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European Journal of Breast Health

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European Journal of Breast Health (Eur J Breast Health) is an international, open access, online-only periodical published in accordance with the principles of independent, unbiased, and double-blinded peer-review.

The journal is owned by Turkish Federation of Breast Diseases Societies and it is published quarterly on January, April, July, and October. The publication language of the journal is English. The target audience of the journal includes specialists and medical professionals in general surgery and breast diseases.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

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Abstract: An English abstract should be submitted with all submissions except for Letters to the Editor. Submitting a Turkish abstract is not compulsory for international authors. The abstract of Original Articles should be structured with subheadings (Objective, Materials and Methods, Results, and Conclusion). Please check Table 1 below for word count specifications.

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Tables

Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are

Table 1. Limitations for each manuscript type

Type of manuscript	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	3500	250 (Structured)	30	6	7 or tatal of 15 images
Review Article	5000	250	50	6	10 or total of 20 images
Case Report	1000	200	15	No tables	10 or total of 20 images
Letter to the Editor	500	No abstract	5	No tables	No media

BI-RADS: Breast imaging, report and data systems

referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

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Books with a Single Author: Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as Author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki Öğrencilerin Beslenme Durumları, Fiziksel Aktiviteleri ve Beden Kitle İndeksleri Kan Lipidleri Arasındaki Ilişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

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Review

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Risk Reduction Strategies in Breast Cancer Prevention

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ABSTRACT

Evaluating the risk of breast cancer makes it possible to identify women with a high risk of developing breast cancer in the future. Adopting a healthier lifestyle, involving diet and exercise, is one way of reducing this risk-but there are other, non-modifiable risk factors, such as family history, genetics and diagnosis of premalignant lesions. In this high-risk population, the tracking must be rigorous and involve the participation of the patient herself, earlier and more frequent clinical assessment, and the use of imaging screening. Agents such as tamoxifen, raloxifene and aromatase inhibitors may be used in chemoprevention and may reduce the risk substantially. The risks and benefits must be assessed, and one must discuss with the patient her adverse events and the decision regarding the best treatment. Women who carry the BRCA1/2 mutation (very high risk) can benefit from prophylactic surgical interventions, such as bilateral mastectomy and/or bilateral salpingo-oophorectomy. This group of patients must be monitored by a multidisciplinary team, providing explanations prior to surgery regarding the surgical treatment offered, the reconstruction techniques, and the risks and complications.

Keywords: Breast, risk, mastectomy, serm oophorectomy

Cite this article as: Costa M, Saldanha P. Risk Reduction Strategies in Breast Cancer Prevention. Eur J Breast Health 2017; 13: 103-112.

Introduction

The strategies for reducing the risk of breast cancer have been increasingly studied, principally for the group of women considered to be at high risk.

The main risk factors are genetic and family factors, reproductive history, lifestyle, dense breasts, previous chest wall radiotherapy prior to the age of 30 and/or breast biopsies with a diagnosis of atypical hyperplasia or lobular neoplasia (Table 1) (1).

The availability of means of identifying women at high risk, such as genetic tests for identifying the mutations in the BRCA1 and BRCA2 oncogenes, and statistical epidemiological indexes such as the Gail model, intensify the need to define the risks and benefits of protective measures for these women.

Approximately 10%-30% of all cases of breast cancer are attributed to hereditary factors; of these, only 5%-10% correlate with hereditary factors linked with high penetrance. Only a small fraction of these cases (4%-5%) is explained by mutations in high penetrance genes transmitted in an autosomal dominant manner (2).

Germinative mutations in the BRCA1 and BRCA2 genes are responsible for approximately 50% of the total risk for hereditary breast cancer. The prevalences estimated for carriers of mutations in BRCA1/2 are, respectively, 0.11% and 0.12% in the general population, and between 12.8%-16% in high risk families with three or more cases of breast or ovarian cancer (Table 2) (3).

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These are associated with tumors in younger women. The risk in the general population is of 1/800, although among Ashkenazi Jews it is 2.3% (4).

Recent technological advances in the area of large-scale parallel sequencing have identified that the remaining 50% of cases of breast cancer are due to a combination of the effects produced by mutations in genes of high, moderate and low penetrance (5). Several of these genes have been identified and associated with other neoplasias (Table 3).

Table 1. Risk factors - family and personal history

1. Family history: women with first-degree relatives who had breast cancer prior to the age of 50, bilateral or multiple relatives with breast cancer or ovarian cancer.
2. Personal history of cancer: women who had breast cancer have a greater risk of developing cancer in the contralateral breast.
3. Presence of genetic mutation in the BRCA1 or BRCA2 genes.
4. Multiple breast biopsies with diagnosis of precursor lesions with atypia and principally in situ lobular carcinoma.
5. Diffuse changes in dense breasts, principally microcalcifications, hinder follow-up, but in isolation do not characterize indication for surgery.
6. History of chest wall radiotherapy before the age of 30, principally for treatment of Hodgkin lymphoma.
7. Two or more first-degree relatives with breast cancer
8. One first-degree relative and two or more second-degree relatives or third-degree relatives with breast cancer
9. One first-degree relative with breast cancer prior to the age of 45, and another relative with breast cancer
10. One first-degree relative with breast cancer and one or more with ovarian cancer

Clinical and research implications

The preventive measures for women at high risk are:

1- Tracking by imaging

The screening of these patients is based initially in the risk assessment (6).

A) Women with previous history of breast cancer: Clinical assessment every 4-6 months in the first 5 years, and annual mammogram. Additional imaging scans follow the same recommendations as for normal risk (7).

B) ≥35 years old, presenting a risk of invasive breast cancer in 5 years ≥1.7% according to the Gail Method: Clinical assessment each 6-12 months with a specialist, and annual mammogram (8, 9).

C) Women with a lifetime risk of breast cancer of >20%, based in dependent models of the family history (Claus, Tyrer-Cuzick) (10): Clinical assessment with a specialist each 6-12 months after the

Table 2. Risk factors from the family history due to being a BRCA1/2 mutation carrier

- Known BRCA1 and 2 mutation
- Breast cancer and ovarian cancer
- 2 or more cases of breast cancer < 50 years old in the family
- Male breast cancer
- One or more cases of cancer in the family when of Ashkenazi descent
- Ovarian cancer in person of Ashkenazi descent

Table 3. Syndrome gene or locus associated neoplasia genes with high penetrance mutations

	Biochemical Mechanisms	
Hereditary breast and ovarian cancer syndrome (HBOC)	BRCA1 (17q12-21) BRCA2 (13q12)	Female breast, ovarian cancer prostate and pancreatic cancers
Li-Fraumeni Syndrome	TP53 (17p13.1)	Breast, sarcomas, leukemias, brain tumors, adrenocortical carcinoma and lung cancers
Cowden Syndrome	PTEN (10q23.3)	Breast, thyroid, endometrium, benign harmatomas and megalencephalies
Peutz-Jeghers Syndrome testicles and colon	STK11(19013.3)	Cancers of the breast, cervix, uterus, ovaries, uterus,
Hereditary gastric cancer	CDH1 (16q22.1)	Hereditary diffuse gastric cancer, breast, lobular and colorectal cancers
	Genes with moderate penetrance mutations	
Syndromes related to ATM	ATM (11q22.3)	Breast and ovarian cancers
Syndromes related to CHEK2	CHECK2 (22q12.1)	Breast, colorectal, ovarian and bladder cancers
Syndromes related to PALB2	PALB2 (16p12.1)	Breast, pancreatic, ovarian, male breast cancers
Moderate risk of Breast and Ovarian Cancer	BARD1, MRE11A, NBN, RAD 50, 51C e 51D XRCC2	Breast and ovarian cancers

Table 4. Biochemical and molecular association between diabetes mellitus Type II and breast cancer

	Biochemical Mechanisms
Insulin	Insulin, which is secreted in increased amounts in type 2 diabetes, was shown to be mitogenic in breast tissue. This is compounded by the fact that insulin receptors tend to be over-expressed in breast cancer cells. In fact, circulating level of C-peptide as a marker for insulin secretion has been shown to be positively associated with risk of breast cancer in some studies
Insulin-like growth factor-1(IGF-1)	Increase in insulin secretion is accompanied by an increase in the serum level of IGF-1, which may also contribute to tumor growth and thus can predict the risk of breast cancer in premenopausal women.
Estrogens and androgens	Increased levels of insulin also lead to higher levels of serum estrogens and androgens through inhibition of sex hormone-binding globulin. Increased levels of estrogen and testosterone have been associated with an increased risk of breast cancer in post-menopausal women.
	Molecular Mechanisms
Insulin Receptor (IR)	IR is a heterotetrameric protein consisting of four subunits; two subunits bind insulin, while the other two subunits span the membrane, protrude into the cytosol, and have tyrosine kinase activity. Two isoforms of the insulin receptor are produced by alternative splicing: IR-A (the fetal isoform) and IR-B. In most cancers, fetal IR-A predominates because it mediates mitogenic rather than metabolic effects.
Insulin-like growth factor-1 receptor (IGF-1R)	(IGF-1R) is 60% homologous with IR and also has tyrosine kinase activity upon ligand binding by IGF-1. It promotes mitogenic, metastatic, and anti-apoptotic processes in breast cancer cells through the PI3K/Akt pathway. Because insulin and IGF-1 can bind to both IR and IGF-1R with different affinities, both ligands can enhance growth and survival
Insulin receptor substrate-1 (IRS-1)	In type 2 diabetes, insulin resistance arises from the up-regulation of cytokines and derivatives of free fatty acids. These lead to activation of protein kinase C-zeta (PKC-zeta), which phosphorylates insulin receptor substrate-1 (IRS-1), impairing its ability to activate the PI3K/Akt pathway upon ligand binding (39). It is possible that hyperglycemia and high insulin levels develop. Activation of IGF-1R by these high insulin levels can therefore lead to activation of the mitogenic and anti-apoptotic pathways, leading to an increased risk of cancer. Metabolic syndrome very often results in these patients; this is characterized by hypertension, insulin resistance, obesity, and dyslipidemia

IGF-1: insulin-like growth factor-1; IR: insulin receptor; IR-A: insulin receptor isoform A (fetal); IR-B: insulin receptor isoform B; IGF-1R: insulin-like growth factor-1 receptor; PI3K: phosphatidylinositol 3-kinase; Akt: protein kinase B; IRS-1: insulin receptor substrate-1; PKC-zeta: protein kinase C-zeta

age of 30, and an annual mammogram – also, consider annual magnetic resonance imaging (11).

D) Previous history of chest wall radiotherapy between the ages of 10-30 years old (12) ≥25 years: annual mammogram, annual magnetic resonance imaging, clinical assessment with a specialist each 6-12 months, beginning 8 to 10 years after exposure to chest wall radiotherapy, or from the age of 40 (whichever comes first). <25 years old: risk counseling and annual clinical assessment with a specialist, 8 to 10 years after exposure (13, 14).

E) Diagnosis of in situ lobular carcinoma (ISLC) or atypical hyperplasia: Clinical assessment each 6-12 months and an annual mammogram subsequent to diagnosis. One retrospective study assessed the use of magnetic resonance imaging associated with mammograms in this group of patients. Breast cancer was detected by the MRI in 4% of the patients for whom the mammograms were normal and diagnosis of ISLC and had no impact on patients with atypical hyperplasia. The routine use of screening with magnetic resonance imaging, therefore, is not indicated (15, 16).

F) Suggestive or known genetic predisposition (BRCA1/2): Clinical assessment each 6-12 months after the age of 25, annual mammogram and magnetic resonance imaging after the age of 25 or based on the earliest age of diagnosis for breast cancer in the family (11, 17-19).

Mammography

The sensitivity of mammograms in women with dense breasts has a significant decrease of <48% (>97% in fatty breasts), culminating in failure to diagnose cases of breast cancer in this population in 37-70% of cases (20). For this reason, and based in the fact that women with dense breasts are considered high risk, the use of imaging examinations in addition to mammograms is sometimes necessary.

Although some studies have suggested the use of ultrasound in conjunction with mammograms in tracking breast cancer in women with dense breasts, there are as yet insufficient studies providing evidence for the routine use of this, when there are no other associated risk factors (6, 21).

Automated breast ultrasound system (ABUS)

A new technology has been developed as an alternative to traditional ultrasound, the aim being to increase its accuracy and reduce the duration of the examination (7 minutes vs. 30 minutes), and the human failure rate (22).

Siemens Healthcare, U-Systems Inc. and SonoCiné developed ABUS, which involves the use of high-frequency waves and 3-D volumetric imaging technology for the entire breast. This 3-D image benefits the population with dense breasts, as it allows the radiologist to assess the breast from various angles, and to produce a better interpretation of the examination. At the time of writing, there are three systems in use worldwide.

Automated breast ultrasound produces a 97% increase in sensitivity when used in conjunction with mammography. As this is a new technology, further studies are necessary, as is the training of the radiologists and the operators (23).

2- Changes in lifestyle

Undertaking physical exercise and changing one's diet are the factors explored most in studies. In the major cities, greater sedentariness and a poor diet have been observed.

Studies assessing the interaction with physical activity have been increasing in frequency, and have already demonstrated a reduction in the levels of insulin and in the inflammatory reaction, and an improvement in cellular immunity, in such a way as to reduce the risk of breast cancer. When the disease is already present, physical activity has been associated with modification of the disease's staging, the body mass index, and the status of the estrogenic receptors (24).

START (Supervised Trial of Aerobic versus Resistance Training) was a Canadian study, involving the participation of 242 women diagnosed with breast cancer that were recruited between 2003 and 2005, and monitored over a minimum period of 7.5 years. They were divided into 3 groups with the objective of assessing the effect of physical exercise during chemotherapy. In the first group, the patients remained with their usual care alone, the second group was composed of those who received supervised aerobic exercise, and the third was made up of women carrying out resistance exercises. This study's main objective was to assess the disease-free survival (DSF), while its secondary objectives were to assess global survival, disease-free survival and the recurrence free interval.

Exercise during chemotherapy helps in the treatment completion rate, without need for changes in the drugs and/or their dosages. Physical activity seems to strengthen the effect of the drugs used in the chemotherapy, due to influence in the distribution and metabolism of the same.

Resistance exercises increase muscular force by 25-30%, and the lean body mass, which has been proven to be linked to lower rates of mortality in the general population. The aerobic exercises, besides leading to weight loss, prevent weight gain. Weight gain-more precisely, the increase in body fat-in patients diagnosed with breast cancer, is associated with the early recurrence of the disease and lower rates of survival. The difficulty of this type of study lies in the recruitment and adherence of the patients, due to the side effects of the chemotherapy treatment.

The daily practice of exercise, consumption of low-calorie food rich in greens, fruits and vegetables, not smoking, not drinking alcohol to excess and keeping oneself within the ideal weight for one's age are simple measures which can make all the difference (25).

3- Chemoprevention (26)

Chemoprevention (tamoxifen, raloxifene, anastrozole, exemestane) is recommended for women ≥35. Its usefulness in women <35 years old is unknown.

The importance of estrogen in the pathophysiology of breast cancer, confirmed by clinical, laboratory and epidemiological evidence, means that chemoprevention-through the use of anti-estrogenic medications, or medications that have an antagonist action on estrogen-is an important alternative in this type of approach.

The selective estrogen receptor modulators (SERMS) are medications which bind to the estrogen receptors and act as estrogenic agonists in specified tissues (e.g. bone tissue) and as antagonists of estrogen in others (the uterus and breasts). Due to the fact that they antagonize the estrogenic effect in the breast, the SERMs are excellent candidates for use in the chemoprevention of breast cancer.

Tamoxifen, a first generation SERM, reduces the risk of breast cancer in women at high risk of this disease. The use of tamoxifen in the prevention of breast cancer has been evaluated in four main clinical studies: the Breast cancer prevention trial (BCPT) undertaken by the National Surgical Adjuvant Breast and Bowel Project (NSABP P-1), the Royal Marsden Trial (RMT), the Italian National Trial (INT) and the International Breast Cancer Intervention Study (IBIS study) (27, 28, 29).

The NSABP P-1 study assessed 13.388 women, and the results showed a reduction in the incidence of invasive and noninvasive breast cancer in approximately 50% of women at high risk, which led to the drug's approval in 1998 by the Food and Drug Administration (FDA), as indicated for the reduction of the incidence of breast cancer in this population. Furthermore, this study showed a reduction of approximately 80% in the risk of invasive breast cancer in those patients with a previous diagnosis of atypical hyperplasia. However, women aged more than 50 years old, using tamoxifen, presented a risk of developing endometrial cancer which was 2.5 times greater, and a threefold increase in the relative risk of pulmonary thromboembolism (28).

The European studies-the Royal Marsden Trial and the Italian National Trial – did not reproduce the results obtained in the NSABP P-1, which was explained by the sample size of the population selected (low risk for breast cancer). A reduction in the risk of breast cancer in the subgroup of women receiving hormone replacement therapy (HRT) when the study began, or who initiated HRT during the study, was observed. In a meta- analysis of three clinical studies, a statistically significant reduction of 38% in the risk of breast cancer, with tamoxifen, was evidenced (30).

The use of tamoxifen for 5 years leads to a statistically significant reduction in the incidence of breast cancer in women at high risk of the disease. This reduction took place through the lower incidence of estrogen-receptor-positive tumors, there being no difference in comparison with placebo in those cases which did not express estrogen receptors. However, the toxicity and the presence of adverse events, such as hot flushes and increase in the risk of pulmonary embolism and endometrial cancer make it important to select patients among whom the benefits should be clearly greater than the possible risks.

Recent studies suggest that the rate of abandonment of chemotherapy with tamoxifen is high, reaching 46% after 4.5 years of use (30).

Raloxifene hydrochloride is a second generation SERM which binds with high affinity to the estrogenic receptors, in particular the alpha receptors, and presents intense antiestrogenic activity in the uterus and breasts, and estrogenic activity in the bone tissue (6, 7). Raloxifene is a well-tolerated drug, and does not increase the incidence of mastalgia, vaginal bleeding or carcinoma of the endometrium. The principal adverse events are vasomotor symptoms (hot flushes), thrombo-embolism and cramps. There is a threefold increase in the relative risk of thromboembolism related to the use of raloxifene, the absolute risk being of 0.8%.

The MORE (Multiple Outcomes of Raloxifene Evaluation) study was a multicenter study undertaken in 25 countries. It was randomized, double-blind and placebo-controlled, and included 7.705 postmenopausal women. The study's primary objective was to assess the efficacy of raloxifene in the reduction of the risk of vertebral fractures. The reduction in the risk of breast cancer was one of the study's secondary objectives. The patients who participated in the MORE study also underwent annual mammograms. A statistically significant reduction of 76% was observed in cases of invasive breast cancer with positive estrogen receptor, in the

women in the raloxifene group, in comparison with the placebo group. When only the cases of tumors with positive estrogen receptors were analyzed, the reduction in relative risk was 84%. There was no reduction in estrogen receptor negative tumors after three years of treatment. The study's follow-up period was four years (31).

The CORE (Continuing Outcomes Relevant to Evista) study was a multicenter study which evaluated the efficacy of the use of raloxifene for over 4 years for preventing invasive breast cancer. A total of 4.011 patients were recruited, who had already participated in the MORE study, totaling 8 years. At the end of the study, a 66% reduction in the risk of invasive breast cancer (independently of the presence of estrogenic receptors in the tumor) was observed among the patients using raloxifene 60 mg/day, in comparison with the placebo group. When the analysis was undertaken separately, taking into account the presence of estrogen receptors in the tumor, the reduction in the risk was of 76% in patients using raloxifene, in comparison with those using placebo. The two analyses were shown to be statistically significant ($p<0.01$) (32).

The effect of raloxifene on breast density was assessed in one study involving 280 postmenopausal women with osteopenia or osteoporosis, divided into two groups: combined hormone therapy (CHT) and raloxifene. In the CHT group, 27.4% of the women presented an increase in breast density in the mammogram, as opposed to 0.9% of the women in the group taking raloxifene. It follows that in postmenopausal women with low bone mass, therapy with raloxifene for 12 months does not increase breast density in the mammography, while CHT leads to a significant increase.

In the MORE study, the incidence of vaginal bleeding and of endometrial cancer among women taking raloxifene was similar to the group using placebos, this data being compatible with the antagonist action of estrogen in the endometrium (31).

The STAR (Study of Tamoxifen and Raloxifene) study was sponsored National Cancer Institute (NCI) and undertaken by a multicenter group of investigators. It included more than 19.000 women who presented a higher risk of invasive breast cancer and who were randomly assigned to take either raloxifene 60 mg/day or tamoxifen 20 mg/day. The study aimed to evaluate raloxifene's efficacy in reducing the risk of developing invasive breast cancer, as well as its safety in the long-term, in comparison with tamoxifen. The women who participated in the STAR study were postmenopausal, were aged at least 35 years old, and had a higher risk of breast cancer. Both raloxifene and tamoxifen reduced

-in a similar manner-the risk of developing invasive breast cancer by approximately 50%. In addition to this, the women using raloxifene had a 36% lower risk of uterine cancer and 29% fewer episodes of deep vein thrombosis and pulmonary embolism in comparison with the women in the group using tamoxifen (33).

Raloxifene was shown to be a drug as efficacious as tamoxifen in reducing the risk of breast cancer in women at high risk of this disease, with fewer adverse events such as uterine cancer.

Aromatase inhibitors

Aromatase inhibitors (AIs) potentially suppress the conversion of androgen to estrogen and block the production of estrogen not only in the normal tissues, but also in the neoplastic cells (29). Due to their different mechanism of action, AIs are better tolerated than tamoxifen and present a lower cardiovascular and endometrial risk. The AIs' safety profile is superior to tamoxifen's, with the exception of the potential increase in osteoporosis due to estrogen depletion.

The results of 5 years of anastrozole in adjuvant therapy for breast cancer demonstrated a striking reduction in the incidence of contralateral breast cancer in comparison with tamoxifen, particularly in patients with positive hormonal receptors (reduction of 53%, CI 95% 25-71, $p=0.0001$). As tamoxifen was capable of reducing contralateral cancer by 50% in comparison with the placebo, one can imagine that anastrozole reduces or delays the risk of developing breast cancer by up to 80% (31).

These results have been reproduced with other AIs, raising the possibility of use of AIs as chemoprevention for breast cancer.

Controlled studies with placebos, exemestane and anastrozole in postmenopausal women with risk factors for breast cancer have demonstrated at least 50% efficacy in reducing invasive breast cancer and that they were well-tolerated. Vasomotor symptoms were experienced, and differences were not observed in fractures or cardiovascular events. The AIs are an alternative for postmenopausal women at high risk who want chemoprevention, but who are contraindicated for SERM.

The data showing a lower incidence of breast cancer with raloxifene, both in postmenopausal women and in the high-risk population analyzed in the STAR study, provide a new perspective in reducing the risk of breast cancer. Tamoxifen continues to be the drug of choice for secondary prevention in the contralateral breast in women who have already undergone mastectomy, as this was not the population evaluated in the STAR study (33).

The use of aromatase inhibitors is restricted to postmenopausal women. We await data from prospective multicenter studies so as to include its use in our practice.

Metformin and new clinical trials

In one meta-analysis with 20 studies, the association between diabetes mellitus and increase in the risk (20%) of developing breast cancer was demonstrated; this increase can reach 23% in menopausal women. An increase in mortality from breast cancer was also evaluated (34).

Biochemical and molecular association between type II diabetes mellitus and breast cancer Table 4 (35).

Recent studies have shown a reduction of 50% in the incidence of cancer among patients using metformin for more than 4 years. The mechanisms explaining metformin's action are complex and as yet difficult to understand. Metformin seems to directly and indirectly regulate (through the insulin) the proliferation rate of tumor progenitor cells in premalignant lesions, preventing or delaying tumor formation. One can also prevent the recurrence of cancer through this regulation in the proliferation of the latent cancer stem cells (36).

Cancer is the second most common cause of death worldwide, with diabetes being the 12th. The use of metformin as an antidiabetic drug and for chemoprevention of breast cancer will bring numerous benefits and positive results.

Risk-reduction surgery

The surgical resources for reducing a woman's risk of developing breast cancer are the prophylactic mastectomy, skin-sparing mastectomy, and salpingo-oophorectomy.

The prophylactic mastectomy may be applied in two situations: contralateral mastectomy synchronous with the treatment of the primary tumor and as a bilateral procedure in women at high risk of developing this disease.

An evaluation by the multidisciplinary team-specialist in breast disease, oncologist, plastic surgeon, psychologist and geneticist-must be undertaken in order to define if surgery is indicated, to ascertain whether the patient is prepared for the possibility of a dissatisfactory esthetic result, and to define the best surgical technique and best option for reconstruction. The individualized selection of the patient is fundamental.

The risk-reduction or prophylactic mastectomy is the surgical removal of the breast tissue. It is worth emphasizing that no mastectomy technique can guarantee the total removal of the mammary gland, due to the impossibility of establishing its real limits, given that it is close to the skin and extends to the axilla. It is estimated that surgery can provide a reduction of 90% in the risk-therefore, the more radical the surgery, the greater the protection it affords (37).

The benefit of prophylactic surgery varies according to the risk of developing the disease: in women with a risk of 40% during their lifetime, prophylactic surgery adds a further 3 years of life; in women for whom the risk is 85%, this number rises to over 5 years (38).

In the case of a woman with a first-degree relative with breast cancer, the ideal is that the mastectomy should be undertaken before the patient reaches the age at which the relative was diagnosed. However, physicians recommend preventive mastectomy only for women who have already finished having children.

Techniques

The techniques consist of: Simple mastectomy (removal of the entire gland and PAC), skin and papillary-areolar complex sparing adenomastectomy (removal of the gland while preserving the skin and PAC)-this technique is the one that leaves the highest

proportion of residual breast tissue, and skin-sparing adenomastectomy (removal of the gland while preserving the skin).

Some patients must be considered to be at greater risk of occult carcinoma-such as those who present with abnormal findings in their mammogram and/or preoperative MRI, those who have not undergone a previous biopsy, or those who have a family history and did not undertake resonance prior to surgery. In these cases, the undertaking of a sentinel lymph node biopsy would be indicated in order to obtain the axillary staging (39, 40).

The reconstruction can be done with silicon prostheses, tissue expanders, or dermo-muscular flaps from the abdomen or back. In some cases, both may be used. The papillary-areolar complex can be reconstructed either with tissue from the vulvar region or through tattooing (Figures 1, 2, 3).

It is important to inform the patient regarding the risks of complications, and to emphasize the possible sequelae such as change in temperature, sensitivity and shape. For women who smoke, one must reinforce the importance of stopping smoking so as to prevent complications.

Currently, there is the possibility of autonomization of the nipple-areola complex. This technique involves dissection through a small incision of 0.5 cm on the inferior margin of the areola, the nipple is detached from the mammary gland, but remains attached to the skin, through which it receives all of its vascularization. The tissue behind the nipple is sent for biopsy. This procedure must be undertaken 15 days prior to the surgery (Figure 4).

While the rate of mastectomy has declined in recent years, more and more women with unilateral breast cancer are opting to have both breasts removed. Researchers have questioned whether the contralateral prophylactic mastectomy has been used more than necessary (41).

In one recent study held in the Sloan-Kettering Memorial Hospital, an increase was observed in the indication of contralateral prophylactic mastectomy, from 6.7% to 24.2% over a period of 8 years. In a genetic study of these 407 women, only 13% were genuinely at greater risk of developing a second breast cancer.

One study published in the National Cancer Institute's Journal (30) showed an improvement in the cancer-specific survival at 5 years in women who had undergone contralateral prophylactic mastectomy in young women with initial breast cancer and negative hormonal receptors (88.5% vs. 83.7%). In contrast, older women-with more advanced disease and with positive hormonal receptors-were not shown to have benefited from contralateral prophylactic surgery.

Figure 1. Inframammary incision with implants

Figure 2. Radial incision and PAC. Immediate post-operative period

Figure 3. Autonomization of the PAC

Figure 4. Risk reduction and sentinel lymph node surgery in the breast, with autonomization of the PAC

In 2011, Dr. Morrow presented a study (42) at the ASCO which demonstrated that women with greater anxiety regarding local recurrence were three times more likely to opt for radical surgery. She questioned whether it is ethical to treat anxiety with surgery, and concluded that further prospective studies were necessary to answer the question of whether the contralateral mastectomy had real benefits, and for which subgroup of patients.

Salpingo-oophorectomy

Prophylactic salpingo-oophorectomy is commonly recommended for carriers of the BRCA1 and BRCA2 mutations, in order to reduce the risk of breast cancer and ovarian cancer. In Canada, approximately 60% of women with the BRCA1 and BRCA2 mutations undergo prophylactic oophorectomy within 1 year of being diagnosed as having a BRCA mutation.

One case-control study in the general population showed that the bilateral oophorectomy in menopausal women is associated with a significant reduction in the risk of breast cancer. Several studies have also shown that the oophorectomy is efficacious in reducing the primary risk and the risk of contralateral breast cancer in BRCA1 and BRCA2 carriers. In that study, among women with the BRCA1 and BRCA2 mutations, the bilateral oophorectomy was associated with a highly significant reduction in the risk of subsequent breast cancer. The oophorectomy provided a substantial reduction in the risk for 15 years after the operation. Further studies will be necessary to establish whether the protection persists for longer than that. These results confirm the findings reported previously, in much smaller studies of women with hereditary susceptibility to breast

cancer and ovarian cancer. The results of these studies support the hypothesis that the suppression of estrogen reduces the risk of breast cancer, whether this is sporadic or hereditary. This result was rather unexpected, given that the majority of the tumors associated with BRCA1 are estrogen receptor negative, but there are various other hormonal modifiers related to the risk of breast cancer in which BRCA1 was identified (3).

The reduction in the risk of breast cancer seemed to be greater for carriers of the BRCA1 mutation who underwent oophorectomy prior to the age of 40, although a protective effect has also been observed in older women. The lowest magnitude in reduction of the risk was observed in BRCA2. It is probable that the lower global effect in BRCA2 is due to the patient's age at diagnosis and, consequently, on average, a greater period of time occurs between the oophorectomy and breast cancer for BRCA2 than for carriers of BRCA1 (10.5 years for BRCA2, as against 7.2 years for carriers of BRCA1). A total of 31% of carriers of BRCA2, who underwent oophorectomy, underwent this procedure 15 years or more before the appearance of their breast cancer, in comparison with 21% of carriers of BRCA1. However, during the 15 year period after oophorectomy, the level of the reduction of risk was similar for both mutation subgroups, although the BRCA2 sample size was far lower, and the result was of borderline significance. It is possible that the difference observed in the risk of breast cancer after the oophorectomy in BRCA1 as against BRCA2 may reflect biological differences in carcinogenesis (43).

Prophylactic oophorectomy is associated with a lower risk of surgical complications, but may result in the sudden beginning of the symptoms of the menopause. The long-term complications of the early surgical menopause include an increased risk of diseases of the heart, and

of osteoporosis, in conjunction with a reduction in libido. Hormone replacement therapy up to 50 years of age is frequently recommended in order to prevent these complications. However, hormone replacement has not been shown to reduce the risk of cardiovascular diseases and it is not yet known to which point hormone replacement reduces oophorectomy's protective effect in relation to the risk of breast cancer (44, 45).

In summary, a significant degree of protection against breast cancer was ascertained among carriers of BRCA1, but no similar significant reduction was observed for BRCA2. The protective effect may be limited to the period of 15 years after the operation. The strongest effects were observed for patients aged 40 years old and for early-age-onset breast cancers (diagnosed before 40 years of age) in carriers of BRCA1. In view of the normally early onset of hereditary breast cancers, we recommend that preventive oophorectomy should be considered for women carrying the BRCA1 or BRCA2 mutations, who are 35 years old and over. This operation is also envisaged to avoid ovarian cancers in this high-risk group.

Recent studies have suggested that ovarian cancer may originate in stem cells located in the distal portion of the fallopian tubes, and recommend salpingectomy as efficient for premenopausal women, leaving the oophorectomy for after the menopause (46).

Possible risks and complications

The complications which can occur are inherent to any surgical procedure-such as infection, hemorrhages, inflammation and breaking of sutures. The surgery can cause emotional sequelae due to the trauma of having the breast removed as-even with the reconstruction-the feeling of loss, and drop in self-esteem, must be worked upon. More specific risks involve the necrosis of the breast and areola and deformation of the silicon prosthesis.

There is also the chance that the patient may not be satisfied with the result of the preventive mastectomy. Patients who have a greater postoperative risk, such as smokers, the obese, or people with comorbidities such as diabetes or hypertension have provisos for undertaking the preventive mastectomy, as a result of which it may be contraindicated in some cases.

The preventive mastectomy surgery is carried out by a specialist in breast disease. However, a multidisciplinary team as indicated, which must include a plastic surgeon, to do the breast reconstruction, and a psychologist to accompany the entire process of removal of the breasts, from the medical consultation through to the postsurgical follow- up, so as to mitigate possible emotional sequelae for the patient.

Conclusions

Prophylactic mastectomy is a good option for prevention of breast cancer in women at high risk of this disease, but the method's efficacy is not totally known. Women who are candidates for the surgery must listen to specialists and gain a thorough understanding of the benefits and limits of the technique. The clinical studies undertaken have shown a reduction in the incidence of breast cancer of 90% in women who undergo the operation the same studies demonstrated a reduction from 81% to 94% in the risk of death from breast cancer.

In the Johns Hopkins University, only 10% of patients who were offered the surgery accepted it. Long-term studies of satisfaction have evidenced that 4% of patients regretted having the operation, and that 44% said that they should have done it 10 years earlier.

In the clinical decision to undertake the surgery, the following factors need to be taken into account:

- The need for reconstructive surgery
- The effect of the surgery on body image and sexuality
- The irreversibility of the decision
- Clarification that not all women who undergo the operation would have had breast cancer.

In relation to the risk-reduction Salpingo-oophorectomy

- These reduce the incidence of breast cancer and ovarian cancer
- They reduce mortality from breast cancer and ovarian cancer
- They present the best results when undertaken prior to the age of 40

Informed Consent: Informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Reference

1. Krishnamurthy A, Soundara V, Ramshankar V. Preventive and Risk Reduction Strategies for Women at High Risk of Developing Breast Cancer: a Review. Asian Pac J Cancer Prev 2016; 17: 895-904. (PMID:27039715) [CrossRef]
2. Ford D, Easton DF, Stratton M, Narod S, Goldgar D, Devilee P, Bishop DT, Weber B, Lenoir G, Chang-Claude J. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. Am J Hum Genet 1998; 62: 676-689. (PMID:9497246) [CrossRef]
3. Risch HA, McLaughlin JR, Cole DE, Rosen B, Bradley L, Kwan E, Jack E, Vesprini DJ, Kuperstein G, Abrahamson JL, Fan I, Wong B, Narod SA. Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. Am J Hum Genet 2001; 68: 700-710. (PMID:11179017) [CrossRef]
4. Warner E, Foulkes W, Goodwin P, Meschino W, Blondal J, Paterson C, Ozcelik H, Goss P, Allingham-Hawkins D, Hamel N, Di Prospero L, Contiga V, Serruya C, Klein M, Moslehi R, Honeyford J, Liede A, Glendon G, Brunet JS, Narod S. Prevalence of BRCA mutations in an unselected population of Ashkenazi Jewish women with breast cancer. J Natl Cancer Inst 1999; 91: 1241-1247. (PMID:10413426) [CrossRef]
5. Banerji S, Cibulskis K, Rangel-Escareno C, Brown KK, Carter SL, Frederick AM, Lawrence MS, Sivachenko AY, Sougnez C, Zou L, Cortes ML, Fernandez-Lopez JC, Peng S, Ardlie KG, Auclair D, Bautista-Piña V, Duke F, Francis J. Sequence analysis of mutations and translocations across breast cancer subtypes. Nature 2012; 486: 405-409. (PMID: 22722202) [CrossRef]
6. NCCN Guidelines Version 1.2016 Breast Cancer Screening and Diagnosis
7. Impact of follow-up testing on survival and health-related quality of life in breast cancer patients. A multicenter randomized controlled trial. The

GIVIO Investigators. JAMA 1994; 271: 1587-1592. (PMID:8182811) [CrossRef]
8. Costantino JP, Gail MH, Pee D, Anderson S, Redmond CK, Benichou J, Wieand HS. Validation studies for models projecting the risk of invasive and total breast cancer incidence. J Natl Cancer Inst 1999; 91: 1541-1548. (PMID:10491430) [CrossRef]
9. Gail MH, Costantino JP. Validating and improving models for projecting the absolute risk of breast cancer. J Natl Cancer Inst 2001; 93: 334-335. (PMID:11238688) [CrossRef]
10. Evans DG, Howell A. Breast cancer risk-assessment models. Breast Cancer Res 2007; 9: 213. (PMID:178881889
11. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, Morris E, Pisano E, Schnall M, Sener S, Smith RA, Warner E, Yaffe M, Andrews KS, Russell CA. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin 2007; 57: 75-89. (PMID:17392385) [CrossRef]
12. Bhatia S, Yasui Y, Robison LL, Birch JM, Bogue MK, Diller L, DeLaat C, Fossati-Bellani F, Morgan E, Oberlin O, Reaman G, Ruymann FB, Tersak J, Meadows AT. High risk of subsequent neoplasms continues with extended follow-up of childhood Hodgkin's disease: report from the Late Effects Study Group. J Clin Oncol 2003; 21: 4386-4394. (PMID:14645429) [CrossRef]
13. Ng AK, Garber JE, Diller LR, Birdwell RL, Feng Y, Neuberg DS, Silver B, Fisher DC, Marcus KJ, Mauch PM. Prospective study of the efficacy of breast magnetic resonance imaging and mammographic screening in survivors of hodgkin lymphoma. J Clin Oncol 2013; 31: 2282-2288. (PMID:23610104) [CrossRef]
14. Children's Oncology Group Long-term Follow-up Guidelines. Version 3. 2008. Available from: www.survivorshipguidelines.org
15. Arpino G, Laucirica R, Elledge RM. Premalignant and in situ breast disease: biology and clinical implications. Ann Intern Med 2005; 143: 446-457. (PMID:16172443) [CrossRef]
16. Lakhani SR. In-situ lobular neoplasia: time for an awakening. Lancet 2003; 361: 96. [CrossRef]
17. Warner E, Plewes DB, Hill KA, Causer PA, Zubovits JT, Jong RA, Cutrara MR, DeBoer G, Yaffe MJ, Messner SJ, Meschino WS, Piron CA, Narod SA. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA 2004; 292: 1317-1325. (PMID:15367553) [CrossRef]
18. Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, Gilbert FJ, Griebsch I, Hoff RJ, Kessar P, Lakhani SR, Moss SM, Nerurkar A, Padhani AR, Pointon LJ, Thompson D, Warren RM. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet 2005; 365: 1769-1778. (PMID: 15910949) [CrossRef]
19. Kuhl CK, Schrading S, Leutner CC, Morakkabati-Spitz N, Wardelmann E, Fimmers R, Kuhn W, Schild HH. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. J Clin Oncol 2005; 23: 8469-8476. (PMID:16293877) [CrossRef]
20. Vachon CM, Sellers TA, Scott CG, Christopher G. Scott, Karthik Ghosh, Kathleen RB, Janet EO, Matthew R. Jensen, Sandhya Pruthi, Marilyn JM, Daniel JS, Pankratz VS. Longitudinal breast density and risk of breast cancer. Cancer Research 2011; 70: 4828. [CrossRef]
21. Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, Pisano ED, Jong RA, Evans WP, Morton MJ, Mahoney MC, Larsen LH, Barr RG, Farria DM, Marques HS, Boparai K. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. JAMA 2008; 299: 2151-2163. (PMID:18477782) [CrossRef]
22. Inciardi M M.D. "Breast Ultrasound: What's New in 2013." Imaging Technology News 2012; 10: 39-41.
23. "FDA Approves First Breast Ultrasound Imaging System for Dense Breast Tissue." FDA Press Release. September 2012
24. Lahmann PH, Friedenreich C, Schuit AJ, Salvini S, Allen NE, Key TJ, Khaw KT, Bingham S, Peeters PH, Monninkhof E, Bueno-de-Mesquita HB, Wirfält E, Manjer J, Gonzales CA, Ardanaz E, Amiano P, Quirós JR, Navarro C. Physical activity and breast cancer risk: the European Prospective Investigation into Cancer and Nutrition. Cancer Epidemiol Biomarkers Prev 2007; 16: 36-42. (PMID:17179488) [CrossRef]
25. Tehard B, Friedenreich CM, Oppert J-M, Clavel-Chapelon F. Effect of physical activity on women at increased risk of breast cancer: results from the E3N cohort study. Cancer Epidemiol Biomarkers Prev 2006; 15: 57-64. (PMID:16434587) [CrossRef]
26. NCCN Guidelines Version 1.2017 Breast Cancer Risk Reduction
27. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005; 365: 1687-1717. [CrossRef]
28. King MC, Wieand S, Hale K, Lee M, Walsh T, Owens K, Tait J, Ford L, Dunn BK, Costantino J, Wickerham L, Wolmark N, Fisher B. Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2: National Surgical Adjuvant Breast and Bowel Project (NSABP- P1) Breast Cancer Prevention Trial. JAMA 2001; 286: 2251-2256. (PMID:11710890) [CrossRef]
29. Cuzick J, Sestak I, Cawthorn S, Hamed H, Holli K, Howell A, Forbes JF. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. Lancet Oncol 2015; 16: 67-75. [CrossRef]
30. Powles TJ, Ashley S, Tidy A, Smith IE, Dowsett M. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. J Natl Cancer Inst 2007; 99: 283-290. (PMID:17312305) [CrossRef]
31. Ettinger B1, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, Christiansen C, Delmas PD, Zanchetta JR, Stakkestad J, Glüer CC, Krueger K, Cohen FJ, Eckert S, Ensrud KE, Avioli LV, Lips P, Cummings SR. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA 1999; 282: 637-645. (PMID:10517716)
32. Martino S, Cauley JA, Barrett-Connor E, Powles TJ, Mershon J, Disch D, Secrest RJ, Cummings SR. Continuing outcomes relevant to Evista: breast cancer incidence in postmenopausal osteoporotic women in a randomized trial of raloxifene. J Natl Cancer Inst 2004; 96: 1751-1761. (PMID:15572757) [CrossRef]
33. Land SR, Wickerham DL, Costantino JP, Ritter MW, Vogel VG, Lee M, Pajon ER, Wade JL 3rd, Dakhil S, Lockhart JB Jr, Wolmark N, Ganz PA. Patient-reported symptoms and quality of life during treatment with tamoxifen or raloxifene for breast cancer prevention: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. JAMA 2006; 295: 2742-2751. (PMID:16754728) [CrossRef]
34. Larsson SC, Mantzoros CS, Wolk A. Diabetes mellitus and risk of breast cancer: a meta-analysis. Int J Cancer 2007; 121: 856-62. (PMID:17397032) [CrossRef]
35. Micallef D, Micallef S, Schembri-Wismayer P, Calleja-Agius J. Novel applications of COX-2 inhibitors, metformin, and statins for the primary chemoprevention of breast cancer. J Turk Ger Gynecol Assoc 2016; 17: 214-223. (PMID:27990091) [CrossRef]
36. Del Barco S, Vazquez-Martin A, Cufí S, Oliveras-Ferraros C, Bosch-Barrera J, Joven J, Martin-Castillo B, Menendez JA. Metformin: multi-faceted protection against cancer. Oncotarget 2011; 2: 896-917. (PMID:22203527) [CrossRef]
37. Hartmann LC, Schaid DJ, Woods JE, Crotty TP, Myers JL, Arnold PG, Petty PM, Sellers TA, Johnson JL, McDonnell SK, Frost MH, Jenkins RB. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Engl J Med 1999; 340: 77-84. (PMID:9887158) [CrossRef]
38. Hamm RM, Lawler F, Scheid D. Prophylactic mastectomy in women with a high risk of breast cancer. N Engl J Med 1999; 340: 1837-1838. [CrossRef]

39. Boughey JC, Khakpour N, Meric-Bernstam F, Ross MI, Kuerer HM, Singletary SE, Babiera GV, Arun B, Hunt KK, Bedrosian I. Selective use of sentinel lymph node surgery during prophylactic mastectomy. Cancer 2006; 107: 1440-1447. (PMID:16955504) [CrossRef]
40. Miller CL, Specht MC, Skolny MN, Jammallo LS, Horick N, O'Toole J, Coopey SB, Hughes K, Gadd M, Smith BL, Taghian AG. Sentinel lymph node biopsy at the time of mastectomy does not increase the risk of lymphedema: implications for prophylactic surgery. Breast Cancer Res Treat 2012; 135: 781-789. [CrossRef]
41. Metcalfe K, Lynch HT, Ghadirian P, Tung N, Olivotto I, Warner E, Olopade OI, Eisen A, Weber B, McLennan J, Sun P, Foulkes WD, Narod SA. Contralateral breast cancer in BRCA1 and BRCA2 mutation carriers. J Clin Oncol 2004; 22: 2328-2335. (PMID:15197194) [CrossRef]
42. Morrow, M Contralateral Prophylatic mastectomy Journal of Clinical Oncology in April 2011.
43. Rebbeck TR, Lynch HT, Neuhausen SL, Narod SA, Van't Veer L, Garber JE, Evans G, Isaacs C, Daly MB, Matloff E, Olopade OI, Weber BL. Reduction in cancer risk after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers. N Engl J Med 2002; 346: 1616-1622. (PMID:12023993) [CrossRef]
44. Colditz GA, Willett WC, Stampfer MJ, Rosner B, Speizer FE, Hennekens CH. Menopause and the risk of coronary heart disease in women. N Engl J Med 1987; 316: 1105-1110. (PMID:3574358) [CrossRef]
45. Aitken JM, Hart DM, Anderson JB, Lindsay R, Smith DA, Speirs CF. Osteoporosis after oophorectomy for nonmalignant disease in premenopausal women. Br Med J 1973; 2: 325-8. (PMID:4704517) [CrossRef]
46. Britt K. Erickson, Michael G. Conner, Charles N. Landen. The role of the fallopian tube in the origin of ovarian cancer. Am J Obstet Gynecol 2013; 209: 409-414. [CrossRef]

Original Article

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Educational Study to Increase Breast Cancer Knowledge Level and Scanning Participation among Women Working at a University

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ABSTRACT

Objective: The aim of the study is to increase the participation level of women in screening programs by increasing the level of knowledge about early diagnosis and screening methods for breast cancer (BC).

Materials and Methods: This was a pretest-posttest one group design study held in Eskişehir Osmangazi University, Turkey. The sample consisted of 405 women in all departments of the University. Data were collected using socio-demographic forms and questionnaires. Training about BC was provided for participants. The questionnaire used prior to the training to measure levels of knowledge about BC was re-administered 3 weeks after the training.

Results: The women were most commonly aware of the breast self-examination (68.1%). The ratio of women who had had mammography in the previous year was 11.4%. The BC knowledge level significantly increased after the training (p=0.001).

Conclusion: This study determined that the level of knowledge about BC in terms of early detection and screening was low and that the percentage of participation in screening was also low.

Keywords: Education, early diagnosis, breast cancer, breast cancer screening

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Introduction

Breast cancer (BC) is the second most common type of cancer in the world and the primary cancer type among women (25.2%) (1). Analyses using Globocan 2012 data have reported that one out of every 25 women in Turkey will develop BC in some period of their lives (2).

The early detection and treatment of BC has an impact on extending the life span, decreasing mortality and raising the quality of life. The methods primarily recommended for early detection include the Breast Self-Examination (BSE), Clinical Breast Examination (CBE) and mammography (3). Developing screening programs, identifying high risk groups and raising individual awareness are important in promoting the early detection of BC. The lack of knowledge about cancer and methods of early detection diminish awareness and have a negative impact on the participation of women in cancer screening programs (4). Studies conducted in Turkey show that women are inadequately informed about early diagnosis and screening methods for breast cancer. Socio-cultural characteristics also have an important influence on the screening behaviors of women (5-8).

Screening programs for BC in Turkey are conducted by the Cancer Early Diagnosis, Screening and Education Centers (CEDSEC). According to the national BC screening standards, women at the ages of 40-69 years are eligible to undergo mammography and CBE every two years (3). The screening rates have not reached the desired levels in Turkey (20-30% of the target population could be screened). The

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Public Health Agency of the Turkish Ministry of Health has stated that one of the three main reasons for this is a lack of awareness (3). It is aimed to increase the participation of women in screening programs by increasing the level of knowledge about early diagnosis and screening methods for breast cancer in this study.

Materials and Methods

Study design and sample

This is a pretest-posttest one group study design conducted at Eskişehir Osmangazi University, Turkey between January and November 2013. The universe of the study comprised a total of 903 women, ages 30 and above (min: 30-max: 59 years), working in 11 academic and administrative departments of university. Women who were at and above 30 years of age and were literate constituted the sample of the study. The women who received BC treatment were not included in this study.

Data collection tool

The first part of the data collection for the study consisted of 36 questions that were formulated to determine the women's sociodemographic characteristics, their risk factors with respect to BC and the status of their use of secondary protection methods; the second part comprised a questionnaire of 20 items designed to measure the level of their knowledge about BC. The questions that determined the level of knowledge were related to the risk factors, symptoms and early diagnosis methods of BC. Questions that were answered correctly were scored as "1", wrong answers were scored "0" (total score min: 0-max: 20).

Breast cancer training program and data collection

The training presentation and booklet related to the risk factors, symptoms and early diagnosis methods of BC were prepared before the training. The training meetings were planned in 11 academic and administrative departments in total. All of the women were visited and invited to attend the training program by the researchers. Out of the 903 women, 405 participated in the training sessions and constituted the study group. The women who did not attend the training program (n=498), were given booklet about BC. Immediately before the start of the training, the women participating in the meeting (n=405) were provided with information about the purpose of the study and their verbal consents were obtained. Later, the data collection tool was distributed and the participants were asked to fill these out. After the completion of the data collection tool, an educational presentation of 25 minutes was given by the same researchers in all the departments. Booklets were distributed after the training. Three weeks after the training, the researchers visited the departments where the women worked to carry out an assessment of the effectiveness of the sessions. At this point, the 20-item questionnaire on BC that had been administered prior to the training to ascertain knowledge levels was re-administered to the 405 women.

Breast cancer screening

The women who were 40 years of age and older were invited to participate in the screening of BC according to National Cancer Screening Standards (144 out of 405). Out of the 144 women, 55 had had mammography scans in the last two years; 32 did not agree to participate in the screening. The contact information (the department they worked in, their phone numbers and email addresses) was obtained from the 57 women who agreed to participate in the screening. Appointments were made at Eskişehir CEDSEC for the women's breast cancer screening process. The women who took part in the screening on the appointment dates were picked up at their work stations and driven to CEDSEC by a vehicle provided by the Eskişehir Osmangazi University. The screening process was completed with 45 women. The women were admitted to CEDSEC and their CBEs and mammography scans were taken. In addition, the women were registered in CEDSEC's screening program for subsequent routine check-ups. The screening results were obtained via courier service from CEDSEC by the researchers, who informed the women of the results and sent them their reports. Cases from which adequate data could not be obtained or that appeared to be dubious according to the mammography test results were referred to the relevant departments for advanced tests.

Statistical analysis

The data obtained from the study were evaluated using the Statistical Package Program. In the data analysis, descriptive statistics (mean, standard deviation) as well as paired sample t-test were used.

Results

Within the study group, 64.4% of the women were aged between 30-39 years (n=261) and 35.6% of them were aged between 40-59

Table 1. Characteristics of the women's knowledge and behavior concerning breast cancer early detection and screening methods

	n	%
Known early detection and screening methods for breast cancer*		
Breast self-exam	276	68.1
Clinical examination	188	46.4
Breast ultrasound	213	52.6
Mammography	252	62.2
Regularly performing a breast self-exam		
Performing it once a month	41	10.1
Performing it irregularly	210	51.9
Not performing it	154	38.0
Times mammography were taken		
In the last 1 year	46	11.4
Every 1-2 years	28	6.9
Every 3-4 years	27	6.7
In more than 5 years	14	3.5
Reasons for women's non-use of detection and screening methods*		
Husband/family does not permit it	1	0.2
Embarrassed	15	3.7
Fear of examination and mammography	22	5.4
Not knowing where to have it done	4	1.0
Not knowing that it should be done	41	10.1
Fear of breast cancer	5	1.2
Neglect	229	56.5

*More than one responses provided

Table 2. Comparison of women's mean knowledge level scores regarding breast cancer before and after the training program

	N	$\bar{X}$±SD	t	p
Pretest	405	8.69±0.283	-3.503	0.001
Posttest	405	10.01±0.273		

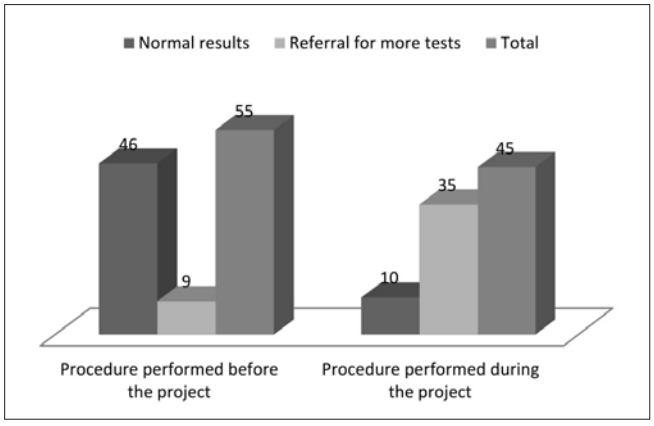

Figure 1. Women's screening results

years (n=144). More than half of the women were married (66.4%) and a large majority (%75) were university graduates. While 50.6% of the women worked as civil servants, 23.5% were academicians. It was found that 7.4% were in the postmenopausal period and 1.2% of the women in menopause were receiving hormone replacement therapy (HRT). Within the whole group, 361 (89.1%) women had no family history of BC (Table 1).

The women were most commonly aware of the BSE method of early detection and screening (68.1%). Although knowledge of this method scored higher than the other methods, the women who regularly used this method represented only 10.1% of the group. The women who had had mammography in the previous year represented 11.4% (Table 1).

A highly significant relationship was found in the statistical analysis of the study group's scores between the women's knowledge levels before the training on BC (pretest) and their knowledge after the training (posttest) (p=0.001) (Table 2).

Women's screening results

According to the mammography test results, CEDSEC assessed the results of 10 out of the 45 women as normal. Thirty-five women were referred to the General Surgery Breast Diseases Clinic for a breast ultrasound and other studies. One individual out of these referred cases was recommended a biopsy. Out of the 55 women who did not participate in the screening but had participated in a screening over the last two years, the screening results of 46 were normal, while 9 were referred for further studies, and 1 received an in situ diagnosis of carcinoma and was started on treatment (Figure 1).

Discussion and Conclusion

It is important to know early diagnosis methods for increasing the participation rate in breast cancer screening programs. In this study, it was aimed to increase the knowledge and participation levels of women in the screening by means of training on BC. Knowledge of early detection and screening methods and the appropriate use of these techniques are of great importance for early diagnosis of BC since this increases the probability of a successful treatment, raises patients' quality of life, and reduces mortality rates.

This study examined known early detection and screening methods and found that the techniques most widely known were consistent with the reports of other studies in Turkey (7, 8), namely BSE (68.1%) and in second place, mammography (62.2%) (Table 1). In a study that looked into the levels of knowledge about early detection and screening tests for BC among women aged 40 and over in Iran, it was reported that 20% knew about BSE, 15% knew about CBE and 10% about mammography (9). In another study conducted in Nigeria, 29% of the women were reported to be aware of the BSE and the BC detection methods (10). When these studies that were carried out in Iran and Nigeria are compared with the results of the present study, it can be seen that the rates reported are low. In Kwok & Fonk's study (2014) about the use of BC screening methods by women in Hong Kong, it was shown that 70%-90% of the women had heard about BSE, CBE and mammography. The knowledge levels of women about screening methods were higher than in our study (11).

The implementation of early detection and screening methods are as important in cancer as the awareness of these methods. Since medical check-ups are not adequately pursued and the BC mortality rate is high due to late detection and treatment in Turkey, it has been pointed out that the practice of BSE is of particular importance in the early diagnosis of BC, as it is in other low-medium income countries, the group of which Turkey is a member (12). The ratio of women in the study group that practiced BSEs was 68%, and only 10.1% among these practiced it regularly, a fairly low rate (Table 1). In community-based studies carried out in Turkey, it is reported that the rate of women practicing BSEs range from 23.7%-84.1% depending upon the characteristics of their particular regions and those they share with the women in the study group. The rate of women practicing BSEs regularly is even lower (9.6%-42.6%) (8, 13).

While the rate of women in the study group undergoing mammography is 28.5%, the women in this group that had a mammography in the previous year represent 11.4% (Table 1). This rate, when compared with the rate of practicing BSE, is considerably low. Studies in Turkey have generally reported low rates of women undergoing mammography, similar to the present study (5.1%-42.7%) (6, 14). According to the European Health Interview Survey (EHIS) conducted by the European Commission EUROSTAT in 17 European countries, the rate of women in the age range of 50-69 who have their mammography scans taken varies between 13.5%-92.9%; Turkey's mammography rate is 28.1% (15).

The main reasons that women cited for not making use of detection and screening methods was neglect, lack of knowledge about the need for the procedure rating second, and lastly, the fear of being examined and undergoing a mammography scan (Table 1). Our results are consistent with the literature in Turkey (5, 14). After reviewing 17 studies on the subject, Alexandraki and Mooradian (2010) have reported the reasons why women do not have mammography done as follows: pain, embarrassment, being financially disadvantaged and not having health insurance, a lack of knowledge, lack of trust in healthcare professionals and hospitals, and language problems (16).

A high level of knowledge about BC has a positive impact on the screening behavior. In order to raise women's awareness about early detection and screening methods in BC, it is recommended that programs of education be organized for this purpose (8, 17). The level of knowledge of women was low before the training. The present study showed that intervention via training was effective in increasing women's knowledge levels about BC (p=.001). Working with 40-to-49-year-old women in a study conducted in Alabama, Bryan et al. (18) provided the women with an educational program designed to extend their information and change their attitudes about BC screening methods. After the program, the knowledge levels of the women about BC screening methods were reported to increase when compared with the scores prior to the training as in the present study, and it was found that their attitudes toward screening methods had taken a positive turn (18). Studies in Turkey have also reported that women's knowledge levels about BC increased after an educational program in a similar way to our research (7, 18, 19).

The fact that training was given to women and they were also taken to the screening sessions makes this study different from many other studies. However, even though the researchers had picked the women up and arranged their appointments for them, the women's level of participation in the screening sessions was not at the desired rate.

In this study that was conducted with women working at a university, it was observed that the levels of knowledge and awareness about early detection and screening for BC were low. The educational program that was organized raised their knowledge levels. To raise these levels to the desired extent and to create a change in behavior, however, it is believed that repeated educational programs must be organized. Although the women in the study group worked at a university that operated in coordination with a research and application hospital that provided training, their rates of benefiting from early detection methods such as mammography were low. The reasons for this should be explored with qualitative studies that will review the issue in detail and suggest a solution.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Eskisehir Osmangazi University Faculty of Medicine Ethics Committee (10.04.2011/0212011).

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

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References

1. Cancer I.A.F.R.O. World cancer report 2014. Geneva: WHO.
2. Eser S. Life time cumulative risks for cancers in Turkey. Turk J Public Health. 2015; 13: 87-96. [CrossRef]
3. Turkey Cancer Control Plan. Turkey Cancer Control Plan 2013-2018. Ankara: Ministry of Health; 2015.
4. Sahin ZA, Ozdemir KF. Assessment of the Knowledge, Beliefs and Attitudes of Women Living in Kars Regarding the Practice of Breast Self-Examination. J Med Res 2015; 13: 54-61.
5. Acikgoz A, Cehreli R, Ellidokuz H. Women's Knowledge And Attıtude About Cancer And The Behaviour For Early Diagnosis Procedures. DEU Medicine Faculty Journal 2011; 25: 145-154.
6. Dündar PE, Özmen D, Öztürk B, Haspolat G, Akyıldız F, Çoban S, Çakıroğlu G. The knowledge and attitudes of breast self-examination and mammography in a group of women in a rural area in western Turkey. BMC Cancer 2006; 6: 43. (PMID: 16504119) [CrossRef]
7. Koc Z, Saglam Z. Determination of the knowledge and the practice of female patients about breast cancer, preventive measures and breast self-examination and effectiveness of education. Eur J Breast Health 2009; 5: 25-33.
8. Kocyigit O, Erel S, Kısmet K, Kılıcoglu B, Sabuncuoglu M, Akkus M. Knowledge About Breast Cancer, Mammography And Breast Self Examination In Women Who Applied To Outpatıent Clınıcs: A Study Conducted In The City Center. Nobel Med 2011; 7: 19-25.
9. Parsa P, Mirmohamadi A. Breast cancer screening behaviors among women above 40 years in Hamadan, Iran. Maturitas 2015; 81: 232-233. [CrossRef]
10. Isara A, Ojedokun C. Knowledge of breast cancer and practice of breast self examination among female senior secondary school students in Abuja, Nigeria. J Prev Med Hyg 2011; 52: 186-190.
11. Kwok C, Fong DY. Breast cancer screening practices among Hong Kong Chinese women. Cancer Nurs 2014; 37: 59-65. [CrossRef]
12. Akyolcu N, Uğraş GA. Breast Self-Examination: How Important Is It In Early Diagnosis? J Breast Health 2011; 7: 10-12.
13. Acikgoz A, Ergör G. Factors Affecting Breast Cancer Risk Perception In Women and Comparison of Risk Levels To The Gail Model. Eur J Breast Health 2013; 9: 156-162. [CrossRef]
14. Sadikoglu G, Ozcakir A, Dogan F, Gokgoz S, Bilgel N. Mammography utilization among Turkish women. Asian Pac J Cancer Prev 2010; 11: 377-381. (PMID: 20843119)
15. Eurostat. Eurostat Breast Cancer Screening Statistics Available from: http://ec.europa.eu/eurostat/statisticsexplained/index.php/Breast_cancer_screening_statistics#cite_ref-4. Access date: 27.02.2015.
16. Alexandraki I, Mooradian AD. Barriers related to mammography use for breast cancer screening among minority women. J Natl Med Assoc 2010; 102: 206-218. (PMID: 20355350) [CrossRef]
17. Mahfouz AA, Hassanein MH, Nahar S, Farheen A, Gaballah II, Mohamed A, Rabie FM, Aftab R. Breast Cancer Knowledge and Related Behaviors among Women in Abha City, Southwestern Saudi Arabia. J Cancer Educ 2013; 8: 516-520. (PMID: 23797712) [CrossRef]
18. Bryan TJ, Estrada CA, Castiglioni A, Snyder ED. Impact of an educational intervention on provider knowledge, attitudes, and comfort level regarding counseling women ages 40-49 about breast cancer screening. J Multidiscip Healthc 2015; 8: 209. [CrossRef]
19. Yılmaz M, Sayın Y, & Cengiz HÖ. The Effects of Training on Knowledge and Beliefs about Breast Cancer and Early Diagnosis Methods among of Women. Eur J Breast Health 2017; 13.

Original Article

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Cost-Effectiveness of Breast Cancer Screening in Turkey, a Developing Country: Results from Bahçeşehir Mammography Screening Project

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ABSTRACT

Objective: We used the results from the first three screening rounds of Bahcesehir Mammography Screening Project (BMSP), a 10-year (2009-2019) and the first organized population-based screening program implemented in a county of Istanbul, Turkey, to assess the potential cost-effectiveness of a population-based mammography screening program in Turkey.

Materials and Methods: Two screening strategies were compared: BMSP (includes three biennial screens for women between 40-69) and Turkish National Breast Cancer Registry Program (TNBCRP) which includes no organized population-based screening. Costs were estimated using direct data from the BMSP project and the reimbursement rates of Turkish Social Security Administration. The life-years saved by BMSP were estimated using the stage distribution observed with BMSP and TNBCRP.

Results: A total of 67 women (out of 7234 screened women) were diagnosed with breast cancer in BMSP. The stage distribution for AJCC stages O, I, II, III, IV was 19.4%, 50.8%, 20.9%, 7.5%, 1.5% and 4.9%, 26.6%, 44.9%, 20.8%, 2.8% with BMSP and TNBCRP, respectively. The BMSP program is expected to save 279.46 life years over TNBCRP with an additional cost of $677.171, which implies an incremental cost-effectiveness ratio (ICER) of $2.423 per saved life year. Since the ICER is smaller than the Gross Demostic Product (GDP) per capita in Turkey ($10.515 in 2014), BMSP program is highly cost-effective and remains cost-effective in the sensitivity analysis.

Conclusion: Mammography screening may change the stage distribution of breast cancer in Turkey. Furthermore, an organized population-based screening program may be cost-effective in Turkey and in other developing countries. More research is needed to better estimate life-years saved with screening and further validate the findings of our study.

Keywords: Mammography screening, breast cancer screening Turkey, cost-effectiveness of breast cancer screening

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Introduction

Mammography screening, which has been shown to reduce breast cancer mortality, has been primarily adopted in developed countries whereas some low-middle income countries (LMIC) such as Turkey are considering to initiate population-based mammography screening as more resources become available (1-3). Mammography screening is becoming potentially more useful in LMIC and/or developing countries including Turkey due to an increase in breast cancer incidence and mortality over time (4-6). For example, while breast cancer incidence in Turkey was 24/100,000 in 1993, it increased to 50/100,000 in 2010 (7, 8).

There was no nationwide organized population-based mammography screening programs in Turkey. However, the Cancer Diagnosis Screening and Education Centers (KETEM) founded by the Turkish Ministry of Health (TMOH) invite women for opportunistic

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mammography screening (i.e. mammography is offered to a woman without symptoms of breast cancer who visits a clinic for unrelated reasons) free of charge (8, 9). Furthermore, TMOH published the first population-based mammography screening guidelines in 2004, which recommended biennial screening for women between 50 and 69 years of age. TMOH updated the guidelines in 2013 and changed the starting age for mammography screening to 40. However, breast cancer screening participation rates in Turkey are still very low, estimated to be less than 10% due to high resource needs, insufficient efforts to publicize screening, and lack of breast cancer awareness in target population (10-12). For example, according to the 2010 Turkish Statistical Institute (TUIK) survey on health care resource utilization, only 17% of women over age 35 reported to have ever had a mammography (both diagnostic and screening) in their lifetime (13).

Breast cancer screening recommendations in Turkey are developed typically by adopting the studies conducted in developed countries such as in the US and Europe. However, Turkish female population has unique characteristics that require a study utilizing Turkish data. For example, the distribution of breast density, a significant breast cancer risk factor also affecting the performance of mammography, is significantly different in Turkey than that in the US and Europe (14). Furthermore, almost 50% of all invasive breast cancers in Turkey are diagnosed in women younger than 50 years of age whereas only 25% of all invasive breast cancers are diagnosed in the same age group in the US (8, 15).

Bahçeşehir Mammography Screening Project (BMSP) is exceptional as it provides primary data for potential effects of mammography screening in Turkish population. Briefly, the BMSP is a 10-year-long program (2009-2019) and it is the first organized population-based screening program implemented in Bahçeşehir, a large region of Istanbul, Turkey. The purpose of the this trial is to demonstrate the feasibility of a population-based organized mammographic screening program in an LMIC country, to determine the effectiveness of a screening program for the early detection of breast cancer and to help identify the appropriate starting age of breast cancer screening in Turkish women. The BMSP study has been screening approximately 7500 women between the ages of 40 and 69 biennially. Recently, the study finished the third round of screening with an overall 82% compliance rate. The BMSP study is unique as it screens women in a LMIC country unlike the previous studies primarily conducted in developed countries.

In this study, we report the results from the first three rounds of screening of BMSP and assess the potential cost-effectiveness of a population-based mammography screening program in Turkey. The results of the study may also provide guidance for other LMICs that consider implementing a population-based mammography screening program. To the best of our knowledge, no other studies have used primary-level data from Turkey to estimate the potential cost-effectiveness of mammography screening in Turkey.

Materials and Methods

Overview of the Bahçeşehir Mammography Screening Project

Bahçeşehir Mammography Screening Project started to screen women living in Bahçeşehir County in Istanbul, one of the largest counties of Istanbul, Turkey, in 2009. An approval by Institutional Review Board of Istanbul University was obtained. Each eligible woman was informed and signed the consent form. Between 2009 and 2015, mammograms were obtained by 2-year intervals from women between the ages of 40-69 years (n=7234). Following physical examination, digital 2-view mammograms (Mammography; Lorad, Danbury, USA) were double-read by two independent breast radiologists. The women were recalled with consensus for additional work-up including spot compression/magnification mammograms or breast ultrasound (Ultrasonography; Toshiba, CA, USA) (16). Ultrasound and biopsy were performed in women with suspicious lesions. One physician, three radiology staff members, one nurse and two secretaries worked over the five years' period. One mammography and one ultrasonography device were allocated. Mammographic findings were classified according to the American College of Radiology's (ACR) Breast Imaging Reporting and Data System (BI-RADS) (17). Recall rates were 16.8% and 25.6% for the first and second rounds, respectively and core biopsy was performed in 1.8% of the patients after the second round (18). More information about the BMSP is available elsewhere (16, 18, 19).

Strategies under consideration

We compared the costs and outcomes of two screening strategies: BMSP (which includes three biennial screens for women between 40-69 years of age) and the existing screening policy utilized in Turkey that is referred to as the Turkish National Breast Cancer Registry Program (TNBCRP). While there exists a recommended screening policy in Turkey, the overall participation in screening programs is very low (less than 10%); therefore, we assumed that the total screening costs associated with TNBCRP was 0, which provided a conservative estimate for our cost-effectiveness estimations. The TNBCRP reports the overall incidence of breast cancer and the stage distribution of the diagnosed cancers throughout Turkey including 22 cities representing diverse populations (8).

Estimating clinical outcomes

We reported the number of women who were diagnosed with breast cancer in the BMSP and classified the stage of breast cancer at the time of diagnosis using the edition of AJCC staging (20). We estimated the stage distribution associated with TNBCRP using a recent study that reports the stage distribution from 13.240 Turkish women, who were diagnosed with breast cancer (8). We used the 5-year survival rates by AJCC stage as reported by the American Cancer Society and calculated by the U.S. National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) database (21). We estimated the stage-specific life expectancies and calculated the expected life-year differences between BMSP and TNBCRP by assuming that survival time follows exponential distribution.

Estimating costs

Total costs associated with BMSP included (a) salaries (b) expenses for recruiting screening group, (c) purchase and maintenance of devices, and (d) diagnosis, treatment, and follow-up & surveillance of detected breast cancer patients. We estimated costs (a)-(c) directly from the BMSP project whereas we used the reimbursement rates of Turkish Social Security Administration (SGK), the organization in charge of reimbursing health expenses in Turkey for (d).

We also considered the additional cost associated with the loss of working months due to cancer treatment as a secondary cost outcome. We estimated the number of work months lost due to being treated by stage to reflect the need for more invasive treatments for advanced breast cancers. We used an annual average cost of minimum salary (869 Turkish Liras on average in 2014) per month to estimate the

Table 1. Stage Distribution according to BMSP with comparison to TNBCRP

Stage (AJCC)	Expected 5-year overall survival by stage (21)	Expected life years at diagnosis	Stage Distribution in BMSP	95% Confidence Intervals	Stage Distribution in TNBCRP (8)	Expected Difference in Stage Distribution (BMSP-TNBCRP)	Work loss (in months)
Stage 0	100%	25.89	19.4%	[10.8%, 30.9%]	4.9%	14.5%	2
Stage 1	100%	25.89	50.8%	[38.2%, 63.2%]	26.6%	24.1%	6
Stage II	93%	18.82	20.9%	[11.9%, 32.6%]	44.9%	-24%	6
Stage III	72%	9.58	7.5%	[2.5%, 16.6%]	20.8%	-13.3%	9
Stage IV	22%	2.93	1.5%	[0.0%, 8.0%]	2.8%	-1.3%	12
Expected life years			22.85		18.68	4.17	
Average work loss (months)			5.54		6.60	-1.06	

AJCC: American Joint Committee on Cancer; BMSP: Bahçeşehir Mammography Screening Project; TNBCRP: Turkish National Breast Cancer Registry Program

total costs associated with loss of work (22). We estimated all the costs using 2014 Turkish Liras (TL) and also converted the costs for summary outcomes into US Dollars using the average exchange ratio of (1 USD=2.2 TL) in 2014 (23).

Cost-effectiveness analysis

We used US dollars as the cost measure and "life years saved" as the effectiveness measure. BMSP has been implemented for five years. Therefore, we calculated the total costs associated with BMSP for five years. Similarly, we estimated the costs under TNBCRP for five years. On the other hand, we used a life-time horizon for the effectiveness outcome, since the full effects of screening on women are observed only until patients die due to breast cancer or non-breast cancer.

We used the society's perspective for our calculations. For this purpose, we obtained all costs related to the diagnosis, treatment, and follow-up & surveillance of cancer cases from SGK's lists of healthcare services and medications. As described earlier, the administrative and operational costs in BMSP were estimated separately using the primary-level data.

Sensitivity analysis

We performed two types of sensitivity analyses. Firstly, we conducted a sensitivity analysis on the stage distribution observed under BMSP. For this purpose, we used the lower and upper bounds for the confidence intervals for the proportion of cancers diagnosed at a particular stage. Namely, we assumed that the proportions of stage 0 and stage I cancers among all cancers under BMSP were equal to the lower bounds for these quantities. We further assumed that the proportion of stage III and stage IV were the same as those observed in TNBCRP and the remaining cancers were observed in stage II and we recalculated the incremental cost-effectiveness ratio (ICER) value. Therefore, this sensitivity analysis considered a scenario where the benefit of screening was smaller than what was observed in our base case. Secondly, we conducted a one-way sensitivity analysis on other inputs and presented them in a tornado diagram (24).

Statistical analysis

All statistical tests were performed in R (25). We used the exact Binomial method for computing confidence intervals and Chi-square test considering continuity correction for comparing stage distributions.

Results

Clinical outcomes and stage distribution observed with BMSP

After the third screening round, a total of 7234 women were screened. Among these, 67 women were diagnosed with breast cancer; therefore, the overall cancer detection rate was 9.3 per 1.000 women (67 out of 7234). We found that 48% of the women diagnosed with breast cancer were women aged 40-49 while 59% of the screened women were in the age group of 40-49 years. The mean age for the women diagnosed with breast cancer was 52. Table 1 includes the breast cancer stage distribution observed in BMSP as well as the stage distribution observed in TNBCRP using the AJCC historical stage definition.

The stage distribution between the BMSP and TNBCRP is statistically significant (p-value<0.0001). The mean life expectancy for the Turkish women in the screened population (40-69) is 25.89 years according to 2010 Turkish life tables (26); therefore, we calculated the rate parameter for survival without breast cancer (β) as 0.0386=1/25.89 using 25.89 years as an input. We found that the total expected life years for 67 patients diagnosed with cancer was 1530.87 years (22.85*67) under the BMSP, and 1251.41 years (18.68*67) under the TNBCRP. Therefore, after three biennial mammography screenings, the BMSP led to a saving of 279.46 life years (1530.87-1251.41) for 67 patients (4.17 saved life years per woman diagnosed with cancer).

Cost outcomes of BMSP

Table 2 shows the costs associated with BMSP and TNBCRP after the third screening round. We provided the details of the computations in the appendix. We assumed that the cost of screening for TNBCRP was 0, which provided a conservative estimate for the cost-effectiveness of BMSP. The costs of diagnosis and treatment are estimated to be higher in TNBCRP than in BMSP due to the additional treatment cost for patients diagnosed at more advanced stages when there is no or limited screening.

Cost-effectiveness analysis

The expected 5-year overall survival rates and expected life years after breast cancer diagnosis by stage, and expected differences among stage distribution of 67 patients were shown in Table 1. Similarly, the cost differences between BMSP and TNBCRP were presented in Table 2.

Table 2. Cost outcomes for BMSP with comparison to TNBCRP

Costs	BMSP	TNBCRP	Expected Difference between BMSP and TNBCRP (in TL)	Expected Difference between BMSP and TNBCRP (in USD)
Cost of screening including false positives	1,875,260 TL	0	1,875,260 TL	852,391 USD
Cost of diagnosis and treatment	1,392,228 TL	1,716,107 TL	-323,879 TL	-147,218 USD
Cost due to work loss	322,214 TL	383,818 TL	-61.604	-28.002 USD
Total Cost	3,579,499 TL	2,087,772 TL	1,491,727 TL	677,171 USD

BMSP: Bahçeşehir Mammography Screening Project; TNBCRP: Turkish National Breast Cancer Registry Program

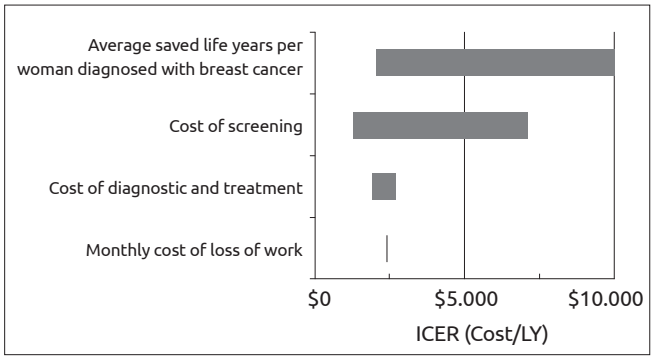

Figure 1. Tornado Diagram. This figure summarizes the results of one-way sensitivity analysis. In this figure, the x-axis represents the ICER per life years (LY) gained by BMSP over TNBCRP and the y-axis lists the parameters that were changed as part of one-way sensitivity analysis that was ordered with respect to their effect on ICER

We estimated that the BMSP program led to an additional 279.46 life years (67*4.17 life years per woman in Table 1) over TNBCRP with an additional cost of $677.171 (Table 2), which implies an incremental cost-effectiveness ratio (ICER) of $2.423 per an additional life year. The World Health Organization recommends that any health care program with an ICER value smaller than the per capita GDP of a nation is highly cost-effective (27). Since the ICER of BMSP program over TNBCRP is smaller than GDP per capita in Turkey ($10.515as of 2014), BMSP program is highly cost-effective (28).

Sensitivity analysis

For our first sensitivity analysis, we assumed that the proportion of cancers diagnosed in Stages 0 and I was equal to the lower bounds of the confidence intervals, 10.8% for Stage 0 (base-case was 19.4%) and 38.2% for Stage I under BMSP (the base case was 50.85). We assumed that the proportions of cancers diagnosed in Stages III and IV were the same as those observed under TNBCRP, i.e., the proportion of cancers diagnosed in Stage III was 20.8% (base case was 7.5%) and the proportion of cancers diagnosed in Stage IV was 2.8% (the base case was 1.5%), respectively. Finally, the proportion of cancers diagnosed in Stage II was (1-10.8%-38.2%-20.8%-2.8%=27.4%) whereas it was 20.9%. We found that this assumed conservative distribution of stages would save 82.89 life years with an additional expense of $698,931 US dollars; therefore, the ICER was $8.433 US dollars per additional life year, implying that BMSP would still remain cost-effective.

Figure 1 presents the results of our one-way sensitivity analysis on four inputs parameters: average life years saved with BMSP, average cost of screening including false positives, monthly cost of loss of work, and cost of diagnosis and treatment. We found in Table 1 that the BMSP led to an average saving of 4.17 life years per woman diagnosed with cancer over TNBCRP; therefore, we chose the range of average saved life years per woman between 1 year and 5 years. Similarly,

Table 2 implies that the average cost of screening including false positives was approximately 1,875,260 TL/(7234*3)=86 TL ($39 US Dollars); therefore, we chose the range for cost of screening between $25 and $100. There were many inputs for the average cost of diagnosis and treatment as explained in the appendix; therefore, for this parameter, we used 50% of all input costs as the minimum value and 200% of all inputs costs as the maximum value. Finally, we used the range of ($350, $500) for the monthly cost of loss of work (the base case was $395 US Dollars, i.e., 869 TL). We found that the most critical input parameter affecting the ICER of BMSP was average life-year savings per woman due to the BMSP. As expected, as the cost of diagnosis and treatment, monthly cost of loss of work, and average saved life years per woman due to BMSP increase, the ICER becomes smaller (i.e. BMSP becomes more cost-effective). On the other hand, as the cost of screening increases, the ICER becomes larger (i.e. BMSP becomes less cost-effective). For all the parameter values, we found the BMSP to remain cost-effective.

Discussion and Conclusion

The potential effects and cost-effectiveness of screening programs in LMIC and developing countries such as Turkey are not extensively studied. It is known that breast cancer is typically diagnosed at more advanced stages in countries with little or no screening and a lack of breast cancer awareness compared to countries that have a population-based screening program. In line with this observation, our present study finds that BMSP, first organized population-based screening program implemented in Turkey, led to a shift in the stage distribution of breast cancers such that a smaller number of breast cancers are diagnosed in regional and distant stages with a significant increase in the proportion of DCIS and localized breast cancers. We conducted a simple modeling study to evaluate the potential cost-effectiveness of screening in Turkey and found that a nationwide biennial mammography screening policy between ages 40-69 may be highly cost-effective in Turkey under our base case assumption. We performed an extensive sensitivity analysis and found that for all scenarios, the ICER would stay below the well-accepted cost-effectiveness threshold of GDP per capita.

While our study does not use any data from the other LMIC and developing countries, it demonstrates that breast cancer screening could

be cost-effective for other LMIC countries, as well. Existing modeling studies that evaluated the value and cost-effectiveness of breast cancer screening in LMIC countries typically focused on evaluating clinical breast exam as a screening tool and reported conflicting results (29-32). Despite the controversy, (31) the Middle Resource Scenarios Working Group of the Breast Health Global Health Initiative concluded that "breast cancer early detection programs continue to be important, should include clinical breast examination with or without mammography, and should be coupled with active awareness programs" (33).

As noted before, there are no cost-effectiveness studies utilizing primary-level screening mammography data from the Turkish female population. There are few studies that report on potential cost-effectiveness of mammography screening in Turkey. While two prospective studies (34,35) found that mammography screening reduced costs compared to the no-screening scenario (i.e. mammography screening is less expensive and leads to better health outcomes than no screening), another recent study (36) found that mammography screening was highly cost-effective (i.e. the ICER of 40-69 biennial screening over no screening is $330 US dollars). Similarly to these studies, we found mammography screening to be cost-effective but with a higher ICER value.

There are several important points as the findings of our study are translated into a nationwide screening program. On one side, it is likely that the positive findings on the benefits of screening with BMSP may not be observed at the same level when a nationwide screening program is implemented. For example, the performance of radiologists in a nationwide program may be worse than that of radiologists working for the BMSP and our findings may have overestimated the benefits of screening. On the other hand, it is also possible that we may have overestimated the cost of screening such as the cost of screening mammography. In summary, there are several similar translational issues that need to be considered carefully before making use of our findings.

Our study has several limitations. Firstly, while this is the first attempt for such a study in Turkey, our study's sample size is still limited. Therefore, we found wider confidence intervals for the breast cancer stage distribution under the BMSP. Secondly, our estimates for costs are very accurate whereas our estimates for life years are based on a simple approach utilizing data from SEER and stage-specific 5-year survival rates due to the unavailability of realistic estimates for stage-specific life expectancies for Turkish women. For example, it is possible that associating the same stage-related survival for the BMSP and the TNBCRP may lead to less favorable outcomes for the TNBCRP (37). Therefore, this assumption may have caused our study to underestimate the benefits of screening. Ideally, one would use an established microsimulation model such as those used as part of NCI's Cancer Intervention Surveillance Network (CISNET) project to estimate the life expectancies for women undergoing screening more accurately (38-40). However, there is no such validated model that uses primary data of Turkish female population; therefore, we leave this for future research. Finally, although our study implicitly accounts for over-diagnosis (i.e. the life-year savings for women diagnosed with cancer are 0 as they may die due to other causes before death due to cancer occurs), we are unable to estimate the rate of over-diagnosis, which is a potential harm of screening.

In summary, we found that mammography screening may significantly shift the stage distribution of breast cancer in Turkey. Furthermore, we found that an organized population-based screening program may be cost-effective in Turkey as well as in other LMIC countries. However, due to the limitations described above, more research is needed to further validate the findings of our study.

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References

1. L. Nyström, S. Wall, L.E. Rutqvist, A. Lindgren, M. Lindqvist, S. Rydén, J. Andersson, N. Bjurstam, G. Fagerberg, J. Frisell, L. Tabár, L.-G. Larsson. Breast cancer screening with mammography: overview of Swedish randomised trials. The Lancet 1993; 341: 973-978. [CrossRef]
2. Otto SJ, Fracheboud J, Looman CW, Broeders MJ, Boer R, Hendriks JH, Verbeek AL, de Koning HJ. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. The Lancet 2003; 361: 1411-1417. (PMID: 12727393) [CrossRef]
3. Smith RA, Duffy SW, Gabe R, Tabar L, Yen AM, Chen TH. The randomized trials of breast cancer screening: what have we learned? Radiol Clin North Am 2004; 42:793-806. (PMID:15337416) [CrossRef]
4. Bray F, Ferlay J, Laversanne M, Brewster DH, Gombe Mbalawa C, Kohler B, Piñeros M, Steliarova-Foucher E, Swaminathan R, Antoni S, Soerjomataram I, Forman D. Cancer Incidence in Five Continents: Inclusion criteria, highlights from Volume X and the global status of cancer registration. Int J Cancer 2015; 137: 2060-2071. (PMID:26135522) [CrossRef]
5. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P. Cancer incidence in five continents, Volume IX: IARC Press, International Agency for Research on Cancer; 2007.

6. Parkin D, Ferlay J, Whelan S, Storm H: Cancer incidence in five continents, vol. 1: Diamond Pocket Books (P) Ltd.; 2005.
7. Fidaner C, Eser SY, Parkin DM. Incidence in Izmir in 1993-1994: first results from Izmir Cancer Registry. Eur J Cancer 2001; 37: 83-92. [CrossRef]
8. Ozmen V. Breast Cancer in Turkey: Clinical and Histopathological Characteristics (Analysis of 13.240 Patients). Eur J Breast Health 2014; 10: 98-105. (PMID:28331652) [CrossRef]
9. Youlden DR, Cramb SM, Dunn NA, Muller JM, Pyke CM, Baade PD. The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. Cancer Epidemiol 2012; 36:237-248. (PMID:22459198) [CrossRef]
10. Ozmen V. Breast cancer in the world and Turkey. Eur J Breast Health 2008; 4: 2-5.
11. Dündar PE, Özmen D, Öztürk B, Haspolat G, Akyıldız F, Çoban S, Çakıroğlu G. The knowledge and attitudes of breast self-examination and mammography in a group of women in a rural area in western Turkey. BMC cancer 2006; 6: 43. (PMID:16504119) [CrossRef]
12. Ozmen V, Boylu S, Ok E, Canturk NZ, Celik V, Kapkac M, Girgin S, Tireli M, Ihtiyar E, Demircan O, Baskan MS, Koyuncu A, Tasdelen I, Dumanli E, Ozdener F, Zaborek P. Factors affecting breast cancer treatment delay in Turkey: a study from Turkish Federation of Breast Diseases Societies. Eur J Public Health 2015; 25: 9-14. (PMID:25096257) [CrossRef]
13. Turkish Statistical Institute (TUIK) 2010 Health Survey, Table 4.21 Health Care Services and Indicators Describing Health. Available from: [http://www.who.int/fctc/reporting/party_reports/turkey_annex2_turkish_health_survey_2010.pdf]
14. Mc Cormack VA, Burton A, dos-Santos-Silva I, Hipwell JH, Dickens C, Salem D, Kamal R, Hartman M, Lee CPL, Chia KS. International Consortium on Mammographic Density: Methodology and population diversity captured across 22 countries. Cancer Epidemiol 2016; 40: 141-151. (PMID:26724463) [CrossRef]
15. DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. CA Cancer J Clin 2014; 64: 52-62. (PMID:24114568) [CrossRef]
16. Kayhan A, Gurdal SO, Ozaydin N, Cabioglu N, Ozturk E, Ozcinar B, Aribal E, Ozmen V. Successful first round results of a Turkish breast cancer screening program with mammography in Bahcesehir, Istanbul. Asian Pac J Cancer Prev 2014; 15: 1693-1697. (PMID: 24641392) [CrossRef]
17. Liberman L, Menell JH. Breast imaging reporting and data system (BI-RADS). Radiol Clin N Am 2002; 40: 409-430. [CrossRef]
18. Ozmen V, Ozkan-Gurdal S, Kayhan A, Ozaydin N, Cabioglu N, Ozcinar B, Aribal E. Abstract P2-04-06: Successful results of a population-based organized mammography screening program in a developing country: The Turkish experience. Cancer Res 2013; 73(24 Suppl): P2-04-06-P02-04-06.
19. Cabioglu N, Ozkan-Gurdal S, Kayhan A, Ozaydin N, Ozcinar B, Aribal E, Ozmen V. Abstract P4-05-07: Molecular profiles of screen detected breast cancers: Final results of Turkish Bahcesehir breast cancer screening project. Cancer Res 2013; 73(24 Suppl): P4-05-07-P04-05-07.
20. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC cancer staging manual, vol. 649: Springer New York; 2010.
21. Breast cancer survival rates, by stage estimated from NCI SEER database. Available from: [http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-survival-by-stage#]
22. Gross and Net Minimum Salaries by Year (in Turkish). Available from: [http://www.csgb.gov.tr/csgbPortal/ShowProperty/WLP%20Repository/csgb/dosyalar/istatistikler/net_brut_asgari_uc]
23. Average Exchange Ratios (Turkish Republic Central Bank Rates). Available from: [http://www.isyatirim.com.tr/p_exchange_avarege.aspx]
24. Briggs AH, Weinstein MC, Fenwick EA, Karnon J, Sculpher MJ, Paltiel AD. Model parameter estimation and uncertainty analysis a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group-6. Med Decis Making 2012; 32: 722-732. (PMID:22990087) [CrossRef]
25. R Core Team: R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available from: URL http://wwwR-projectorg2015.
26. Turkey 2010 Life Tables for Females (in Turkish). Available from: [http://www.sbm.org.tr/tr/Documents/TRH_2010_1507_k_e.pdf]
27. Table: Threshold values for intervention cost-effectiveness by Region, WHO Web site. Available from: [http://www.who.int/choice/costs/CER_levels/en/]
28. GDP per Capita (current US$). Available from: [http://data.worldbank.org/indicator/NY.GDP.PCAP.CD]
29. Okonkwo QL, Draisma G, der Kinderen A, Brown ML, de Koning HJ. Breast cancer screening policies in developing countries: a cost-effectiveness analysis for India. J Natl Cancer Inst 2008; 100: 1290-1300. (PMID:18780864) [CrossRef]
30. Pisani P, Parkin D, Ngelangel C, Esteban D, Gibson L, Munson M, Reyes MG, Laudico A. Outcome of screening by clinical examination of the breast in a trial in the Philippines. Int J Cancer 2006; 118: 149-154. (PMID:16049976) [CrossRef]
31. Smith RA, Caleffi M, Albert US, Chen TH, Duffy SW, Franceschi D, Nyström L. Breast Cancer in Limited-Resource Countries: Early Detection and Access to Care. Breast J 2006; 12: 16-26. (PMID:16430395) [CrossRef]
32. Barfar E, Rashidian A, Hosseini H, Nosratnejad S, Barooti E, Zendehdel K. Cost-Effectiveness of Mammography Screening for Breast Cancer in a Low Socioeconomic Group of Iranian Women. Arch Iran Med 2014; 17: 241-245. (PMID:24724599)
33. Yip CH, Cazap E, Anderson BO, Bright KL, Caleffi M, Cardoso F, Elzawawy AM, Harford JB, Krygier GD, Masood S. Breast cancer management in middle-resource countries (MRCs): consensus statement from the Breast Health Global Initiative. Breast 2011; 20: 12-19. (PMID:21388811) [CrossRef]
34. Astim E. Cost-effectiveness analysis of a prospective breast cancer screening program in Turkey. Middle East Technical University; 2011.
35. Yazihan N, Yilmaz HH. Breast cancer in Turkey: economic efficiency and cost effectiveness. Cancer Control in Turkey, Cancer Control in Turkey Health Ministry Publication 2006.
36. Ada K. A Simulation Model for Breast Cancer Epidemiology in Turkey. Bilkent University; 2014.
37. Elkin EB, Hudis C, Begg CB, Schrag D. The effect of changes in tumor size on breast carcinoma survival in the US: 1975-1999. Cancer 2005; 104: 1149-1157. (PMID:16088887) [CrossRef]
38. Mandelblatt JS, Stout NK, Schechter CB, van den Broek JJ, Miglioretti DL, Krapcho M, Trentham-Dietz A, Munoz D, Lee SJ, Berry DA, Nicolien T. Collaborative modeling of the benefits and harms associated with different US breast cancer screening strategies. Ann Intern Med 2016. [CrossRef]
39. Kim JJ, Tosteson AN, Zauber AG, Sprague BL, Stout NK, Alagoz O, Trentham-Dietz A, Armstrong K, Pruitt SL, Rutter CM. Cancer Models and Real-world Data: Better Together. J Natl Cancer Inst 2016; 108: djv316. (PMID: 26538628) [CrossRef]
40. Lee C, Cevik M, Alagoz O, Sprague B, Tosteson A, Miglioretti D, Kerlikowske K, Stout N, Jarvik J, Ramsey S, Lehman CD. Comparative effectiveness of combined digital mammography and tomosynthesis screening for women with dense breasts. Radiology 2015; 274: 772-780. (PMID:25350548) [CrossRef]

Original Article

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Translation and Validation of the Turkish Version of Lymphedema Quality of Life Tool (LYMQOL) in Patients with Breast Cancer Related Lymphedema

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ABSTRACT

Objective: Breast cancer related lymphedema (BCRL) is a drastic situation that affects patients who have undergone breast cancer surgery. The impact of this condition on individuals' quality of life should be investigated in more detail to obtain better treatment results.

Materials and Methods: In total, 65 patients with BCRL participated in this study. Nottingham Health Profile (NHP) was used to evaluate the validity of associated domains in Lymphedema Quality of Life Tool (LYMQoL). Both the LYMQoL and NHP were filled out by BCRL patients. To evaluate its test-retest reliability, the LYMQoL was subsequently performed seven days following its initial application. Measurement properties such as internal consistency, test-retest reliability, criterion validity and factor structure were tested. The internal consistency was assessed via Cronbach's alpha; test-retest reliability was assessed by the intra-class correlation coefficient (ICC).

Results: Cronbach's alpha values ranged from 0.74 to 0.91 for the LYMQoL total and domain scores. Test-retest reliability was excellent (ICC=0.92-0.99). When the relation between LYMQoL and NHP was investigated, 'good' to 'very good' correlations were obtained (r=0.539-0.643, p<0.05) for all domains of LYMQoL. Exploratory factor analyses demonstrated a four-factor structure.

Conclusion: Turkish version of LYMQoL is a valid and reliable measurement tool to evaluate the quality of life in patients with BCRL.

Keywords: Validity, Reliability, Lymphedema Quality of Life Tool, Turkish version, Breast Cancer Related Lymphedema

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Introduction

Breast cancer is the most frequent cancer and the major reason of cancer related deaths among women in the world. Incidence in Turkey was 39/100.000 in 2010 and increased to 46/100.000 in 2013 (1, 2). Since the incidence of breast cancer among Turkish women is increasing, the number of women affected by complications of its treatment is increasing, as well. Breast cancer-related lymphedema (BCRL) is one of the most distressing complication of breast cancer treatment (3). BCRL can manifest directly after surgery or, in most cases, in the first two years after breast cancer treatment (4, 5). Systematic reviews suggest that more than one in five women who survive breast cancer will develop arm lymphedema (6). BCRL can be described as the excessive accumulation of protein-rich fluid in interstitial tissue of the arm, hand, and/or chest wall that can occur after breast cancer surgery or radiation therapy (7). This chronic and incurable condition causes physical and psychological disorders. Patients may develop symptoms such as heaviness, tightness, stiffness, impaired upper limb function and body image, which are all related with swelling (8). Apart from these symptoms, situations such as inability to find a proper outfit, to wear watch or ring trigger psychosocial problems that affect the quality of life (QoL) among breast cancer survivors. Breast cancer survivors with BCRL have a significantly lower QoL than patients without BCRL (9). Therefore, QoL is an important outcome measure in many breast cancer studies. In clinical settings, generic health-related quality of life (HRQoL) questionnaires are used due to lack of lymphedema-specific questionnaires specific questionnaires... along with cultural adaptation and validation studies are not exist yet. However, HRQoL questionnaires are incapable of evaluating both the symptoms and treatment outcome; therefore, they cannot evaluate problem specific conditions. Thus, the use of disease specific questionnaires has a role in this manner. Disease-specific HRQoL questionnaires such as Lymphedema Quality of Life (LYMQoL) are more likely to track changes more specifically in QoL in comparison with HRQoL measures. The LYMQoL is a comprehensive questionnaire designed to measure QoL in patients with BCRL.

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LYMQoL was developed by Keeley et al, which is a self-report questionnaire that assesses upper limb lymphedema symptoms and ability to perform common functional activities in patients with BCRL (10). The LYMQoL has been validated in the English and Dutch languages. However, validation of LYMQoL for upper limb lymphedema in the Turkish language has not been performed yet (11). The aim of this study was to translate the English version of LYMQoL to Turkish and to test the reliability and validity of the Turkish version of the questionnaire among patients with BCRL in Turkey.

Material and Methods

Instrument

The LYMQoL was designed as a disease-specific HRQoL measure by Keeley in 2010 (10). Its questions can be gathered under four domains being function, appearance, symptoms and mood. It consists of 21 questions. The last question 'overall quality of life' scale investigates the general QoL. Item scoring in each domain is as follows: Not at all=1, A little=2, Quite a bit=3, A lot=4. The total score for each domain is calculated by adding up all the scores together and dividing it by the total number of questions answered. If fewer than 50% of the items were answered, the whole domain is scored as 0. The LYMQoL total score and each domain score have a range between 1 and 4. Higher scores indicate lower quality of life. The last question about the 'overall quality of life' item is scored through 0 to 10. Higher scores indicate a better overall QoL (8).

Translation and constitution of the Turkish version of LYMQoL

After permission was granted for translation and use of LYMQoL from the copyright holder Keeley the standard translation method was followed, which was established by previous studies (12). The English version was first translated independently to Turkish by two native Turkish speakers (a physiotherapist specialized in lymphedema and a professional translator). A panel consisting of these two translators and one bilingual author (Y.B) critically reviewed the translations to reveal the first draft of Turkish version of LYMQoL. Two other bilingual speakers who did not know the original questionnaire translated this draft back to English. The discrepancies among the original version and the translated versions were analyzed by the panel (consisting of all five members). Semantic and conceptual equivalences were discussed, and a draft version of the questionnaire was developed. In the next step, the Turkish LYMQoL was firstly tested on a sample of 20 Turkish female patients with BCRL as a pilot study. The aim was to detect problems with the questionnaire such as wording, terminology, instructions, items and whether the questionnaire was understandable or not. After completion of the questionnaire, an interview was held with patients to investigate the understandability of each item. They were asked to comment on items and offer recommendations for improvement. All patients reported that the questionnaire was easily understandable, readable and culturally relevant. No problematic items were observed in the Turkish translated version of LymQoL.

Nottingham health profile

Nottingham Health Profile (NHP) was used to measure the generic HRQoL. NHP is a self-administered questionnaire which is used to evaluate perceived health problems. NHP includes 38 questions with assigned individual score under six domains as energy level, pain, emotional reaction, sleep, social isolation, and physical abilities. The sum of maximum scores for all domains is 100. For the calculation of final score in each domain, variation in the number of items per domain was estimated by computing the percentage score (i.e., each sum was multiplied by 100 and divided by the number of items in the domain). Possible scores ranged from 0 (indicating all "no" answers in that domain or absence of distress) to 100 (all "yes" answers indicating maximal distress). Lower NHP scores indicate a better QoL. The reliability and validity of Turkish NHP was demonstrated (13).

Study sample

Eighty-seven women with BCRL were recruited to the study between June 2016 and December 2016 at the lymphedema outpatient clinic in School of Physical Therapy and Rehabilitation in Abant Izzet Baysal University. BCRL was diagnosed by the medical oncologist and patients were also evaluated by the circumference measurement method in which the diagnostic criteria was chosen as having a circumferential difference of 2 cm or above in their arms compared to the contralateral arm. The sample size for this study comprised of patients who were referred to the lymphedema outpatient clinic for being informed and learning treatment options about BCRL. The inclusion criteria for this study were as follows: having BCRL, 18 years of age or older, able to read, speak, and understand Turkish, being a volunteer to be recruited in this study. Patients with acute infection, lymphangitis, breast cancer recurrence, ongoing chemotherapy, radiotherapy, history of trauma, thrombosis in upper limbs and having open wounds in the affected limb were excluded from the study. All patients were asked to fill in the LYMQoL and NHP questionnaires. Then, they were asked to refill the LYMQoL one week later. This study was approved by the local ethics committee. (31 May 2016; number 2016/98). Written informed consent was taken from the participants after oral and written information was given to them.

Reliability

The reliability of LYMQoL was evaluated by means of the internal consistency and test-retest analysis. Internal consistency measures the consistency of responses across the questionnaire and the subscales. Internal consistency was determined by using Cronbach's alpha coefficient. Commonly accepted values for Cronbach's alpha are described as excellent ($a>0.9$), good ($0.9>a>0.7$), acceptable ($0.7>a>0.6$), poor ($0.6>a>0.5$) and unacceptable ($a<0.5$) (14). Test-retest reliability was tested by administering a questionnaire to the patient on two separate times without any substantial changes in her symptoms. Retest analysis was done after seven days. It was calculated by using intraclass correlation coefficient (ICC). Correlation coefficient power was categorized as poor (<0.40), fair to good (0.40-0.75), and excellent (>0.75). A correlation coefficient of 0 indicates no reliability, whereas a value of 1 indicates excellent reliability (15).

Validity

Criterion validity means the degree to which an instrument measures what it is intended for. The criterion validity of the LYMQoL was determined by calculating Pearson's correlation coefficient between the patients' LYMQoL and the NHP scores. The Pearson's r correlation coefficient is used for the criteria of poor (r<0-0.20), fair (r=0.21-0.40), moderate (r=0.41-0.60), good (r=0.61-0.80), and excellent (r>0.81-1) (16).

Factor analysis

The main purpose of factor analysis is to reduce items into smaller groups, which are called factors. Factors contain correlated variables and are typically quite similar in terms of content. Exploratory factor analysis allows the researcher to determine the underlying domains or factors that exist in a set of data (17).

Statistical analysis

Descriptive analyses were used to calculate means and standard deviations of the demographic variables. The distribution was determined by the normality tests. 'Overall quality of life', total score of LYMQoL and differences between baseline and last measurements in four domains were compared via the Wilcoxon Signed Rank Test. Internal consistency was assessed by Cronbach's alpha coefficient between items. Test-retest reliability of each item was investigated via the Kappa coefficient while test-retest reliability, which consisted of four domains' total scores, was assessed with the (ICC). Pearson correlation analysis was used for correlations between values of total scores of LYMQoL and NHP for the investigation of the validation of LYMQoL questionnaire. Exploratory factor analysis was used to investigate the structure of questionnaire. Within this analysis, the Kaiser-Meyer-Olkin test was used to investigate whether factor analysis was appropriate for data structure or not. The factor structure was assessed with maximum likelihood extraction and Varimax rotation (18).The internal consistency was assessed by using Cronbach's alpha coefficient. Alpha values ≥0.7 are considered as satisfactory. Test- retest reliability was assessed using (ICC). Criterion validity was assessed by Pearson's correlation coefficient. Correlation coefficient was categorized as poor (0-0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), and excellent (0.81-1). The statistical significance level accepted as $p<0.05$. PASW (SPSS Institute, Chicago, IL, USA. versiyon 18) was used for the statistical analyses.

Results

In total, 87 patients with BCRL were screened for participation in the study. Ten patients were excluded from the study due to their inability to meet inclusion criteria. Six participants had acute infection, 2 of them had active metastasis and 2 of them had no ability to read and write. The second evaluations were missed in 12 participants. Thus, this study was started and completed with 65 participants in total with an attrition rate of 25% (22/87).The mean age was 50.6±12.45 years. Forty-nine patients (75.4%) had unilateral arm lymphedema. Demographic characteristics and clinical features of the patients are shown in Table 1.

Cronbach's Alpha value of the total score of LYMQoL and domains (Functional Aspects, Appearance/Body image, Symptoms, Mood/Emotions) were recorded as 0.91, 0.76, 0.79, 0.70 and 0.94, respectively. These values indicated that the questionnaire has 'good to excellent' internal consistency. Test-retest ICC value (95% confidence interval) of each domain varied between 0.92 and 0.99, $p<0.001$ (Table 2). According to the ICC values, it was shown that the LYMQoL had excellent test-retest results.

The LYMQoL correlated very well with the 'overall quality of life' and NHP as having a good criterion validity of the LYMQoL in this population. The 'overall quality of life' had negative correlation with all the domains of LYMQoL. The p values were found significant in all parameters except for correlation between Energy Level (EL) of NHP and symptoms domain of LYMQoL. The p values of 'overall quality of life' and NHP total scores were all significant (Table 3).

The floor and ceiling effects were determined by calculating the rate of participants in which lowest and highest scores in each item most The floor-ceiling effect was calculated for the first measurement of questions within LYMQoL and possibility of participants who replied to "1" in 15th question was much more when compared to other ques-

Table 1. Demographic characteristics and clinical features of the patients (n=65)

	Minimum	Maximum	X±SD
Age (years)	24	75	50.6±12.45
Height (m)	1.48	1.78	1.60±0.06
Weight (kg)	45	103	71.0±14.06
BMI (kg/m2)	15.76	41.98	27.82±5.79
Lymphedema duration (year)	1	18	4.32±3.06

BMI: body mass index; X±SD: mean±standard deviation

Table 2. Reliability of Lymphedema Quality of Life Questionnaire (LYMQoL) (n=65)

LYMQoL Domain	ICC (95% CI)	p
Functional Aspects	0.99 (0.983-0.994)	<0.001
Appearance/Body image	0.99 (0.983-0.994)	<0.001
Symptoms	0.98 (0.982-0.993)	<0.001
Mood/Emotions	0.99 (0.986-0.995)	<0.001
Total LYMQoL	0.99 (0.993-0.997)	<0.001

ICC: intra-class correlation coefficient $p<0.05$

Table 3. Criterion validity of Lymphedema Quality of Life Questionnaire (LYMQoL)

	NHP		Energy Level		Pain		Emotional Reactions		Social Isolation		Sleep		Physical Activity'		Overall Quality of Life'	
LYMQoL Domains	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Functional Aspects	0.539	0.000	0.328	0.008	0.559	0.000	0.329	0.007	0.310	0.013	0.322	0.009	0.446	0.000	-0.642	0.000
Appearance/Body image	0.541	0.000	0.405	0.001	0.503	0.000	0.309	0.012	0.272	0.030	0.412	0.001	0.367	0.003	-0.655	0.000
Symptoms	0.543	0.000	0.153	0.224	0.562	0.000	0.481	0.000	0.388	0.002	0.468	0.000	0.337	0.006	-0.571	0.000
Mood/Emotion	0.555	0.000	0.311	0.012	0.580	0.000	0.403	0.001	0.345	0.005	0.412	0.001	0.317	0.010	-0.535	0.000
Total LYMQoL	0.643	0.000	0.365	0.003	0.646	0.000	0.446	0.000	0.382	0.002	0.484	0.000	0.421	0.000	-0.707	0.000

r: pearson correlation coefficient $p<0.05$; NHP: Nottingham Health Profile

Table 4. Factor analysis loadings of the LYMQoL

	Factors			
Item	1	2	3	4
1.Affect daily activities	.679	.208	.133	.273
2. Affect leisure activities	.624	.276	.504	.253
3. Depend on the other people	.912	.276	.123	-.055
4. Affect appearance	.227	.876	.267	-.147
5. Difficulty finding clothes to fit	.301	.610	.305	-.343
6. Difficulty finding clothes to wear	.369	.764	.186	-.311
7. Affect feel about yourself	-.036	.594	.535	.071
8. Affect relationship with other people	.296	.587	.233	.520
9. Cause you pain	-.002	.150	.731	.244
10. Numbness in your swollen arm	.200	.056	.866	-.261
11. Feelings pins and needles	.119	.016	.817	.063
12. Feel weak	-.011	.203	.376	.157
13. Feel heavily	.132	.240	.448	.352
14. Feel tired	-.222	-.147	.720	.215
15. Trouble sleeping	-.250	.048	.198	.795
16. Difficulty concentrating on things	.210	.406	.036	.788
17. Feel tense	.205	.195	.048	.851
18. Feel worried	.270	.219	.101	.861
19. Feel irritable	.146	.211	.172	.848
20. Feel depressed	.211	.186	.140	.855

tions, while the replies "4" were much higher in number than others in the 5th question.

When exploratory factor analysis was conducted with items within the questionnaire, considered...as...appropriate-Olkin test value was found 0.781. It was considered appropriate to conduct a factor analysis with the questionnaire due to value is above 0.50. Besides, the sphericity test resulted in the conclusion that the correlation matrix did not have a spherical structure ($p<0.0001$). This result shows that correlations were significant between items of questionnaire and the factor analysis was suitable. Furthermore, it was deduced that it was not necessary to eliminate any items from questionnaire since all the diagonal elements were above the value of 0.50 in anti-image matrix. After factor loadings were gained, they were rotated with the Varimax rotation method; factor loadings were obtained and finally, four significant factors were achieved in the Turkish version of LYMQoL and the factor structures were the same as in the original version. The same items appeared in the same factors. We selected four factors which explained 74.9% of the total variance, each accounting for 44.3%, 13.9%, 10.7% and 6.1% of the total variance, respectively. Factor loadings constituted in the study and factor names are shown in Table 4.

Discussion and Conclusion

During the data collection period, there were no validated Turkish versions of any lymphedema questionnaires. Thus, the aim of this study was to translate the original version of the LYMQoL to Turkish for Turkish-speaking patients with BCRL and to evaluate its validity and reliability. The results of the current study showed that the Turkish version of LYMQoL was a reliable, internal consistent and valid questionnaire for determining the HRQoL in patients with BCRL.

Breast cancer related lymphedema is a chronic condition which can occur after removal of axillary lymph nodes and radiotherapy. Some women with BCRL can fall into depression and think that this condition is much worse than breast cancer itself when they figure out that lymphedema is a chronic disease and only its symptoms could be brought under control (19). In this situation, attention should be paid on quality of life of women with BCRL (20). Velonovich et al (21) showed that lymphedema-related symptoms (swelling, heaviness, firmness, pain, hardness, reduced extremity mobility etc.) have negative impact on physical and functional well-being and these affect the QoL negatively. Ridner et al (22) stated that patients who have more symptoms and more need for self-care have a lower QoL. Yet, the generic HRQoL measurements which are used often do not provide detailed information in comparison with disease-specific HRQoL questionnaires since they can only show the picture of general deficit (23). For instance, the volume of the lymphedematous extremity cannot completely reflect the effect of disease of an individual. The social and psychological problems, which are primarily caused by the disease, and the patient's well-being are ignored. The effect of the disease on daily life is reflected better by the evaluation of disease-specific HRQoL. Thus, evaluation of disease-specific HRQoL is important for the determination of both the patient's situation and effectiveness of the administered treatment (23). The LYMQoL is a specific questionnaire which assesses the QoL in BCRL patients (10). In this study, LYMQoL was translated and validated for Turkish-speaking patients with BCRL. Patients answered the Turkish version of LYMQoL without any difficulties.

In version studies, for test-retest analyses, various time intervals were selected between test-retest periods. In the original version of LYMQoL, the time interval between test-retest was one week, and in the Dutch version for lower limb lymphedema it was two weeks. It was reported that no significant differences were found between two days and two weeks of test-retest time intervals. In the present study, the time interval between test-retest was selected as seven days based on the report of Marx et al (24).

Cronbach's Alpha value of the total score of LYMQoL was recorded as 0.91 and the ICC values were recorded in the range of 0.92 and 0.99. According to the results, the Turkish version of LYMQoL has an excellent internal consistency and test-retest reliability. Keeley et al (10) did not report the ICC value for the test-retest reliability and Cronbach's Alpha value of total LYMQoL, while they indicated only Cronbach's Alpha values for the domains of LYMQoL. The internal consistency of the English version of the LYMQoL was reported to be in the range of 0.83-0.88. Similar findings were obtained in the Turkish version of LYMQoL. In this study, the Cronbach's Alpha values of the domains of LYMQoL were in the range between 0.70-0.79. For criterion validity in the English version, the correlation was investigated ..between..the...domains of EORTC QLQ-C30 and LYMQoL. It was reported that a good correlation was found. During the study process, NHP was used for criterion validity due to the absence of a Turkish lymphedema-specific HRQoL questionnaire since it is widely used in Turkish population and it also has relatively good readability and comprehensibility. 'Good' to 'very good' correlations were found between domains of the Turkish version of the LYMQoL and the

NHP total scores (0.539-0.643) and as expected, negative correlations were found between LYMQoL and 'overall quality of life' (-0.535, -0.707). Based on these findings, the Turkish version of the questionnaire appears to have 'good' to 'very good' validity. It was thought that if Turkish disease specific HRQoL questionnaire had been used, it could was obtained for criterion validity. There is already only one specific questionnaire translated into Turkish, the Lymphedema Functioning, Disability and Health Questionnaire (Lymph-ICF) (25). Nevertheless, this questionnaire could not be used since it was published while we were in the data collection period. When investigating the factor analyses, four domains existed in the original questionnaire. It was seen that the Turkish version has four domains in the factor analysis that was conducted, as well. Besides, the floor-ceiling effect analyse was not done in the original questionnaire whereas it was also applied to the Turkish version of the LYMQoL in our study. In the 5th item, "Difficulty finding to clothes", the possibility of "4: A lot" answer was much higher than the other answers; while in the 15th item, "Trouble sleeping" the answer "1: Not at all" was much more common than the others. These were expected results since difficulty with finding clothes is natural in lymphedema patients because of their severe swelling as it was investigated in the 5th item "Trouble sleeping", which was also less in proportion. This can be explained with the generally painless characteristic of lymphedema. We could not evaluate the responsiveness of the questionnaire due to the lack of treated patient population because most patients who referred to the outpatient clinic had no insurance for treatment costs. Keeley et al (10) assessed the responsiveness of the questionnaire one week and one month after the treatment; yet they stated that there were no significant differences although improvement was observed with the treatment in the resulting LYMQoL scores. They also concluded that was occurred due to the small sample size. Patel et al (26) stated that LYMQoL was a condition-specific instrument that could be used to track changes in the QoL throughout a lymphedema treatment. They also noted that the use of LYMQoL indicated that some domains improved earlier than others. In a similar manner, Terumi Iuchi et al (27) stated that improvements in QoL could be evaluated by using the LYMQoL measure regarding the Complex Decongestive Therapy.

There is a number of questionnaires that evaluate disease-specific HRQoL in upper limb lymphedema such as Wesley Clinic Lymphedema Scale (WCLS) (28), Upper Limb Lymphedema-27 (ULL-27) (29), Lymph-ICF (25). However, all of these questionnaires have disadvantages in their own way. There is no responsiveness analysis of Lymph-ICF even though the Turkish version was published this year (30) and the scoring system is not completely understood by patients (25). Wesley Clinic Lymphedema Scale is a questionnaire derived from the questionnaire Functional Living with Cancer. Yet, the words "disease" and "cancer" were replaced with "lymphedema" in WCLS. Furthermore, no validity and reliability studies currently exist. Thus, it is not appropriate for evaluating lymphedema. In the original version of the LYMQoL, it was indicated that the questionnaire could not evaluate the trunk, genital, head and neck lymphedema, which was considered a limitation (10). This limitation is not specific to LYMQoL only as all the questionnaires mentioned above cannot evaluate the lymphedema separately from the extremity.

A measurement tool should not take a long time for both the clinician and patient. Additionally, it should be easy to use. 93% of patients indicated that they completed the original version of LYMQoL easily and 99% indicated that the items were easily understandable, only 1% of patients indicated that the questionnaire was too long (10). In our point of view, LYMQoL is short and compact and these could be assumed as the most important advantages as compared to other questionnaires. Our patients remarked that the questionnaire was easily understandable and they spent five minutes on average to complete the questionnaire. As shown in the pilot study, no incomprehensible questions were found. Since questions were found understandable by patients, no changes were necessary to take into consideration. During the data collection process, no negative situations were observed in the light of feedbacks received from our patients. We believe that more detailed and specific questions about lymphedema such as compression and infection-related questions should have been included in original questionnaire based on our clinical experiments.

In conclusion, the Turkish version of LymQoL is a disease specific HRQoL questionnaire for BCRL patients and it is appropriate to use in the Turkish population. Because it is short and easy-to-apply, it can be recommended as a clinical outcome measure for disease-specific HRQoL evaluation in patients with BCRL. As a future study, the responsiveness of Turkish LYMQoL for BCRL patients in the Turkish population should be investigated. Besides, another disease specific Turkish HRQoL tool should be used regarding criterion validity.

Ethics committee approval: All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Abant Izzet Baysal University Ethics Committee (31 May 2016; number 2016//98).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Y.B.; Design - Y.B.; Supervision - Y.B.; Resources - A.T., Y.B.; Materials - Y.B., A.T., O.C., E.D.; Data Collection and/or Processing - A.T., O.C., E.D., U.U.; Analysis and/or Interpretation - E.D., O.C.; Literature Search - A.T., O.C., E.D.; Writing Manuscript - Y.B., A.T.; Critical Review - Y.B., A.T.

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Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Gultekin M, Boztas G. Türkiye kanser istatistikleri. Sağlık Bakanlığı, Türkiye Halk Sağlığı Kurumu (Turkish Only). 2014; 43.
2. Kibar S, Dalyan Aras M, Ünsal Delialioglu S. The risk factors and prevalence of upper extremity impairments and an analysis of effects of lymphoedema and other impairments on the quality of life of breast cancer patients. Eur J Cancer 2016; 13.
3. Thomas-MacLean R, Miedema B, Tatemichi SR. Breast cancer-related lymphedema: women's experiences with an underestimated condition. Can Fam Physician 2005; 51: 246-247. (PMID:16926934)
4. Paskett ED, Naughton MJ, McCoy TP, Case LD, Abbott JM. The epidemiology of arm and hand swelling in premenopausal breast cancer survivors. Cancer Epidemiol Biomarkers Prev 2007; 16: 775-782. (PMID:17416770) [CrossRef]

5. Bakar Y, Berdici B, Sahin N, Pala OO. Lymphedema after Breast Cancer and its Treatment. Eur J Breast Health 2014; 10: 6-14. [CrossRef]
6. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol 2013; 14: 500-515. [CrossRef]
7. Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Ung OA, Dylke ES, French JR, Yee J, Koelmeyer L, Gaitatzis K. Risk factors for lymphoedema in women with breast cancer: A large prospective cohort. The Breast 2016; 28: 29-36. (PMID:27183497) [CrossRef]
8. Shi S, Lu Q, Fu MR, Ouyang Q, Liu C, Lv J, Wang Y. Psychometric properties of the breast cancer and lymphedema symptom experience index: the Chinese version. Eur J Oncol Nurs 2016; 20: 10-16. (PMID:26071198) [CrossRef]
9. Smoot B, Wong J, Cooper B, Wanek L, Topp K, Byl N, Dodd M. Upper extremity impairments in women with or without lymphedema following breast cancer treatment. J Cancer Surviv 2010; 4: 167-178. (PMID:20373044) [CrossRef]
10. Keeley V, Crooks S, Locke J, Veigas D, Riches K, Hilliam R. A quality of life measure for limb lymphoedema (LYMQOL). J Lymphoedema 2010; 5: 26-37.
11. van de Pas CB, Biemans AA, Boonen RS, Viehoff PB, Neumann HA. Validation of the Lymphoedema Quality-of-Life Questionnaire (LYMQOL) in Dutch Patients Diagnosed with Lymphoedema of the Lower Limbs. Phlebology 2016; 31: 257-263. (PMID:25956549) [CrossRef]
12. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000; 25: 3186-3191. (PMID:11124735) [CrossRef]
13. Kücükdeveci A, McKenna S, Kutlay S, Gürsel Y, Whalley D, Arasil T. The development and psychometric assessment of the Turkish version of the Nottingham Health Profile. Int J Rehabil Res 2000; 23: 31-38. (PMID:10826123) [CrossRef]
14. Bhatnagar R, Kim J, Many JE. Candidate surveys on program evaluation: Examining Instrument reliability, validity and program effectiveness. Am J Educ Res 2014; 2: 683-690. [CrossRef]
15. Shamliyan T, Kane RL, Dickinson S. A systematic review of tools used to assess the quality of observational studies that examine incidence or prevalence and risk factors for diseases. J Clin Epidemiol 2010; 63: 1061-1070. (PMID:20728045) [CrossRef]
16. Feise RJ, Menke JM. Functional rating index: a new valid and reliable instrument to measure the magnitude of clinical change in spinal conditions. Spine 2001; 26: 78-87. [CrossRef]
17. Hooper D. Exploratory factor analysis.Approaches to Quantitative Research -Theory and its Practical Application: A Guide to Dissertation Students, Cork, Ireland. Oak Tree Press 2012.p.1-32.
18. Osborne JW, Costello AB. Best practices in exploratory factor analysis: Four recommendations for getting the most from your analysis. Pan-Pac Manage Rev 2009; 12: 131-146.
19. Ridner SH, Bonner CM, Deng J, Sinclair VG. Voices from the shadows: living with lymphedema. Cancer Nurs 2012; 35: E18. (PMID:21558848) [CrossRef]
20. Fayers PM, Machin D. Quality of life: the assessment, analysis and interpretation of patient-reported outcomes. 2nd ed. Sussex, England. John Wiley & Sons; 2013.
21. Velanovich V, Szymanski W. Quality of life of breast cancer patients with lymphedema. Am J Surg 1999; 177: 184-188. [CrossRef]
22. Ridner SH, Dietrich MS, Kidd N. Breast cancer treatment-related lymphedema self-care: education, practices, symptoms, and quality of life. Support Care Cancer 2011; 19: 631-637. (PMID:20393753) [CrossRef]
23. Morgan PA, Franks PJ, Moffatt CJ. Health-related quality of life with lymphoedema: a review of the literature. Int Wound J 2005; 2: 47-62. (PMID:16722853) [CrossRef]
24. Marx RG, Menezes A, Horovitz L, Jones EC, Warren RF. A comparison of two time intervals for test-retest reliability of health status instruments. J Clin Epidemiol 2003; 56: 730-735. [CrossRef]
25. Devoogdt N, Van Kampen M, Geraerts I, Coremans T, Christiaens M-R. Lymphoedema Functioning, Disability and Health questionnaire (Lymph-ICF): reliability and validity. Phys Ther 2011; 91: 944-957. (PMID:21493748) [CrossRef]
26. Patel KM, Cheng M-H. A prospective evaluation of lymphedema-specific quality of life outcomes following vascularized lymph node transfer. Ann Surg Oncol 2015; 22: 2424-2430. (PMID:25515196) [CrossRef]
27. Iuchi T, Dai M, Sanada H, Okuwa M, Nakatani T, Sugama J. Associations between the treatments and outcomes of patients with upper and lower lymphoedema in Japan: A cross-sectional observational study. Int J Nurs Stud 2015; 52: 913-919. (PMID:25769476) [CrossRef]
28. Mirolo BR, Bunce IH, Chapman M, Olsen T, Eliadis P, Hennessy JM, Ward LC, Jones LC. Psychosocial benefits of postmastectomy lymphedema therapy. Cancer Nurs 1995; 18: 197-205. (PMID:7600551) [CrossRef]
29. Viehoff P, van Genderen F, Wittink H. Upper limb lymphedema 27 (ULL27): Dutch translation and validation of an illness-specific health-related quality of life questionnaire for patients with upper limb lymphedema. Lymphology 2008; 41: 131-138. (PMID:19013881)
30. Kostanoglu A, Hosbay Z, Tarakci E. Lymphoedema functioning, disability and health questionnaire Turkish version: translation, cross-cultural adaptation and validation. J Phys Ther Sci 2016; 28: 1728-1732. (PMID:27390404) [CrossRef]

Original Article

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Top 100 Cited Classic Articles in Breast Cancer Research

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ABSTRACT

Objective: This study aimed to analyze 100 most cited articles in breast cancer research.

Materials and Methods: The data in this study were obtained by a search conducted on the Web of Science (WOS). In brief, the term "breast cancer" was typed in the search box of WOS basic research including all the years and the data. The analysis was carried out by compiling the top 100 cited articles in the shortlist as sorted by the journals, categories of the studies, the countries, the centers, the authors and the publication date. No statistical methods were used in the study. All data were reported as percentages, numbers and bar charts on tables.

Results: Our findings showed that the most frequently cited article received 7609 citations to date. Most articles were published in the New England Journal of Medicine. 81% of the studies originated from the USA. The National Institutes of Health (NIH USA) was ranked the first with 21% and it was followed by Harvard University in terms of number of published articles. 42% of the articles were published under the category of medicine and general internal medicine.

Conclusion: Top 100 most cited articles originated from the United States. The highest number of articles among the top 100 articles were published in New England Journal of Medicine and National Institutes of Health NIH USA was the leading institutes published the most articles.

Keywords: Breast cancer, citation, research

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Introduction

There has been a growing increase in the incidence of breast cancer (1), which is still the most significant cancer-related cause of female mortality (2). In spite of significant progress in the management of breast cancer, the search for a curative treatment is still ongoing. Although a number of crucial studies and clinical trials have significantly contributed to the improvement of breast cancer care, many often remain unknown to the majority of clinicians, suggesting a need to identify at least the top 100 most cited studies in the field. Actually, in the past, there were a couple of studies which identified the most cited articles in several fields such as digestive disease and psychology (3, 4), which helped the researchers in this field to easily access them. This identification is important because the decisions made by the clinicians are generally based on the evidence and the studies with a high impact (5). The most significant component of the methodological qualities of studies is associated with an increase of citation and a high impact factor of the journal where it is published (6). The object of this study was to identify and analyze the qualities of the top 100 cited papers in breast cancer-related studies.

Materials and Methods

The data in this study were obtained by a search conducted on the Web of Science (WOS) (Clarivate Analytics, United States). The journals indexed in the Science Citation Index Expanded were included. There were no restrictions on the journals. The Science Citation Index Expanded in WOS covers more than 8,500 notable and major journals encompassing 150 disciplines. The coverage time extends from 1900 to the present (7). The term "Breast cancer" was typed into the search box of WOS basic research with the selection of all the years and the data were searched in Title setting. Our search produced 189.235 published articles between 1978-2017. Thereafter, they were listed based on the citation frequency-from the highest to the lowest. The analysis was carried out by compiling the Top 100 cited classical articles in a shortlist as sorted by the journals, categories of the studies, countries, centers where the studies were published, authors and publication date. Since this was not invasive study, an approval from the ethical committee was not requested. The study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

No statistical methods were used in the study. All the data were given in percentages, numbers and bar charts.

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Table 1. The top 100 cited articles in breast cancer research

No	Author	Title	Journal	No of Cite
1	Slamon DJ..	Human breast cancer: correlation of relapse and.	Science. 1987;3798106(177):235	7609
2	Slamon, Dennis J., et al.	"Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2."	New England Journal of Medicine 344.11 (2001): 783-792.	5760
3	Slamon, Dennis J., et al.	"Studies of the HER2/neu proto-oncogene in human breast and ovarian cancer."	Science 244.4905 (1989): 707.	5300
4	Al-Hajj, Muhammad, et al.	"Prospective identification of tumorigenic breast cancer cells."	Proceedings of the National Academy of Sciences 100.7 (2003): 3983-3988.	5087
5	Van't Veer, Laura J., et al.	"Gene expression profiling predicts clinical outcome of breast cancer."	Nature 415.6871 (2002): 530-536.	4798
6	Miki Y1, Swensen J, et al.	A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1.	Science 266 (1994): 7.	3948
7	Early Breast Cancer Trialists' Collaborative Group.	"Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials."	The Lancet 365.9472 (2005): 1687-1717.	3643
8	Van De Vijver, Marc J., et al.	"A gene-expression signature as a predictor of survival in breast cancer."	New England Journal of Medicine 347.25 (2002): 1999-2009.	3599
9	Fisher, Bernard, et al..	"Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study."	Journal of the National Cancer Institute 90.18 (1998): 1371-1388	3548
10	1Elston, Christopher W., and Ian O. Ellis.	"Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up."	Histopathology 19.5 (1991): 403-410.	3330
11	Li, Jing, et al.	"PTEN, a putative protein tyrosine phosphatase gene mutated in human brain, breast, and prostate cancer."	Science 275.5308 (1997): 1943-1947.	3210
12	Müller, Anja, et al	"Involvement of chemokine receptors in breast cancer metastasis."	Nature 410.6824 (2001):50-56.	3139
13	Romond, Edward H., et al.	"Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer."	New England Journal of Medicine 353.16 (2005): 1673-1684.	2903
14	Paik, Soonmyung et al.	"A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer."	New England Journal of Medicine 351.27 (2004): 2817-2826.	2826
15	Early Breast Cancer Trialists' Collaborative Group.	"Tamoxifen for early breast cancer: an overview of the randomised trials."	The Lancet 351.9114 (1998): 1451-1467.	2665
16	Malkin, David, et al.	"Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms."	Science 250.4985 (1990): 1233.	2636
17	Piccart-Gebhart, Martine J., et al.	"Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer."	New England Journal of Medicine 353.16 (2005): 1659-1672.	2605
18	Fisher, Bernard, et al.	"Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer."	New England Journal of Medicine 347.16 (2002): 1233-1241.	2450
19	Early Breast Cancer Trialists' Collaborative Group.	"Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials." The	Lancet 366.9503 (2006): 2087-2106.	2223
20	Wooster, Richard, et al.	"Identification of the breast cancer susceptibility gene BRCA2."	Nature 378.6559 (1995): 789.	2085
21	Sjöblom, Tobias, et al.	"The consensus coding sequences of human breast and colorectal cancers."	science 314.5797 (2006): 268-274.	2034
22	Iorio, Marilena V., et al.	"MicroRNA gene expression deregulation in human breast cancer."	Cancer research 65.16 (2005): 7065-7070.	2028
23	Wolff, Antonio C., et al.	"American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer."	Journal of clinical oncology 25.1 (2006): 118-145.	1967
24	Vogel, Charles L., et al.	"Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer."	Journal of Clinical Oncology 20.3 (2002): 719-726.	1901
25	Cristofanilli, Massimo, et al.	"Circulating tumor cells, disease progression, and survival in metastatic breast cancer."	New England Journal of Medicine 351.8 (2004): 781-791	1849
26	Ford, Deborah, et al.	"Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families."	The American Journal of Human Genetics 62.3 (1998): 676-689.	1824

Table 1. The top 100 cited articles in breast cancer research

No	Author	Title	Journal	No of Cite
27	Cobleigh, Melody A., et al.	"Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease."	Journal of Clinical Oncology 17.9 (1999): 2639-2639.	1812
28	Miller, Kathy, et al.	"Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer."	New England Journal of Medicine 357.26 (2007): 2666-2676.	1773
29	Wood, Laura D., et al.	"The genomic landscapes of human breast and colorectal cancers."	Science 318.5853 (2007): 1108-1113.	1746
30	Million Women Study Collaborators.	"Breast cancer and hormone-replacement therapy in the Million Women Study."	The Lancet 362.9382 (2003): 419-427.	1707
31	Veronesi, Umberto, et al.	"Twenty-year follow-up of a randomized study comparingbreast-conserving surgery with radical mastectomy for early breast cancer."	New England Journal of Medicine 347.16 (2002): 1227-1232.	1704
32	Gail, Mitchell H., et al.	"Projecting individualized probabilities of developing breast cancer for white females who are being examined annually."	Journal of the National Cancer Institute 81.24 (1989): 1879-1886.	1688
33	Carey, Lisa A., et al.	"Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study."	Jama 295.21 (2006): 2492-2502.	1684
34	Wang, Yixin, et al.	"Gene-expression profiles to predict distant metastasis of lymph-node-negative primary breast cancer."	The Lancet 365.9460 (2005): 671-679.	1668
35	Giuliano, Armando E., et al.	"Lymphatic mapping and sentinel lymphadenectomy for breast cancer."	Annals of surgery 220.3 (1994): : 391.	1660
36	Collaborative Group on Hormonal Factors in Breast Cancer.	"Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer."	The Lancet 350.9084 (1997): 1047-1059.	1657
37	Geyer, Charles E., et al.	"Lapatinib plus capecitabine for HER2-positive advanced breast cancer."	New England Journal of Medicine 355.26 (2006): 2733-2743.	1623
38	Hall, Jeff M., et al.	"Linkage of early-onset familial breast cancer to chromosome 17q21."	Science 250.4988 (1990): 1684.	1623
39	Overgaard, Marie, et al.	"Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy."	New England Journal of Medicine 337.14 (1997): 949-	1570
40	Antoniou, Anthony, et al.	"Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies	The American Journal of Human Genetics 72.5 (2003): 1117-1130	1539
41	Neve, Richard M., et al..	"A collection of breast cancer cell lines for the study of functionally distinct cancer subtypes."	Cancer cell 10.6 (2006): 515-527	1486
42	Karnoub, Antoine E., et al.	"Mesenchymal stem cells within tumour stroma promote breast cancer metastasis."	Nature 449.7162 (2007): 557-563.	1473
43	Early Breast Cancer Trialists' Collaborative Group.	"Polychemotherapy for early breast cancer: an overview of the randomised trials."	The Lancet 352.9132 (1998): 930-942.	1442
44	Carter, Christine L., Carol Allen, and Donald E. Henson.	"Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases."	Cancer 63.1 (1989): 181-187.	1417
45	Easton, Douglas F., et al.	"Genome-wide association study identifies novel breast cancer susceptibility loci."	Nature 447.7148 (2007): 1087-1093.	1416
46	Ma, Li, Julie Teruya-Feldstein, and Robert A. Weinberg.	"Tumour invasion and metastasis initiated by microRNA-10b in breast cancer."	Nature 449.7163 (2007): 682-688.	1413
47	Minn, Andy J., et al.	"Genes that mediate breast cancer metastasis to lung."	Nature 436.7050 (2005): 518-524.	1409
48	Doyle, L. Austin, et al.	"A multidrug resistance transporter from human MCF-7 breast cancer cells."	Proceedings of the National Academy of Sciences 95.26 (1998): 15665-15670.	1394
49	Tabar, Lazio, et al.	"Reduction in mortality from breast cancer after mass screening with mammography: randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare."	The Lancet 325.8433 (1985): 829-832.	1371
50	Krag, David, et al.	"The sentinel node in breast cancer—a multicenter validation study."	New England Journal of Medicine 339.14 (1998): 941-946	1356
51	Howell, Anthony.	"Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer."	Lancet 365.9453 (2005): 60.	1350

Table 1. The top 100 cited articles in breast cancer research

No	Author	Title	Journal	No of Cite
52	Veronesi, Umberto, et al.	"Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes."	The Lancet 349.9069 (1997): 1864-1867.	1342
53	Kang, Yibin, et al.	"A multigenic program mediating breast cancer metastasis to bone."	Cancer cell 3.6 (2003): 537-549.	1327
54	Liaw, Danny, et al.	"Germline mutations of the PTEN gene in Cowden disease, an inherited breast and thyroid cancer syndrome."	Nature genetics 16.1 (1997): 64-67.	1302
55	Spiegel, David, et al.	"Effect of psychosocial treatment on survival of patients with metastatic breast cancer."	The Lancet 334.8668 (1989): 888-891.	1296
56	Hankinson, Susan E., et al.	"Circulating concentrations of insulin-like growth factor I and risk of breast cancer."	The Lancet 351.9113 (1998): 1393-1396.	1286
57	Fisher, Bernard, et al.	"Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer."	New England Journal of Medicine 312.11 (1985): 665-673	1264
58	Fisher, Bernard, et al.	"Effect of preoperative chemotherapy on the outcome of women with operable breast cancer."	Journal of Clinical Oncology 16.8 (1998): 2672-2685.	1261
59	Cummings, Steven R., et al.	"The effect of raloxifene on risk of breast cancer in postmenopausal women: results from the MORE randomized trial."	Jama 281.23 (1999): 2189-2197.	1259
60	Baum, M., et al.	"for the ATAC (Arimidex, Tamoxifen Alone or in Combination) Trialists' Group (2002) Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial."	Lancet 359: 2131-2139.	1257
61	Anzick, Sarah L., et al.	"AIB1, a steroid receptor coactivator amplified in breast and ovarian cancer."	Science 277.5328 (1997): 965-968.	1242
62	Dupont, William D., and David L. Page.	"Risk factors for breast cancer in women with proliferative breast disease."	New England Journal of Medicine 312.3 (1985): 146-151.	1232
63	Dent, Rebecca, et al.	"Triple-negative breast cancer: clinical features and patterns of recurrence."	Clinical cancer research 13.15 (2007): 4429-4434.	1217
64	Wooster, Richard, et al.	"Localization of a breast cancer susceptibility gene, BRCA2, to chromosome 13q12-13."	Science 265.5181 (1994): 2088-2091.	1214
65	Parker, Joel S., et al.	"Supervised risk predictor of breast cancer based on intrinsic subtypes."	Journal of clinical oncology 27.8 (2009): 1160-1167.	1207
66	Colditz, Graham A., et al.	"The use of estrogens and progestins and the risk of breast cancer in postmenopausal women."	New England Journal of Medicine 332.24 (1995): 1589-1593.	1200
67	Fisher, Bernard, et al.	"Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer."	New England Journal of Medicine 320.13 (1989): 822-828.	1197
68	Harris, Lyndsay, et al.	"American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer."	Journal of clinical oncology 25.33 (2007): 5287-5312.	1194
69	Harvey, Jennet M., et al.	"Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer."	Journal of clinical oncology 17.5 (1999): 1474-1474.	1159
70	Allred, D. C., et al.	"Prognostic and predictive factors in breast cancer by immunohistochemical analysis." Modern pathology: an official journal of the United States and Canadian	Academy of Pathology, Inc 11.2 (1998): 155-168.	1151
71	Goldhirsch, A. 2011 et al.	. "Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011."	Annals of oncology (2011): mdr304.	1149
72	Coombes, R. Charles, et al.	"A randomized trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer."	New England Journal of Medicine 350.11 (2004): 1081-1092.	1143
73	Fisher, Bernard, et al.	"A randomized clinical trial evaluating tamoxifen in the treatment of patients with node-negative breast cancer who have estrogen-receptor–positive tumors."	New England Journal of Medicine 320.8 (1989): 479-484.	1137
74	Sotiriou, Christos, et al.	"Breast cancer classification and prognosis based on gene expression profiles from a population-based study."	Proceedings of the National Academy of Sciences 100.18(2003): 10393-98	1124
75	Sotiriou, Christos, et al.	"Breast cancer classification and prognosis based on gene expression profiles from a population-based study."	Proceedings of the National Academy of Sciences 100.18 (2003): 10393-10398.	1112

Table 1. The top 100 cited articles in breast cancer research

No	Author	Title	Journal	No of Cite
76	Easton, Douglas F., Deborah Ford, and D. Timothy Bishop.	"Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium."	American journal of human genetics 56.1 (1995): 265.	1109
77	Ragaz, Joseph, et al.	"Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer."	New England Journal of Medicine 337.14 (1997): 956-962.	1101
78	Easton, D. F., et al.	"Genetic linkage analysis in familial breast and ovarian cancer: results from 214 families. The Breast Cancer Linkage Consortium."	American journal of human genetics 52.4 (1993): 678.	1097
79	Veronesi, Umberto, et al.	"Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast."	New England Journal of Medicine 305.1 (1981): 6-11.	1096
80	Goss, Paul E., et al.	A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer."	New England Journal of Medicine 349.19 (2003): 1793-1802.	1095
81	Berry, Donald A., et al.	"Effect of screening and adjuvant therapy on mortality from breast cancer."	New England Journal of Medicine 353.17 (2005): 1784-1792.	1091
82	Chlebowski, Rowan T., et al.	"Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial."	Jama 289.24 (2003): 3243-3253.	1086
83	Tavazoie, Sohail F., et al.	"Endogenous human microRNAs that suppress breast cancer metastasis."	nature 451.7175 (2008): 147-152.	1083
84	Hedenfalk, Ingrid, et al.	"Gene-expression profiles in hereditary breast cancer."	New England Journal of Medicine 344.8 (2001): 539-548.	1083
85	Remmele, W., and H. E. Stegner.	"Recommendation for uniform definition of an immunoreactive score (IRS) for immunohistochemical estrogen receptor detection (ER-ICA) in breast cancer tissue."	Der Pathologe 8.3 (1987): 138.	1080
86	Veronesi, Umberto, et al.	"A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer."	New England Journal of Medicine 349.6 (2003): 546-553.	1077
87	Skobe, Mihaela, et al.	"Induction of tumor lymphangiogenesis by VEGF-C promotes breast cancer metastasi"s.	Nature medicine 7.2 (2001): 192-198.	1074
88	Yu, Fengyan, et al.	"let-7 regulates self renewal and tumorigenicity of breast cancer cells."	Cell 131.6 (2007): 1109-1123.	1057
89	King, Mary-Claire, Joan H. Marks, and Jessica B. , et al.	"Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2."	Science 302.5645 (2003): 643-64	1028
90	Ritchie, Marylyn D., et al.	"Multifactor-dimensionality reduction reveals high-order interactions among estrogen-metabolism genes in sporadic breast cancer."	The American Journal of Human Genetics 69.1 (2001): 138-147.	1027
91	Ponti, Dario, et al.	"Isolation and in vitro propagation of tumorigenic breast cancer cells with stem/progenitor cell properties."	Cancer research 65.13 (2005): 5506-5511.	1007
92	Sotiriou, Christos, et al..	"Gene expression profiling in breast cancer: understanding the molecular basis o f histologic grade to improve prognosis."	Journal of the.National Cancer Institute 984 (2006): 262-272	1006
93	Saslow, Debbie, et al.	"American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography."	CA: a cancer journal for clinicians 57.2 (2007): 75-89.	1004
94	Krag, D. N., et al.	"Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe."	Surgical oncology 2.6 (1993): 335-340.	1000
95	Giuliano, Armando E., et al.	"Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial."	Jama 305.6 (2011): 569-575.	981
96	Lehmann, Brian D., et al.	"Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies."	The Journal of clinical investigation 121.7 (2011): 2750-2767.	973
97	Thurlimann, B., et al.	"Goldhirsch Breast International Group (BIG) 1-98 Collaborative Group, A, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer."	N Engl J Med 353 (2005): 2747-57.	962
98	Carver, Charles S., et al.	"How coping mediates the effect of optimism on distress: a study of women with early stage breast cancer."	Journal of Personality and social psychology 65.2 (1993): 375.	962
99	Knabbe, Cornelius, et al.	"Evidence that transforming growth factor-β is a hormonally regulated negative growth factor in human breast cancer cells."	Cell 48.3 (1987): 417-428.	962
100	Rouzier, Roman, et al.	"Breast cancer molecular subtypes respond differently to preoperative chemotherapy."	Clinical Cancer Research 11.16 (2005): 5678-5685.	960

Table 2. Distribution of articles by publication date

Publication Years	Record Count	% of 100	Bar Chart
2005	12	12.000 %	
2007	11	11.000 %	
1998	9	9.000 %	
2003	9	9.000 %	
1997	7	7.000 %	
1989	6	6.000 %	
2002	6	6.000 %	
2006	6	6.000 %	
2001	5	5.000 %	
1985	3	3.000 %	
1987	3	3.000 %	
1994	3	3.000 %	
1995	3	3.000 %	
1999	3	3.000 %	
2004	3	3.000 %	
2011	3	3.000 %	
1990	2	2.000 %	
1993	2	2.000 %	

Table 3. Journals in which the top 100 cited articles were published

Source Titles	Record Count	% of 100	Bar Chart
New England Journal of Medicine	25	25.000 %	
Lancet	13	13.000 %	
Science	11	11.000 %	
Journal of Clinical Oncology	8	8.000 %	
Nature	8	8.000 %	
American Journal of Human Genetics	5	5.000 %	
Jama Journal of The American Medical Association	4	4.000 %	
Journal of The National Cancer Institute	3	3.000 %	
Proceedings of The National Academy of Sciences of The United States of America	3	3.000 %	
Cancer Cell	2	2.000 %	
Cancer Research	2	2.000 %	
Cell	2	2.000 %	
Clinical Cancer Research	2	2.000 %	
Nature Genetics	2	2.000 %	

Results

The articles included in the study were ranked according to the frequency of citation (Table 1). Our search demonstrated that among the top 100 articles, the most frequently cited article received 7609 citations while the least cited article received 960 citations. We found that 93 of the articles received more than 1000 citations and determined that the top 100 articles were published between 1985 and 2011 (Table 2). The number of most cited articles peaked in 2005 with 12 publications, while the number of least cited in articles peaked in 1990 and 1993 with only two publications.

These top 100 articles were published in 14 high-impact journals where 25 out of 100 articles were published in the New England Journal of Medicine (Table 3).

81% of the studies originated from the USA while the rest originated from the UK, Canada and Italy (Table 4). These top 100 articles

Table 4. Countries of origin of the top 100 cited article

Source Titles	Record Count	% of 100	Bar Chart
United States Of America	81	81.000 %	
England	26	26.000 %	
Canada	18	18.000 %	
Italy	13	13.000 %	
France	12	12.000 %	
Netherlands	12	12.000 %	
Australia	11	11.000 %	
Switzerland	9	9.000 %	
Belgium	7	7.000 %	
Denmark	7	7.000 %	
Germany	7	7.000 %	
Sweden	7	7.000 %	
Scotland	6	6.000 %	
Finland	5	5.000 %	
Poland	5	5.000 %	
Iceland	4	4.000 %	
Spain	4	4.000 %	
Ireland	3	3.000 %	
Israel	3	3.000 %	
Peoples R China	3	3.000 %	
Russia	3	3.000 %	
Austria	2	22.000 %	
Greece	2	2.000 %	
Hungary	2	2.000 %	
Japan	2	2.000 %	
Mexico	2	2.000 %	

Table 5. Institutions of origin

Institutions	Record Count	% of 100	Bar Chart
National Institutes of Health Nih Usa	21	21.000 %	
Harvard University	18	18.000 %	
National Cancer Institute Nci	18	18.000 %	
University of California System	14	14.000 %	
Memorial Sloan Kettering Cancer Center	13	13.000 %	
University of London	13	13.000 %	
Va Boston Healthcare System	13	13.000 %	
Institute of Cancer Research Uk	11	11.000 %	
Dana Farber Cancer Institute	10	10.000 %	
Utmd Anderson Cancer Center	9	9.000 %	
European Institute of Oncology	8	8.000 %	
Fondazione Irccs Istituto Nazionale Tumori Milan	8	8.000 %	
Pennsylvania Commonwealth System of Higher Education	8	8.000 %	
Roche Holding	8	8.000 %	
Unicancer	8	8.000 %	
University of Oxford	8	8.000 %	
University of Pittsburgh	8	8.000 %	
Mcgill University	7	7.000 %	
University of California Los Angeles	7	7.000 %	
International Agency For Research On Cancer	6	6.000 %	
Johns Hopkins Oncology Center	6	6.000 %	
Johns Hopkins University	6	6.000 %	
Mayo Clinic	6	6.000 %	
National Surgical Adjuvant Breast Bowel Project	6	6.000 %	
University of California San Francisco	6	6.000 %	
University of Cambridge	6	6.000 %	
University of Toronto	6	6.000 %	
University of Utah	6	6.000 %	
Utah System of Higher Education	6	6.000 %	
World Health Organization	6	6.000 %	
British Columbia Canc Agcy	5	5.000 %	
Duke University	5	5.000 %	
Howard Hughes Medical Institute	5	5.000 %	
Leiden University	5	5.000 %	
Northshore University Health System	5	5.000 %	
Northwestern University	5	5.000 %	
University of Michigan	5	5.000 %	
University of Michigan System	5	5.000 %	
Erasmus University Rotterdam	4	4.000 %	
Karolinska Institutet	4	4.000 %	
Rush University	4	4.000 %	
University of British Columbia	4	4.000 %	
University of Copenhagen	4	4.000 %	
University of Edinburgh	4	4.000 %	
University of Helsinki	4	4.000 %	
University of North Carolina	4	4.000 %	
University of North Carolina Chapel Hill	4	4.000 %	
University of Texas Health Science Center San Antonio	4	4.000 %	

NIH: National Institutes of Health; UK: United Kingdom; CANC AGCY: Cancer Agency; IARC: International Agency for Research on Cancer; NCI: National Cancer Institute; USA: The United States of America

that originated from 50 different centers and National Institutes of Health (NIH USA) ranked as the first with 21% of total articles followed by Harvard University and NIH National Cancer Institute (NCI). The University of Washington ranked the last with 4% (Table 5).

Among top 100 authors in these articles, Wolmark N. was determined to be the mostly cited common author with 12% followed by Fisher

Table 6. Most common the first 20 authors

Source Titles	Record Count	% of 100	Bar Chart
Wolmark N	12	12.000 %	
Fisher B	9	9.000 %	
Bryant J	8	8.000 %	
Easton DF	7	7.000 %	
Norton L	7	7.000 %	
Peto J	7	7.000 %	
Veronesi U	7	7.000 %	
Cuzick J	6	6.000 %	
Davidson NE	6	6.000 %	
Ford D	6	6.000 %	
Gelber RD	6	6.000 %	
Goldhirsch A	6	6.000 %	
Klijn Jgm	6	6.000 %	
Peto R	6	6.000 %	
Redmond C	6	6.000 %	
Baum M	5	5.000 %	
Brown A	5	5.000 %	
Collins R	5	5.000 %	
Costa A	5	5.000 %	
Devilee P	5	5.000 %	

Table 7. Most common the first 20 authors

Categories of articles	Record Count	% of 100	Bar Chart
Medicine General Internal	42	42.000 %	
Multidisciplinary Sciences	22	22.000 %	
Oncology	21	21.000 %	
Genetics Heredity	7	7.000 %	
Cell Biology	6	6.000 %	
Biochemistry Molecular Biology	3	3.000 %	
Pathology	3	3.000 %	
Medicine Research Experimental	2	2.000 %	
Surgery	2	2.000 %	

B. and Bryant J., respectively (Table 6). Furthermore, 42% of these articles were categorized under the title of medicine and general internal medicine followed by studies under the category of multidisciplinary sciences, oncology and genetic hereditary diseases, respectively. The rate of studies under the surgery category was found to be the lowest with 2% (Table 7).

Discussion and Conclusion

Bibliometric analysis can be conducted in many areas for different purposes (8, 9) and can be used to reveal the historical development in a field (9). In this study, we aimed to identify the top 100 most cited articles in breast cancer research to help researchers easily access and analyze them. In that respect, this study is one of the early studies under the title of breast cancer.

Although analyzing the top 100 most cited articles was relatively difficult, we identified that the top 100 articles were published between 1985 and 2011 thanks to systems such as WOS. The citations mostly peaked between 2005 and 2007. The number of citations to the studies conducted in the areas of orthopedics and neurosurgery peaked between 1965 and 1980 (10, 11). However, the citation frequency of studies in the field of cardiology peaked between 2001 and 2010 (12). This result may suggest that the development and progression in the area of breast cancer may have occurred within a short period of time. In parallel with the technological advances that have occurred in the last two decades, a significant progress in breast cancer research has been also achieved.

The number of citations is closely associated with the publishing date, and has been increasing with time (9). For this reason, the vast majority of articles with a high number of citations consisted of early-published articles. No papers published after 2011 appeared in our list. However, the number of citations is not solely depended on publication date. For example, one article in our list published in 2005 received more citations than other articles published between 1985 and 1995.

Another interesting point of our analysis is that all the articles were published in journals with a high impact factor. The New England Journal of Medicine, Lancet and Science were the journals which mostly published top 100 articles, indicating that the vast majority of the studies were published in the best-known general medical journals rather than specific journals in this field. It may be speculated that the audience of a general medical journal may be closely interested in the issue of breast cancer or it is possible to consider that the authors of studies on breast cancer preferentially choose the journals with a high impact.

Another point of our study is that the top 100 articles most often originated from the United States. The bibliometric analyses in other areas also showed that the United States ranked high on the list (13, 14). These findings clearly show that the United States is at the forefront of studies on breast cancer. A wide range of patient population and a substantial amount of financial support to researchers can be the main reason behint this.

The authors who have received the highest number of citations are the people who are prominent in their field. For example, Wolmark N. authored 12 articles in the top 100 articles whereas Slamon Dennis J. was not in the list of the first 20 authors who have the highest number of articles although he was the first author in the first 3 articles that received the highest number of citations.

Breast cancer research has progressed historically and gone through milestones in various areas in this process. These areas include breast cancer gene associations, breast cancer treatment modalities, hormonal therapies, HER2 and breast cancer involvement, sentinel lymphadenectomy, breast conserving surgery, breast cancer metastasis, survival, neoadjuvant chemotherapy and breast screening.

Slamon Dennis J. was observed as the first author in first 3 articles with the highest number of citations. All three articles were about the oncogene HER2 / neu. It has been emphasized that HER2 / neu amplification gene has a high prognostic value and this gene may play a role in the pathogenesis of breast cancer. The first three articles with the highest number of citations are very important in terms of revealing the correlation between HER2 / neu and breast cancer. Prognosis is very low in patients with HER2 / neu positive breast cancer. For this reason, HER2-targeting therapies are thought to have positive effects on outcomes. Romond, Edward H., et al. showed an improvement in the outcomes of women with HER2-positive breast cancer treated with trastuzumab, a monoclonal antibody targeting the extracellular domain of HER2. Piccart-Gebhart, Martine J. et al also demonstrated the efficacy of trastuzumab in HER2-positive breast cancer patients after adjuvant chemotherapy. Vogel, Charles L., et al., showed that trastuzumab is safe and effective as a single agent in the first-line treatment of HER2-positive metastatic breast cancer patients. Seven of the top 100 articles are related to HER2 and trastuzumab and they are an important milestone in this field.

Today, hormonal treatments in breast cancer have an important place in therapy. Remmele, W., and H.E. Stegner identified estrogen receptors immunohistochemically from breast cancer tissues in 1987. Fisher, Bernard, et al. published a paper in 1989, showing a randomized clinical trial which demonstrated the efficacy of tamoxifen on breast cancer in patients that are estrogen- and progesterone-receptor-positive. This study provided significant progress in breast cancer treatment. The Early Breast Cancer Trialists' Collaborative Group investigated the efficacy of tamoxifen in early breast cancers in 1998. Fisher, Bernard et al. explained the protective effects of tamoxifen on breast cancer in 1998.

Gene-based studies have been conducted on breast cancer through the demonstration of the effects of genetic factors in many types of cancer. Miki Y, Swensen J, et al. reported the association of the BRCA-1 gene with breast cancer and ovarian cancer in 1994. Wooster, Richard, et al, showed a relationship between BRCA-2 gene and breast cancer in 1995.Easton, Douglas F. et al. investigated the incidence of breast and over-cancer in BRCA-1 gene mutation carriers. Ford, Deborah et al. showed that families with breast cancer have BRCA-1 and BRCA-2 identified in their gene analysis in relation to breast cancer in 1998. Antoniou, Anthony et al. published a study entitled '' "Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies" in 2003. Today, BRCA1 and 2 genes can be examined and prophylactic mastectomy can be decided upon (Table 1).

Veronesi, Umberto et al. showed that using sentinel-node biopsy can help avoid axillary dissection in breast cancer patients with clinical negative lymph-nodes. Krag, David et al. emphasized the importance of sentinel node in breast cancer. In another study by Krag, D. N., et al., they showed that sentinel-node can be found by radiocalization with gamma probe. In 1994, Giuliano, Armando E. et al. described sentinel lymphadenectomy by lymphatic mapping. In 2003, Veronesi, Umberto

et al. published a paper entitled "A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer", and stated that sentinel-node biopsy was a safe and reliable method. All these papers constituted the milestones for avoiding unnecessary axillary dissection in breast cancer patients, and helped reduce morbidity associated with breast surgery (Table 1).

While radical mastectomy surgery was commonly used as the conventional breast cancer treatment, modified radical mastectomy and especially preventive breast surgery are generally chosen as a curative treatment at the present time. The reason behind this change in treatment method actually is rooted in the findings of the following milestone papers: in 1981, the paper published by Veronesi, Umberto et al. compared radical mastectomy to quadrantectomy, and they found that there were no differences between these groups in terms of disease-free or overall survival rate. Fisher, Bernard et al. published a paper in 1985 entitled "Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer." and they determined that segmental mastectomy with breast irradiation and adjuvant chemotherapy was the appropriate treatment method in stage I and II breast cancer (less than 4 cm).

The rest of the top 100 cited articles were associated with adjuvant and neoadjuvant treatments, survival, breast cancer metastasis, and breast screening. These studies contribute to breast research by providing significant improvements.

In this bibliometric analysis, the vast majority of the top 100 articles were in the category of general internal medicine. It was followed by multi-disciplinary sciences, and the third in rank was oncology research. Surgery was at the bottom of the list. However, surgeons have significantly contributed to the area of breast cancer. The effects of significant studies which have been conducted in recent years will be seen during the upcoming years.

There are some limitations to our study. Only the studies having breast cancer in their title were included in the study. However, breast cancer as the topic of the studies was not taken into consideration. The studies on the topic of breast cancer with a high number of citations can also be separately analyzed. The results which have been found by typing 'breast, breast neoplasm' in the search box of WOS can be separately added to the analysis. In order to ensure homogenization in our study, analyses have been conducted under only one title and search.

As a result, it was found that top 100 most cited publications predominantly originated from the United States. The largest part of top 100 articles was published in New England Journal of Medicine. Most articles were published under the category of general internal medicine. The highest number of publications was in 2005. The articles about HER2 / neu were listed as the first three articles. It was determined that National Institutes of Health NIH USA and Harvard University were the institutes which published the highest number of articles.

Analysis of highly cited articles with 'breast cancer' in their title provided the opportunity to recognize the progress made in studies on breast cancer. It also provides a historical perspective on the development of breast cancer studies.

Ethics Committee Approval: Ethics committee approval was not requested for this study.

Informed Consent: Informed consent is not necessary as our work is a retrospective international data study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - EU.; Design - EU.; Supervision - EU.; Resources - EU.; Materials - EU.; Data Collection and/or Processing - EU.; Analysis and/or Interpretation - EU.; Literature Search - EU.; Writing Manuscript - EU.; Critical Review - EU.; Other - EU.

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References

1. J. Ferlay, I. Soerjomataram, M. Ervik, R. Dikshit, S. Eser, C. Mathers. GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide International Agency for Research on Cancer, IARC CancerBase No. 11. Lyon, France (2013) http://globocan.iarc.fr Accessed January 1, 2016
2. World Cancer Report". International Agency for Research on Cancer. 2008. Retrieved 26 February 2011.
3. Ho YS, Hartley J. Classic articles in psychology in the Science Citation Index Expanded: a bibliometric analysis. Br J Psychol 2016; 107: 768-780. (PMID:26607573) [CrossRef]
4. Loomes DE, van Zanten SV. Bibliometrics of the top 100 clinical articles in digestive disease. Gastroenterology 2013; 144: 673-676. (PMID:23439236) [CrossRef]
5. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312: 71-72. (PMID:8555924) [CrossRef]
6. Moed HF. The impact-factor debate: the ISI's uses and limits. Nature 2002; 415: 731-732. (PMID:11845176) [CrossRef]
7. Jo Yong-Hak. Web of Science. Thomson Reuters, 2013.
8. Khan MS, Ullah W, Riaz IB, Bhulani N, Manning WJ, Tridandapani S, Khosa F. Top 100 cited articles in cardiovascular magnetic resonance: a bibliometric analysis. J Cardiovasc Magn Reson 2016; 18: 87. (PMID:27866473) [CrossRef]
9. Li Q, Jiang Y. Top classic citations in pancreatic cancer research. World J Surg Oncol 2016; 14: 298. (PMID:2789914) [CrossRef]
10. Lefaivre KA, Shadgan B, O'Brien PJ. 100 most cited articles in orthopaedic surgery. Clin Orthop Relat Res 2011; 469: 1487-1497. (PMID:20922583) [CrossRef]
11. Ponce FA, Lozano AM. Highly cited works in neurosurgery. Part I: the 100 top-cited papers in neurosurgical journals. J Neurosurg 2010; 112: 223-232. (PMID:20078192) [CrossRef]
12. Shuaib W, Khan MS, Shahid H, Valdes EA, Alweis R. Bibliometric analysis of the top 100 cited cardiovascular articles. Am J Cardiol 2015; 115: 972-981. (PMID:25670637) [CrossRef]
13. Joyce CW, Sugrue CM, Joyce KM, Kelly JL, Regan PJ. 100 citation classics in the melanoma literature: a bibliometric analysis. Dermatol Surg 2014; 40: 1284-1298. (PMID:25357170) [CrossRef]
14. Tao T, Zhao X, Lou J, Bo L, Wang F, Li J, Deng X. The top cited clinical research articles on sepsis: a bibliometric analysis. Crit Care 2012; 16: R110. (PMID:22731930) [CrossRef]

Original Article

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The Effect of Peer Education upon Breast Self-Examination Behaviors and Self-Esteem among University Students

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ABSTRACT

Objective: The current study was semi-experimentally designed in order to identify the effect of peer education upon breast self-examination (BSE) behaviors and self-esteem among university students.

Materials and methods: The study was undertaken with 100 female students who studied at Erzincan University. Peer educators were recruited from the 4th year students. The data were collected with a questionnaire form, BSE skill form and Rosenberg Self-esteem Scale in two phases one month before and after the BSE peer education. For the data assessment; percentage distributions, frequency, mean, standard deviation and Simple T test were employed.

Results: The mean age of the participant students was 20.45±1.67 year and all of them were single. It was found that during the first data collection phase, only 16 % of the students performed BSE while during the final data collection phase, the rate of the students performing BSE rose to 77 %. During the first data collection phase, students received a mean score of 2.36±4.13 from BSE skill form while during the last data collection phase they had a mean score of 10.70±3.40 from BSE skill form.

When the scores obtained from Rosenberg Self-esteem Scale by the students were examined, it was seen that they received a mean score of 1.20±1.34 during the first data collection phase while they had a mean score of 0.84±1.07 during the final data collection phase.

Conclusion: Although short-term feedback was obtained, it was noted that students' BSE knowledge and skills increased considerably.

Keywords: Breast self-examination, self-esteem, peer education, student

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Introduction

One of the most significant health problems of today is cancer. Globally, breast cancer is the one detected most among women and ranks as the second cause of death from cancer among women. More than 1.15 million of breast cancer diagnoses are made worldwide each year and 502.000 women die from breast cancer annually (1-3). In Turkey, breast cancer is among the most commonly seen cancer types and its incidence is 48.6 per 100.000 (4). Although breast cancer is a widespread and important health problem, it is one of those cancers for which early diagnosis is possible (5). Key methods recommended for early diagnosis are BSE, clinical breast examination (CBE) and mammography (6).

Breast self-examination is an examination method which is used by women to detect breast cancer as much early as possible and in which they examine breast and the surrounding site for unusual mass and shape changes at regular intervals and in a systematic way using the same method (7). BSE practiced at regular intervals and in a systematic way is a simple and affordable method in which women's confidentiality is protected and which can be performed alone at home for the diagnosis of breast cancer. Therefore, it is recommended that those women aged ≥20 years should regularly practice BSE (8, 9). However, although the benefits of regularly performed BSE are well explained, few women are interested in this practice (10).

Self-esteem is another important term that affects BSE behaviors. Rosenberg defines self-esteem as positive or negative orientation/attitude towards oneself. Positive peer report increases self-esteem. Therefore, high self-esteem encourages positive health behaviors among the

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adolescents. Peers -in other words- friends are one of the most effective support and help sources of people in life. Exchange of personal, social and moral experiences of peers enables personal and social development among friends. Peer education -a training activity that focuses on the fact that youngsters interact and identify with their friends and peers better- is based on social learning theory and aims at training voluntary and pioneer youngsters about certain issues and making them share the knowledge and information they have already learnt with their peers. Thus, positive peer reports regarding BSE improve BSE knowledge and practices of the adolescents (11-14).

The current study aimed at identifying the effect of peer education upon BSE behaviors and self-esteem among university students.

Materials and Methods

Aim, design, population and sampling of the study

The study was semi-experimentally designed in order to identify the effect of peer education upon BSE behaviors and self-esteem among university students. The population of the study was composed of all the female students who studied at different departments of Erzincan University (Faculty of Education, Faculty of Engineering, Faculty of Justice, Faculty of Theology, Faculty of Science and Letters). The sample of the study was consisted of 100 female students who studied at other departments of Erzincan University - Health School students not included- and who were contacted through 10 female students recruited among the 4th year students of Health School.

Sampling method:

In order to provide BSE peer education, peer educators were recruited among the 4th year female students of Health School thanks to their nursing education and health knowledge. Names of the 4th year female students were written down on a piece of paper and put in a bag to draw lots. The 10 students who accepted to participate in the study were trained about BSE and breast cancer. Each of the 10 nursing students who were trained gave peer education to 10 female peer students coming from other departments about BSE and breast cancer. Criteria for the participants to whom peer education was given were as follows: they should be female, should share the same social settings as peer educators, should not have mastectomy before and should study at a department of Erzincan University except Health School.

Data collection method

The study was carried out between April and July, 2015. Firstly, 10 peer educators recruited among the 4th year female students of Health School were trained about prevalence, risks, early diagnosis methods, symptoms and importance of breast cancer and BSE in Turkey through a power point presentation so that they could provide the peer education. The Presentation was designed by the researchers and examined by experts (one expert from the department of public health, two experts from the department of obstetrics and women's health and disease). Study topics were demonstrated in a total of 4 sessions in order to minimize any bias in the researcher and students' performance. Each session lasted 30-minutes. Each female nursing student who participated in 4 sessions of the training was called as peer educators. Brochures to be used in the peer education and questionnaire forms to be administered were distributed to the female peer educators. Then, each peer educator provided 10 female students -one by one- with an applied peer education on BSE that lasted nearly 30 minutes in one session. Before the educations, oral informed consents of the participants were obtained and then questionnaire forms and scales were administered. The participants who filled in the questionnaire and scale were given one to one peer education by peer educators about breast cancer and BSE and were asked to practice BSE on their own bodies once. At the end of the education, brochures that were designed and illustrated BSE steps were given to the participants. One month after the peer education, the participants again filled in questionnaire forms and scales again through peer educator.

Data Collection Tools

Questionnaire form: The questionnaire form included a total of 14 questions; 4 questions about students' socio-demographic characteristics (age, income status, etc.), 5 questions about BSE and breast cancer (whether or not they have knowledge about breast cancer; if yes, who the person from whom they get the information is, whether or not the family has breast cancer history) and 5 questions about BSE practice status (whether or not they practice BSE; if yes, how often they practice BSE).

BSE skill form: The form included a total of 13 questions about whether or not they performed steps of BSE in order. The form was designed in line with the literature and expert opinion was obtained (one expert from the department of public health, two experts from the department of obstetrics and women's health and disease).

Rosenberg self-esteem scale: The scale was designed by M. Rosenberg and adapted for Turkish language by Füsun Çuhadaroğlu (15). The scale is composed of 63 items and 12 subscales. In the current study, only self-esteem subscale was used. In the test based on Guttman scale, positive and negative items are successively organized. According to scale scoring system, scores that subjects receive range from 0 to 6. In the comparisons made on the basis of numeric measurements, a score between 0 and 1 indicates high self-esteem, a score between 2 and 4, moderate self-esteem and a score between 5 and 6, low self-esteem. High scores indicate low self-esteem while low scores indicate high self-esteem. Validity coefficient of the scale was found to be .71 whereas reliability coefficient of the scale was .75.

Ethical principals

Written official permissions and approvals to undertake this study were gained from government agencies. The study was started with the decision dated 13.02.2015 and numbered 01. All patients were informed of the purpose of the study and were explained that participation was voluntary and could withdraw from the study anytime. Also, the participants were assured of confidentiality and individual responses would remain confidential, not be disclosed and be used nowhere.

Data analyses and data assessment

Statistical Package for the Social Sciences (SPSS) for Windows software Version 22.0 (IBM Corp., Armonk, New York, USA) was used for statistical analysis. In assessing the data, it was found that the data were homogenous and parametric tests were employed. Statistical methods used were percentage, frequency, mean, standard deviation and simple t-test. Results were considered significant at $p<0.05$.

Results

All of the participant students were single and their descriptive characteristics were presented in Table 1. It was found that mean age of the participant students was 20.45±1.67 years and 35% of the female students were 1st year graders, 52% of them had an income equal to expenses and 78% of them lived in nuclear families.

Table 1. Descriptions of the students in terms of descriptive characteristics (n=100)

Socio-demographic characteristics	Number	%
Age	20.45±0.16	
Grade		
1st graders	35	35
2nd graders	21	21
3rd graders	20	20
4th graders	24	24
Income level		
Income<expenses	24	24
Income=expenses	52	52
Income>expenses	24	24
Family type		
Extended family	22	22
Nuclear family	78	78

Table 2. Knowledge level of breast cancer and BSE of the participant students (n=100)

	Number	%
Status of whether or not information on breast cancer was received before		
Yes	35	35.0
No	65	65.0
Information-source where participants got the information about breast cancer		
Health care personnel	14	40.0
Books, magazines, brochures	9	25.7
Mass media	12	34.3
Whether or not 1st degree relatives have breast cancer history		
Yes	13	13.0
No	87	87.0
Whether or not you had information/ education on BSE		
Yes	32	32.0
No	68	68.0
Information-source where participants got the information/education about BSE		
Health care personnel	17	53.2
Books, magazines, brochures	10	31.2
Mass media	5	15.6

BSE: breast self-examination

Table 3. Comparison of status of students' BSE knowledge and practices before and after BSE peer education (n=100)

	Before BSE peer education		After BSE peer education	
	Number	%	Number	%
At what age should a woman start BSE?				
Following the first menstruation	25	25.0	19	19.0
After the age of 30	9	9.0	2	2.0
After the age of 15	14	14.0	4	4.0
After the age of 20	24	24.0	75	75.0
I do not know	28	28.0	0	0.0
Do you perform BSE?				
Yes	16	16.0	77	77.0
No	84	84.0	23	23.0
The reason why you do not do BSE				
I do not know how to do BSE	58	69.0	2	8.7
Possibility that something bad may take place	10	11.9	4	17.4
I do not think that I should	12	14.3	2	8.7
I forgot	4	4.8	15	65.2
What is the frequency that you perform BSE?				
From time to time	7	41.2	23	29.9
Once a month	5	29.4	48	62.3
Other (when I remember)	5	29.4	6	7.8
When do you practice BSE?				
Whenever I remember	22	62.9	17	19.5
Before menstruation	3	8.6	1	1.1
During menstruation	3	8.6	4	4.6
5-7 days later following menstruation	7	20.0	65	74.7

BSE: breast self-examination

Table 2 demonstrates the level knowledge that participants had about breast cancer and BSE. It was identified that 65% of the students did not get any information on breast cancer before but 40% of those who got information on breast cancer received that information from health care personnel mainly and 87% of them did not have breast cancer history among their first degree relatives. On the other hand, when the status of getting BSE information/education and from whom the students got this BSE information/education were examined, it was found that 68% of them received information/education on BSE before and 53.2% of them received this information/education from health care personnel mainly.

Table 4. Students' ability to do BSE and mean scores of Rosenberg Self-esteem Scale (n=100)

Scales	Before BSE peer education X±SD	After BSE peer education X±SD	t	P
Ability to do BSE	2.36±4.13	10.70±3.40	-16.895	0.000
Rosenberg Self-esteem Scale	1.20±1.34	0.84±1.07	2.78	0.006

BSE: breast self-examination; SD: standard deviation

Table 3 includes comparisons about BSE knowledge level of the students before and after the BSE peer education in terms of whether or not students received BSE information. Before the BSE peer education, 28% of the students answered "I do not know." for the question "At what age should BSE be initiated?" whereas after the BSE peer education 75% of the students answered that BSE should be initiated after the age of 20. It is significant that before the BSE peer education, 16% of the students practiced BSE regularly whereas after the BSE peer education, the rate of those performing BSE regularly rose to 77%. Before the BSE peer education, 69% of the students did not practice BSE because they did not know how to do BSE whereas after the BSE peer education, 65% of the students told that they did not perform BSE because they forgot. When the frequency at which students practiced BSE was examined, the following was found: before the BSE peer

Table 5. Distribution of students' ability to do BSE before and after BSE peer education

	Before BSE peer education				After BSE peer education				
	Knowledge		No knowledge		Knowledge		No knowledge		
Breast self-examination information form	n	%	n	%	n	%	n	%	
You stand before a mirror that reflects upper part of body.	26	26	74	74	87	87	13	13	t=11.513 p=0.000
Breasts are checked in front of a mirror in terms of shapes, size, appearance with arms at sides, arms on hips and overhead.	24	24	76	76	90	90	10	10	t=12.771 p=0.000
Hands are pressed against hips, shoulders and elbows are placed in front by bending . towards mirror slowly and breasts are observed	14	14	86	86	81	81	19	19	t=13.577 p=0.000
Control nipples for discharge by gently squeezing.	17	17	83	83	74	74	26	26	t=11.456 p=0.000
Use 2nd, 3rd and 4th fingers of your hand to touch every part of your breast. Fingers should be kept close.	21	21	79	79	88	88	12	12	t=11.764 p=0.000
Site to be examined are upper part of bra, collar bone, middle of thorax and under armpits.	20	20	80	80	80	80	20	20	t=11.282 p=0.000
Examination should be done over breasts by circle and horizontal movements slowly and carefully.	21	21	79	79	90	90	10	10	t=13.625 p=0.000
During the examination, all layers of breast should gradually be felt –first- by slow, moderate and strong pressures.	20	20	80	80	73	73	27	27	t=9.485 p=0.000
Hand examination should be done by both lie-flat position and standing position. Each breast is checked at least for 5 minutes.	16	16	84	84	80	80	20	20	t=12.726 p=0.000
While in the shower, use your right hand to examine your left breast and vice versa.	21	21	79	79	89	89	11	11	t=13.331 p=0.000
Clasp your hand behind your head in the shower and look carefully for any changes in the shape or contour of your breasts.	18	18	82	82	85	85	15	15	t=13.046 p=0.000
Put a pillow or towel under your shoulder for the breast to be examined while lying down.	9	9	91	91	69	69	31	31	t=11.282 p=0.000
While standing or lying down, underpins are examined by hand after breasts by palpation.	19	19	81	81	85	85	15	15	t=13.863 p=0.000

BSE: breast self-examination

education, 41.2% of the students performed BSE from time to time whereas after the BSE peer education, the rate of those practicing BSE once a month increased to 62.3%. Before the BSE peer education, 62.9% of the students practiced BSE when they remembered whereas after the BSE peer education, 74.7% of the students performed BSE after 5-7 days following menstruation.

Table 4 showed students' knowledge level and mean scores of Rosenberg Self-esteem Scale before and after BSE peer education. It was identified that students' ability to do BSE before and after BSE peer education and mean scores of Rosenberg Self-esteem Scale increased considerably ($p<0.001$).

Table 5 demonstrated distributions regarding students' ability to do BSE before and after the BSE peer education. When students' abilities to perform each step of BSE were examined, it was noted that there were statistically significant differences between students' abilities to perform each step of BSE before and after BSE peer education ($p<0.01$). Accordingly, students' abilities to perform each step of BSE increased and enhanced following BSE peer education.

Discussion and Conclusion

Breast cancer is the most commonly seen cancer type among women both in the developing countries and the developed countries. A treatment that prevents breast cancer has not been found yet but when early diagnosis is made, expected life span can be extended and a complete recovery can be achieved. Mammography, clinical breast examination and BSE are the methods used for screening in the early detection of breast cancer (16, 17). According to the literature, BSE is a cheap, simple, safe and effective method and acquiring BSE behaviors and practices will increase the possibility to continue BSE in the future (18). The study was done in order to determine the effects of peer education upon BSE practices and self-esteem among the university students.

The mean age of the participant students was 20.45±1.67 years, 35% of the female students were 1st year graders, 52% of them had an income equal to expenses and 78% of them lived in nuclear families (Table 1). 35% of the participant students told that they got information on breast cancer before (Table 2). The rate of those receiving information on breast cancer before was 64.2% in the study by Tahmasebi and Noroozi, 52.4% in study by Segni et al. (19) , 50% in the study by Özkahraman et al. (20) and 50.2% in the study by Özen et al. (21). Therefore, it is very crucial to promote and to enhance awareness level of young women about breast cancer, which has increased in the recent years, to inform women about breast cancer screenings and to help them gain health promoting behaviors (21).

When information-source where participants got the information about breast cancer was examined, it was identified that 40% of the students received the information on breast cancer from health care personnel (Table 2). It was found that participants received the information on breast cancer from health care personnel (27.6%) in the study by Suleiman, again from health care personnel (12.2%) in the study by Tahmasebi and Noroozi, from mass media in the study by Özen et al. (21) (29%) while 11.2% of them received the information from nurses (10, 22). Although healthcare workers play a key role in preventing and early diagnosis of cancer, the studies indicate that their effect is quite poor.

When family history of breast cancer, another important risk factor, was examined, 13% of the participant students stated that they had breast cancer history among their first degree relatives (Table 2). The rate of those who told that they had breast cancer history among their first degree relatives was 9.2% in the study by Al Sharbatti et al. (23), 13% in the study by Koç and Sağlam (24), 17.6% in the study by Al Zalabani et al. (25), 5% in the study by Ertem and Koçer (26) and 11% in the study by Ogunbod et al. (27). The results of the current study concurred with the results of the literature.

Breast cancer, prevalence of which has been increasing all over the world, is the one that is most seen among women. Many studies emphasize that BSE, which plays a key role in early diagnosis of breast cancer, is not known by Turkish women much and those who know BSE do not practice it enough (24, 28, 29). In this sense, 32% of the participant students told that they had education on BSE before (Table 2). Similarly, 37.4% of the university students in the study by Nde et al. (3) and 30.1% of the students in the study by Karayurt et al. (30) told that they had education on BSE before. On the contrary, 77.3% of the teachers had education on BSE before in the study by Marzo and Salam. (31) The reason why the rate of those receiving education on BSE before in the study by Marzo and Salam (31) is high may have resulted from the age of the participants. The idea that people catch illnesses more whey they grow old and the fact that importance of early diagnosis of breast cancer is not known at younger ages confirm the finding above.

When the source of information from which the participants got information about BSE was examined, it was identified that 53.2% of them received information about BSE from health care personnel, 31.2% from books, magazines, brochures and 15.6% from mass media (Table 2). Similarly to our study findings, in the Turkish study by Koç and Sağlam (24), it was reported that women received information about BSE from health care personnel, newspapers, magazines, TVs and radio, respectively (24). In another study, Gençtürk et al. (32) reported that students of midwifery stated that undergraduate education, publications such as TVs and newspapers, nurses and doctors -respectively- were influential upon BSE practice.

When the students' BSE knowledge and practices before and after the BSE peer education were compared, it was identified that their BSE knowledge and practices before the BSE peer education was poor but after the BSE peer education a big change took place in BSE knowledge and practices (Table 3). Similar to our study results, the study by Öztürk et al. (33) indicated that there were significant differences in terms of BSE knowledge and practices before and after the education. Similarly, the study by Seif and Aziz (34) pointed out that rate of participants' knowledge and BSE practices was 15% and 5.2% before the education whereas it rose to 95.1% and 86% after the education; respectively.

When the students' abilities to do BSE before and after the BSE peer education and their mean self-esteem scores were compared, it was found that there were significant increases in BSE ability/skills and self-esteem scores (Table 4). Similarly, in the study by Tuna et al. (35), too, it was identified that there were significant increases in BSE ability/skills and self-esteem scores before and after the BSE education. Self-esteem is people's evaluation and approval of their own worth and is a positive mood that enables them to be satisfied and pleased with themselves and find themselves positive without considering themselves inferior or superior (36). In line with the definition, it is thought that one who loves and accepts his/her own body seeks for healthy lifestyle behaviors and cares about his/her health while those who do not care about their own bodies neglect both their health and body.

In the current study, it was seen that there were significant differences in BSE skill levels before and after BSE peer education given to enhance the ability to do BSE (Table 5). Besides, when the finding that 84% of the students did not do BSE at all and 41.2% of those doing BSE performed BSE from time to time was considered, it may be argued that applied peer education regarding BSE became effective upon BSE practice. The outcome that the BSE peer education produced significant knowledge and information changes supports the conclusion that a strong scientific ground has been built in terms of developing awareness about breast cancer and early diagnosis among the students. The study results were in line with literature (24, 16, 37).

In conclusion, with the current study, students had the opportunity to fill knowledge gap about epidemiology, risk factors, protection of BSE and other BSE topics through peer education. Although short-term feedback was obtained, it was noted that students' BSE knowledge increased and they enhanced their BSE skills considerably. Besides, the study results demonstrated effects of peer education upon self-esteem, which were not studied before. In light of these results, it may be recommended that peer education models should be used in larger samples in order to increase students' knowledge and awareness levels, to provide more extensive information in curriculum, to extend educations and to increase their efficacy. Trainings to be given at an early age will draw attention of youngsters and raise their awareness. Meanwhile, a long-term follow up will be useful in determining sustainability of behavior change and knowledge preservation.

Limitation of the study

The study was conducted with the female students at the Erzincan University. Therefore, the results are generable only for these students. The study is limited with the points included in the questionnaire form that addressed socio-demographic characteristics, breast cancer and BSE. Although the participants were not forced to report increased performance of BSE, participants may have been inclined to give biased answers towards the expected outcomes/actions after the training.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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References

1. Al-Naggar RA, Al-Naggar DH, Bobryshev Y, Chen R, Assabri A. Practice and Barriers Toward Breast Self-Examination Among Young Malaysian Women. Asian Pac J Cancer Prev 2011; 12:1173-1178. (PMID: 21875261)
2. Karayurt Ö, Coşkun A, Cerit K. Nurses' beliefs about breast cancer and breast self examination and their breast self examination performance. Eur J Breast Health 2008; 4:15-20.
3. Nde FP, Assob JC, Kwenti TE, Njunda AL, Tainenbe TR. Knowledge, attitude and practice of breast self-examination among female undergraduate students in the University of Buea. BMC Res Notes 2015; 8:43. (PMID: 25889644) [CrossRef]
4. Şencan I, Keskinkılıç B. The Turkish Ministry of Health, Public Health Agency of Turkey, Cancer Statistics Turkey. (Accessed November 20 2016) http://www.kanser.gov.tr.
5. Şen S, Başar F. Breast cancer and breast self examination knowledge of women who live in kütahya region Eur J Breast Health 2012; 8:185-190.
6. Duran O. Effect of Planned Education Provided on Breast Self-Exam on the Health Beliefs and Perceived Health Statuses of Women. C.U. Health Sciences Institute, PhD Thesis. 2008. https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp
7. Akyolcu N, Uğraş G. Kendi Kendine Meme Muayenesi: Erken Tanıda Ne Kadar Önemli? Meme Sağlığı Dergisi 2011; 7:10-14.
8. Karayurt Ö, Dramalı A. Adaptation of Champion's Health Belief Model Scale for Turkish women and evaluation of the selected variables associated with breast self-examination. Cancer Nurs 2007; 30: 69-77. (PMID: 17235224). [CrossRef]
9. Güner İ, Tetik A, Görener A. Identification of the Knowledge, Attitudes and Behaviours of Women Regarding Breast Self-Exam (BSE). Gaziantep Journal of Medicine 2007; 55-60.
10. Tahmasebi R, Noroozi A. Is Health Locus of Control a Modifying Factor in the Health Belief Model for Prediction of Breast Self-Examination? Asian Pac J Cancer Prev 2016; 17:2229-2233. (PMID: 27221923). [CrossRef]
11. The relation between self-esteem and social anxiety levels of adolescents and the effects of personal variables. International Periodical for the Languages, Literature and History of Turkish or Turkic 2013; 8:179-193. http://www.turkishstudies.net/Makaleler/121209375_13ErisYaseminsos-179-193.pdf
12. Aladağ M, Tezer E. What is the Peer Helping and What is Not? Turkish Psychological Counseling and Guidance Journal 2007; 3:139-155. dergipark.ulakbim.gov.tr/tpdrd/article/view/1058000028
13. Aladağ M, Tezer E. Need Assessment Study For A Peer Helping Program For University Students. Ege Journal of Education 2007; 2:19-36.
14. Richmond C, Ross N. Social support, material circumstance and health behaviour: influences on health in First Nation and Inuit communities of Canada. Soc Sci Med 2008; 67:1423-1433. (PMID: 18676079). [CrossRef]
15. Çuhadaroğlu F. Adolesanlarda Benlik Saygısı. H.Ü. Tıp Fakültesi, Uzmanlık Tezi. 1986.
16. Gür K, Kadıoğlu H, Sezer A. Breast Cancer Risks and Effectiveness of BSE Training among Women Living in a District of İstanbul. Eur J Breast Health 2014; 10:154-160. [CrossRef]
17. Erkin Ö, Ardahan M. Meme Kanseri ve Kendi Kendine Meme Muayenesinin Pullardaki Tarihi. Lokman Hekim Journal, 2014; 4:22-28.
18. Gürsoy A, Yiğitbaş Ç, Yılmaz F, Erdöl H, Bulut H, Mumcu H, Yeşilçiçek K, Kahriman İ, Hindistan S, Nural N. The Effect of Peer Education on University Students' Knowledge of Breast Self-Examination and Health Beliefs. Eur J Breast Health 2009; 5: 135-140. [CrossRef]
19. Segni MT, Tadesse DM, Amdemichael R, Demissie HF. Breast Self-examination: Knowledge, Attitude, and Practice among Female Health Science Students at Adama Science and Technology University, Ethiopia. Gynecol Obstet (Sunnyvale) 2016; 6:4.
20. Özkahraman Ş, Vural BK, Bayık A. Development of the Skills for Breast Self-Exam in Public Education Center Course Participants. Atatürk University Journal of Nursing College 2006; 9:1-9.
21. Özen B, Zincir H, Erten Z, Özkan F, Elmalı F. Knowledge and Attitudes of Women about Breast Cancer, Self Breast Examination and Healthy Life Style Behaviours. Eur J Breast Health 2013; 9:200-204. [CrossRef]
22. Suleiman AK. Awareness and attitudes regarding breast cancer and breast self-examination among female Jordanian students. Journal of Basic and Clinical Pharmacy 2014; 5:74-78. (PMID: 25278670). [CrossRef]
23. Al-Sharbatti SS, Shaikh RB, Mathew E, Al-Biate MA. Breast Self Examination Practice and Breast Cancer Risk Perception among Female University Students in Ajman. Asian Pac J Cancer Prev 2013; 14:4919-4923. (PMID: 24083768). [CrossRef]

24. Koç Z, Sağlam Z. Determination of the knowledge and the practice of female patients about breast cancer, preventive measures and breast self-examination and effectiveness of education. Eur J Breast Health 2009; 5:25-33.
25. Al-Zalabani AH, Alharbi KD, Fallatah NI, Alqabshawi RI, Al-Zalabani AA, Alghamdi SM. Breast Cancer Knowledge and Screening Practice and Barriers Among Women in Madinah, Saudi Arabia. J Cancer Educ 2016 Jun 7 doi:10.1007/s13187-016-1057-7. [Epub ahead of print]. (PMID: 27271153). [CrossRef]
26. Ertem G, Koçer A. Breast self-examination among nurses and midwives in Odemis health district in Turkey. Indian J Cancer 2009; 46:208-213. (PMID: 19574672). [CrossRef]
27. Ogunbode AM, Fatiregun AA, Ogunbode OO. Breast self-examination practices in Nigerian women attending a tertiary outpatient clinic. Indian J Cancer 2015 Oct-Dec; 52:520-524. doi: 10.4103/0019-509X.178376. (PMID: 26960463). [CrossRef]
28. Vicdan A, Koçyiğit C, Kabak N. Identification of the Levels of Knowledge of University Students about Breast Cancer and Breast Self-Exam. Maltepe University, Journal of Nursing Science and Art, Symposium Special Issue 2010.
29. Beydağ KD, Karaoğlan H. Influence of Breast Self-Exam Education on the Knowledge and Attitudes of Students. Turkish Armed Forces Preventive Medicine Newsletter 2007; 6:106-111.
30. Karayurt Ö, Özmen D, Çetinkaya AC. Awareness of breast cancer risk factors and practice of breast self examination among high school students in Turkey. BMC Public Health 2008; 8:359. (PMID: 18928520). [CrossRef]
31. Marzo RR, Salam A. Teachers' Knowledge, Beliefs and Practices of Breast Self-Examination in a City of Philippine: A Most Cost-Effective Tool for Early Detection of Breast Cancer. Journal of Applied Pharmaceutical Science 2016; 6:016-021. http://imsear.li.mahidol.ac.th/handle/123456789/176906
32. Gençtürk N, Demirezen E, Ay F. Health Beliefs of Midwifery Students at Istanbul University about Breast Cancer and Breast Self-Examination Acknowledgements. J Canc Educ 2016 DOI: 10.1007/s13187-016-1014-5. [CrossRef]
33. Öztürk M, Engin VS, Kişioğlu AN, Yılmazer G. Effects of Education on Knowledge and Attitude of Breast Self Examination Among 25+ Years Old Women. Eastern Journal of Medicine 2000; 5(1):13-17. http://www.eastjmed.org/jvi.aspx?pdir=ejm&plng=eng&un=EJM-29650
34. Seif N, Aziz M. Effect of Breast Self Examination Training Program onçKnowledge, Attitude and Practice of a Group of Working Women. Journal of the Egyptian Nat. Cancer Inst 2000; 12:105-115.http://www.nci.cu.edu.eg/Journal/00_06_05.pdf
35. Tuna A, Bektash M, Turgay A, Tuna A, Genç R. Effects of Peer Education, Social Support and Self Esteem on Breast Self Examination Performance and Knowledge Level. Asian Pac J Cancer Prev 2009; 10:605-608. (PMID: 19827878).
36. Özcan H, Subaşı B, Budak B, Çelik M, Gürel Ş, Yıldız M. Relationship between self-esteem, social appearence anxiety, depression and anxiety in adolescent and young adult women. Journal of Mood Disorders 2013; 3:107-113. [CrossRef]
37. Gölbaşı Z, Kutlar Z, Akdeniz H. The effect of education given by nursing students on womens' knowledge and practice of breast cancer / breast self examination in a public training center. Eur J Breast Health 2007; 3:53-57.

Original Article

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The Relationship Between Breast Cancer and Risk Factors: A Single-Center Study

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ABSTRACT

Objective: To determine the relationship between breast cancer and known risk factors in patients who had mammography (MG) for breast cancer screening or ultrasonography and/or MG for diagnostic purposes.

Materials and Methods: In the period of January-December, 2011, a questionnaire composed of 17 questions was applied to 2862 female patients and MG and/or US examination was performed afterwards. Chi-square and Kruskal-Wallis tests were used for statistical analysis.

Results: The mean age was 51.05±8.98, age at menarche was 13.0±1.6 and age at menopause was 47±5.2. The first pregnancy was at 20±4.6. Out of 2862 cases, 242 had breast cancer diagnosis and 32 were newly diagnosed. There was no correlation between menarche age, age at menopause or first pregnancy and breast cancer. There was no relationship between breast cancer risk and hormone replacement therapy or oral contraceptive use. In patients with the diagnosis of breast cancer (242 cases), 61 had (25%) a positive family history. There was a significant correlation between the presence of a positive family history and having breast cancer (p=0.003).

Conclusion: The presence of breast cancer in the family has the strongest relationship among all risk factors. It is important to have regular follow-up of these patients and to raise the awareness of patients.

Keywords: Breast cancer, screening, risk factors

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Introduction

Breast cancer is the most frequently observed type of cancer among women (40.6/100,000) in Turkey (1). According to the national cancer statistics, it has had an increasingly rising incidence in the past decade (1). Today, mammography (MG) is the most effective screening method for the early diagnosis of breast cancer (2, 3).

Hereditary and non-hereditary factors are effective in the etiology of breast cancer. It is accepted that the majority of hereditary breast cancer cases are related to the BRCA1 and BRCA2 mutation (4). Among the non-hereditary factors, the most important factor that contributes to breast cancer is the female sex and age. Age-specific breast cancer incidence increases rapidly starting at the age of 40 (5, 6). The other risk factors include menarche, age at menopause, age at first birth, number of births, breastfeeding, smoking, radiation exposure, oral contraceptive and postmenopausal hormone use, fatty diet and obesity (4, 7, 8).

In our study, the risk factors in cases presenting to the breast screening unit were inquired by means of a survey. The aim of our study is to identify the relationship between cases diagnosed with breast cancer and risk factors.

Materials and Methods

In this retrospective study, 2878 cases that presented to the breast imaging unit for the purposes of breast cancer screening and diagnosis between January, 2011 and December, 2011. The patient information form of 17 questions referring to the risk factors for breast cancer

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Table 1. Breast screening - patient information form

Date:

Name Surname:

Age:

Citizenship ID No:

Educational background: O Primary school O Secondary school O High school O University

Employment status: O Employed O Housewife

Age at menarche: Date of the last menstrual period:

Age at first pregnancy: Age at menopause:

Number of live births: The longest breastfeeding duration:

Have you ever used contraceptive pills? (Trademark and duration):

Did you take hormones during the menopause period? (Trademark and duration):

If you have any disorders or a diagnosed disease, please specify:

If there is a medicine that you regularly, please specify its name and duration of use:

Please specify if you have diagnosed cancer involving an organ:

What is Your Reason to Present for Mammography?

O I have no complaints; I am here only for control purposes (for screening).

O I have a breast-related complaint (you can mark multiple options):

Palpable mass-gland: O Right O Left

Pain in breast: O Right O Left

Discharge from the nipple: O Right O Left

Nipple shrinkage: O Right O Left

Skin thickening-shrinkage: O Right O Left

Mass in the armpit: O Right O Left

Other:.....

Have you ever had mammography scans?: O Yes O No

Have you ever undergone breast ultrasonography?: O Yes O No

Have you ever had breast surgery or breast biopsy?: O Yes O No

X-ray therapy: O Yes O No

Chemotherapy: O Yes O No

Has Breast Cancer Been Detected in Any of Your Close Relatives?

O No

O Yes (please mark the relationship degree)

O Mother O Maternal Aunt O Sister O Father O Paternal Aunt O Grandmother

O Other:.....

RESULT: BI-RADS- (0) (1) (2) (3) (4) (5) (6)

was applied before the study upon consent by patients (Table 1). 16 cases were excluded from the study due to omissions in the survey form and the study was completed with 2862 cases.

All the cases that presented to the imaging unit for diagnosis and screening purposes were included in our study. The screening was opportunitic in type and included female cases that presented at their own will or were referred by the clinician. As for the diagnostic group, it was composed of patients who had breast-related symptoms or follow-up patients diagnosed with breast cancer. All the cases were included in the study towards the aim of creating a more homogeneous group.

The patient information form included the socio-demographic and personal information (age, educational level, civil state, number of children had, family and personal history of breast cancer, breastfeeding, menarche, menopause, etc.). The information requested the form was filled in by 2 members of staff at the department before the study in a 'question and answer' format. The cases that were not willing to answer the questions were excluded from the study. The patient information form was completed by the participants in approximately 5-10 minutes. The cases received mammography and/or ultrasonography imaging studies after the survey. The examination results were categorized according to the BI-RADS classification. The cases with known breast cancer and newly diagnosed cases were compared with cases not identified to have cancer in terms of risk factors.

For statistical analysis, the Chi-square and Kruskal-Wallis tests were used. The statistical significance was considered to be as p≤0.05. The study was approved by the Ethics Committee of the Ankara Numune Hospital. The study meets the standards of the Helsinki Declaration. All the participants were informed using an informed consent form.

Results

The average age of our cases was 51.05±8.98, average at menarche 13.0±1.6, average age at menopause 47±5.2 and average age at pregnancy 20±4.6 years (Table 2).

It was determined that 68.2% of the cases (n=1952) that presented to our clinic for diagnostic and screening previously received MG studies and 30.6% of the cases (n=861) were about to have their first MG study. The most frequent symptoms at diagnosis were mastalgia with %23.3 (n=655) and palpable mass with %16.5 (n= 464).

83.9% of the cases (n=2360) had previous breast-related biopsy procedure and 11% (n=311) had breast-related surgery.

Out of the 2862 cases, 242 were patients diagnosed with breast cancer. 210 of them were cases in the follow-up period for breast cancer and 32 patients were newly diagnosed bresat cancer cases. In the group that did not have breast cancer, the average age at menarche was found to be 13.0±1.6, average age at menopause 47±5.1 and the age at first pregnancy 20±4.5 (Table 2). Among the cases diagnosed with breast cancer, the average age at menarche was found to be 14±1.5, average at menopause 48.5±5.4 and average age at first pregnancy 21±4.8. As a result of the statistical analysis, no relationship was identified among the age at menarche, age at menopause, age at first pregnancy and breast cancer (p=0.67, p=0.61, p=0.70).

When the intervals between the age at menarche and age at menopause was examined, this period was measured at 32.9±5.9 years for the breast cancer cases and at 32.7±5.3 years for the non-patient group. No statistically significant relationship was identified (p=0.99).

Table 2. Distribution of patients with and without breast cancer according to demographic and reproductive factors

Variables	Breast cancer cases (%)	Non-breast cancer cases (%)	All patients
Age	51.1±6.7	49.5±7.8	51.05±8.98
Age at menarche	14±1.5	13.0 ±1.6	13.0±1.6
Age at menopause	48.5±5.4	47±5.1	47±5.2
Age at first pregnancy	21±4.8	20±4.5	20±4.6
Breastfeeding			
Yes	211	2356	2567
No	31	264	295
OCS use	50	503	553
HRT use	15	177	192

HRT: hormone replacement therapy; OCS: oral contraceptive

When examination was made regarding breastfeeding, it was identified that 295 (11.4%) cases never breastfed and 31 (1.1%) of those were cases diganosed with breast cancer. The breastfeeding periods of women that breastfed were assessed and it was determined that 45% breastfest for more than 12 years, 22.7% for 6-12 months and 20% for 0-6 months. Regarding the distribution of breastfeeding women diagnosed with breast cancer, it was found that 47.1% breastfed for more than 12 months, 24.7% for 6-12 months and 15.2% for 0-6 months. As a result of the statistical analysis, no relationship was identified between the presence and duration of breastfeeding and breast cancer. (p=0.39, p=0.6)

With respect to the use of oral contraceptives and hormone replacement therapies, it was seen that 553 (20.2%) of all the cases used OCS and 192 (7%) used hormone replacement therapy (HRT) in one period of their lives. The number of people diagnosed with breast cancer who took OCS was 50 (9%) and those who used HRT was 15 (7.8%). As a result of the statistical analysis, the use of OCS and HRT was not identified to be associated with breast cancer (p=0.39, p=0.6, respectively).

When the presence of breast cancer in family was assessed, it was seen that 575 (20%) of the cases had history of breast cancer in their family. Out of 242 cases diagnosed with breast cancer, 61 (25%) had family history. Family history was present most frequently in the sister (n=17) and the mother (n=12). A statistically signifcant relationship was identified between the presence of breast cancer in family and having breast cancer (p=0.003).

When the presence of endometrium, ovary and gastrointestinal system cancer genetically associated with breast cancer was assessed, it was identified that 2054 patients did not have the types of cancer specified in the family, 220 cases had tumors of gastrointestinal origin, 7 cases ovarian cancer and 43 cases endometrium cancer. In the cases diagnosed with breast cancer, n=25 cancers of GIS origin and n=3 cases associated with endometrium cancer were identified. A statistically significant relationship between the presence of non-breast cancer in family and breast cancer was identified (p=0.07).

Discussion

Family history of breast cancer is a very important factor. Approximately 3-10% of breast cancer cases are hereditary cancers. It is stated

that approximately 85% of them are associated with BRCA1 and BRCA2 mutations (9). In breast cancer, the relationship degree of the family member that has history of breast cancer and the start date of the disease are important (10, 11). A women who lives until the age of eighthy has a cancer incidence of 7.8% if she has no 1. degree relatives with breast cancer while the risk goes up to 13.3% if one 1. degree relative has breast cancer and to 21.1% if two 2. degree relatives have cancer (12). Similarly, our study also found a significant relationship between the presence of family history and breast cancer. In 20% of all the cases and in 25% of those with breast cancer had positive family history. Those who had family history of breast cancer, it was present most frequently in their sister (n=17) and mother (n=12).

An early age of first menarche and a late age of menopause increase the risk of developing breast and endometrium cancer. It is estimated that every year of delay after the age of 12 reduces the premanopausal breast cancer risk by 7% and postmenopausal cancer by 3% (13, 14). Women with a menopause age of 55 have 2 times higher risk for developing breast cancer as compared to those with a menopause age of 45 (15, 16). In our study, the average age at menarche of cases diagnosed with breast cancer was found to be 14±1.5, the average at menopause 48.5±5.4, the age at menarche of the non-breast cancer group 13.0±1.6 and the average age at menopause 47±5.1. There were no statistically significant differences between the two groups.

The relationship between breastfeeding and breast cancer is controversial. An analysis conducted on this subject spanning 30 countries, 47 epidemiological studies, 50302 breast cancer and 96973 non-breast cancer patients demonstrated that breastfeeding for 12 months decreased the risk for breast cancer by 4.3% (8). A study with meta-analysis and case control encompassing four cohort studies reported that every act of breastfeeding for 5 months reduced cancer risk by 2% (17). On the other hand, Stuebe et al. identified breast cancer in 608 out of 60.705 cases that they followed during the period of 1997-2005. They did not identify any significant relationship between premenopausal breast cancer and breastfeeding then they assessed the duration and intensity of breastfeeding (18). Similarly, in our study, no relationships were identified in terms of the presence and duration of breastfeeding when cancer cases were compared with the non-patient group.

The relationship between oral contraceptives and breast cancer is controversial. In the year 1996, a study that reviewed 53297 breast cancer patients and 100239 non-breast cancer patients reported that 40% of the patients took OCS at one period of their lives and the use of OCS resulted only in a small increase of risk (relative risk=1.24) for breast cancer (19). They demonstrated that there was no significant difference in the development of breast cancer during 10 years after the discontinuation of oral contraceptive use. Ban and Godellas conducted a recent study where they reported that women taking oral contraceptives had 24% higher risk of developing cancer compared to those who never took them in their lives and that this risk especially materialized during the use of oral contraceptives (11). Westhoff CL did not identify any relationship between oral contraceptives and breast cancer risk in a way similar to our study (12). Changes in the formulation of oral contraceptives overtime, the duration of their use and different oral contraceptive formulation may result in a differentiation of breast cancer risk. In our study, only 9% of cases with breast cancer (n=50) were using OCS. No relationship was identified between the use of OCS and breast cancer. We suggest that the difference may not have been significant since the use of OCS was low.

It is thought that hormone replacement therapy increases the levels of sex hormone in circulation and breast cancer risk (20, 21). However, the relationship between HRT and breast cancer development is complex and heterogeneous. HRT combination and types, age at menopause, age of starting HRT and other breast cancer risk factors are associated with the cancer risk. People of black race, obese women and those with breast tissue of mostly fatty content may benefit from HRT with only minimal breast cancer risk increase. According to the guidelines, the use of HRT for less than 5 years does not change the risk (20). In the study conducted by Bae et al., it was stated that the use of HRT did not change the cancer risk (21). In our study, no relationship was identified between HRT and breast cancer risk (p=0.6). We attribute this to the fact that HRT use rates in our series were low (7% in the entire series).

It is accepted that a great majority of reproductive cancers associated with breast, especially ovarian cancer, are related to genetic mutations. Breast cancer associated with these cancers is seen at a younger age (22). Claus et al. (22) conducted a case-controlled study on 4730 women with breast cancer aged 20-54 and stated that cases with family history of ovarian cancer developed breast cancer at an earlier age than the expected age. In our study, a statistically significant relationship between the presence of non-breast cancer in family and breast cancer was identified (p=0.07). We believe that the reason why this difference, which is very close to statistical significance, arose out of the fact that the number of cases in our series was not adequate. On the other hand, all the cancer types in the family were inquired jointly and no sub-group analyses were carried out. We believe that this association can be demonstrated through more detailed studies.

The fundamental limitation of our study is that the cases included in the study were not cases that participated in the general community screening, but were cases that presented to our hospital for opportunistic screening or diagnostic purpose mostly upon clinician's referral. There may be statistical differences between general community screening cases and cases that present to the hospital. The other limitation is the limited number of cases included in the study. Studies with larger series are needed to be able to more clearly identify the risk factors pertaining to the community in Turkey.

Conclusion

In our study, the presence of breast cancer in family was found to be the most important risk factor among the risk factors for breast cancer. Performing regular follow-ups on this group and raising the awareness of patients gain importance in early diagnosis and therapeutic efficacy for breast cancer.

Ethics Committee Approval: Ethics committee approval was received for this study from Ankara Numune Hospital.

Informed Consent: Informed consent was obtained from patients who participated in this study.

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References

1. The Ministry of Health of Turkey, Turkish National Public Health Agency, Head of Cancer Department. Turkey Cancer Statistics. 2015 [updated 2015; cited 2015 10 Sep]; Available from: URL: http://kanser.gov.tr/Dosya/kayitcilik/2011Caistatistikleri.pdf.
2. Luke C, Priest K, Roder D. Changes in incidence of in situ and invasive breast cancer by histology type following mammography screening. Asian Pac J Cancer Prev 2006; 7:69-74. (PMID: 16629519)
3. World Health Organization. WHO position paper on mammography screening. 2014. Available from: URL: http://apps.who.int/iris/bitstream/10665/137339/1/9789241507936_eng.pdf?ua=1
4. Park MJ, Park EC, Choi KS, Jun JK, Lee HY. Sociodemographic gradients in breast and cervical cancer screening in Korea: the Korean National Cancer Screening Survey (KNCSS) 2005-2009. BMC Cancer 2011; 11: 257. (PMID: 21682886) [CrossRef]
5. Berg WA. Tailored supplemental screening for breast cancer: what now and what next? AJR Am J Roentgenol 2009; 192: 390-399. (PMID: 19155400) [CrossRef]
6. Berg WA. Beyond standard mammographic screening: mammography at age extremes, ultrasound, and MR imaging. Radiol Clin North Am 2007; 45: 895-906. (PMID: 17888776) [CrossRef]
7. Steiner E, Klubert D, Knutson D. Assessing breast cancer risk in women. Am Fam Physician 2008; 78: 1361-1366. (PMID: 19119554)
8. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002; 360: 187-195. [CrossRef]
9. Pharoah PD, Day NE, Duffy S, Easton DF, Ponder BA. Family history and the risk of breast cancer: a systematic review and meta-analysis. Int J Cancer 1997; 71: 800-809. (PMID: 9180149) [CrossRef]
10. Berg WA. Tailored supplemental screening for breast cancer: what now and what next? AJR Am J Roentgenol 2009; 192: 390-399. (PMID: 19155400) [CrossRef]
11. Ban KA, Godellas CV. Epidemiology of breast cancer. Surg Oncol Clin N Am 2014; 23: 409-422. (PMID: 24882341) [CrossRef]
12. Westhoff CL. Breast cancer risk: perception versus reality. Contraception 1999; 59: 25S-28S. (PMID: 10342093) [CrossRef]
13. Clavel-Chapelon F. E3N-EPIC Group. Differential effects of reproductive factors on the risk of pre- and postmenopausal breast cancer. Results from a large cohort of French women. Br J Cancer 2002; 86: 723-727. (PMID: 11875733) [CrossRef]
14. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, Morris E, Pisano E, Schnall M, Sener S, Smith RA, Warner E, Yaffe M, Andrews KS, Russell CA; American Cancer Society Breast Cancer Advisory Group. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin 2007; 57: 75-89. (PMID: 17392385) [CrossRef]
15. Slattery ML, Kerber RA. A comprehensive evaluation of family history and breast cancer risk. The Utah Population Database. JAMA 1993; 270: 1563-1568. (PMID: 8371466) [CrossRef]
16. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993; 15: 36-47. (PMID: 8405211) [CrossRef]
17. Parkin DM. 15. Cancers attributable to reproductive factors in the UK in 2010. Br J Cancer 2011; 105: S73-76. (PMID: 22158326) [CrossRef]
18. Stuebe AM, Willett WC, Xue F, Michels KB. Lactation and incidence of premenopausal breast cancer: a longitudinal study. Arch Intern Med 2009; 169: 1364-1371. (PMID: 19667298) [CrossRef]
19. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Lancet 1996; 347: 1713-1727. (PMID: 8656904) [CrossRef]
20. Santen RJ, Allred DC, Ardoin SP, Archer DF, Boyd N, Braunstein GD, Burger HG, Colditz GA, Davis SR, Gambacciani M, Gower BA, Henderson VW, Jarjour WN, Karas RH, Kleerekoper M, Lobo RA, Manson JE, Marsden J, Martin KA, Martin L, Pinkerton JV, Rubinow DR, Teede H, Thiboutot DM, Utian WH; Endocrine Society. Postmenopausal hormone therapy: an Endocrine Society scientific statement. J Clin Endocrinol Metab 2010; 95: s1-s66. (PMID: 20566620) [CrossRef]
21. Bae JM, Kim EH. Hormone Replacement Therapy and Risk of Breast Cancer in Korean Women: A Quantitative Systematic Review. J Prev Med Public Health 2015 48: 225-230. (PMID: 26429288) [CrossRef]
22. Claus EB, Schildkraut JM, Thompson WD, Risch NJ. The genetic attributable risk of breast and ovarian cancer. Cancer 1996; 77: 2318-2324. (PMID: 8635102)[CrossRef]

Original Article

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Evaluation on the Practice and Behaviour of Women Applied for Gynecology Outpatient Clinics About Screening Methods for Early Diagnosis of Breast Cancer

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ABSTRACT

Objective: Breast self-examination (BSE), clinical breast exam (CBE), mammography and ultrasound imaging (UI) are screening methods used for early diagnosis of breast cancer (BC). The purpose of this study is to put forth the utilization frequency of these screening methods among women presenting to the gynecology outpatient clinics and the relation of these data with the socio-demographic characteristics of the women.

Materials and Methods: A survey was conducted among 429 women (age, 16-80 years) who were admitted to the gynecology outpatient clinics. The survey inquired about the rate and frequency of the performance of BSE, CBE, mammography and UI; personal and family history of breast cancer and social-demographic characteristics of the women.

Results: The mean age was 40.08 (SD: 3.67). More than half of the women above 40 years of age (59.7 %) had never undergone mammography. 99.8 % of the women who had undergone mammography had also received ultrasound imaging. A significant relationship was identified between the BSE performance and having mammography. 57.4% of the women above 40 years of age (117) had UI, 53.9% (110) had CBE and 57.3% (117) performed BSE. There was a significant relationship between the age, education status and regular BSE; positive family history of BC and having CBE and mammography.

Conclusion: The results reveal that the rate of BSE performance, having mammography and CBE are at less-than-ideal levels. In this context, it is apparent that breast cancer screening methods are needed to be introduced and guidance about their application frequency should be provided for women in gynecology outpatient clinics.

Keywords: Breast cancer, mammography, breast self-exam, clinical breast exam, ultrasound imaging

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Introduction

Breast cancer accounts for more than one million cases globally per year; it is the most frequently diagnosed type of cancer among the women. Also it ranks the first among reasons for death among patients (1). It is the cancer type with the highest incidence rate among women in the United States of America and ranks the second among reasons for death (2).

In Turkey, breast cancer incidence is 45.9/100000. One out of every four cancer cases diagnosed in the year 2013 is breast cancer. It is seen that 45% of patients diagnosed with breast cancer in Turkey are aged 50-69 while 40% are in the age range of 25-49 years. Regarding the breast cancer stages, only 10% of invasive cases in the database are in the distant stage (3).

The fact that it is a frequently seen type of cancer and ranks the first among reasons for death of patients demonstrates how important the breast cancer screening programs are. A practicable and effective screening program may reduce morbidity and cancer-related deaths. There are several studies reporting that screening mammography and regularly conducted breast self-examinations (BSE) decrease breast cancer-related mortality (4-7).

The aim of breast cancer screening is to capture malignancy at the early phase before any clinical signs occur; mortality reduction is thus achieved (8). However, the current protocols indicating the age when screening should start and the frequency with which it should be

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maintained and when it should be ended vary among countries and per individual risk status.

Mammography ranks the first among the imaging methods used for breast cancer screening. Breast ultrasonography (USG), breast magnetic resonance imaging (MRI), tomosynthesis and molecular imaging are often used as methods that aid in mammography. Furthermore, an important step of screening includes clinical breast exam (CBE) and breast self-exam (BSE).

The aim of this study is to identify the behaviors of women aged between 16-80 presenting to the gynecology outpatient clinic to undergo mammography, breast USG, CBE and perform BSE as part of early breast cancer diagnosis methods, to determine their frequency of implementing these methods and to demonstrate their correlations with the socio-demographic characteristics of women. Another aim of the study is to emphasize the important role of gynecologists and obstetricians in ensuring that early breast cancer diagnosis methods are known and applied by the patients.

Materials and Methods

This study, which was defined as a descriptive study, was conducted at the Istanbul Medeniyet University Göztepe Research and Training Hospital gynecology outpatient clinic between May-July, 2016. Approval was obtained from the Istanbul Medeniyet University Faculty of Medicine ethics committee to be able to conduct this study. 429 women aged between 16 and 80 presenting to the gynecology outpatient clinic and were examined, who volunteered to participate, were included in the study. The study data were obtained by receiving responses to a questionnaire with 11 questions by means of face-to-face interview conducted by the examining physician after the informed consent forms were signed by the women. The women were asked about which methods they perform among mammography, breast USG, clinical breast exam and breast self-exam and the frequency at which they perform them, presence of breast cancer in them and their family as well as demographic characteristics such as age, menopause, profession and education.

Statistical analysis

The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS) version 22 statistics software (IBM Corp.; Armonk, NY, USA). To analyze the data, the percentage distributions and Fisher (Fisher's Exact Test) t-test, Chi-square test and logistic regression model were used.

Results

In total, 429 people took part in the study. Two people in the study were 77 and two people were 79 years old. The ages of these people were higher than the other patients participating in the study. The average age of study participants was 40.08 and standard deviation was 13.67. The median age was 39 and the age range was 16-79. 332 people were not in menopause and 97 people (23%) were in the postmenopausal period. Among the patients who took responded to the questionnaire, 336 people (78%) were not working while 84 people (20%) were working. Six people (2%) were retired. 276 people among the questionnaire respondents (64%) were primary school graduates constituting the biggest group. It was learned that 11.7% of the patients had relatives with breast cancer in their family. 8% (35) reported that they had 1st degree relatives with breast cancer and 3% (13) reported that they had 2nd degree relatives with breast cancer. The socio-demographic characteristics of patients are provided in Table 1. 4 of the patients (0.9%) that took part in the study were diagnosed with breast cancer. These women were not included in the investigation for their behaviours related to early breast cancer diagnosis methods.

Table 1. Patients' socio-demographic characteristics

Socio-demographic characteristics	(n)	(%)
Age Group		
<40 years	221	51.5
40-49 years	111	25.9
50-59 years	50	11.7
60-69 years	34	7.9
>70 years	13	3.0
In menopause		
Not in menopause	332	77
Post-menopause	97	33
Occupation		
Unemployed	339	79
Employed	84	19.6
Retired	6	1.4
Educational Status		
No Education	19	4.4
Primary School	276	64.3
High School	69	16.1
University	64	14.9
Master	1	0.2
Breast Cancer Patient		
Yes	4	0.9
No	425	99.1
Breast Cancer in Family		
Yes	50	11.7
No	379	88.3
Total	429	100

The distribution of women according to their performance of undergoing mammography, breast ultrasonography, CBE and BSE is provided in Table 2 as per their age group.

Based on the latest gynecological examination date, it was learned that 57.3% of women (240) above the age of 40 had mammography scan at least once in their life while 42.7% of them (87) never underwent mammography. The data according to the last date of mammography scan are given in Table 3. It was seen that 99.8% of women undergoing mammography had received breast USG. Furthermore, it was identified that 93.5% of patients undergoing mammography received CBE. A statistically significant relationship was found between the status of undergoing mammography and BSE (p=0.000). According to the

Table 2. Distribution of mammography, breast USG, CBE and BSE according to the age groups

	Mammography		Breast USG		CBE		BSE	
Age Group	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n (%)
<40 years	44 (19.9)	177 (80.1)	42 (19.0)	179 (81.0)	42 (19.0)	179 (81.0)	93 (42.1)	128 (57.9)
40-49 years	55 (50.5)	55 (50.5)	55 (50.5)	55 (50.5)	53 (48.6)	56 (51.4)	59 (54.1)	50 (45.9)
50-59 years	37 (75.5)	12 (24.5)	37 (75.5)	12 (24.5)	35 (71.4)	14 (28.6)	31 (63.3)	18 (36.7)
60-69 years	21 (61.8)	13 (38.2)	21 (61.8)	13 (38.2)	18 (52.9)	16 (47.1)	21 (61.8)	13 (38.2)
>70 years	4 (33.3)	8 (66.7)	4 (33.3)	8 (66.7)	4 (33.3)	8 (66.7)	6 (50.0)	6 (50.0)
Total	161 (37.9)	264 (62.1)	159 (37.4)	266 (62.6)	152 (35.8)	273 (64.2)	210 (49.4)	215 (50.6)

USG: ultrasonography; CBE: clinical breast exam; BSE: breast self-exam

Table 3. Last date of undergoing mammography according to the women's age groups

Mammography Date	<40 years	40-49 years	50-59 years	60-69 years	>70 years	Total
No	177	54	12	13	8	264
2016	6	7	5	2	1	21
2015	14	24	9	10	0	57
2014	10	11	12	1	0	34
2013	5	6	3	2	0	16
2012	0	2	1	0	0	3
2011	2	0	0	1	1	4
5-10 years	7	4	6	4	2	23
11-15 years	0	0	1	0	0	1
16-20 years	0	1	0	1	0	2
Total	221	109	49	34	12	425

Table 4. Last date of undergoing breast ultrasound according to the women's age groups

Ultrasound Scan Date	<40 years	40-49 years	50-59 years	60-69 years	>70 years	Total
No	179	54	12	13	8	266
2016	4	7	5	2	0	18
2015	14	24	9	10	1	58
2014	10	11	12	1	0	34
2013	5	6	3	2	0	16
2012	0	2	1	0	0	3
2011	2	0	0	1	1	4
5-10 years	7	4	6	4	2	23
11-15 years	0	0	1	0	0	1
16-20 years	0	1	0	1	0	2
Total	221	109	49	34	12	425

Table 5. Last dates of undergoing clinical breast examination (CBE) according to the women's age groups

CBE Date	<40 years	40-49 years	50-59 years	60-69 years	>70 years	Total
No	179	56	14	16	8	273
2016	6	7	4	0	0	17
2015	15	25	9	7	1	57
2014	7	9	11	2	0	29
2013	4	5	3	2	0	14
2012	1	1	1	0	0	3
2011	0	0	0	2	1	3
5-10 years	9	5	6	4	2	26
11-15 years	0	0	1	0	0	1
16-20 years	0	1	0	1	0	2
Total	221	109	49	34	12	425

CBE: clinical breast exam

logistic regression analysis performed, it was identified that one unit of increase in the women's age increased their chance of undergoing mammography by 5.6% (p value<0.01).

Based on the date of the latest gynecological examination, it was found that 57.4% of women above the age of 40 (117) received mammography at least once in their lives while 42.6% (87) never received breast USG. The data according to the date of the latest breast ultrasound are specified in Table 4.

Based on the date of the latest gynecological examination, 53.9% of women above the age of 40 (110) underwent CBE at least once while 46.1% (94) never received CBE. The data according to the last date when a clinical breast examination was performed are specified in Table 5. It was determined that one unit of increase in the women's age increased the chance of undergoing clinical examination by 5.5% with all the other variables being unchanged (p<0.01).

Based on the date of the latest gynecological examination, it was identified that 49% of all women (210) and 57.3% of women above the

Table 6. Women's status of performing breast self-exam (BSE) according to their age groups

BSE Frequency	<40 years	40-49 years	50-59 years	60-69 years	>70 years	Total
None	128	50	18	13	6	215
Every Day	3	2	0	0	0	5
Twice a week	7	7	6	4	0	24
Once a week	18	12	6	10	1	47
Once a month	42	22	12	5	5	86
Once every 1-3 months	2	2	0	0	0	4
Once every 3-6 months	10	11	3	1	0	25
Once a year	11	3	4	1	0	19
Total	221	109	49	34	12	425

BSE: clinical breast exam

Table 7. Multivariate analysis results explaining the relationship between breast cancer early diagnosis methods and socio-demographic characteristics

Breast Cancer Early Diagnosis Methods and Characteristics	p	OR	95% CI
Mammography			
Age	0.000*	1.056	1.029-1.085
Education	0.963	1.007	0.759-1.336
Family History of Breast Cancer	0.037*	1.965	1.041-3.707
CBE			
Age	0.000*	1.055	1.027-1.084
Education	0.678	0.941	0.707-1.253
Family History of Breast Cancer	0.012*	2.261	1.200-4.261
BSE			
Age	0.003*	1.038	1.013-1.064
Education	0.003*	1.498	1.148-1.955
Family History of Breast Cancer	0.314	1.382	0.736-2.595

OR: odds ratio; CI: confidence interval; CBE: clinical breast exam; BSE: breast self-exam; *: significant at the level of 0.05

age of 40 performed BSE. 11.2% of those performing BSE remarked that they were performing examinations regularly on a weekly basis. The largest group among patients performing BSE (20%) was those who stated that they did it once a month. The data according to the last date when a BSE was performed are specified in Table 6. It was found that one unit of increase in the women's age increased their possibility of performing BSE by 3.8% (p value=0.03). Furthermore, a significant relationship was also identified between their educational background and BSE (p value=0.003). It was found that having family history of breast cancer increased the possibility to undergo mammography by 9.65% (p value=0.037). No significant relationships were identified between the educational background of women and their status of undergoing mammography (p=0.96). It was found that the chance of a women with no family members with breast cancer to undergo a clinical examination was 2.26 times higher than that of a person who does not have a family member with breast cancer (p=0.037). The data are provided in Table 7.

Discussion and Conclusion

Similarly to the European countries and the USA, breast cancer is the most frequently diagnosed type of cancer in Turkey (2, 3, 9). It is well known that breast cancer-related deaths can be reduced if the disease is diagnosed early and an effective treatment is administered (4, 10). The effectiveness of a screening program provides information on the level of development of countries. While breast cancer is diagnosed at an early stage in developed countries (Stages 0 and 1), it is made at later stages in developing countries (11). For that reason, it is extremely critical to conduct a cost-effective and sufficient screening program and raise the awareness of healthcare professionals.

Mammography for screening purposes is performed on women with no complaints, signs and symptoms. There are differences among countries in terms of the time to start screening by mammography. American Congress of Obstetricians and Gynecologists (ACOG) recommends that screening start at the age of 40 (12). According to the breast cancer screening program national standards, it is recommended that screening mammography be performed in women aged between 40-69 once every 2 years (13).

Based on the latest gynecological examination date, it was learned that 57.3% of women above the age of 40 had mammography scan at least once in their lives. While the rate of undergoing mammography in the USA is 72.4%, this rate is 34.2% in Japan (14-16). In Turkey, a study conducted on women attending the educative meeting found that the ratio of women above the age of 40 undergoing at least once in their lives was 40.6%, another community-based study found that the ratio of undergoing mammography within the last two years was 41.6% (17, 18). In our study, the rate of undergoing mammography was found low as compared to developed countries and high as compared to the average rate in Turkey. Considering that all women aged between 40-69 need to be included in a screening program, the number of women undergoing mammography is still insufficient according to the data in our study. The gynecologists and obstetricians informing and guiding women who present for a gynecological examination with regards mammography would greatly increase the number of women included in the scope of screening programs.

93.5% of women undergoing mammography had CBE. In a study from Turkey, this ratio was 6.2% (19). It is seen that the majority of patients undergoing mammography present to the clinic and are thus included in the screening program.

A significant relationship was found between the presence of breast cancer in the family and the rate of undergoing mammography. However, it was determined that no statistically significant difference existed between educational background and undergoing mammography. Two separate studies conducted in the urban and rural areas in Turkey identified that the rate of undergoing mammography was not significantly influenced by the educational background in a way similar to our study (20, 21). In another study, it was stated that women with a higher educational level underwent mammography more often (18).

Breast USG is not one of the primary diagnostic methods for breast cancer screening. It is preferred for the diagnostic assessment of masses palpated during examination or identified during mammography. There is very limited scientific evidence supporting the primary use of ultrasound for breast cancer screening in any age group (22). In our study, it was found that 99.8% of women undergoing mammography received breast ultrasound. It has been understood that almost all of the women undergoing mammography had received ultrasound.

Clinical breast exam is not a screening modality per se; it is administered in conjunction with mammography. ACOG recommends that clinical breast examination be performed once every 1-3 years for women aged between 20-39 and every year after the age of 39 (12). According to the national screening standards, women above the age of 20 are recommended to undergo clinical breast examination once every two years and women above 40 once a year (23). In our study, it was found that 53.9% of women above the age of 40 underwent CBE at least once while 46.1% (94) never received CBE in their lives based on the date of the latest gynecological examination. In Sinop, a study conducted with patients presenting to a secondary care hospital found that the ratio of women undergoing CBE was 24% (24). A study conducted with female members of faculty reported that 20.9% of the participants received CBE (25). Another study stated that 32.9 of women received CBE (19). In Turkey, the perception about breast cancer screening in general is concentrated on mammography, which starts as of the 40s. It was determined in our study that 81% of women (179) below the age of 40 never had CBE. Similarly to our study, it is seen in studies conducted elsewhere than Turkey that a significant part of women do not know the importance of CBE for themselves with respect to breast cancer screening (19, 24).

American Congress of Obstetricians and Gynecologists recommends BSE to the patients in the high risk group rather than the general population (12). BSE has certain limitations; today, it is considered as an auxiliary method for essential breast cancer screening methods (26, 27). There are several studies from the past mentioning the effectiveness of BSE and the requirement to recommend its administration (6, 28, 29). It is a economical method that is easy to implement and keeps the patients' awareness alive. It may be considered that patients performing BSE would also be willing to undergo mammography. Based on the date of the latest gynecological examination, it was identified that 49% of all women (210) and 57.3% of women above the age of 40 performed BSE. The largest group among women performing BSE (20%) was those who stated that they did it once a month. The other studies conducted in Turkey specified the rates of performing BSE regularly every month as 24%-56.6% (19, 30, 31). In two different studies conducted in Nigeria with patients and teachers presenting to a tertiary care hospital, the rates of performing BSE were 62.1% and 54.8% (32, 33). It was found in our study that the age and educational levels of women were directly proportional to their possibility to perform BSE. A study investigating the educational levels of women and their status of performing BSE found a positive relationship between a high educational level and performing BSE (34). In that case, raising the educational level of women increases their awareness, thereby facilitating their adoption of methods for protecting against breast cancer.

The fact that breast cancer is the type of cancer with the highest rate of incidence in the female population has an important role in the practice of gynecology. In Turkey, breast diseases are in the scope of training and practices of gynecology and obstetrics. However, it is required that patients which present to a gynecology outpatient clinic for any reason be informed about the breast cancer modality they should perform and the frequency thereof. Thereby, the malignant diseases of the breast that do not lead to any complaints, signs and symptoms can be captured at an early phase to reduce morbidity and mortality. Within this framework, gynecologists and obstetrics have important roles to play.

Our study was conducted at a tertiary care reference hospital providing healthcare services to people from every socioeconomic group. Important data about the types of breast cancer screening methods and the frequencies thereof have been provided for the literature. Furthermore, the important role of gynecologists and obstetricians in the implementation of a breast screening program based on the principle of a holistic approach to the patient has been demonstrated.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Istanbul Medeniyet University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patient who participated in thisstudy.

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References

1. Globocan 2012. Fast Stats. Most frequent cancers: both sexes. (Accessed on December 12, 2013). Available from: URL: http:/ www.uptodate.com
2. Siegel RL, Miller KD, Jemal A, Cancer statistics, 2016. CA Cancer J Clin 2016; 66: 7-30. [CrossRef]
3. Türkiye Halk Sağlığı Kurumu-Kanser Daire Başkanlığı. Available from: http://kanser.gov.tr/daire-faaliyetleri/kanser-istatistikleri/1793-2013-yılı-türkiye-kanser-istatistikleri.html.
4. Njor S, Nyström L, Moss S, Paci E, Broeders M, Segnan N, Lynge E. Breast cancer mortality in mammography screening in Europe: a review of incidence- based mortality studies. J Med Screen 2012; 19: 33-41. (PMID: 22972809) [CrossRef]
5. Myers ER, Moorman P, Gierisch JM, Havrilesky LJ, Grimm LJ, Ghate S, Davidson B, Mongtomery RC, Crowley MJ, McCrory DC, Kendrick A, Sanders GD. Benefits and Harms of Breast Cancer Screening: A Systematic Review. JAMA 2015; 314: 1615. (PMID: 26501537) [CrossRef]
6. Pillay AL. Rural and urban South African women's awareness of cancer of the breast and cervix. Ethn Health 2002; 7: 103-114. (PMID: 12511197) [CrossRef]
7. Underwood SM. Breast cancer in African American women: Nursing Essentials. ABNF J 2006; 17: 3-14. (PMID: 16596895).
8. Arda Kayhan, Erkin Arıbal. Meme Kanseri Taraması neden Yapıyoruz? Ne Zaman? Değerlendirmede Yaşanan Sorunlar. Trd Sem 2014; 2: 230-240. [CrossRef]
9. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, Forman D, Bray F. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013; 49: 1374-1403. (PMID: 23485231) [CrossRef]
10. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, Mandelblatt JS, Yakovlev AY, Habbema JD, Feuer EJ. Effect of screening

and adjuvant therapy on mortality from breast cancer. N Engl J Med 353: 1784-1792. (PMID: 16251534) [CrossRef]
11. Anderson BO, Braun S, Carlson RW, Gralow JR, Lagios MD, Lehman C, Schwartsmann G, Vargas HI. Overview of breast health care guidelines for countries with limited resources. Breast J 2003; 9: 42-50 (PMID: 12713496) [CrossRef]
12. American College of Obstetricians-Gynecologists. Practice bulletin no. 122: Breast cancer screening. Obstet Gynecol 2011; 118: 372-382. (PMID: 21775869) [CrossRef]
13. Türkiye Halk Sağlığı Kurumu-Kanser Daire Başkanlığı. http://kanser.gov.tr/ /Dosya/tarama/meme.pdf
14. Tsuchida J, Nagahashi M, Rashid OM, Takabe K, Wakai T. At what age should screening mammography be recommended for Asian women? Cancer Med 2015; 4: 1136-1144. (PMID: 25914223) [CrossRef]
15. National Cancer Center. Center for Cancer Control and Information Services. Estimation of cancer incidence Available from URL: http://ganjoho.jp/reg_stat/statistics/stat/screening_p01.html. Accessed 5 Apr 2015.
16. Uematsu T. The need for supplemental breast cancer screening modalities: a perspective of population-based breast cancer screening programs in Japan. Breast Cancer 2017; 24: 26-31. (PMID: 27259342) [CrossRef]
17. Dişcigil G, Şensoy N, Tekin N, Söylemez A. Breast health: knowledge, behaviour and performance in a group of women living in the Aegean region. Marmara Medical Journal 2007; 20: 29-36
18. Ozmen V, Nilüfer Ozaydin A, Cabioglu N, Gulluoglu BM, Unalan PC, Gorpe S, Oner BR, Aribal E, Thomas DB, Anderson BO. Survey on a mammographic screening program in Istanbul, Turkey. Breast J 2011; 17: 260-267. (PMID: 21450016) [CrossRef]
19. Açıkgöz A, Çehreli R, Ellidokuz H. Determination of knowledge and behavior of women working at a hospital on breast cancer early detection methods, and investigation of efficiency of planned education. Eur J Breast Health 2015; 11: 31-38. [CrossRef]
20. Dündar PE, Özmen D, Öztürk B, Haspolat G, Akyıldız F, Coban S, Cakiroglu G. The knowledge and attitudes of breast self-examination and mammography in a group of women in a rural area in western Turkey. BMC Cancer 2006; 6: 43. (PMID: 16504119) [CrossRef]
21. Seçginli S, Nahcivan NO. Factors associated with breast cancer screening behaviours in a sample of Turkish women: a questionnaire survey. Int J Nurs Stud 2006; 43: 161-171. (PMID: 16427965) [CrossRef]
22. Teh W, Wilson AR. The role of ultrasound in breast cancer screening. A consensus statement by the European Group for Breast Cancer Screening. Eur J Cancer 1998; 34: 449-450. (PMID: 9713292) [CrossRef]
23. Türkiye Halk Sağlığı Kurumu-Kanser Daire Başkanlığı http://kanser.gov.tr/Dosya/Kitaplar/turkce/DunyadaveTurkiyedeMamografiProgramlari.pdf
24. Koç Z, Sağlam Z. Determination of the knowledge and the practice of female patients about breast cancer, preventive measures and breast self examination and effectiveness of education. Eur J Breast Health 2009; 5: 25-33.
25. Ekici E, Utkualp N. Women instructors behaviors towards breast cancer. Eur J Breast Health 2007; 3: 136-139.
26. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, Porter P, Hu YW, Zhao GL, Pan LD, Li W, Wu C, Coriaty Z, Evans I. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst 2002; 94: 1445-1457. (PMID: 12359854) [CrossRef]
27. World Health Organization. Breast cancer: prevention and control; 2015; Available from: URL: http:/ www.uptodate.com
28. Dorsay RH, Cuneo WD, Somkan CP, Tekawa IS. Breast self-examination: improving competence and freguency in a classroom setting. Am J Public Health 1988; 78: 520-522. (PMID: 3354734) [CrossRef]
29. Gastrin G, Miller AB, To T, Aronson KJ, Wall C, Hakama M, Louhivuori K, Pukkala E. Incidence an mortality from breast cancer in the mama program for screening in Filland, 1973-1986. Cancer 1994; 73: 2168-2174. (PMID: 8156521) [CrossRef]
30. Şen S, Başar F. Breast cancer and breast self examination knowledge of women who live in Kutahya region. Eur J Breast Health 2012; 8: 185-190.
31. Kabataş MS, Kızıl H, Duman D. Evaluation on information, attitude and behavior about breast cancer and breast self- examination (bse) of female teachers. Eur J Breast Health 2010; 6: 150-155.
32. Ogunbode AM, Fatiregun AA, Ogunbode OO. Breast self examination practices in Nigerian women attending a tertiary outpatient clinic. Indian J Cancer 2015; 52: 520-524. (PMID: 26960493) [CrossRef]
33. Kayode FO, Akande TM, Osagbemi GK. Knowledge, attitude and practice of breast self examination among secondary school teachers in Ilorin, Nigeria. Eur J Sci Res 2005; 10: 42-47.
34. Gürdal SÖ, Saraçoğlu GV, Oran EŞ, Yankol Y, Soybir GR. The Effects of Educational Level on Breast Cancer Awareness: A Cross-Sectional Study in Turkey. Effects of Educational Level on Breast Cancer Awareness: A Cross-Sectional Study. Asian Pac J Cancer Prev 2012; 13: 295-300. (PMID: 22502688) [CrossRef]

Case Report

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Intraparenchymal Leiomyoma of the Breast: A Rare Location for an Infrequent Tumor

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ABSTRACT

Intraparenchymal leiomyoma of the breast are among benign non-epithelial tumors with the lowest incidence. Although it displays a benign histology, it may be confused with malignant lesions and create diagnostic confusion. In this paper, we report a 44-year-old woman with a painless mass with a diameter of 1.5 cm in the upper medial quadrant of her right breast. The lesion was removed surgically. The lesion's histologic examination and immunohistochemical analysis revealed a smooth muscle tumor of the breast. The patient was initially diagnosed with fibroadenoma and was followed in terms of the epicenter for six months before she underwent surgery. Her mammography and histopathology results are discussed in this report.

Keywords: Breast neoplasm, diagnosis, leiomyoma

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Introduction

Leiomyoma is a non-malignant tumor of smooth muscle origin, which is an important member of mesenchymal neoplasms involving the gastrointestinal tract and uterus. Leiomyoma of the breast is an extremely rare stromal tumor, constituting less than 1% of all breast neoplasms (1). It most commonly involves the subareolar area of the breast and occurs in both sexes (2). Herein, we report a 44-year-old woman with leiomyoma of the breast and provide the lesion's immunohistochemical and histological properties along with a discussion of the relevant literature.

Case Presentation

A 44-year-old woman was admitted with a history of a painless lump growing in her right breast for six months. She experienced neither nipple discharge nor morphological changes of the areola and nipple. She was not lactating or taking hormone therapy, either. Her family history of breast cancer was negative. On physical examination, she had a mobile, well-circumscribed mass lesion measuring 1.5x1 cm localized to the upper medial quadrant (UMQ) of the right breast, 7 cm away from the nipple. The mass had no attachment to the overlying skin and lacked any signs of inflammation. There was no axillary or supraclavicular lymph node involvement, nor was there any abnormality of the contralateral breast and axillary region.

A mammogram revealed a dense, oval, non-calcified lesion in the corresponding region (Figure 1), but no other lesions. There appeared no axillary lymphadenopathy. The final classification of the mass was considered to be in BIRADS category 4A. The clinical and mammographic findings prompted an excisional biopsy collected from the lesion. The gross examination of the mass revealed a fleshy, pale whitish tissue; the histological study of the lesion showed that it contained spindle cells forming bundles in an intermingling fashion. The microscopic examination demonstrated spindle cells without atypia, which were arranged in fascicles. There were also no necrosis, mitotic activity, or vascular invasion (Figure 2a-d). Immunohistochemical study indicated diffuse, intense staining for smooth muscle actin (SMA) (Figure 2c) and desmin (Figure 2d). Based on the results, intraparenchymal leiomyoma of the breast was diagnosed. An informed consent was obtained from the patient for the publication of this manuscript.

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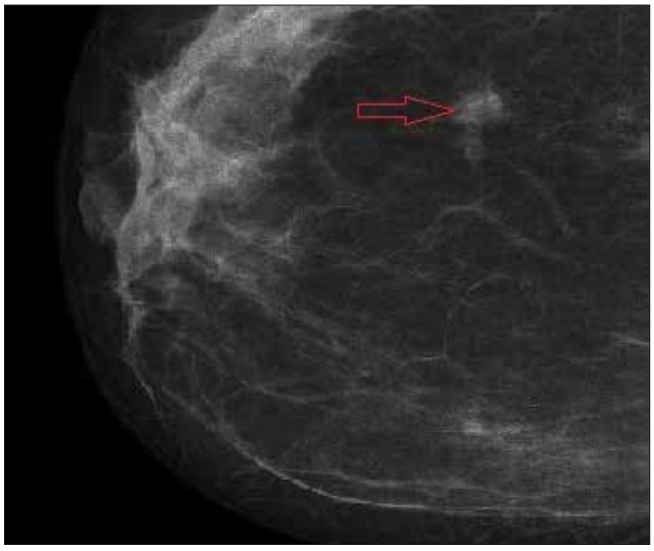

Figure 1. Craniocaudal mammografic view of the right breast, which shows a dense, oval mass (red arrow)

Discussion and Conclusion

Leiomyomas are extremely uncommon (1). The first description of a leiomyoma of the breast parenchyma was done by Strong LW in 1913 (3). When it involves the breast tissue, it usually occurs in the subareolar area. There are multiple theories as to the origin of these tumors. Kaufman and Hirsch (4) advocated that they originate from the myocytes around the capillaries in the subcutaneous tissue of the mammary gland. According to Diaz-Arias et al. (5), there may be five alternatives: teratoid origin coupled with significant overgrowth of the myomatous elements, smooth muscle cells that migrate from the nipple during embryological life, a multipotent mesenchymal cell, angiomatous smooth muscle and myoepithelial cells. Although the common location of this tumor around the nipple suggests a relationship with a high amount of smooth muscle cells in these regions, the histological evolution of these lesions remains obscure (6). Tumors of smooth muscle origin are rare in general and even rarer in the human breast. Their ratio is less than 1% among all breast tumors. They usually involve the right breast and are usually seen in women of 30-60 years of age with

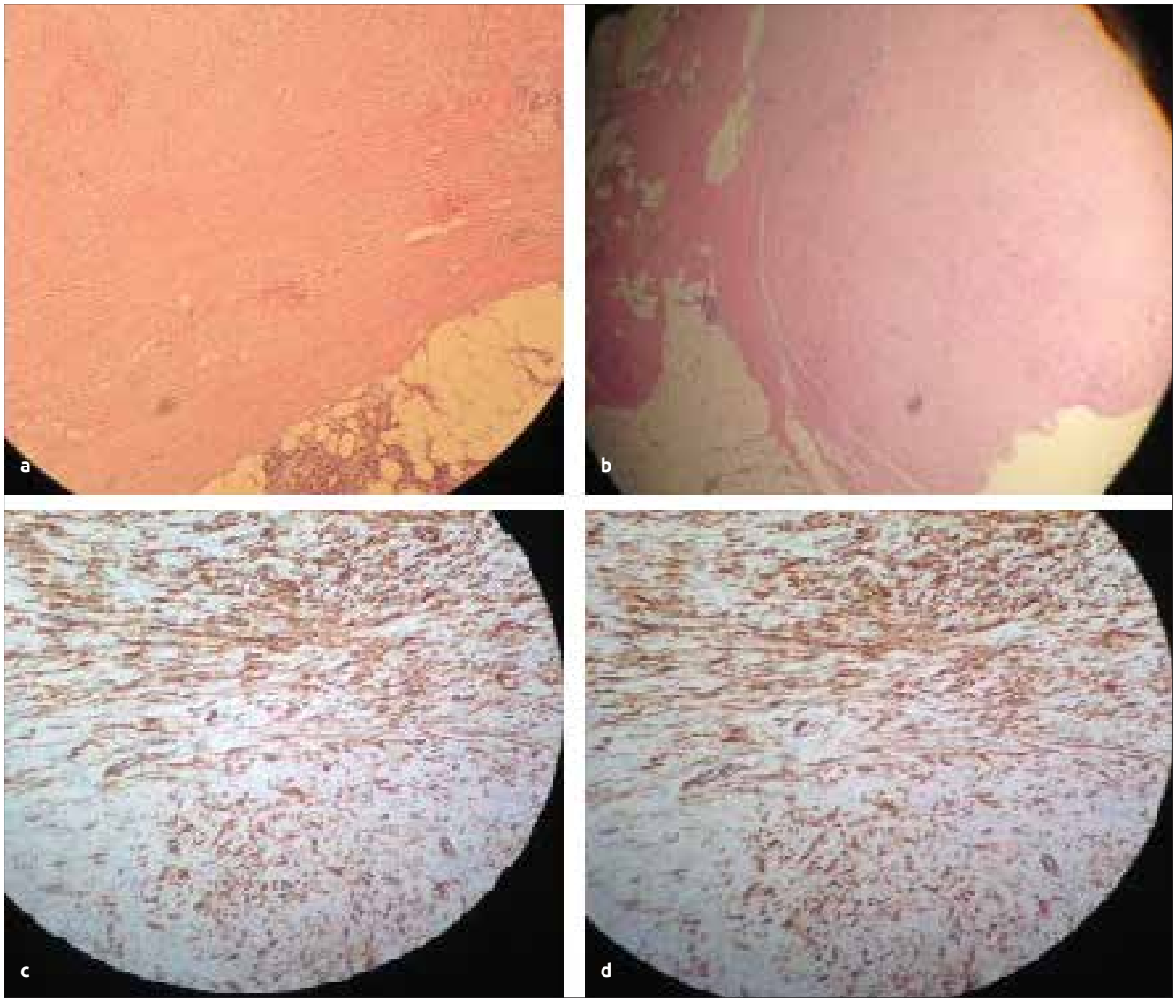

Figure 2. a-d. Microscopic view of sections of surgical specimen; positive reaction in smooth muscle cells in immunohistochemical examination (H&E:10x, H&E:5x, SMA: 20x, Desmin:20x)

an average age of 47.5 years; consistent with this, our patient was 44 years old. Parenchymal leiomyomas have a well-defined border and usually measure 1.0-14.0 cm in diameter (7). As no definite radiological criteria exist for their identification, histopathological and immunohistochemical studies are necessary. The histopathological properties of all leiomyomas are the same irrespective of the involved organ. The cells of this tumor have an eosinophilic cytoplasm and form intermingling bundles. They are stained positively for vimentin, desmin and SMA (5). h-Caldesmon (h-CD) is a protein combined with actin and tropomyosin that regulates cellular contraction. h-CD has been thought to be expressed exclusively in vascular and visceral smooth muscle cells (SMC). h-CD is also a specific marker of both SMC and its neoplasms and that immunohistochemical detection of h-CD may facilitate the differential diagnosis between leiomyosarcomas and other tumors with SMC-like differentiation, including myofibroblastic tumors (8).

This tumor's differential diagnoses include adenomyoepithelioma, phyllodes tumor, adenoleiomyoma, fibroadenoma with prominent smooth muscle, fibromatosis, benign spindle cell tumor of the breast, fibrous histiocytoma, myoid hamartoma, myoepithelioma, fibromatosis-like low-grade metaplastic carcinoma and leiomyosarcoma of the breast (9).

Among these, the most important one is leiomyosarcoma, which shows similar properties with leiomyomas in that it appears as a dense, well-demarcated non-invasive lesion on mammography and arises many years before being diagnosed. The distinction between the two is important since leiomyosarcomas may show local recurrence or distant metastasis by hematogenous route long after excision. These tumors also feature marked cellular atypia, high grade of mitosis (2-16 mitotic figures per 10 high-power fields), atypical mitoses, vascular invasion, and necrosis (10). Son et al. (11) reported an increase in the prevalence of leiomyomas of breast with tamoxifen use. A similar potential association was also reported for antiobesity drugs sibutramine and orlistat (6). These tumors are best treated with simple excision, and extensive surgery is not justified given the benign nature of these lesions. No evidence yet has been reported as to any potential of the tumor for malignant transformation or distant spread (9).

In conclusion, intraparenchimal leiomyoma of the breast is quite rare, but it can mimic other lesions of the mammary gland, both clinically and radiologically. Malignant and benign lesions cannot be reliably distinguished using physical examination or imaging studies. Hence, simple excision followed by a careful histological evaluation is necessary for a definitive diagnosis.

Informed Consent: Informed consent was obtained from patient who participated in this study.

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References

1. Sidoni A, Lüthy L, Bellezza G, Consiglio MA, Bucciarelli E. Leiomyoma of the breast: case report and review of the literature. Breast 1999; 8: 289-290. (PMID:14965748) [CrossRef]
2. Ende L, Mercado C, Axelrod D, Darvishian F, Levine P, Cangiarella J. Intraparenchymal leiomyoma of the breast: a case report and review of the literature. Ann Clin Lab Sci 2007; 37: 268-273. (PMID:17709693)
3. Shah SD, Gupta A, Roy S, Mukhopadhyay S. Intraparenchymal leiomyoma of the breast: a case report. Indian J Surg 2013; 75: 88-9. (PMID:24426524) [CrossRef]
4. Kaufman HL, Hirsch EF. Leiomyoma of the breast. J Surg Oncol 1996; 62: 62-64. [CrossRef]
5. Diaz-Arias AA, Hurt MA, Loy TS, Seeger RM, Bickel JT. Leiomyoma of the breast. Hum Pathol 1989; 20: 396-399. [CrossRef]
6. Pourbagher A, Pourbagher MA, Bal N, Oguzkurt L, Ezer A. Leiomyoma of the breast parenchyma. ACR 2015; 185: 1595-1597.
7. Vecchio GM, Cavaliere A, Cartaginese F, Lucaccioni A, Lombardi T, Parenti R, Salvatorelli L, Magro G. Intraparenchymal leiomyoma of the breast: report of a case with emphasis on needle core biopsy-based diagnosis. Pathologica 2013; 105: 122-127. (PMID:24466762)
8. Watanabe K, Kusakabe T, Hoshi N, Saito A, Suzuki T. h-Caldesmon in leiomyosarcoma and tumors with smooth muscle cell–like differentiation: its specific expression in the smooth muscle cell tumor. Hum Pathol 1999; 30: 392-396. [CrossRef]
9. Granic M, Stefanovic-Radovic M, Zdravkovic D, Ivanovic N, Nikolic D, Radovanovic D, Stojiljkovic M. Intraparenchimal leiomyoma of the breast. Arch Iran Med 2015; 18: 608-612. (PMID:26317604)
10. Stafyla VK, Gauvin JM, Farley DR. A 53–year– old woman with a leiomyosarcoma of the breast. Curr Surg 2004: 61: 572-575. (PMID:15590026) [CrossRef]
11. Son EJ, Oh KK, Kim EK, Son HJ, Jung WH, Lee HD. Leiomyoma of the breast in a 50-year-old woman receiving tamoxifen. Am J Roentgenol 1998; 171: 1684-1686. (PMID:9843313) [CrossRef]

Case Report

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Extraction of a Foreign Body from the Breast Using Radio-guided Occult Lesion Localization (ROLL): Metallic Foreign Body in the Breast

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ABSTRACT

The most common clinical causes of metallic foreign body in the breast are surgical clips, pieces of guide-wire and gunshot wounds. Metallic foreign bodies can lead to local breast pain, abscesses, pneumothorax after granulomas or migration, and cardiac tamponade. Mammotome biopsy, fluoroscopy, guide-wire biopsy and radio-guided occult lesion localization (ROLL) are the standard techniques applied for surgical excision of non-palpable breast lesions. This article presents the second case in the literature undergoing the ROLL technique for the removal of a metallic foreign body from the breast.

Keywords: Breast, gunshot injury, metallic body, mammography

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Introduction

Metallic foreign bodies (MFB) within the breast develop out of surgical clips, broken pieces of guide-wires and gunshot injuries (GSI) (1). As such, metallic foreign bodies can cause local breast pain, abscess, cardiac tamponade, granuloma or pneumothorax, which are clinically significant (1-2). In this report, we aim to present a 35-year-old female patient diagnosed with a metallic foreign body in the left breast as the second case in the literature in which radio-guided occult lesion localization (ROLL) was used for the excision of the foreign body.

Case Presention

A 35-year-old female patient presented to the general surgery department with pain in the left breast. She had a history of a gunshot wound in the breast four months ago, shortly after which the symptoms had started. The patient told that the bullet was still in her breast. Physical examination revealed tenderness in the upper outer quadrant of the left breast. The breast ultrasound indicated a 10 mm hyperechoic formation in the upper outer quadrant of the left breast. The mammography and chest x-ray confirmed the presence of a 10 mm hyperdense MFB within the breast. The object was not fragmented (Figure 1-2). It was decided to surgically remove the foreign body and written informed consent from the patient was obtained. On the morning of surgery, the MFB was marked using the ROLL technique in the radiology unit. The foreign body was excised along with the surrounding fibrosis and inflammatory breast tissue by applying a gamma probe through a 3 cm incision in a 20-minute operation. Specimen mammography was performed on the excision material to confirm that the MFB was located within the tissue (Figure 3).

Discussion and Conclusion

Since metallic foreign bodies can cause symptoms such as local breast pain, abscess, cardiac tamponade, granuloma or pneumothorax, they have clinical importance (1-2). Korbin et al. (3) reported broken guide-wire pieces in 5 of 3500 patients who underwent guide-wire biopsy. Montrey et al. (4) reported that the most common types of MFB in the breast are surgical clips and broken pieces of guide-wires. In that same study, the prevalence of MFB related to broken guide-wire pieces was found to be 0.2%. As reported in several studies addressing MFB in the breast, surgical clips, pieces of guide-wires and GSIs are the most common factors in etiology. Mammography is usually helpful for the diagnosis (1, 2, 5). In our case, the patient had a history of GSI as well as pain in the left breast as consistent with the literature. The MFB was clearly visualised in ultrasound, mammography and chest x-ray.

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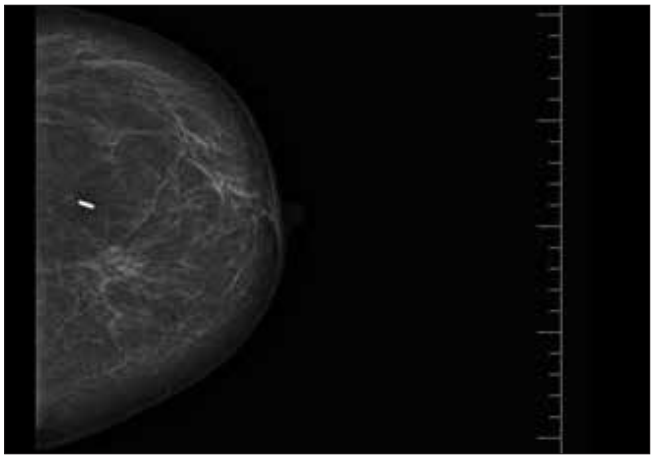

Figure 1. Mammography of left breast and the foreign body

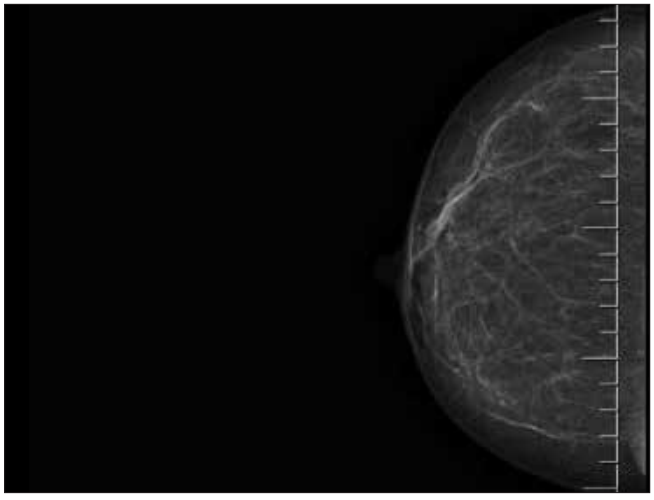

Figure 2. Mammography of right breast

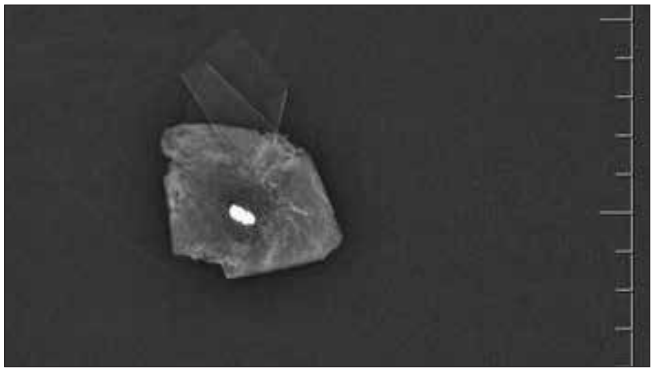

Figure 3. Specimen mammography

Metallic foreign bodies within the breast are treated through surgical excision. Guide-wire, fluoroscopy, mammotome biopsy and ROLL are the guiding techniques reported in the literature for non-palpable MFBs (1, 2, 4-6). The ROLL technique was first introduced in 1996 and has since been successfully applied for various cases including non-palpable breast lesions, parathyroid adenoma, recurrent papillary thyroid cancer and extraction of MFBs from the breast (5, 7, 8, 9). The use of ROLL for the extraction of a foreign body from the breast was first reported in 2010 (5). Moreno et al. (10) stated the ROLL technique to be an effective method for excision of non-palpable breast lesions due to its advantages such as good cosmetic outcomes, lower cost and shortened duration of operation and hospitalization. As the required radionuclide dose in clinical use is low, there is no need for additional safety precautions (11). Our case is the second case in the literature having the ROLL technique applied for the removal of a metallic foreign body from the breast with similar advantages like smaller incision, shorter operative time and shorter hospital stay.

In conclusion, considering the advantages it offers such as three-dimensional localization, smallness of incision, reduced aesthetic concern, shortened duration of operation and hospitalization and reduced cost, the ROLL technique can be conveniently used for extracting non-palpable organic, inorganic and metallic foreign bodies from the breast.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

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References

1. Akyol C¸ Akmak A, Kepenekci I, Erkek AB, Baskan S. Metallic foreign body in the breast. Eur J Breast Health 2008; 4: 125-126.
2. Bozdag A, Baykara M. Metallic Foreign Bodies in the Breast: ACase Report. Fırat University Medical Journal of Health Sciences 2014; 28: 33-34.
3. Korbin CD, Denison CM, Lester S. Metallic particles on mammography after wire localization. Am J Roentgenol 1997; 169: 1637-1638. (PMID:9393182) [CrossRef]
4. Montrey JS, Levy JA, Brenner RJ. Wire fragments after needle localization. Am J Roentgenol 1996; 167: 1267-1269. (PMID:8911193) [CrossRef]
5. Aydogan F, Atasoy D, Olgun DC, Dikici AS, Aliyev A, Gazioglu E. Extraction of a foreign body from the breast parenchyma using radioguided occult lesion localisation (ROLL) technique: a new approach. Br J Radiol 2010; 83: 147-149. (PMID:20603400) [CrossRef]
6. Parker SH, Kercher JM, Dennis MA. Sonographically guided mammotome extraction of retained localization wire. Am J Roentgenol 1999; 173: 903-904. (PMID:10511145) [CrossRef]
7. Luini A, Zurrida S, Galimberti V, Paganelli G. Radioguided surgery of occult breast lesions. Eur J Cancer 1998; 34: 204-205. (PMID:9624261)
8. Ilgan S, Ozbas S, Bilezikci B, Sengezer T, Aydin OU, Gursoy A, Kocak S. Radioguided occult lesion localization for minimally invasive parathyroidectomy: technical consideration and feasibility. Nucl Med Commun 2014; 35: 1167-1174. (PMID:25153058) [CrossRef]
9. Giles YS, Sarici IS, Tunca F, Sormaz IC, Salmaslioglu A, Adalet I, Ozgur I, Tezelman S, Terzioglu T. The rate of operative success achieved with radioguided occult lesion localization and intraoperative ultrasonography in patients with recurrent papillary thyroid cancer. Surgery 2014; 156: 1116-1126. (PMID:24953276) [CrossRef]
10. Moreno M, Wiltgen JE, Bodanese B, Schmitt RL, Gutfilen B, Da Fonseca LM. Radioguided breast surgery for occult lesion localization- correlation between two methods. J Exp Clin Cancer Res 2008; 27: 29. (PMID:18706096) [CrossRef]
11. Rampaul RS, Dudley NJ, Thompson JZ, Burrell H, Evans AJ, Wilson AR, Macmillan RD. Radioisotope for occult lesion localisation (ROLL) of the breast does not require extra radiation protection procedures. Breast 2003; 12: 150-152. [CrossRef]

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Erratum

In the article by Yati Vaidya et al., entitled "Somatic Cell Count: A Human Breast Wellbeing Indicator" (Eur J Breast Health 2017; 13: 88-93) that was published in the April 2017 issue of European Journal of Breast Health, one of the contributing authors's institution information erroneously misspelled due to an author error. Upon the receipt of the written request of the contributing authors, the Editorial Board reviewed the case and approved Dev Nauriyal's affiliation corrected as "Department of Veterinary Medicine, College of Veterinary Science and Animal Husbandry, Anand Agricultural University, Anand, India".

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