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Factors affecting breast cancer treatment delay in Turkey: a study from Turkish Federation of Breast Diseases Societies

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Background: One of the most important factors in breast cancer (BC) mortality is treatment delay. The primary goal of this survey was to identify factors affecting the total delay time (TDT) in Turkish BC patients. **Methods**: A total of 1031 patients with BC were surveyed using a uniform questionnaire. The time between discovering the first symptom and signing up for the first medical visit (patient delay time; PDT) and the time between the first medical visit and the start of therapy (system delay time; SDT) were modelled separately with multilevel regression. **Results**: The mean PDT, SDT and TDT were 4.8, 10.5 and 13.8 weeks, respectively. In all, 42% of the patients had a TDT >12 weeks. Longer PDT was significantly correlated with disregarding symptoms and having age of between 30 and 39 years. Shorter PDT was characteristic of patients who: had stronger self-examination habits, received more support from family and friends and had at least secondary education. Predictors of longer SDT included disregard of symptoms, distrust in success of therapy and medical system and having PDT in excess of 4 weeks. Shorter SDT was linked to the age of >60 years. Patients who were diagnosed during a periodic check-up or opportunistic mammography displayed shorter SDT compared with those who had symptomatic BC and their first medical examination was by a surgeon. **Conclusion**: TDT in Turkey is long and remains a major problem. Delays can be reduced by increasing BC awareness, implementing organized population-based screening programmes and founding cancer centres.

Introduction

Breast cancer (BC) is the most common cancer among women both in developed and developing countries, with an estimated 1.38 million new cancer cases diagnosed worldwide in 2008 (23% of all cancers).[1] The incidence of BC has been steadily increasing in developing countries.[2–5] BC incidence in Turkey was 24/100,000 in 1993 and increased to 50/100,000 in 2010.[6,7] Changes in reproductive factors, lifestyle (westernized lifestyle) and age structure (aging) have increased incidence and mortality rates, especially in western Turkey.[7]

However, incidence and mortality rates are decreasing in developed countries because of early detection and improved

treatment.[8,9] In contrast, in the developing world, lack of public awareness, absence of organized screening programmes and lack of accessible and effective treatment for BC are cited as reasons for delays in treatment and higher mortality rates.[10]

There is no organized nationwide mammographic screening programme in Turkey.[7] The first and continuing organized population-based screening programme started in 2008 in Bahcesehir County, Istanbul and included >10,000 women aged 40–69 years.[11] The first results of this programme were successful regarding implementation and cost effectiveness, and will be used nationwide by the cancer control department (CCD). There are 82 Cancer Diagnosis Screening and Education Centers founded by the CCD in 81 cities in Turkey. All centres have been screening for breast and cervical cancer and inviting women for opportunistic mammography. The screening of women aged 40–69 years is free of charge.

A recent Turkish study about BC awareness and knowledge showed that 77% of women had heard or read about BC; however, only 11% of them had ever received mammography in their life, and 56% of them had sufficient knowledge on BC.[12] In another study, most of the BC patients aged <50 years, and 25% of those >50 years had breast imaging during BC diagnosis.[13] In our previous study, we found that only half of all healthy women aged between 40 and 69 years had a mammogram at least once in their life, without being involved in a regular screening programme.[11]

Treatment in BC is often delayed because of a variety of factors related to the patient's health-care provider or health-care system. Long delays are associated with worsened prognoses, reduced survival rates and a higher incidence of mastectomy.[14–16] Many previous studies have examined delays in diagnosis and treatment of BC.[17] However, only few studies have analysed in detail how delay is related to patient- and system-specific factors. The aim of this study was to investigate factors influencing patient- and system-related delay.

Methods

The study was conducted between October 2011 and March 2012. The target population was women aged ≥18 years who had been diagnosed with BC within 6 months before completing the questionnaire, and undergoing or being processed for treatment. The sample was collected following a cluster sampling procedure where the medical units were first selected with probability proportional to the number of patients treated in each facility related to the whole number of BC patients in Turkey in the year 2010. In total, 13 medical units were chosen and a designated number of interviews completed in each proportional to the number of BC patients in respective facilities. Almost half of the sample was enrolled from different sites in Istanbul, a city making up ∼20% of the Turkish population.

All respondents gave written participation consents, and the study was approved by local ethics committees. The data were collected either by nurses or medical doctors, which contributed to almost 100% reply rate. The answers provided by the respondents were not cross-validated with their individual medical records.

The questionnaire was developed in English for a larger multinational study and then translated into local languages including Turkish (18). The items on the questionnaire, including a 14-item Likert-type scale for measuring behavioural and psychological determinants of patient delay time (PDT), were developed based on previous studies on similar topics as well as a series of in-depth interviews with oncologists and patients organized specifically for the project. The testing of validity and reliability of the Likert scale with exploratory factor analysis revealed almost identical patterns of latent variables in each of 12 participant countries, which implies a good quality of measuring instrument allowing high replicability of the outcomes in various independent national environments.

The questionnaire consisted of 25 questions addressing patient- and system-related factors, demographic data and cancer stage evaluation. In particular, the questions asked about the way of detecting first signs and symptoms of BC, the nature of symptoms that were identified by the patients, the speciality of the MD who made the first diagnosis, the type of medical facility where the first BC examination was performed and possible causes of delays. In addition, the patients were asked about availability of mammography screening programmes by two variables encompassing receiving invitation to free-of-charge mammography and actual participation in the screening.

The study investigated two types of delays in treatment: PDT and system delay time (SDT). PDT was defined as the number of weeks between the first symptom discovery and registering for the first medical examination and was calculated only for patients with self-detected symptoms. On the other hand, SDT was conceptualized as the time between registering for the first medical visit and the actual start of therapy and was relevant for patients with both self-diagnosed and clinically diagnosed symptoms. On the questionnaire, there were eight categorized scales with identical time intervals: one for measuring PDT and seven for subsequent steps in a typical diagnosis process amounting to SDT. The sum of PDT and SDT was total delay time, denoted by TDT.

Statistical methods

All statistical analyses were performed using SPSS, version 22. Statistical methods included chi-square tests and one-way analysis of variance (ANOVA) for studying group differences, principal components analysis for variable reduction and multiple regression analysis to build predictive models of PDT, SDT and TDT.

Principal component analysis allowed for extracting five latent constructs from a set of 14 variables representing Likert-scale statements denoting possible behavioural, attitudinal and emotional antecedents of delay time (Kaiser-Meyer Olkin (KMO) measure of sampling adequacy = 0.682; total variance retained from the original data = 67.8%; component solution rotated with varimax method). Based on factor loadings of original scale items the five components were interpreted as (i) disregard or trivialization of BC symptoms, (ii) distrust in medical system and success of therapy, (iii) fear of consequences of BC, (iv) influence of family and friends and (v) appropriate habits of regular self-examination. These components were used in subsequent analysis as predictors in three separate multiple regression models with PDT, SDT and TDT as outcome variables (table 3). The regression equations were enhanced with additional independent variables representing personal and contextual characteristics of patients through a stepwise procedure. In total, 17 variables were considered as potential predictors in the PDT model and 19 in the PDT and SPD models. Because of a strong asymmetry in distributions of PDT, SDP and TDT (see figure 1), to increase the reliability of regression models, the base-10 logarithmic transformation was applied to the original variables.

Results

Demographics

Of 1031 surveyed respondents, 32% were aged 40–49 years, and 15% were younger than 40 years. Most respondents had primary education (53%), were vocationally inactive (67%) and lived in large cities with a population over 500,000 (60%). About one-third of respondents (39%) reported incidents of cancer among the closest female family members.

BC symptoms detection

BC symptoms were predominantly self-detected (67%), and breast lump was the most frequent symptom (75.2%), followed by breast

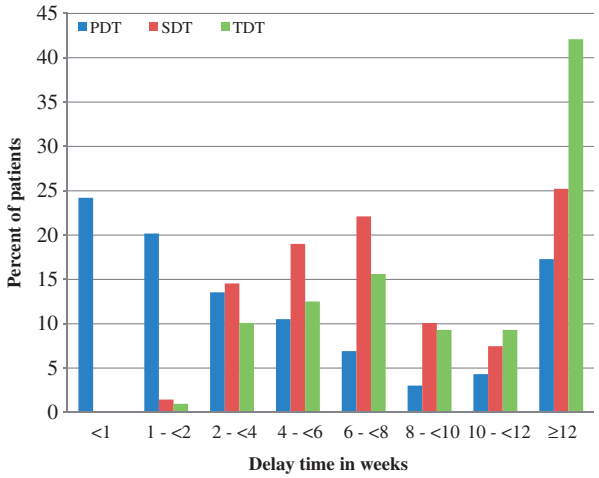

Figure 1 Frequency distributions of PDT, SDT and TDT for BC in Turkey. PDT: Patient delay time in weeks between discovering the first symptom by the patient and registering for the first medical examination. SDT: System delay time in weeks between registering for the first medical examination by the patient and the start of BC treatment. TDT: Total delay time in weeks between discovering the first symptom by the patient and start of therapy calculated as the sum of PDT and SDT

Table 1 Patient characteristics and circumstances of BC detection in Turkish patients surveyed in 2011 and 2012

Patient characteristics and diagnosis	*N*	%
Identification of first symptoms of BC		
Symptoms of BC detected at routine medical examination	112	10.9
Symptoms of BC detected by mammography	225	21.8
Symptoms of BC detected by patients themselves	694	67.3
First detected symptoms		
Breast lump	522	75.2
Breast pain	96	13.8
Changes in breast skin or nipple	35	5.0
Nipple discharge	18	2.6
Other	23	3.3
Number of symptoms before first medical examination		
Single symptom	337	48.6
Multiple symptoms	357	51.4
First appointment		
General practitioner or family physician	74	10.7
Gynaecologists	30	4.3
Oncologist	10	1.4
Internist	8	1.2
Surgeon	558	80.4
Other	14	2.0
First admission		
Private hospitals	230	33.1
Public hospitals	464	66.9

pain (13.8%), nipple or skin changes (5.0%), nipple discharge (5.0%) and other symptoms (3.3%). Diagnosis during a regular check-up or opportunistic mammography was 10.9% and 21.8%, respectively. Medical care was mostly sought from surgeons (80.4%), and 66.9% of presentations were made at public hospitals (table 1).

In Turkey, free-of-charge mammography screening programmes are available for women aged between 40 and 69 years. Patients in that age were asked if they had received and accepted a mammography invitation. Among 797 eligible patients, 173 (22%) admitted having received a mammography invitation. Despite the low coverage, a high attendance was observed among those who received remainders, equal to 60% for the 40–49 year group and 72% for the 50–69 year group.

Cancer staging

Surgical treatment and tumour staging are summarized in table 2. Most of the patients (76%) had early stage BC (Stages I and II). No lymph node metastasis was found in 42% of the patients, and breast conserving surgery (BCS) was the most frequently performed surgical procedure (60%).

Table 2 Surgical treatment and tumour staging of Turkish BC patients surveyed in 2011 and 2012

Surgical treatment and tumour staging	*N*	%
Surgery		
Mastectomy with axillary lymph node dissection	277	30.9
Mastectomy with sentinel lymph node biopsy	83	9.3
BCS with sentinel lymph node biopsy	344	38.4
BCS with axillary lymph node dissection	192	21.4
Tumour size		
<1 cm	105	12.4
1–<2 cm	329	39.0
2–<4 cm	283	33.5
≥4 cm	127	15.0
Lymph node metastasis		
No metastasis	305	41.7
Only sentinel lymph node	137	18.7
Sentinel lymph node plus other lymph nodes	289	39.5
Pathologic stage		
Stage I	204	38.3
Stage II	201	37.8
Stage III	98	18.4
Stage IV	29	5.5

Patient-related delays

Almost half of the patients sought medical care within 2 weeks (44.6%) of their first symptoms presenting, whereas 17.3% of patients delayed seeking medical care for ≥3 months. Interestingly, this group of "laggards" did not display any systematic differences from other patients across known demographic characteristics including age, education and place of living. Mean PDT was 4.8 weeks.

Multiple regression analysis indicated that disregard of symptoms ($P<0.001$) and belonging to 30–39 age group ($P<0.001$) were significantly correlated with longer PDT. Patients with stronger self-examination habits ($P<0.001$), more support from friends and family ($P<0.001$) and at a minimum secondary education ($P=0.028$) tended to report shorter PDTs (table 3). Interestingly, neither fear of BC nor distrust in medical system and positive effects of therapy were adding meaningfully to the predictive capacity of the model. This fact sets Turkey apart from the multinational sample investigated with the same method in the same period where high levels of fear coincided with shorter PDTs, and distrust was tied to longer delays.[18]

System-related delays

Mean SDT was 10.5 weeks and ranged between 4.9 and 27.0 weeks. Of the seven stages in a typical BC diagnostic process, the longest wait time of 3.2 weeks was found for the stage of seeing an oncologist. The shortest delay time of 1.6 weeks characterized registering for a physician's appointment.

Regression analysis revealed that predictors of longer SDT were disregarding discovered symptoms ($P<0.001$), distrusting in healthcare system and the success of therapy ($P=0.034$), PDT >4 weeks ($P<0.001$) and having the first medical examination in a public hospital ($P=0.014$). Shorter SDTs were characteristic of females >60 years ($P=0.0276$) (table 3).

Table 3 Multiple regression models for predicting PDT, SDT and TDT of female BC patients in Turkey

Model 1 (Dependent variable: Log 10 PDT; R = 0.447; R^2 = 0.200)					
Model variables	Unstandardized Coefficients		*P* values	Transformed B coefficients	
	B	Standard error		10^B	Average % change in PDT with 1 unit change in predictor
Constant	0.44	0.02	<0.001	–	–
Disregard of BC	0.18	0.02	<0.001	1.52	52%
Self-examination habits	−0.08	0.02	<0.001	0.83	−17%
Support from family and friends	−0.11	0.02	<0.001	0.78	−22%
At least secondary education	−0.10	0.04	0.028	0.80	−20%
Age: 30–39 years	0.10	0.05	0.044.044	1.25	25%
Model 2 (Dependent variable: Log 10 SDT; R = 0.301; R^2 = 0.091)					
Model variables	Unstandardized Coefficients		Sig.	Transformed B coefficients	
	B	Standard error		10^B	Average % change in SDT with 1 unit change in predictor
Constant	0.78	0.04	<0.001	–	–
Patient delay: > 4 weeks	0.11	0.02	<0.001	1.30	30%
Disregard of BC	0.05	0.01	<0.001	1.13	13%
First diagnosis in public versus private facility	0.06	0.03	0.014	1.15	15%
Age ≥ 60 years	−0.06	0.03	0.026	0.87	−13%
Distrust in medical system and effects of therapy	0.02	0.01	0.034	1.06	6%
Model 3 (Dependent variable: Log 10 TDT; R = 0.358; R^2 = 0.128)					
Model variables	Unstandardized coefficients		Sig.	Transformed B coefficients	
	B	Standard error		10^B	Average % change in TDT with 1 unit change in predictor
Constant	1.05	0.02	<0.001	–	–
Disregard of BC	0.10	0.01	<0.001	1.25	25%
Self-examination habits	−0.03	0.01	0.012	0.93	−7%
First examination by general practitioner vs. other MD	0.14	0.05	0.003	1.37	37%
Support from family and friends	−0.03	0.01	0.006	0.93	−7%
Participation in mammography	−0.12	0.05	0.016	0.76	−24%
Breast lump as the first sign vs. other symptoms	−0.06	0.03	0.047	0.88	−12%

Total delay time

Mean TDT was 13.8 weeks and varied in different cities between 9.1 and 33.8 weeks. Almost half (42%) of the patients had a TDT of at least 12 weeks.

Predictors of longer TDT included disregard ($P < 0.001$) and having the first medical examination by a general practitioner vs. other MDs ($P = 0.003$). In contrast, shorter TDTs were observed for respondents with stronger self-examination habits ($P = 0.012$), having more support from family and friends ($P = 0.006$), having participated in mammography screening programme ($P = 0.016$) and presenting breast lump as the first symptom ($P = 0.047$).

The relationship between TDT and cancer progression indicators (tumour size, nodal spread and metastasis) was also analysed. Findings showed that for all three indicators there were statistically significant differences ($P < 0.001$) in mean TDT depending on how advanced the symptoms were. Specifically, longer diagnostic times were associated with larger tumour sizes, affected lymph nodes and metastasis.

Discussion

Delays in BC diagnosis and treatment increase morbidity and mortality, and there are big differences in delay times among developed and developing countries. The mean TDT in the USA was reported as 4.9 weeks,[19] and the median in Denmark was 9.3 weeks.[20] Longer delays were observed in Kenya,[21] Malaysia[22] and India.[23] Globally, our mean TDT of 13.8 weeks (median 10.0) was an average delay.

Factors found to influence PDT were distrust of the health-care system, disregarding symptoms, lack of breast self-examination (BSE) and a low level of education.[24] In a Danish survey, system delay in secondary health care accounted for a substantial part of the total delay experienced by cancer patients.[20] Patients who saw their general practitioner before diagnosis experienced significantly longer system delays in secondary health care than those who were admitted directly to hospital. Another study conducted in the UK compared the delay times of six types of cancer. Patients with BC had the shortest mean PDT of 4 weeks. This was related to clearer referral guidance, a national screening programme and a high public awareness of BC.[25] We conducted a similar study investigating delay times in 11 countries and found that the longest PDT was experienced in India and Latvia with mean PDTs of 6.1 and 6.2 weeks, respectively.[26] The mean PDT in our study was 4.8 weeks (median 3.0), which was average compared with the results of estimated PDTs from developed and developing countries.[20,24,25]

Longer PDTs in developed countries were found to be associated with older age (>65 years), lower education (≤5 years), lack of routine breast examinations and health-care providers.[27] In our

study, we found that longer PDT was correlated with disregarding the detected symptoms and belonging to the 30–39 age category. Shorter PDT's were predicted by regular BSE, family and friend's support and at least secondary education, which was consistent with our previous international survey.[24]

The median SDT was reported as 5.7 weeks in Denmark, 6.0 weeks in Scotland and 4.9 weeks in the USA.[19,20,28] In China, the mean SDT and TDT were 8.7 and 21.7 weeks, respectively, with the average PDT of 13.1 weeks constituting the largest component of the delay (60%).[29] The mean SDT and TDT in the present study were 10.5 (median 7.0) and 13.8 (median 10.0) weeks, respectively, which implies that SDT in Turkey was longer than in other developed countries.

Our results revealed that longer SDTs were associated with higher scores on disregard of BC and distrust in medical system and effectiveness of therapeutic procedures. Also, longer delays were noticed for those with PDTs >4 weeks, suggesting that tardiness of some patients carried over from PDT to SDT. Shorter SDTs were associated with age >60 years, suggesting that this group of patients was prioritized in the diagnostic process. Analysis of antecedents of TDT revealed additional drivers of delay time. Consistent with previous research,[20,25] the present study showed that having the first examination by a general practitioner was a predictor of a longer TDT. The patients with shorter delays more often reported participating in mammography screening and presenting with breast lump as a first sign of BC, which was probably easier to diagnose.

The majority of patients in this study sought medical advice after identifying the symptoms of BC (67.3%), most commonly with breast lump (75.2%). Only 22% of members of this survey were asymptomatic and were diagnosed by opportunistic mammography, underlining the need for nationwide mammographic screening programmes in Turkey.[30]

Demographic characteristics of BC patients vary across the world. Populations of developed countries have grown older, which was the likely reason for only 25% of BC patients being premenopausal and aged <50 years, with 5–6% of them <40 years, as reported by other studies.[31] Our demographic findings showed that almost half of our patients were premenopausal, and 16% of them were younger than 40 years. These differences may be related to a younger population in Turkey because the percentage of women aged <40 years is 65%, as compared with 45% in the USA.[32,33] Thus, age should be taken into consideration while implementing local BC policies.

Women's awareness of BC has an important role in attending mammography. Our previous study surveyed women aged 40–69 years on their knowledge and attitudes towards BC and mammography, and showed that only 50% of them ever had a mammogram in their lives. Also, women aged >50 years, who regularly participated in gynaecological examinations and had higher educational levels, were more likely to have a mammogram.[13] Another study from Turkey showed that women who underwent mammography either had a family history of BC or they had been informed about BC before and had previous mammographic examinations.[34] The number of women screened by mammography may be improved by increasing public knowledge, which may result in more asymptomatic cases detected during screening, and may decrease the number of advanced BC patients.

The lower participation rate in mammography screening was associated with low socio-economic status, and could be increased through free-of-charge programmes and repeated invitation.[35] Only 21.7% of the participants in the present study received an invitation for mammographic screening with participation rate of 66%. This rate of participation is lower than that in Sweden (92%) and Denmark (79%), which are the countries with a reputation for high-quality medical documentation.[35,36] The presence of population-based screening programmes also decreases the incidence of diagnosis of BC at advanced stages. The rate of locally advanced BC was 5% in developed countries and 18.4% in this study.[37]

Our results showed that one-fifth of the patients were diagnosed during an opportunistic mammography, and younger patients (40–49 years) constituted almost 40% of the sample. The results of Turkish Breast Cancer Registry Program showed almost 50% of Turkish patients with BC were younger than 50 years.[7] Consequently, the CCD changed the mammographic screening age from 50–69 years to 40–69 years in 2012.

Consistent with our results, a low level of education was found to be related to longer PDT in many studies.[23,27,35–38] Despite a free-of-charge programme in Denmark, non-participants were more likely to be older, single, have low income and low educational attainment.[35]

BCS with radiation therapy is today's standard therapy for early BC. Mammography screening and increased awareness are associated with a noticeable increase in non-palpable BC and breast surgery rates.[39,40] Despite inadequate mammographic screening and low awareness, the BCS rate in our study is close to these rates (59.8%). This may be related to an increasing number of opportunistic mammograms, breast experts in different disciplines and Cancer Education and Screening Centers founded by Medical Schools and CCDs in each city of Turkey.

In conclusion, the delay in diagnosis and treatment of BC remains a serious problem. Several factors, mainly related to health-care systems and patients' psychological and behavioural attributes, appear to determine both the delay in diagnosis and treatment. Therefore, an increase in cancer awareness among women and health-care professionals, an implementation of nationwide organized screening programmes and founding of new cancer centres seem to be necessary measures to reduce TDT.

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Conflicts of interest: Co-authors, Esra Dumanli and Fatih Ozdener, are currently staff members of Roche, Istanbul. Other authors declare that they have no conflict of interest.

Key points

- This was the first study in Turkey evaluating delay times in BC patients as a part of a multinational survey.
- Mean TDT was high (13.8 weeks) in Turkey, and almost half (42%) of the patients had a mean TDT of ≥12 weeks.
- SDT was two times longer than PDT and calls for implementation of nationwide organized screening programmes and comprehensive cancer centres by health-care providers.
- The factors that affected delay times the strongest were psychological and behavioural attributes of patients.

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