Breast Cancer in Men: Risk Factors, Treatment Options, Quality of Life: Systematic Review

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ABSTRACT

Objective: The aim was to systematically examine the risk factors that have a role in the development and prognosis regarding the breast cancer among men and patients' survival rate, and the studies performed to determine the treatment methods and patients' quality of life.

Methods: The databases of PubMed, Scopus, Cochrane Library, OVID-LWW, Medline Complete, Science Direct, Taylor&Francis, ULAKBIM, Ethos, OpenThesis, Open Dissertation, ProQuest Dissertations & Theses Global, and National Center of Theses were used to screen the literature. Case-control and cohort studies published between 2000 and 2020 were included. Following the screening activity, 14 studies were included in the systematic review.

Results: This study involved seven cohort and seven case-control studies. Most of the patients were followed with invasive carcinoma diagnosis. These studies aimed to examine the genetic mutations and impacts of environmental, anthropometric and hormonal factors in regard to the risk factors. The factors such as the molecular classification of cancer, presence of genetic mutation, cancer stage and treatment methods affected the prognosis and survival rate. Mastectomy was used as the first treatment option, and this process had adverse impacts on patients' quality of life physically, mentally and emotionally.

Conclusion: This study indicated that many risk factors played a role in the development and prognosis of breast cancer among men and their survival rate, that mastectomy was the primary treatment option, and that patients' quality of life was adversely affected during/following the disease.

Keywords: male breast cancer, risk factors, treatment, quality of life.

1. INTRODUCTION

Breast cancer is the most frequent type of cancer among women but is quite rare among men. Although the prevalence of breast cancer among men was 1% or less, this rate has been increasing in recent years (1,2). According to 2020 estimations made by the American Cancer Society, 2620 people in United States of America will be diagnosed with this disease, and 520 of them will lose their lives (3). Although many aspects of breast cancer have been understood due to various reasons such as high number of studies conducted with women or effective operation of screening programs, informational deficiencies are experienced as the number of cases among men is limited, samples of these studies are limited or relevant studies are retrospective. Thus, diagnoses are generally made at a later period (2,4,5). Moreover, the amount of information on the ethology of male breast cancer is quite limited compared to the information on breast cancer among women (6,7). The literature indicates genes, age, hormones boosting the estrogen level, factors related to lifestyle or environmental factors (1,8,9)). The treatment methods used on women are also used on men. However, while lumpectomy is often preferred for women while mastectomy is the procedure performed on men (4). The treatment method is shaped by different factors such as tumor type, stage, or hormone receptor (10)). The presence of informational deficiency in the society may direct people to believe that men do not have breast tissue and thus they cannot suffer from breast cancer (11)). Therefore, people diagnosed with breast cancer may suffer from concerns related to embarrassment and stigma, which may affect their quality of life (1).

This study aimed to systematically examine and present the data of the studies reviewing the risk factors which have a role in the development and prognosis regarding the breast cancer among men and patients' survival rate, and the results of studies performed to determine the treatment methods and patients' quality of life following the diagnosis.

2. METHODS

The systematic review was carried out in accordance with the PICOS format. It was determined as: P (population): Male breast cancer patients, I (Intervention): Not applicable, C (Comparator(s)): Men that didn't have breast cancer, O (Outcome(s)): risk factors, prognostic factors, treatment options, quality of life, S (Study design): case-control and cohort studies. This systematic review was conducted from PubMed, Scopus, Cochrane Library, OVID-LWW, Medline Complete, Science Direct, Taylor&Francis, ULAKBIM databases and Ethos, Open Thesis, Open Dissertation, ProQuest Dissertations & Theses Global, and National Center of Theses databases. The screening was performed using the Turkish and English keywords. To determine the English keywords, Medical Subject Headings (MeSH) were used, and to determine the Turkish keywords, Turkish Science Terms Dictionary (TBT) was utilized. Then, the keywords of "male breast cancer", "male breast tumors", "male breast neoplasm", "risk factors", "treatment", "life quality", "quality of life" and "health-related quality of life" and relevant combinations were used, and screening was performed between January and April 2020. The last screening activity was performed at 5 April 2020. The flow chart regarding the literature screening is presented in Figure 1. The case-control and cohort studies were included as the number of cases was limited. The protocol of the study was registered by PROSPERO (ID: CRD420.201.78399).

The inclusion criteria were as follows:

- Samples containing people aged 18 years or older,
- Publication in English or Turkish,
- Publication between 2000 and 2020,
- Accessibility to the full text,
- Breast cancer as the primary diagnosis among men.

Manuscripts with, qualitative studies, systematic review, meta-analyses, case reports, editorial reports, short reports and descriptive, or cross-sectional study designs were excluded.

Ethic Consideration

This study was a systematic review; no ethics committee approval was required. The researcher also declares that there was no conflict of interest in this study.

Risk of Bias in Individual Studies

Two researchers independently reviewed full texts. Newcastle Ottawa Scale used to evaluate the study criteria. The scale is scored between 0-9 and the higher the score, the higher the quality of the study (12). Total quality scores were shown in Table 1 and Table 2.
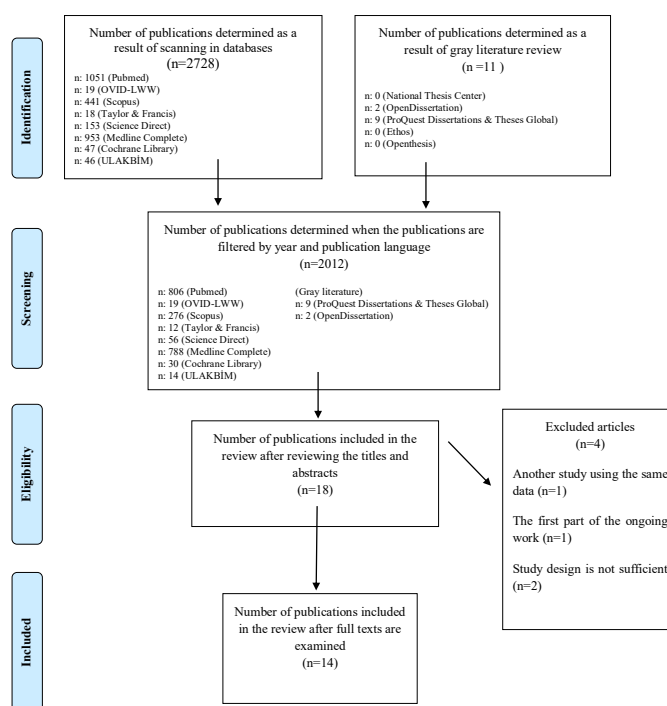

Figure 1. PRISMA chart regarding the literature screening

Table 1. Properties of the reviewed cohort studies

Author/year and country	Study objective	Sample	Duration of monitoring	Age*	Cancer type	Main results	Newcastle Ottawa Scale Score (0-9)
André et al. (2019) Portugal	Determining the parameters used to define the treatment and characterization of male breast cancer and assessing the relationship between these parameters and healthy and general survival	196	Mean 84.9 months	Diagnostic age: 66.5 (min-max: 31-89) of the patients, 55.1% were aged between 40 and 69 years maximum	of the patients, 39.2% were diagnosed with invasive carcinoma	Forty-four patients were assessed in terms of BRCA mutation and 15 had BRCA2 mutation. A relationship was found between BRCA2 mutation, family history, bilateral cancer, high Ki-67 presence, PR (progesterone receptor)-(negative), and Luminal B-like tumors. A relationship was found between Luminal B-type, BRCA2 mutation, high Ki-67 presence, second and third stage, short and healthy survival and general survival period. Moreover, a relationship was found between the ages below 70 years and low survival rate. The treatments performed on patients included; • Surgical (90.3%) / 4.6% lumpectomy • Radiotherapy (63.3%) • Hormonotherapy (60.2%) • Chemotherapy (37.2%)	8
Keinan Boker, Levine, Leiba, Derazne & Kark (2018) Israel	Assessing the relationship between the body mass index of adolescent men aged between 16 and 19 years and male breast cancer	1,382,093 people were monitored. Breast cancer was found in 100 male people.	21.3±12.5 years on average	17.3±0.4 at the early stages of monitoring 38.6±12.6 at the end of monitoring 46.9±8.7 years as the diagnostic age	of the patients, 75% were diagnosed with infiltrative ductal carcinoma	People with excessive weight and obesity were found to have a higher risk of breast cancer compared to those with normal weight. Minimal risk among adolescents was seen among those with a body mass index of 21.0 kg/m² ; the risk was found to be significantly high among the adolescents with a body mass index higher than 24.2 kg/. European people had higher risk compared to Asians, Africans and Israelis.	7
Rugo et al. (2013) USA	Assessing the demographic characteristics of black and Caucasian people diagnosed with HER-2 (human epidermal factor receptor) positive metastatic breast cancer, treatment methods and clinical results	919 Caucasian: 793 Black: 126	Duration of monitoring for Caucasian people: 28.4 months Duration of monitoring for black people: 21 months	Caucasian: 54 (min-max: 22-92) Black: 50 (min-max: 20-90)	61% of Caucasian people and 50.8% of black people had stage 1-3 for more than 12 months following the first diagnosis Cancer type not specified	Compared to the Caucasian people, black people had; • breast cancer at an earlier age • higher obesity prevalence • diabetes at a rate higher than two times • and a co-morbid cardiovascular disease higher than two times. Adjuvant systematical treatment was performed in both races (Caucasian: 75.4%, black: 66.7). Transtuzumab was used as the preliminary medication for both people before the first progression. ER/PR (estrogen receptor/progesterone receptor) was negative for most black people, but it was positive for most of the Caucasian people. As hormonotherapy could not be preferred as a treatment method, number of those who received chemotherapy was higher compared to Caucasian people. In addition, the progression-free survival duration of black people was shorter than that of Caucasian people, and black people had a higher mortality risk. The regional metastasis risk was higher among black people, and only the bone or bone-breast metastasis development rate was higher among Caucasian people.	8

Author/ year and country	Study objective	Sample	Duration of monitoring	Age*	Cancer type	Main results	Newcastle Ottawa Scale Score (0-9)
Turashvili et al. (2018) USA	Assessing the relationship between the 21-gene recurrence score of male patients with ER+(positive)/HER2-(negative) breast cancer and treatment type.	38	34 months (1.05-133.3)	70 (min-max: 40-84)	Diagnosis of invasive ductal carcinoma for 63.2%	21-Gene recurrence score; • Low in 26 cases (<17) • Moderate in 9 cases (18-30) • High in 3 cases (≥31). Total mastectomy was performed for all patients. Radiotherapy was administered to a patient thereafter. As a hormonal therapy; • 31 patients received tamoxifen • Three patients received aromatase inhibitor. Five patients were treated with adjuvant chemotherapy along with the hormonal treatment (moderate recurrence score for three patients, and high recurrence score for two patients) Consequently, only one patient experienced distant metastasis 29 months after the monitoring, but other patients showed no distinctive symptoms.	8
Zhou et al. (2010) China	Determining the changes in the treatment methods used for male breast cancer patients and effectiveness of radical mastectomy and modified radical mastectomy	70 patients in total Two groups Cohort A (1969-1997): 35 Cohort B (1998-2009): 35	3-391 months (median 55 months) **Cohort A** 1969-1997 **Cohort B** 1998-2009	Of all patients: 61 (min-max: 27-90) Cohort A: 60 (min-max: 27-90) Cohort B: 62 (min-max: 32-80)	of the patients, 81.4% were diagnosed with infiltrative ductal carcinoma	**Cohort A** • Multidisciplinary treatment was performed for 26 patients (74.3%). • Adjuvant chemotherapy was not conducted for 23 patients (65.7%). • Radiotherapy was not conducted for 25 patients (71.4%). • Hormonal treatment was not performed for 26 patients (74.3%). • Radical mastectomy was performed for 26 patients (74.3%) **Cohort B** • Multidisciplinary treatment was performed for 33 patients (94.3%). • Adjuvant chemotherapy was conducted for 23 patients (65.7%). • Radiotherapy was not conducted for 31 patients (88.6%). • Hormonal treatment was conducted for 23 patients (65.7%). • Radical mastectomy was performed for 19 patients (54.3%). No difference regarding the five-year survival rates was found between the groups that underwent radical mastectomy and modified mastectomy. The treatment methods were monitored in ten-year periods and modified radical mastectomy was found to be preferred more in the last 10 years. Therefore, both methods were found to be equally effective. Presence of axillary node involvement, advancement of cancer stage and performing post-operative radiotherapy were found as the potential factors that may adversely affect the five-year survival rate.	8

Author/year and country	Study objective	Sample	Duration of monitoring	Age*	Cancer type	Main results	Newcastle Ottawa Scale Score (0-9)
Zongo et al. (2018) Burkina Faso (Western Africa)	Determining the diagnostic stages, treatment models and five-year survival rates of male patients with breast cancer	51	1990-2009	60.9±8.4	Of the patients, 91.1% were found to have epithelial tumors (ductal and lobular carcinoma)	The disease stage was three and four for 88.8%. Surgery was the primary treatment method. 31 patients were operated. Of the patients who underwent surgery, 80.6% underwent mastectomy with axillary dissection, 12.9 had mastectomy and 6.5% had lumpectomy. 15 patients (29.4%) underwent chemotherapy while 11 received (21.6%) hormonal treatment. Radiotherapy was performed in two cases. The five-year survival rate was found to be 49.9%. The survival duration of stage one and two patients was found to be longer than five years while the survival rate of stage three and four were found to decrease from 54 months to 36 months.	7
Son et al. (2012) Korea	Determining the BRCA1/2 mutation prevalence among the patients of high-risk, non-familial breast cancer	758 patients in total Female: 741 Male: 17	May 2007-May 2010	Not specified	Not specified	65 out of 758 patients (8.6%) had mutation in BRCA1/2 genes. None of 17 patients had BRCA1 gene mutation, while only one of them had BRCA2 mutation. BRCA1/2 mutation prevalence was found to be higher than 10% for the people with a history of cancer diagnosis before the age of 35 years, bilateral breast cancer, and personal breast and ovary cancer.	7

*Median (min-max); Mean±Standard deviation (SD)

Table 2. Properties of the reviewed case-control studies

Author/year and country	Study objective	Sample	Age*	Cancer Type	Main Results	Newcastle Ottawa Scale Score (0-9)
Andrykowski (2012) USA	Determining the physical and mental states of men following the development of breast cancer and specifying their medical behaviors	Case: 66 Control: 198	Case: 66.2±15.9 Control: 65.9±15.8	Not specified	Data were collected using Behavioral Risk Factor Surveillance System (BRFSS) The duration after the diagnosis was made was found to be 12±10.9 years. Compared to the control group, the case group; • had more co-morbid disease history • had less satisfaction from their lives • had poor general, mental and physical health statuses in the last month • Due to the physical, mental and emotional problems, they had more limitations in their activities. 16 indicators were assessed in regard to medical behaviors. No significant different was found between the medical behaviors of the case group, with only one exception that case group had less exercising time in the last month.	8
Guenel et al. (2004) Denmark, France, Germany, Italy, Sweden	The role of alcohol consumption for male breast cancer was examined.	Case: 74 Control: 1432	Not specified Patients aged between 35 and 70 were included	-	Alcohol consumption varied between 30.2 to 46.9 g/day within the case groups; Regarding the control groups, this rate ranged from 19.8 to 38.3 g/day, meaning the case group had higher alcohol consumption rate. Alcohol consumption of 60g/day significantly increased the risk for cancer. In cases where this rate was higher than 90 g/day, the risk was found to increase by six times. In addition to alcohol consumption; gynecomastia, diabetes, male factor fertility problems, injuries to head and every 1 kg/m^2 increase in body mass index had a significant relationship with the cancer risk. A daily alcohol consumption routine of 10g was found to increase cancer risk by 16%.	8
Orr et al. (2011) England	Determining whether the single nucleotide polymorphism changes within 2q35, 5p12, 6q25.1, 10q26.13 and 16q12.1 chromosomes, which create breast cancer among women, cause the development of male breast cancer.	Case: 433 Control: 1569	Median diagnostic age 65.5 (Interquartile range: 59-72)	of the patients, 92% were diagnosed with invasive carcinoma	A significant relationship was found between five single-nucleotide polymorphism and male breast cancer. These are • rs13387042 (2q35) • rs10941679 (5p12) • rs9383938 (6q25.1) • rs2981579 (FGFR2) • rs3803662 (TOX3) A comparison between the male breast cancer risk rates and published risk rate for women indicated a significant difference regarding genders within three polymorphism. These are • rs13387042 (2q35) (riskier for men than women) • rs3803662 (TOX3) (riskier for men than women) • rs6504950 (COX11) (riskier for women than men)	8

Author/year and country	Study objective	Sample	Age*	Cancer Type	Main Results	Newcastle Ottawa Scale Score (0-9)
Ottini et al. (2014) Italy	Assessing the impact of the changes within the Arg213His [638G(A)], a functional polymorphism of sulfotransferase 1A1 (SULTH1A1) enzyme that plays a key role in estrogen metabolism, on the development of male breast cancer	Case: 394 Control: 786	Not specified	-	A significant difference regarding the SULT1A1 Arg213His genotype distributions was found between the case and control groups. SULT1A1 Arg213His variant could be a risk factor with low penetration for male breast cancer. Moreover, a significant relationship was found between SULT1A1 risk genotype and HER2.	8
Palli et al. (2007) Italy	Determining the relationship between BRCA2 N372H variant and male breast cancer risk.	Case: 99 Control: 261	Case: 67.9±11.8 Control: 55.9±6.9	-	Of the people in case group, eight (8.1%) were found to have BRCA1/BRCA2 gene mutations. Six (6.1%) had BRCA2 mutation while two (2.0%) were found to have BRCA1 mutation. No significant difference was found between the BRCA2 N372H genotypes and case and control groups. In addition, people over the age of 60 years had increased cancer risk rate. HH homozygote genotype was found to increase the risk for the men aged over 60 years.	7
Silvestri et al. (2018) Italy	Assessing the FANCM mutation on male breast cancer	Case: 506 (negative BRCA1 and BRCA2 mutations) Control: 854	Mean diagnostic age: 61.5 (min-max: 22-90)	of the patients, 80.2% were diagnosed with invasive ductal carcinoma	Two FANCM mutations, c.1432C>T (p.Arg478Ter) and c.1972C>T (p.Arg658Ter), were found in two people from the case group. Although the frequency of mutation was higher in the case group, no significant difference was found between both groups. FANCM c.5101C>T mutation was not be found in the case group, but FANCM c.5791C>T mutation was seen in two people in the control group. In addition to these two mutations, other rare partial mutations could play a role in increasing the sensitivity to cancer.	7
Villeneuve et al. (2018) Denmark, France, Germany, Italy, Sweden	Assessing the role of environmental chemicals and profession on the male breast cancer	Case: 104 Control: 1901	Not specified.	-	• Cancer risk was high for wood processing sector, paper manufacturers, • machinists of motor vehicles, • painters, • paper manufacturers, • people of wood crafting sector, • medical and social service staff • and those who sell and repair motor vehicles. Risk rate increased for every ten year or longer for the machinists of motor vehicles, and the risk was found to decrease for farmers and agricultural workers, despite being not significant. A significant relationship was found between the alkyl phenolic compounds, which are environmental chemicals, and risks. The risk could increase for the machinists of motor vehicles due to petrol, petrol solvents or polycyclic hydrocarbons.	8

*Median (min-max); Mean±Standard deviation (SD)

3. RESULTS

Keywords were used in the first section of the literature screening activity, and 2739 studies were found. Within the second section, studies were filtered based on the year of publication and language. Consequently, 2012 studies were found. These studies were systematically organized examining the relevant titles and abstracts and using Mendeley reference management program to review 18 full study texts with suitable study designs. Following the quality assessment, 14 studies were included in the systematic review (Figure 1). Moreover, seven cohort and seven case-control studies were found among these studies. The characteristics of cohort studies are present in Table 1 while the qualities of case-control studies are provided in Table 2.

3.1. General Properties of Cohort Studies

Cohort studies were found to have been published in 2010, 2012, 2013, 2018 and 2019. Of these studies, two were conducted in the United States of America (USA) while others were conducted in Portugal, Israel, China, Burkina Faso and Korea. The number of people monitored in those studies varied between 38 and 1,382,093, and the duration of monitoring ranged from 21 to 391 months. The patients within those studies were mostly diagnosed with invasive carcinoma (Table 1). A cohort study examining the quality of life was not found. Cohort studies included one study that reviewed the risk factors directly affecting the development of breast cancer. The study by Keinan Boker et al. (2018) indicated that people with obesity or extra weight had a higher risk of developing breast cancer compared to the people with normal weight. Moreover, European people had a higher risk of developing breast cancer compared to Asian, African and Israeli people (2). In the study by Son et al. (2012) who assessed the gene mutation prevalence of BRCA1/2 in terms of the risk factor after developing breast cancer, only one out of 17 patients in the sample of 758 patients (both genders) had BRCA2 mutation. In addition, BRCA gene mutations were found to be capable of having a greater role for the patients who developed cancer before the age of 35 years and had bilateral breast cancer, breast and ovary cancer histories (13).

Other cohort studies reviewed the factors that affected prognosis and/or survival rate. André et al. (2019) examined 196 people for 84.9 months and found a relationship between Luminal B type cancer, BRCA2 mutation, high Ki-67 value, age over 70 years, advanced cancer stage and survival rate (4). Rugo et al. (2013) examined 917 people for racial differences and found that prognosis of black people was worse than that of Caucasian people, and that black people's survival rate was lower (14). Zhou et al. (2010) conducted a study on 70 people to compare treatment options and activities for breast cancer among men and found that presence of axillary node involvement, implementation of postoperative radiotherapy and failure to perform hormonal treatment adversely affected prognosis and/or survival (15).

The treatments performed in the studies indicated that mastectomy was used as the first treatment option and that surgical procedure were assisted with radiotherapy, hormonotherapy and chemotherapy. Turashvili et al. (2018) found in their study that mastectomy was initially performed on almost all patients (n=38), and that surgical procedure was assisted with hormonotherapy rather than radiotherapy (5). André et al. (2019) found that 90.3% of 196 patients underwent a surgical procedure, followed by radiotherapy, hormonotherapy and chemotherapy, respectively (4). Zhou et al. (2010) found in their study where they compared the treatment options for 70 patients with breast cancer that multidisciplinary treatment methods were mostly used and that there was no difference between radical mastectomy and modified radical mastectomy (15). Zongo et al. (2018) revealed that 31 patients out of 51 underwent a surgical procedure, and that 80.6% of these patients underwent mastectomy along with axillary dissection mastectomy while 12.9% underwent mastectomy and 6.5% experienced lumpectomy. Moreover, within the same study, 15 patients (29.4%) underwent chemotherapy while 11 received (21.6%) hormonal treatment (16).

3.2. General Characteristics of Case-control Studies

Case-control studies were published in 2004, 2007, 2011, 2012, 2014 and 2018. Of these studies, three were conducted in Italy, two were performed in more than one country (Denmark, France, Germany, Italy and Sweden), and the others were conducted in England and USA. The number of participants in case groups ranged from 66 to 506, and the number of people in control groups were between 198 and 1901. Regarding the risk factor, four studies reviewed the genetic factor while one examined the alcohol consumption, and one investigated the professional factors (Table 2).

Regarding the studies examining the genetic factors, Orr et al. (2011) found that there could be a relationship between the single-nucleotide polymorphisms of rs13387042 (2q35), rs10941679 (5p12), rs9383938 (6q25.1), rs2981579 (FGFR2), rs3803662 (TOX3) and development of breast cancer, while Ottini et al. (2014) indicated that variant of sulfotransferase 1A1 (SULTH1A1) enzyme SULT1A1 Arg213His could have a relationship with the development of breast cancer, and Silvestri et al. (2018) revealed that there could be a relationship between two partial FANCM mutations of c.1432C>T (p.Arg478Ter) and c.1972C>T (p.Arg658Ter) and development of breast cancer (8,17,18). The study conducted by Palli et al. (2007) to examine the relationship between BRCA2 N372H variant and breast cancer development risk for men indicated that there was no significant difference regarding the mutations between the case and control group but people younger than 60 had higher cancer risk and HH homozygote genotype could increase the risk for the men younger than 60 (7).

Two articles on the relationship between men's habits, current diseases, professions and cancer development were examined, and among them, the study by Guenel et al. (2004)

on the impact of alcohol consumption on breast cancer development found that an alcohol consumption rate of >60 g (gram)/day increased the risk significantly (a 16% increase in the risk for every increase on 10 g in the consumption). In cases where this rate was higher than 90 g/day, the risk was found to increase by six times. In addition to alcohol consumption; gynecomastia, diabetes, male factor infertility problems, injuries to head and every 1 kg/m^2 increase in body mass index were found to have a significant relationship with cancer risk (6). Villeneuve et al. (2018) performed a risk assessment based on professional groups and found that people working in wood processing sector, machinists of motor vehicles, painters, paper manufacturers, people of wood crafting sector, medical and social service staff, and those who sell and repair motor vehicles had higher cancer development risk (19).

Treatment methods were not included in these studies, but one study was found to have examined the quality of life. The study conducted by Andrykowski (2012) to assess patients' physical and mental statuses following the diagnosis of breast cancer found that general, mental and physical statuses of those in the case group were not good compared to those of the control group, that they had more limitations in their activities due to physical, mental or emotional problems, and that their quality of life was poor (1).

4. DISCUSSION

The results of this systematic review that examined the risk factors, treatment options and quality of life which play a role in the development and prognosis of male breast cancer and men's survival rate will be compared to the information in the literature.

This review indicated that many genetic and environmental factors, excessive weight or obesity, and variables such as alcohol consumption, diabetes, age or cancer stage affected the development/prognosis of breast cancer, thus the survival rate, which was also mentioned in the results section (2,4,18,19,6–8,13–17). Brinton et al. (2014) examined the anthropometric and hormonal risk factors that played a role in the development of male breast cancer and found that body mass index was the most important factor in regard to the risk and that conditions that create hormonal changes such as Klinefelter syndrome, gynecomastia, diabetes, cryptorchidism or orchid could create risks related to the breast cancer (20). Moreover, another study by Brinton et al. (2008) that examined the risk factors found that family history and obesity significantly increased the breast cancer risk and that alcohol consumption had no relationship with the risk, which contradicts with the relevant result in this compilation (21). The study conducted by Ewertz et al. (2001) revealed that cancer history in the family, obesity that started ten years before the diagnosis, and use of digoxin and methyldopa could be a risk factor for the development of male breast cancer (22). Regarding the studies examining the factors that had an impact on the prognosis and/or survival rate, Ravi et al. (2012) found that advanced age, high

cancer stage and increased tumor size adversely affected the prognosis (23). Yadav et al. (2020) similarly indicated that advanced age, black race, and increase in tumor grade and disease stage adversely affected the prognosis, and therefore reduced survival rate (24).

According to the studies examined within the review, the first method preferred for the treatment of male breast cancer was mastectomy. Moreover, lumpectomy was found to be performed less, and treatment methods such as radiotherapy, chemotherapy and hormonotherapy were used as supportive treatment methods (4,5,15,16). The studies examining the treatment methods used for the male people diagnosed with breast cancer included the study by Ravi et al. (2012) who found that modified radical mastectomy was used as the standard treatment method and that radiotherapy, chemotherapy and hormonotherapy were performed as the post-surgical adjuvant treatment methods (23). Another similar study by Yadav et al. (2020) found that 71.3% of the patients underwent total mastectomy and 23.7% had lumpectomy (24). Rushton et al. (2014) examined 73 female and 73 male patients and found that all of men underwent mastectomy while 38 out of 73 women had this procedure (25). The retrospective study conducted by Wan et al. (2018) to examine 161 male patients found that 88.8% of them had a surgical procedure, and the most frequent surgical procedure was mastectomy (93%) (26).

Result of one study reviewed about of the quality of life following the breast cancer development was stated that people's physical, mental and emotional health statuses were not good and that people had limitations in their activities due to the their problems (1). The study by Ruddy et al. (2013) evaluated the quality of life of the male patients who survived the breast cancer and found that patients had hormonal and sexual problems and that these problems affected their quality of life (27). Moreover, another study examining the quality of life collectively assessed the women and men with breast cancer and compared their results with the results of healthy male population. That study found that men with breast cancer had higher scores from the physical function, role function-physical, pain, vitality, social function, role function-emotional and mental health subdimensions of quality of life compared to the women with the same disorder, meaning men had higher quality of life than women in these subdimensions. Results of men with breast cancer indicated that they gained lower scores from all subdimensions compared to the scores of healthy male population and male population aged between 61 and 70 years, meaning the quality of life of men with breast cancer was lower (28).

The limitation of our review is that we excluded all studies that did not report cohort and case control, another limitation of the review process may lead to a restriction (English, Turkish).

5. CONCLUSION

This systematic review was found that many factors such as age, body mass index, occupation, alcohol consumption, genetic factors (mutations), hormonal factors, diabetes, injuries to head and fertility had a role in the development of male breast cancer. Moreover, factors such as the molecular classification of cancer, presence of genetic mutation, cancer stage and treatment method affected the prognosis and survival rate. Although the treatment type varied by the factors such as cancer type, tumor size and stage, and axillary lymph node involvement, the main treatment method was surgery. Mastectomy was generally performed as the surgical procedure, but lumpectomy was preferred less. Regarding the quality of life, development of breast cancer adversely affected patients' physical, mental and emotional statuses.

Due to the fact that there is an informational deficiency regarding the male breast cancer in the literature, awareness of the risk factors and treatment methods to be used and supporting the people bio-psychosocial so that they are affected from this period to the lowest degree are important. Therefore, multi-centered prospective studies are needed to increase the sample size.

Conflict of interest

The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript

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