Breast Cancer Prognosis: A Literature Review.

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ABSTRACT

Breast cancer is the most prevalent malignancy among women in all around the world. Every year substantial numbers of women develop to this malignancy. Study about effective factors on survival and prognosis of these patients can lead to promote the quality of treatment protocols. There are some known genetic factors, drugs, environmental or nutritional factors those effect on prognosis of breast cancer. So in this review article, we decided to discuss about prognosis of patients with breast cancer and it's effective factors.
Keywords: Breast cancer, prognosis, review article.
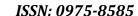
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INTRODUCTION

Currently, breast cancer stands as a major cancer-induced mortality factor among women all over the world. In 2008, about 1.3 million of new types of breast cancer were reported through the world. 458,000 of these patients were estimated to have died. One out of every 8 women born in America is likely to be afflicted by invasive breast cancer in her lifetime. Such risk factors which may increase affliction chance to this disease includes; age, familial history of the disease, radiation exposure, hormonal factors, obesity, alcohol consumption, smoking, immobility, white race, and breast density. The progression stage of the disease is the key factor determining the disease clinical outcome. Moreover, breast cancer is the most prevalent malignancy during pregnancy. About .2% to 2.6% of the total numbers of breast cancers occur during pregnancy (1). Among women suffering from breast cancer at the outset of its metastasis, the risk of metastasis to distant areas depends on the number of axillary lymph nodes as well as the tumor size. Since 1990, the prognosis of patients has improved and the mortality rate has decreased due to supplementary therapies and a higher precision of diagnostic tests (2). Although the prevalence of breast cancer was reported to be higher among the white race, the survival and prognosis of black patients after the diagnosis of the disease has been reported to be worse than the white. In addition, the presentation of the black and the Hispanic has been found to be worse in highly developmental stages of the disease (3). Breast cancer stage is considered to be the most important factor for determining the prognosis of the disease. The most prevalent categorization method of breast cancer stage is TNM system which consists of: T (tumor size), N (number and location of the lymph nodes involved) and M (existence or non-existence of metastasis). Breast cancer has five stages: 0, I, II, III, and IV. Broadly speaking, the initial stages have a better prognosis. A tumor's being invasive or non-invasive is another factor involved in predicting the prognosis of the disease(4). If ductal carcinoma in situ, as one type of non-invasive cancers, is treated properly, it will have an excellent prognosis. If it does not treat among patients afflicted with this type of cancer, the tumor cells turn into malignant types. Different types of invasive cancers do commonly originate from milk ducts or lobules (5). The prognosis of this type of cancer depends on the developmental stage of the disease. For diagnosis, some of these tumors require estrogen and progesterone. In fact, these cancers are hormone receptor positive. They can be improved using prognostic hormone therapy. Existence or non-existence of Human epidermal growth factor receptor-2 (HER2) is another factor influencing prognosis among these patients. Tumor cells, which have this protein on their surface, would show a more invasive pattern than the poor prognostic (3, 4). Proliferation rate indicates the invasion degree of cancerous cells. Lower proliferation rate leads to a slower rate of tumor growth and finally a better prognosis of the disease. In addition the mentioned issues, the type of the therapeutic protocol used for these patients could affect the prognosis process (6). Considering the remarkable prevalence of breast cancer and the significance of planning to treat the disease, in this review article, we investigate some of the therapeutic factors involved in the prognosis of the disease.

METHODOLOGY

In this review research which seeks to investigate the prognosis of breast cancer Pubmed database was explored. Reference was made to the clinical trials carried out and registered during the past 5 years in this database. To do the investigation, the key word 'breast cancer prognosis' was searched for. Inclusion criteria supposed all articles to be written in English; their research population needed to consist of human beings; the key terms searched for were supposed to be in their titles. Moreover, the articles were filtered for their age range. Eventually, those articles were selected which were carried out on women participants aged between 19 and 44 years.

Literature review:

In a study conducted by Labbezoo et al. to investigate the survival rate and the effect of the subgroups of breast metastatic cancer (HR and HER2), 815 patients afflicted with breast cancer between 2007 and 2009 were examined for an average of 21.8 months. In this research, patients were divided in 4 groups in terms of hormonal receptors HR and HER2: 1. HR+/HER2- 2. HR+/HER2+ 3. HR-/HER2+ 4. HR-/HER2- (Triple negative=TN). The findings of this research revealed that 66% of patients belonged to group 1, 15% to group 4, 11% to group 2, and 8% belonged to group 3. The longest survival time of an average 34.4 months belonged to group 2. According to the results of this study, sub-groups of breast metastatic cancer are recognized as an independent factor of prognosis (6).

In another research carried out by Scott et al. which aimed to investigate the effects of sports and a low-calorie diet on biomarkers correlated with long-term prognosis of breast cancer at primary stages (I to III) 90 women who suffered from this disease acted as the control group. Their age was 55.6±10.2 years. They had three sessions of physical exercises a week under supervision. They also attended nutrition seminars. In this study, waist/hip ratio, blood biomarkers correlated with breast cancer, risk of cardiovascular diseases and life quality were measured once at the outset of the study and once again after six months. The results obtained revealed that solo sports along with low-calorie diets positively affect long term prognosis among overweight women at lower stages of the disease (7).

In their investigation, Amant et al. examined prognosis among women afflicted with primary breast cancer whose disease had been diagnosed during pregnancy. In this study, 447 pregnant women at the age of 45 who suffered from BCP were compared prospectively and retrospectively with non-pregnant patients. Findings included that the total survival rate among BCP patients was the same as non-pregnant patients (8). In another research conducted by Jacques et al., the effect of neoadjuvant on operable triple negative tumors of breast cancer was investigated. In this study, the pathologic response made by patients who received consecutive chemotherapy with gemcitabine together with docetaxel and vinorelbine along with epirabicin was investigated. 74 women at the second and third stages of breast cancer received 6 two-week medical courses using gemcitabine 100 mg/m^2 along with docetaxel 75 mg/m^2 on the first and 15th days, and vinorelbine 25 mg/m^2 along with epirabicin 100 mg/m^2 on their 29th and 43rd days. Those patients who responded on the 56th day, received an additional course using docetaxel/gemcitabine on the 57th day and vinorelbine/epirabicin on the 71st day. Findings revealed the total pathologic response to be 22% which was higher among triple negative patients than others. Finally based on the results of this study, using a high dose of 4 medicines created an acceptable pathologic response in operable patients (9).

In their study, Frasci et al. investigated the effect of a weekly treatment before breast cancer operation using cisplatin, epirabicin and paclitaxel. In this study, the 12-week treatment using the three medicines was compared to the treatment which used paclitaxel and epirabicin together in patients suffering from locally advanced breast cancer. This study investigated the pathologic response before and after the treatment, relapse free survival, overall survival and distant metastasis free survival (DMFS). According to the findings of this research, the weekly diet with three medicines, as compared to the three-week treatment significantly improved OS and DMFS (4).

Muntch et al. conducted a study to compare the effect of neoadjuvant therapy in the form of an intensive or standardized dose of epirabicin and cyclophosphamide on the survival of patients afflicted with primary breast cancer. 733 patients received four therapeutic courses: Epirabicin 90 along with Cyclophosphamide 600 (EC to T treatment) every three weeks followed by 4 courses of Paclitaxel 175 every three week, or 3 courses of Epirabicin every two weeks followed by 3 courses of Paclitaxel 225 every two weeks followed by 3 courses of mixed treatments using Cyclophosphomide, methotrexate and Fluorouracil (E$_{dd}$ toT$_{dd}$ to CMF treatment). Results indicated that the degree of DFS in the 3-year EC to T treatment was 75.8%, compared to 78.8% in the E$_{dd}$ toT$_{dd}$ to CMF treatment. Therefore, this study revealed that the intensive dose of neoadjuvant treatment, as compared to the standardized dose, does not improve DFS (10).

Sherene Loi et al. investigated the prognostic effects of the known somatic mutations of breast cancer. In this study, 705 women were examined for an average of 62 months. A group of them were randomly selected and received Transluzumab for 9 weeks. According to the findings of this research, PIK3CA mutations are accompanied by better prognoses. Although this effect would disappear after 3 years, no significant correlation was observed between the mutations and improvement using Transluzumab (11).

In another research conducted by Uo.Huang et al., the effect of Grb14 on breast cancer patients' prognosis was investigated. The results of this research indicated that a high Grb14 expression is significantly correlated with a high overall survival. Moreover, the investigations in this study revealed that a high expression of Grb14 is a strong independent prognostic factor correlated with overall survival. Therefore, a high expression of Grb14 in breast cancerous cells can help to diagnose the disease in low-risk patients and help the extra therapies after neoadjuvant chemotherapy (5).

In their research, Saquib et al. investigated the effect of the supplementary treatment of CAM on the prognosis of breast cancer. In this study, 2,562 women who survived breast cancer participated. According to

the finding of this study, those women who received no systemic treatment were prone to a higher risk of breast cancer side effects and mortality. Finally, according to this study, the risk of the side effects and mortality of breast cancer was higher among patients who received no systemic treatments. The use of food supplements or CAM therapy would not alter this risk. Therefore, CAM therapy would not change the result of breast cancer and should not be used as a standardized treatment (12).

In another investigation carried out by Mishra, the correlation of vitamin D receptor gene polymorphisms (VDR) and breast cancer prognosis was explored among Hispanic and African-American women. Blood samples of 232 patients suffering from breast cancer and 349 healthy women were gathered and were analyzed in terms of 4 VDR genotypes via PCR-RFLP. According to the findings of this research VDR haplotypes were found to be correlated with FOKI FF genotype of VDR in African-American women afflicted with breast cancer was correlated with low prognosis (13).

In Jian-YiLi et al.'s study, distribution of MiR-374o in breast tumors was investigated as a main factor in the development of this disease. In this research, breast tissue samples of 40 patients afflicted with breast cancer were obtained and divided into two: 1. a highly invasive metastatic group (HIMG), and 2. a low invasive metastatic group (LIMG). The samples were extracted from the center and wedges of tumors. In each group, 6 samples were analyzed through microRNA and the other 14 samples through Western blot and immunohistochemistry. In this study, patients were monitored for 28 to 68 months after the surgery. Findings of this research revealed that the distribution of MiR-374o varies in breast cancer. In this study, VEGFA and VCAM-amRNA had a synchronous distribution. The results of this study can probably explain the divergent distribution of Micro Vessel density in breast cancer and the difference of prognosis of this cancer. No significant correlation was found between the distribution of MiR-374o and an improved prognosis (14).

CONCLUSION

Breast cancer is one of the major diseases a woman might encounter in her life. Its precise diagnosis is made possible only through microscopic methods. Upon diagnosis, the next immediate step would be to opt for a therapeutic method. This step is dependent on patient's prognosis. Several factors are involved in these patients' prognosis. Only some of them are investigated in this study. One key factor affecting cancerous patients' survival and prognosis is the expression of HR and HER2 hormonal receptors. That is to say those patients who have these two hormonal receptors have a higher prognosis (6). On the other hand, the nutritional diet was another influential factor in prognosis. In Frasci's study it was revealed that the weekly 3-medicine treatment (Cisplatin, Epirubicin and Paclitaxel) improved the overall survival and also distant metastasis free survival more than the monthly two-medicine (Paclitaxel and Epirobicin) treatment (4). In another study it was revealed that a treatment based on an intensive dose of neoadjuvant does not change the disease free survival as compared to the standard dose (10). Conducting a systemic therapy is part of the medical protocol of these patients. Although supplementary treatments can also be effective, they cannot replace systemic therapies. Therefore, the chances of the occurrence of breast cancer side effects are higher in women who have not received any systemic therapy (12). The expression of some genes can also affect prognosis in patients afflicted with breast cancer. Among them is Grb14. The expression of this gene is indirectly correlated with an increased survival chance among these patients (5). Sports and nutritional diet are among other factors influencing patients' prognosis. In Scotte et al.'s study it was revealed that solo sports and low-calorie diets positively influence the prognosis of obese women who are at the early stages of breast cancer (7). Findings of this study show that various factors either medical or non-medical can affect the prognosis and survival of patients suffering from breast cancer. Therefore, we suggest further cohort studies to investigate the effect of each and every factor influencing prognosis.

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