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ORIGINAL ARTICLE

Evaluation of Survival Rates and Patterns of Risk Factors and Recurrence Rates in Patients with Triple-Negative Breast Cancer with Other Subtypes

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ABSTRACT

Introduction: Breast cancer a major health concern, especially in industrialized countries. Despite extensive research, a consensus does not yet exist regarding the association between breast cancer risk factors and its many outcomes. Because of the increasing rate of breast cancer in Iran, including in Yazd City, in this study we evaluated the relationship between survival and recurrence rates and patterns of risk factors in breast cancer patients. **Methods:** This analytical study was conducted retrospectively on 333 patients with breast cancer over an 8-year period (2005-2013). Total survival and recurrence rates were recorded in monthfor all patients; then the data were analyzed with the chi-square and log-rank tests and compared to other obtained data. Kaplan-Meier curves were used to analyze survival data. **Results:** The mean patient age was 57.02 ± 12.32 years. The mean total survival rate was 93.15 ± 1.25 months (97.9%). The mean total recurrence rate was 84.59 ± 1.91 months (89.8%). Patients in all breast cancer subgroups had no significant relationship with risk factors (P>0.05), although body mass index (BMI) and recurrence rate were significantly related (P=0.045). Other risk factors were not significantly related to total survival and recurrence rates. The mean duration of oral contraceptive pill consumption was significantly longer in patients in the estrogen receptor-progesterone receptor-HER2-positive subgroup than in other groups (P=0.03). **Conclusion:** We found that BMI lower than 25 kg/m^2 was strong prognostic factor for recurrence in patients with triple-negative breast cancer. Because of the high survival rate of patients with breast cancer during our 8-year study period, we recommend that studies with larger sample sizes that are focused on survival period be conducted.

INTRODUCTION

Breast cancer has four main subgroups that are classified based on the expression of estrogen receptor-progesterone receptor (ER-PR) and HER2 genes (1). Currently, considering the increasing prevalence of breast cancer, it is important to evaluate treatment status and follow-up on patients from different subgroups (2). Recent reports have suggested that there is a significant relationship between recurrence rate and breast cancer subgroups in terms of response to treatment (3,4).

However, what is still unclear, and what shows the importance of research in major cancer registry centers worldwide, is the relationship between breast cancer subgroups and their diagnostic factors and risk factors (5). One group of researchers has suggested that breast cancer subgroups in different parts of the world vary in terms of outbreak, diagnostic patterns, surgical findings, response to treatment, and ultimately survival rate (6). To understand and devise the correct treatment plan for patients, comprehensive information should be available for all breast cancer subgroups in different societies. Therefore, we designed this study to evaluate the patterns of risk factors, survival rates, and recurrence rates in patients with triple-negative breast cancer (TNBC) and other subtypes.

Our aim was to help improve the diagnosis and follow-up of patients and provide a basis for additional studies.

METHODS

This analytical study was conducted retrospectively on 333 women with breast cancer who were referred to private medical centers during an 8-year period (2005-2013). Patients were selected using the convenience sampling method, and all patients who were referred to the private Oncology Clin-

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ic and Hospital Shah Wali were included. All information was extracted from patient medical records and from direct contact with the patients. After collecting the necessary information and recording it in a questionnaire prepared for this purpose, the data were categorized based on breast cancer subtypes, including TNBC, triple-positive breast cancer (TPBC), and ER-PR-negative-HER2-positive breast cancer. Data were analyzed using SPSS software (SPSS Inc., Chicago, IL, USA), and tables related to the required indicators were prepared. Statistical analysis was performed using analysis of variance (ANOVA), the log-rank and chi-square tests, and the Kaplan-Meier survival curve. P values less than 0.05 were considered statistically significant.

RESULTS

The mean patient age was 57.02 ± 12.32 years; since P=0.76, no significant difference was observed between breast cancer subgroups and patient age. Patients were studied in terms of educational level, residence, and marital status. We found no significant relationship among educational level, residence, or marital status with breast cancer subgroups, as well as no significant relationship between rate of survival and recurrence. Patients were evaluated for age (first pregnancy), number of pregnancies, history of breastfeeding, lactation duration (months), history of oral contraceptive pill (OCP) consumption, and duration of OCP consumption (months). No relationship was observed between the frequency distribution of breast cancer subgroups and possible risk factors (P>0.05). The difference in duration of OCP consumption (months) was evaluated by ANOVA. Significant differences were observed between duration of OCP consumption in patients with breast cancer subgroups (P=0.03). In the subgroup of patients with ER-PR-HER2-positive breast cancer, the mean duration of OCP consumption was 22.22±15.03 years, which showed significant differences compared to other subgroups (Figure 1). However, no significant relationship was observed between duration of OCP consumption and breast cancer subgroups and the rates of survival and recurrence.

In our population, 2 patients were smokers and alcohol consumers; they were excluded from the study before the data were analyzed. The mean total survival rate was 93.15 ± 1.25 months (97.9%). The mean survival rate of patients in the breast cancer subgroups was analyzed by the log-rank test, and no significant differences were observed (P=0.33; Figure 2). The mean recurrence rate was 84.59±1.91 months (89.8%). The mean recurrence rate after treatment in patients was analyzed in the breast cancer subgroups by the log-rank test, and no significant differences were observed (P=0.93; Figure 3). In the TNBC group, a significant relationship was observed between body mass index (BMI) and recurrence rate (P=0.045). Other risk factors had no significant relationship with the rate of survival and recurrence in the studied subgroups.

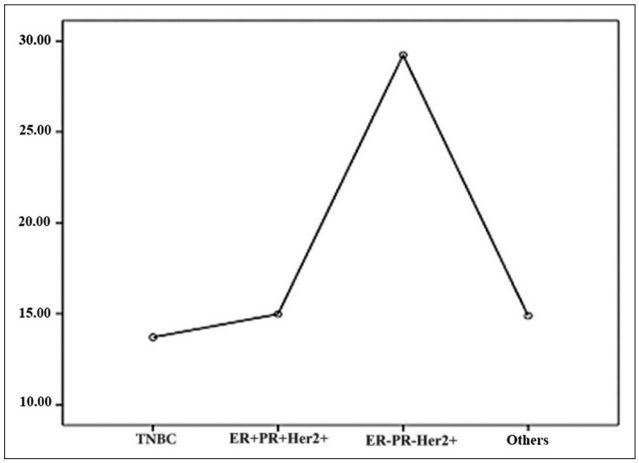

Figure 1. Mean duration of oral contraceptive pill consumption in the studied population according to the breast cancer subgroups (TNBC: triple-negative breast cancer)

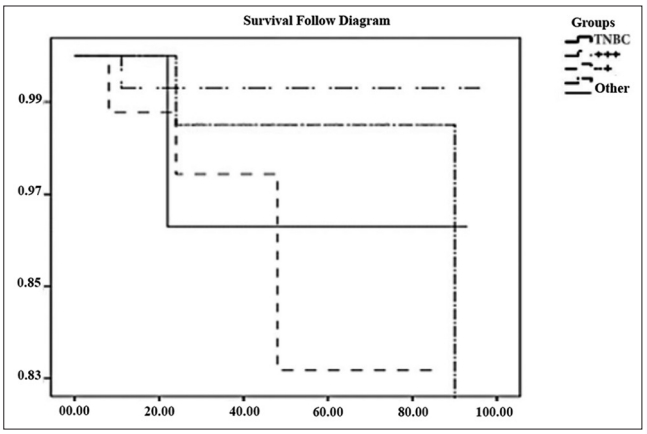

Figure 2. Mean survival rate in the studied population according to the breast cancer subgroups (TNBC: triple-negative breast cancer)

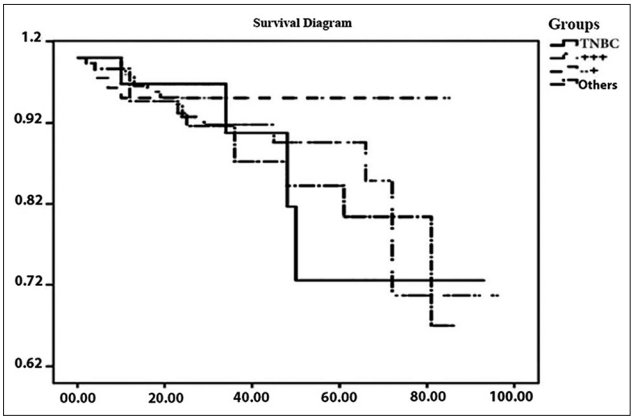

Figure 3. Mean recurrence rate after treatment (months) in the studied population according to the breast cancer subgroups

DISCUSSION

In our study, the mean total survival rate was 93.15 ± 1.25 months (97.9%). This survival rate was related to an 8-year period, which is a longer period compared to other existing reports and studies in other countries. In a similar study (2012) in France, the mean survival rate was reported to be 78.2% over a 10-year period (7). Another study in Italy showed that the mean survival rate was 82.7% over a 5-year period (8). It appears that these findings, apart from

the different time periods studied, also depend on other predictive factors, which are fundamentally the reason for the differences in various reports on the survival rate of patients with breast cancer (9, 10).

Age has always been a controversial factor in relation to survival rate. In our study, we found no significant correlation between age and breast cancer subgroups. Dialla et al., according to reports from the National Cancer Registry Center in Paris (7), suggested that age was an ineffective factor in predicting survival rates in breast cancer. However, this report was in contrast to a similar report from the Netherlands that was published in 2011 (11). Weggelaar et al. introduced age as a strong predictor. They recommended that age be considered when devising patient treatment plans; furthermore, they suggested that age has a predictive role in response to treatment and can be effective in increasing survival (11).

Pregnancy and related factors can also affect survival rate; this has been discussed repeatedly in various studies. In our study, first gestational age was analyzed, and no significant relationship was observed between it and the survival and recurrence rates of the patients. Not even the frequency distribution of the first gestational age groups was significant in the different subgroups. In this regard, some studies reported no relationship between pregnancy and prognosis and the survival rate of patients with breast cancer (12-16). Conversely, some reports were based on the relationship between the survival rate of patients and their pregnancy status and the first gestational age (17, 18); these studies suggested that pregnancy was effective at increasing the survival of breast cancer patients. Papatestas et al. (19) and Green et al. (20) suggested that history of pregnancy and childbirth was a negative factor in predicting the status of breast cancer; but, recently, many researchers have reported a direct relationship between age of last childbirth and the diagnosis of breast cancer with the survival rate of patients (21-23). Rosner and Lane reported that this was an inverse relationship (24).

In our study, we also considered OCP consumption history as a factor in breast cancer survival and recurrence rates, as well as mean duration of OCP consumption (months). We found no significant relationship in any case with survival of patients, which was consistent with the findings of other studies (12,24). Another study reported a significant relationship between OCP consumption and survival rate. The only significant finding in our study was that patients in the ER-PR-HER2-positive subgroup had a significantly longer history of OCP consumption; however, this relationship was not observed in any other study that we reviewed. Only Chlebowski et al. reported OCP consumption as a negative prognostic factor in prognosis and the survival rate of breast cancer. They observed a direct relationship between tumor size and long-term OCP consumption (25). However, several studies (26-29) suggested that OCP consumption was an effective factor in better prognosis of patients.

McDonald et al. (30) reported that alcohol consumption was a major factor in reducing the survival rate of breast cancer patients. In our study, no patient had a history of alcohol consumption, which is rooted in cultural beliefs and is reliant upon patients' reporting honestly. Some studies found no relationship between alcohol consumption and the survival rate of breast cancer patients (32, 31). Smoking history was reported in less than 1% of our population (2/333 patients); however, it was impossible to assess the association of smoking with survival factors. Two studies found that smoking reduced the survival rate of breast cancer patients (33,34).

Finally, regarding the relationship in our study between BMI and survival and recurrence rates, patients in the TNBC subgroup with a BMI less than or equal to 25 kg/m^2 had a significantly higher recurrence rate than patients with a BMI between 25 kg/m^2 and 35 kg/m^2 and more than 35 kg/m^2. In terms of the possible mechanism of the role of BMI in survival, we can point to the relationship between obesity and plasma levels of hormones, including the growth hormone, especially when adipose tissue is the most important source of external estrogen in postmenopausal women. In addition, obesity is associated with a decrease in plasma levels of globulins bound to sex hormones (34,35). In other words, the incidence of hyperinsulinemia and hyperandrogenism is enhanced with increasing BMI in middle-aged women, while the current thinking is that estrogen levels do not change or they decrease only mildly. Insulin-like growth factor 1 and insulin are two important markers in explaining the mechanism for how the survival rate of breast cancer patients is reduced following an increase in BMI. Because this marker also stimulates cell proliferation, it also prevents apoptosis (36); in other words, while stimulating the production of sex steroids, it reduces the production of glucose bound to sex hormones (35).

Considering the increasing prevalence of breast cancer in Iran, especially in Yazd City, it is important to conduct similar studies and obtain more accurate results to develop experimental therapeutic programs for the design and implementation of a comprehensive breast cancer registry system. Even though we included all possible patients in our study, the sample size was still small and was a limitation. Considering the high survival rate of breast cancer patients, it is necessary to consider longer study periods or multicenter studies and provide access to more patients, so that more accurate and generalizable results can be obtained. Based on our findings, we suggest that accounting for the BMI of patients and the duration of their OCP consumption, especially in the TNBC subgroup, can be effective at predicting and setting treatment schedules.

CONCLUSION

In our study, the mean survival rate of breast cancer patients was higher than that reported in similar studies worldwide. However, no significant correlation was observed between total survival and recurrence rates of patients with possible risk factors, except for BMI in the TNBC subgroup. Because of the relatively small sample size, it was impossible to evaluate the relationship between risk factors and survival rate. Finally, a significant relationship was observed between the mean duration of OCP consumption and breast cancer in the ER-PR-HER2-positive subgroup. However, investigating

the mechanism of this phenomenon was beyond the scope of this study.

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AUTHOR CONTRIBUTIONS

All authors contributed to this work and manuscript equally. All authors read and approved the final manuscript.

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