 departments and in those 62 distinguished Turkish and international faculty members are assigned for academic work. SENATURK's scope includes Turkey, the Balkans, the Middle East, North Africa, Caucasia, and the Caspian region. Its utmost objectives are to establish accredited high-quality cancer units and excellent centres for breast health care, train and certify health professionals and disseminate the philosophy of quality assurance, data acquisition, benchmarking in regional health systems which are natural evolving procedures for globalisation process in training and health care provision. Besides, SENATURK publishes Breast Case as its official journal which is an international peer-reviewed open access on-line publication (SENATURK, 2012).

Advocacy

Currently there are three advocacy groups in Turkey which are exclusively involved in breast cancer. All three have their offices in Istanbul. MEVA (Meme Vakfı; Breast Foundation), as being the oldest among the three, supports efforts for early diagnosis and awareness in the society. EuropaDonna Turkey is a department of the global EuropaDonna organization. This organization concentrates more on rehabilitation of already treated breast cancer patients. MEMEDER (Meme Sağlığı Derneği; Society for Breast Health), as being the youngest among the three, was founded in 2007. MEMEDER has projects on awareness (Figure 25.8) and coordinates the Bahcesehir Mammograhy Screening Project in Istanbul. MEMEDER is also currently one of official partners of TFNBS (Gulluoglu, 2009). Each October, a fun run for breast cancer awareness over the Bosphorus Bridge is organized by the coalition of Turkish MoH and the above mentioned advocacy groups (NGOs).

Clinical Research

Figure 25.8: A MEMEDER Project: Istanbul Bosphorus Bridge in pink for the Breast Awareness Week in 2011

In a recent report, Turkey was found to be the leading country which contributed to evidence-base literature among developing

countries in the EURO (European) region of the World Health Organization. In this report articles originating from Turkey constituted 16% of all those coming from developing countries in the EURO region (Lodge and Corbex, 2011). In addition to these efforts, TFNBS started a randomized clinical trial that compares surgical removal of primary cancer to primary systemic treatment in breast cancer patients with distant metastasis. This study is the very first one with this objective and continues to recruit patients since 2008. It is expected that authors will report their early results within the next few years (Soran et al, 2009). This trial is the first collaborative multicentric project coordinated by TFNBS.

Marmara University Pendik Training & Research Hospital Breast Center

The Marmara University Pendik Training & Research Hospital Breast Center was founded in late 2001. It has radiology, surgery and pathology staff who are providing breast care services within one unit. Comprehensive breast care is given to patients at a multidisciplinary setting. The Center has dedicated consultants on breast surgery, radiology, pathology, nuclear medicine, medical oncology, radiation oncology, medical genetics, physical medicine and rehabilitation, gynaecology, plastic & re-constructive surgery and psychiatry. Breast diagnostic meetings and tumour boards are regularly held weekly. The Center received quality assurance certifications for its management as well as information technology systems in 2006. It also hosts multidisciplinary postgraduate education program for breast health since 2004. The Center's first objective is to serve as a one-stop diagnostic unit and secondly to provide high standard breast cancer care and postgraduate education for its residents and medical students. The unit is affiliated with the European Academy of Senology in Germany and the European Institute of Oncology in Italy. Also, it is the full member of the SenoNetwork which is a joint project of the European Society of Mastology (EUSOMA) and the European School of Oncology (ESO). It took place at the Breast Units Directory of both institutions. The Breast Center and the Marmara University Pendik Training & Research Hospital are both members of the European Organization for Research and Treatment of Cancer (EORTC), the Breast Cancer Group since 2001. The Marmara University Hospital received an EORTC affiliation and the Breast Center received the Senology International Society (SIS) honorary membership in 2005.

In 2010, the center moved to its new building in Pendik, Istanbul (Figure 25.9). In its new place, there are two dedicated breast surgeons and one dedicated plastic & re-constructive surgeon working at the breast surgery unit. So far, immediate breast reconstruction with various types of oncoplastic and re-constructive techniques were available at the unit. Day-case surgery facilitated to shorten the waiting list. Currently, one operating room and more than 10 beds at one specific ward are available for breast patients (Figures 25.10 and 25.11). One specialized breast nurse is providing specified health care for breast patients at the unit. In 2010, 158 new breast cancer cases were admitted to the breast center and the case load had a slight decrease early after its move to its new building at the end of 2010.

Figure 25.9: Marmara University Pendik Research & Training Hospital in Istanbul: a modern comprehensive institution for breast cancer care (courtesy of Furkan Tatar)

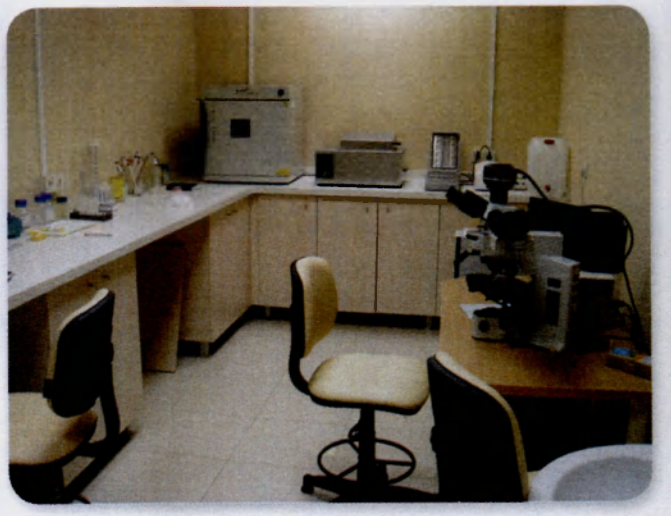
Figure 25.10: Operating room for breast surgery at Marmara University Pendik Research & Training Hospital

Figure 25.11: Surgical ward for breast care at Marmara University Pendik Research & Training Hospital

In Marmara University Hospital Breast Center, there is one dedicated radiologist who is one of the leading radiologists with necessary experience and skills. There are mammography, USG and MRI equipments. Interventional methods such as mammography, USG and MRI guided biopsy systems are available at the unit. Radio-guided occult lesion localization (ROLL) and hook-wire localization methods are used for nonpalpable lesions. Also, there is one dedicated pathologist for breast diseases at the hospital and she works exclusively on breast pathology. Immuno-histo-chemistry and florescent in-situ hybridization assessments are available at the hospital's pathology department (Figures 25.12 and 25.13).

Figure 25.12: Macroscopy unit in Department of Pathology at Marmara University Pendik Research & Training Hospital

Figure 25.13: FISH unit in Department of Pathology at Marmara University Pendik Research & Training Hospital



There is one large outpatient oncology (systemic treatment) unit in which nearly 30 patients can receive their treatments at one setting

(Figure 25.14). Unfortunately, the radiation treatment (RT) unit is still under construction at its new place in Pendik. However, until August 2010 all breast cancer patients received their RT at its previous location in Altunizade, Istanbul whenever indicated (Figure 25.15). At its new place the RT unit is expected to be completed in late 2012 and equipped with at least two latest generation LINAC devices. The whole breast RT and external beam partial breast irradiation systems will be available at the unit, as well.

Figure 25.14: Chemotherapy unit at Marmara University Pendik Research & Training Hospital

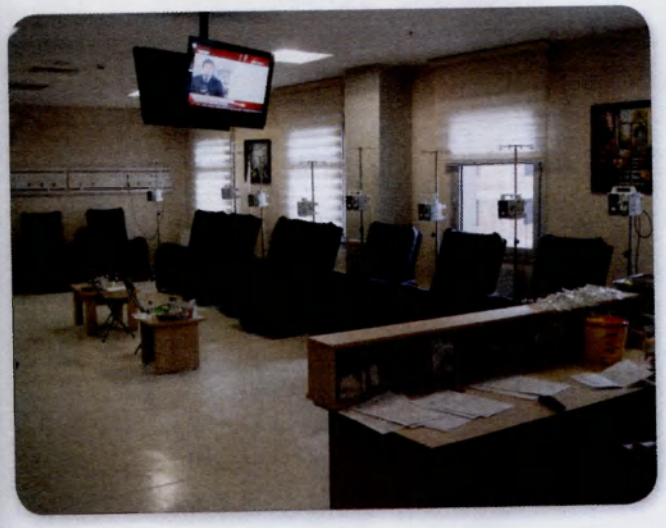
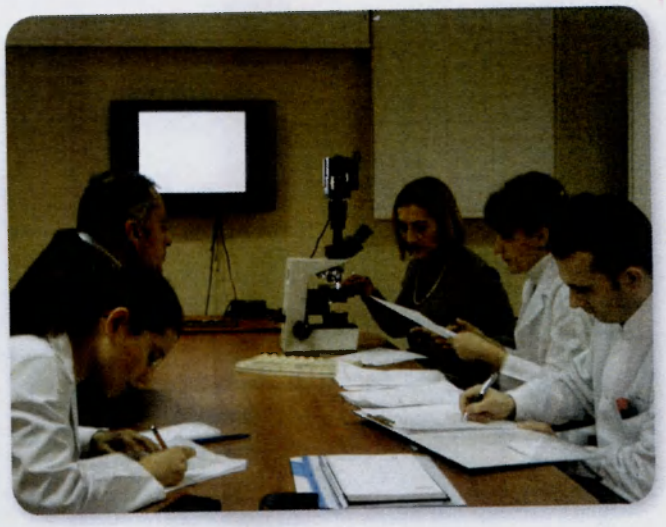


Figure 25.15: LINAC unit for radiation treatment at Marmara University Hospital, Altunizade, Istanbul

Multidisciplinary meetings are held twice weekly. One for diagnostic purposes in which all biopsies are reviewed by radiologists, surgeons and pathologists. The other for cancer patients in which the adequacy and planning of all cancer-related treatments are discussed (Figure 25.16).

Figure 25.16: Multidisciplinary meeting for breast diseases at Marmara University Pendik Research & Training Hospital



At the hospital's Nuclear Medicine Unit, PET/SPECT images are available. Sentinel lymph node biopsy by the aid of both blue-dye and radiotracer is performed routinely. The high-risk outpatient clinic is available and genetic tests can be done to those whose probability to carry a mutation is high. Psycho-oncology, lymphedema, pain, sports medicine (physical exercise) and dietary / nutritional counselling units are also available for breast cancer patients in the hospital. Nearly 50% of the breast cancer patients who were admitted to the center are included in one of the clinical trials conducted at the unit (Breast Centres Network, 2010).

In the Marmara University Pendik Research & Training Hospital, annual new breast cancer case load is around 125. Data regarding the latest consecutive 50 new breast cancer cases admitted to the Breast Center between June 2011 and January 2012 are provided in Table 25.2.

Table 25.2: Data regarding latest consecutive 50 new breast cancer cases at Marmara University Hospital, Istanbul, Turkey between June 2011-January 2012

Gender	n (%)
Male	0 (0%)
Female	50 (100%)
Age; *median years (range)*	49 (28-81)
Clinical stage	n (%)
0	2 (4%)
I	13 (26%)
II	24 (48%)
III	7 (14%)
IV	4 (8%)
Type of diagnostic biopsy	n (%)
FNAB[a]	8 (16%)
Core bx[b]	38 (76%)
Open surgical bx (excl. frozen section)	4 (8%)
Only frozen section	0 (0%)
Neoadjuvant systemic treatment	n (%)
No	46 (92%)
Yes	4 (8%)
Breast surgery	n (%)
Total mastectomy	26 (52%)
BCS[c] (lumpectomy)	24 (48%)
Axillary management	n (%)
None	2 (4%)
Only RT[d]	0 (0%)
SLNB[e] only	16 (32%)
SLNB + axillary dissection	4 (8%)
Axillary dissection	24 (48%)
Histologic type	n (%)
DCIS[f]	2 (4%)
Invasive ductal	36 (72%)
Invasive lobular	1 (2%)
Mixt	3 (6%)
Other	8 (16%)
Histologic grade	n (%)
I	3 (6%)
II	18 (36%)
III	27 (54%)
Undetermined/unknown	2 (4%)
Pathologic tumour size; *median mm (range)*	20 (7 – 60)

pT[g] stage	n (%)
Tx	0 (0%)
Tis	2 (4%)
T1	18 (36%)
T2	24 (48%)
T3	4 (8%)
T4	2 (4%)
pN[h] stage	n (%)
Nx	0 (0%)
N0	27 (54%)
N1	18 (36%)
N2	3 (6%)
N3	2 (4%)
ER[i] expression	n (%)
Negative	8 (16%)
Positive (at least 1% positive)	40 (80%)
Undetermined/unknown	2 (4%)
PR[j] expression	n (%)
Negative	5 (%10)
Positive (at least 1% positive)	43 (86%)
Undetermined/unknown	2 (4%)
HER-2 expression	n (%)
Negative (IHC[k] 0 or 1 and/or ISH[l] negative)	32 (64%)
Positive (IHC 3 and/or ISH positive)	7 (14%)
Borderline (IHC +2 without ISH)	9 (18%)
Undetermined/unknown	2 (4%)
Molecular subtyping	n (%)
Luminal A	27 (54%)
Luminal B	16 (32%)
HER-2+	3 (6%)
Triple negative	2 (4%)
Undetermined	2 (4%)
Adjuvant RT to breast after BCS	n (%)
No	2 (8%)
Yes	22 (92%)
Adjuvant RT to chest wall and/or regional lymph nodes	n (%)
No	27 (54%)
Yes	23 (46%)
Adjuvant chemotherapy	n (%)
No	14 (38%)
Yes	36 (72%)
Adjuvant trastuzumab	n (%)
No	43 (86%)
Yes	7 (14%)

Adjuvant hormone treatment	n (%)
No	7 (14%)
Yes	43 (86%)
Perioperative mortality	**n (%)**
No	50 (100%)
Yes	0 (0%)

aFNAB; fine needle biopsy, bbx; biopsy, cBCS; breast conserving surgery, dRT; radiation treatment, eSLNB; sentinel lymph node biopsy, fDCIS; ductal carcinoma in situ, gpT; pathological T stage, hpN; pathological N stage, iER; oestrogen receptor, jPR; progesteron receptor, kIHC; immuno-histochemistry, lISH; in situ hybridization.

Briefly, all patients were female and the median age was 49 years (28-81). During their first admittance, patients mostly had clinical stage II (48%) disease. Most common tool for tissue diagnosis was core-biopsy (76%). Only four patients (8%) received neoadjuvant chemotherapy. Among patients 52% underwent total mastectomy. There was no perioperative mortality. All patients with clinical stage IV (metastatic) disease were included in a prospective randomized study where they all underwent resection of the primary tumour according to the protocol. Median tumour size at surgical specimens was 20 (7-60) mm. 36 patients (72%) had invasive ductal cancer as the most common histology. Most patients (54%) had grade III tumours. Axilla was not involved in tumour metastasis (pN0) in 54% of patients. In surgical specimens, ER, PR, and HER-2 neu were expressed in 80%, 86%, and 14% of patients, respectively. Luminal A type cancers (48%) were most common. Among those who underwent BCS, 92% of patients received adjuvant radiotherapy to the whole breast. Adjuvant chemotherapy was planned or already administered in 72% of all patients. Among those, CEF (cyclophosphamide, epirubicin and 5-fluorouracil) regimen was common. Also, 86% of patients are currently receiving or planned to receive either tamoxifen or one of aromatase inhibitors. Besides, trastuzumab treatment is planned or given to 14% of patients to those whose HER-2 neu expression is positive.

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