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Surgical Trends in Breast Cancer in Turkey: An Increase in Breast-Conserving Surgery

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PURPOSE Breast cancer is the most frequent cancer in women, and there is a great variability in surgical practice for treating that cancer in different countries. The aims of this study were to analyze the effect of guidelines from the Turkish Federation of Breast Diseases Societies on academic institutions that have breast centers and to evaluate surgical practice in Turkey in 2018.

PATIENTS AND METHODS Between January and March 2019, a survey was sent to breast surgeons who were working in breast centers in academic institutions. The sampling frame included 24 academic institutions with breast centers in 18 cities in Turkey to evaluate interdisciplinary differences among breast centers and seven regions in Turkey regarding patients' choices, surgical approaches, and academic institutions.

RESULTS All surgeons responded to the survey, and all 4,381 patients were included. Most of the surgeons (73.9%) were working in a breast center. Multidisciplinary tumor boards were performed in 87% of the breast centers. The average time between clinical evaluation and initiation of treatment was 29 days; the longest time was in Southeast Anatolia (66 days). Only 6% of patients had ductal carcinoma in situ. Sentinel lymph node biopsy was available in every region across the country and was performed in 64.5% of the patients. In 2018, the overall breast-conserving surgery rate was 57.3% in Turkey, and it varied from 72.2% in the Black Sea region to 33.5% in Central Anatolia ($P < .001$). Oncoplastic breast surgery options were available at all breast centers. However, 25% of the breast centers from the Black Sea region and half the breast centers from Eastern Anatolia and the Mediterranean region did not perform this type of surgery.

CONCLUSION Increasing rates of nonpalpable breast cancer and decreasing rates of locoregional recurrences favored breast-conserving surgery, especially in developed countries. Guidelines from the Turkish Federation of Breast Diseases Societies resulted in more comprehensive breast centers and improved breast health in Turkey.

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INTRODUCTION

Breast cancer (BC) is the most frequent cancer in women, accounting for almost one in four cancers worldwide, and it is also the leading cause of cancer-related deaths with an estimated 627,000 deaths in 2018.[1] Despite the increase in incidence rates, BC mortality rates decreased in developed countries. But BC incidence and mortality rates have been increasing in low- and middle-income countries because of changing life styles (westernizing), aging, increasing population, diagnosis at advanced stage, and lack of modern treatment. In 1993, the incidence of BC was 24 per 100,000, and it increased to 50 per 100,000 in 2013; the number of new patients was 22,345 in Turkey in 2018.[2-4]

In the last three decades, there has been a great paradigm shift in BC surgery.[5] Patient management using primarily radical surgery was replaced with more conservative approaches by incorporating multimodality therapy and individualized care with patient-centered decision making.[6] Evidence shows that early detection, microscopic confirmation of negative margins, and widespread use of new drugs has reduced local recurrence rates by at least 50%, and breast-conserving surgery (BCS) rates reached 75% in comprehensive breast centers.[7-11] In addition, management of the axilla changed from axillary lymph node dissection (ALND) to sentinel lymph node biopsy (SLNB), even if patients had two or fewer positive sentinel lymph nodes.[12,13] The initiation of personalized and tailored medicine with shared decision making has led to less invasive interventions with fewer complications.[14,15]

There is great variability in the surgical practice patterns in Turkey. In our previous study, only 35% of patients had BCS in 2008, but the rate increased to

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39% in 2014 and to 57% in 2018.[10,16] Thus, it is imperative to develop national quality standards for a surgical approach after BC diagnosis. This will ensure that each patient receives standardized and evidence-based surgical management regardless of which region they live in or which institution they are treated at. The attitudes of the surgeons and academic institutions, in terms of type and timing of breast and axillary surgery with or without first-line systemic therapy, are of paramount importance. The Turkish Federation of Breast Diseases Societies (TFBDS), which was established in 2001, provided guidelines that included once-per-week tumor boards with practitioners having different BC specialties in attendance; each society is required to conduct tumor boards to be a full member. The aims of this study were to demonstrate the efficiency of the TFBDS guidelines and to evaluate current comprehensive breast centers and levels of surgical practice in different academic institutions in Turkey in 2018.

PATIENTS AND METHODS

The study was conducted between January and March 2019. The target population was breast surgeons who were working in breast centers in academic institutions. The sample was collected from medical schools, which were selected according to the number of patients treated in each breast center related to the total number of patients with BC in Turkey in 2018.

All respondents gave written consent for participation, and the study was approved by local ethics committees. The data were extracted from individual patient medical records at their breast center by breast surgeons who had a 100% reply rate.

The survey was developed in Turkish and included six domains and 15 questions. The domains were academic institutions, patient volume and characteristics, BCS rate, axillary management algorithm, pathologic evaluation, and oncoplastic reconstructive surgery options. Items on the survey evaluated regional and institutional surgical actions related to each domain. The sampling frame included 24 academic institutions from 18 cities in seven regions in Turkey to evaluate interdisciplinary differences among academic institutions and regions as a result of patients' choices, surgeons' attitudes, and the academic institutions themselves. The regions included Marmara, Aegean, Central Anatolia, Mediterranean, Black Sea, Eastern Anatolia, and Southeast Anatolia. The survey was prepared in Turkish and was sent to all participants by e-mail. A cover letter accompanied the survey that explained the purpose and rationale, ensured confidentiality, and estimated the time required to complete the survey.

Statistical Analyses

Data were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows 22.0 (IBM, Armonk, NY). A descriptive analysis of baseline characteristics of the six domains were expressed as mean plus standard deviation or median plus range. Categorical variables were expressed as their frequency with respective proportion in percentage. χ^2 (Fisher's exact test) was used to compare regions regarding rates of SLNB and BCS, and $P < .05$ was considered significant.

RESULTS

Academic Institutions

The characteristics of the institutions are listed in Table 1. In all, 73.9% of the surgeons in 24 academic institutions were working in a comprehensive breast center. This rate was higher (up to 100%) in western and lower (50%) in eastern and southeastern regions of Turkey. General academic institutions, in terms of the presence of a breast center and breast-specific inpatient and outpatient clinics, revealed that a breast center and inpatient breast clinic were already established in 39.1% of the regions. The average rate of outpatient clinics was 56.5%. The number of breast centers, breast-specific inpatient clinics, and breast-specific outpatient clinics in Eastern Anatolia, Southeast Anatolia, Black Sea, and Mediterranean regions was low. The average rate of multidisciplinary tumor boards presented once per week was 87%, with the lowest rate (50%) in Southeast Anatolia and the Mediterranean region. An analysis regarding various breast disciplines revealed that breast surgery, radiology, and pathology were available in every region, and medical oncology, radiation oncology, and genetics were available in 96%, 87%, and 78% of breast centers. Central Anatolia, Eastern Anatolia, and Southeast Anatolia had insufficient radiation oncology clinics (50%, 50%, and 75%, respectively). Similarly, 50% of breast centers in East Anatolia and Southeast Anatolia and 25% of breast centers in the Black Sea region had genetics departments (Table 1).

Patient Volume and Characteristics

The total number of patients treated for BC was 4,381 with a median age of 45 years (range, 22 to 87 years) in 2018 at the abovementioned academic institutions in seven regions in Turkey. Practice volume varied among the regions: there were 1,523 patients in the Marmara region and 258 patients in Southeast Anatolia. The average duration of symptoms (patient-related delay) was 3 months, differing from 2 months (2 ± 0.5 months) in the Mediterranean region and 4 months (4 ± 1 month) in the Aegean region and Southeast Anatolia. The average time between clinical evaluation and initiation of treatment (system-related delay) was 29 ± 4 days; the longest delay was in Southeast Anatolia (66 ± 3 days), and the shortest was in Eastern Anatolia (20 ± 3 days). The rates of ductal carcinoma in situ (DCIS), stage I, stage II, stage III, and stage IV BC were found to be 6.1%, 26.3%, 38.6%, 23%, and 6.1%, respectively. Although DCIS comprises only 6.1% of all cases, the rate of DCIS was 10.2% in Central Anatolia and 0.5% in Southeast Anatolia. There was substantial variation in rates of stage IV disease in different regions. The lowest rate of metastatic disease was in the Mediterranean region

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TABLE 1. Institutional Characteristics

Survey Question	Total (%)	Region in Turkey						
		Marmara (%)	Aegean (%)	Central Anatolia (%)	Mediterranean (%)	Black Sea (%)	Eastern Anatolia (%)	Southeast Anatolia (%)
Do you work at an institute specific for breast cancer?	73.9	100.0	75.0	75.0	100.0	50.0	50.0	50.0
Which of the following are available at your institute?								
Breast unit	39.1	60.0	50.0	25.0	50.0	50.0	0.0	0.0
Inpatient clinic	39.1	40.0	25.0	75.0	50.0	0.0	50.0	50.0
Outpatient clinic	56.5	80.0	50.0	50.0	0.0	50.0	50.0	100.0
Do you organize weekly breast boards regularly?	87.0	100.0	100.0	75.0	50.0	100.0	100.0	50.0
Which of the following disciplines are available at your institute?								
Surgery	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Radiology	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Clinical oncology	95.7	100.0	100.0	100.0	100.0	100.0	100.0	50.0
Radiation oncology	87.0	100.0	100.0	75.0	100.0	100.0	50.0	50.0
Pathology	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Genetics	78.3	100.0	100.0	50.0	100.0	75.0	50.0	50.0

(1%) and the highest rate was in Central Anatolia (8.5%; Tables 2 and 3). These data are of paramount importance in analyzing the differences in BC surgical management that result from the economic and sociocultural variations among regions, academic institutions, and economical and educational status throughout Turkey.

Axillary Management Algorithm

SLNB with blue dye was available in every region of Turkey. The time of initiation of SLNB differed among regions, with a median time of 13 years. SLNB has been in use in the Marmara region (22 years in the Istanbul Faculty of Medicine) longer than in any other region in Turkey, for 17 years in the Black Sea region, and for only 8 years in Southeast Anatolia (the shortest time of any region). Most of the breast centers (79.3%) had experience with the dual SLNB method (blue dye plus radioisotope). None of the breast centers used the radioisotope technique alone. There was no significant difference among regions regarding the use of the dual method for SLNB. In 2018, 64.5% of 4,381 patients underwent SLNB because of clinically negative axilla (cN0); other patients underwent ALND. The rate of SLNBs was higher in the Black Sea (86.4%; $P < .001$) and Marmara (76.6%; $P < .001$) regions and lower in Eastern Anatolia (29.9%; $P < .001$) and Central Anatolia (43.6%; $P < .001$). The overall SLN positivity rate was 40.7%, with the highest rate (74.8%) in Southeast Anatolia ($P < .001$) and the lowest rate (27%) in

TABLE 2. Patient Volume and Characteristics

Characteristic	Total	Region in Turkey						
		Marmara	Aegean	Central Anatolia	Mediterranean	Black Sea	Eastern Anatolia	Southeast Anatolia
How many new BC patients did you treat at your institute in 2018?	4,381	1,523	858	539	310	582	311	258
About the patients treated at your institute in 2018								
Median age, years	45	53	48	49	48	51	46	51
Mean age, years	45	53	51	49	49	48	44	49
Symptom period, months	3	3	4	3	2	3	3	4
Symptoms at clinical admission, months	2	3	3	2	1	2	1	2
Evaluation-initiation of treatment, days	29	24	34	22	50	22	20	66

Abbreviation: BC, breast cancer.

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TABLE 3. BC Stage at Diagnosis

Stage at Time of Diagnosis	Total (%)	Region in Turkey						
		Marmara (%)	Aegean (%)	Central Anatolia (%)	Mediterranean (%)	Black Sea (%)	Eastern Anatolia (%)	Southeast Anatolia (%)
DCIS	6.1	5.7	6.7	10.2	4.1	7.8	1.5	0.5
Stage								
I	26.3	30.9	22.0	25.8	24.8	29.8	17.5	27.5
II	38.6	39.5	34.6	41.8	35.0	38.0	38.0	43.5
III	23.0	17.6	31.1	13.5	35.1	18.5	34.5	24.5
IV	6.1	6.3	5.5	8.8	1.0	6.0	8.5	4.0

Abbreviations: BC, breast cancer; DCIS, ductal carcinoma in situ.

the Mediterranean and Black Sea regions ($P < .001$; Table 4).

BCS

All breast centers were able to perform BCS and had been doing so for different periods of time ranging from 8 to 23 years, with a median duration of 18 years. In Turkey in 2018, the overall rate for BCS was 57.3%. BCS rates varied among regions: 72.2% in the Black Sea region and 33.5% in Central Anatolia ($P < .001$). It should be emphasized that BCS was a surgical option for less than half the patients in Eastern Anatolia and Southeast Anatolia (Table 5).

Pathologic Evaluation

Preoperative diagnosis by means of core biopsy was performed in all patients. However, the rate of preoperative molecular subtype analysis was 75% in the Black Sea and Aegean regions and 50% in Eastern Anatolia. The overall use of adjuvant systemic therapy in breast centers was 87%; it ranged from 50% in the Mediterranean region and Eastern Anatolia to 75% in the Black Sea region. The median reporting period for permanent histopathologic results was 12 days (range, 9 to 20 days; Table 6).

Oncoplastic-Reconstructive Surgery Options

Oncoplastic-reconstructive surgery options were available in all breast centers. However, 25% of breast centers from the Black Sea region and half the breast centers from Eastern Anatolia and the Mediterranean region were not performing these procedures because of patient preferences or for economic reasons.

DISCUSSION

Screening mammography and increased awareness have increased the rates of early-stage and nonpalpable BC in developed countries.[17,18] But rates of locally advanced and metastatic BC are still high in developing countries because there is a lack of awareness, infrastructure, and nationwide screening programs.[19-26] In this study, rates of DCIS, stage I, and stage III BC were 6%, 26.3%, and 23%, respectively.

BCS has become a standard surgical approach for early-stage BC after the long-term follow-up results of the NSABP B-06 and Milan trials were published.[21,27] The increasing rates of nonpalpable BC and more effective treatments have increased the rate of BCS by more than 50% and decreased locoregional recurrence rates by less than 5% in 10 years in developed countries.[1,4,9,12,21,27] But BCS rates are low in low- and middle-income countries because of advanced stage at diagnosis and lack of modern diagnostic tools and therapeutic institutions.[1,17,18] The primary aim of this study was to reveal the current surgical practice patterns in academic institutions in different regions of Turkey. Overall, the rate of BCS was 35% in 2008 and 39% in 2014 in Turkey.[3,19] It was found to be 57.3% in this study. This increase may be related to use of the TFBDS guidelines, an increase in the number of breast centers, and an increase in the number of BC specialists.[3,19] The rate of BCS was 33% in Central Anatolia and 50% in both Eastern Anatolia and Southeastern Anatolia, which might be attributed either to the lack of radiation oncology institutions or to patients' choice of mastectomy.

Using a multidisciplinary approach to providing individualized treatment is of paramount importance in managing BC.[6] In Turkey, the first comprehensive breast center was founded in the Istanbul Faculty of Medicine Department of Surgery in 1986.[9] Four breast societies in Istanbul, İzmir, Bursa, and Ankara established TFBDS in 2001 and created guidelines to increase the number of nationwide breast societies, including comprehensive breast centers to improve breast health in Turkey. Today, TFBDS has 21 societies, and most of them (87%) have breast centers. Unfortunately, 50% of the patients in the Mediterranean region and Southeastern Anatolia and 25% of patients in Central Anatolia have been treated without their disease being discussed at weekly tumor boards, probably because of the work overload and lack of radiation oncologists, medical oncologists, and geneticists in their clinics. Our data revealed that many clinics in Turkey do not have weekly tumor boards to discuss managing their patients with BC and improving quality of patient care.

Another important issue is the volume of patients with BC who undergo surgery in breast centers. Volume has been one of the major determinants of successful surgical outcomes.[28,29] It has been documented that high-volume breast centers offer more BCSs as well as more SLNBs than

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TABLE 4. Axillary Management Algorithm

			Region in Turkey													
	Total		Marmara		Aegean		Central Anatolia		Mediterranean		Black Sea		Eastern Anatolia		Southeast Anatolia	
Variable	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
The rate of SLNB		100.0		100.0		100.0		100.0		100.0		100.0		100.0		100.0
No. of years of experience with SLNB	13		17		13		13		9		17		12		8	
Blue dye		16.3		20.0		0.0		0.0		0.0		25.0		100.0		0.0
Radioisotope		0.0		0.0		0.0		0.0		0.0		0.0		0.0		0.0
Dual technique		79.3		80.0		100.0		100.0		100.0		75.0		0.0		100.0
P				1.000		.562		.562		1.000		1.000		.059		1.000
In 2018																
Patients with BC	4,381		1,523		858		539		310		582		311		258	
SLNB	2,824		1,166		507		235		181		503		93		139	
Rate of SLNB		64.5		76.6		59.1		43.6		58.4		86.4		29.9		53.9
P				.000		.000		.000		.024		.000		.000		.000
Patients with SLNB	1,150		497		212		112		48		136		41		104	
Rate of patients with SLNB		40.7		42.6		41.8		47.7		26.5		27.0		44.1		74.8
P				.092		.615		.028		.000		.000		.572		.000

NOTE. All data are either No. or percent as indicated, except for rows containing *P* values. χ^2 (Fisher's exact test) was used and $P < .05$ was considered significant.
Abbreviations: BC, breast cancer; SLNB, sentinel lymph node biopsy.

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TABLE 5. BCS

	Total		Region in Turkey											
			Marmara		Aegean		Central Anatolia		Mediterranean		Black Sea		Eastern Anatolia		Southeast Anatolia	
Variable	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
BCS		100.0		100.0		100.0		100.0		100.0		100.0		100.0		100.0
No. of years of experience with BCS	18		23		19		22		13		19		8		11	
In 2018																
Patients with BC	4,381		1,523		858		539		310		582		311		258	
BCS	2,508		950		530		181		168		420		132		128	
Rate of BCS		57.3		62.4		61.7		33.5		54.2		72.2		42.5		49.5
P				.000		.003		.000		.285		.000		.000		.013

NOTE. All data are either No. or percent as indicated, except for rows containing *P* values. χ^2 (Fisher's exact test) was used and $P < .05$ was considered significant.

Abbreviation: BCS, breast-conserving surgery.

low-volume centers.[28,29] These data were in accordance with the rates in the Marmara, Black Sea, and Aegean regions: BCS rates are higher (≥ 60%) in these regions when compared with BCS rates in other regions with a lower volume of cases. Similarly, rates for SLNBs were higher in these regions.

The management of the axilla is one of the most important aspects of the surgical paradigm shift from ALND to SLNB.[13,30] In Turkey, SLNB is available in each of the regions we evaluated. Nevertheless, the technique that will be used is dependent on the academic institution. In Eastern Anatolia, only blue dye is used to identify sentinel nodes because there are no radioisotope or gamma probes. Dual SLNB methods can be used in all other regions, if necessary.

Delay in BC treatment resulted in higher disease stage and tumor burden for the patients, which is related to fewer BCSs and poor survival rates. In our previous study, total delay time (the time between the onset of first symptoms and the start of therapy) for treating BC in Turkey was found to be 13.8 weeks[31] as a result of patient- and system-related factors. In particular, patient-related delays (time between the onset of first symptoms and the first medical visit) resulted from lack of awareness of BC, distrust of the health care system, ignoring symptoms, and lack of education. System-related delay (time between the first medical visit and the start of therapy) in Turkey was found to be two times longer than patient-related delay because of higher scores on disregarding BC and distrust of the medical system and effectiveness of therapeutic procedures.[31] Similar to the patient-related delay time in our previous study, it was too long in this study (it changed from 2 to 4 months), with no major differences in patient-related delay between the western and eastern parts of Turkey. However, it is worth mentioning that the time between the first medical visit and the initiation of therapy was more than 2 months in Southeast Anatolia. The delay in initiating treatment could be a result of the long time it took to receive histopathologic reports. Other factors, including patient profile and access to treatment facility should be assessed to determine the major reasons for delay.

TABLE 6. Pathologic Evaluation

	Total		Region in Turkey											
			Marmara		Aegean		Central Anatolia		Mediterranean		Black Sea		Eastern Anatolia		Southeast Anatolia	
Variable	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Preoperative core biopsy and receptor expression analysis		100.0		100.0		100.0		100.0		100.0		100.0		100.0		100.0
Molecular subtype analysis available		87.0		100.0		75.0		100.0		100.0		75.0		50.0		100.0
Adjuvant chemotherapy		87.0		100.0		100.0		100.0		50.0		75.0		50.0		100.0
Pathologic evaluation		100.0		100.0		100.0		100.0		100.0		100.0		100.0		100.0
Mean reporting period, days	12		10		13		9		9		13		20		10	
Oncoplastic-reconstructive options available		87.0		100.0		100.0		100.0		50.0		75.0		50.0		100.0

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Increasing disease-free survival rates take into consideration oncoplastic breast surgery (OBS) for improving cosmetic outcomes.[32] The duration of training for OBS differs among countries and within each country.[20] In Turkey, OBS options are available in 87% of the regions. However, half the breast centers from Eastern Anatolia and the Mediterranean region and a quarter of the breast centers from the Black Sea region were not able to provide this service, which confirms the necessity for national accredited harmonized and standardized training for breast surgical oncologists.

Analysis of our survey showed that there has been important progress in surgical management of BC because of the recent increase in comprehensive breast centers, BCS, and rates of SLNB in Turkey. In addition, there are significant differences among regions because of social, economic, educational, and cultural factors. To our knowledge, improvements may be related to TFBDS guidelines that have been published in the bylaws of the federation since its establishment in 2001. Many postgraduate courses have been established by TFBDS in different cities to increase the number of breast centers and breast surgeons in Turkey. The data might help determine aspects of breast care that need to be improved or revised in the context of establishing national quality measures.

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