ISSN:2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 4, Issue, 6, pp. 1220-1223, June, 2014

International Journal of
DEVELOPMENT RESEARCH

Full Length Research Article

SURVIVAL RATE OF BREAST CANCER PATIENTS WITH DIFFERENT AGE GROUPS AND THE SUBTYPE OF BREAST CANCER

***Mansur Ahmed and Christian Bach**

Department of Biomedical Engineering, University of Bridgeport, Bridgeport, Connecticut, USA

ARTICLE INFO

Article History:
Received 31st March, 2014
Received in revised form
12th April, 2014
Accepted 08th May, 2014
Published online 25th June, 2014

Key words:
Survival rate,
Age,
Subtype,
Luminal A,
Luminal B,
HER2,
Estrogen Receptor (ER) and
Progesterone Receptor (PR).

ABSTRACT

Purpose – The study includes the comparison between older patience having the breast cancer with the younger ones, on the basis of their survival rate and characteristics of the tumor. The tumor characteristics is a crucial to be known for the increase in survival rate of the patient. The study elaborates the tumor characteristics and helps to identify the risk factors to be considered. Methodology – Retrospective analysis of several papers were done and there analysis are being compared to provide vital information on breast cancer patient and their survival rate. Findings – Patients who are >70 years old are commonly experiencing this types of breast cancer phenotypes – HER2+, positive axillary nodes. They also have lower breast cancer specific survival. As well as their distant metastasis free survival rates are low. Younger and older patients who have ER(−)/PR(−)/HER2(−) phenotypes of breast cancer had lower survival when compared to other age groups. Research limitations/implications – The status of the phenotypes ER, PR, and HER-2 phenotypes are not based on genotype assessment which brings a biasness to the selection of patients. Also the patients might experience multiple phenotypes of cancer which might hamper the result. The breast cancer subtype is done by immunochemistry or FISH method and not on genotype evaluation which increase the bias-ness in the selection of patients. Practical implications – Development of a standard treatment for older patients is very much required. Identifying the risk factors will bring light to the discussion of a proper procedure for the treatment of patients. More clinical researches on different age group of patients contributes to the discussion. Originality/value – The paper provides an adequate information on the relation with age of the patients with their survival rate along with emphasizing the particular phenotype of cancer they had.

Copyright © 2014Mansur Ahmed and Christian Bach. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Breast cancer diagnostics and treatment is adjusted with the age of patients (Baranovsky and Myers,1986). Younger breast cancer patients seem to have worse scenario then older patients (Kroman *et al*., 2000; Swanson and Lin, 1994; Colleoni *et al*., 2002 and Albain *et al*., 1994). Researches in the past few years have led to properly classify breast cancer according to the estrogen receptors (ER), progesterone receptors (PR) and HER-2 expressions (Sotiriou *et al*., 2003; Sørlie *et al*., 2001; Sørlie *et al*., 2003 and Perou*et al*., 1999), which is done by study of immunohistochemistry (Spitale *et al*., 2009). Breast cancer tumors can be classified using the statuses of ER, PR, and HER-2 (human epidermal growth factor 2) which are tumors. According to this the breast cancer subtype can be categorized as follows: luminal A (ER+ or PR+ and HER-2–), luminal B (ER+ or PR+ and HER-2+), HER-2 (ER– and PR– and HER-2+), and basal (ER– and PR– and HER-2–) (Brenton *et al*., 2005; Carey *et al*., 2006). The classified phenotypes each show different behavior and clinical outcomes with each age groups (Nguyen et a., 2008; Parise *et al*., 2009 and Sanpaolo *et al*., 2011). The purpose of this retrospective study is to provide an insight on the occurrence of each phenotype of breast cancer patients among different age subgroups and its prediction in a group of patients affected by breast cancer.

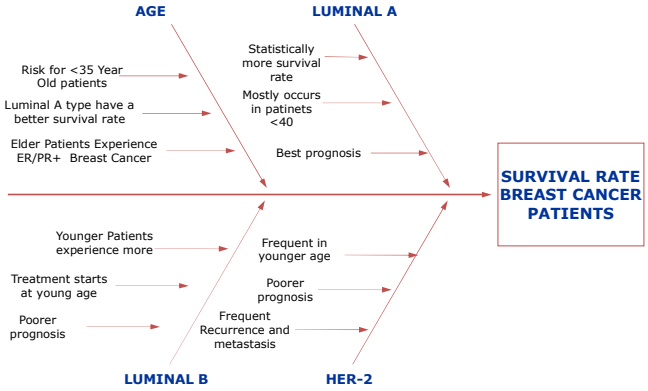
****Corresponding author: Mansur Ahmed***
Department of Biomedical Engineering, University of Bridgeport, Bridgeport, Connecticut, USA

MATERIALS AND METHODS

This research was based on the study of several articles mainly (Sanpaolo *et al*., 2012; Daidone *et al*., 2003; Nikolic-Vukosavljevic *et al*., 2001 and Molino *et al*., 2006) evaluating several medical records. The information compiled contained the record of age at diagnosis, tumor size, surgical margins,

estrogen and progesterone receptor status and HER-2 status. Hormonal therapy was administered after the surgery or after chemotherapy schedule was completed. Information was analyzed firstly by graphical methods in the article and then the survival rate was compared on the basis of breast cancer specific survival (BCSS) which is the interval between the date at which the surgery was done and the expiration date of the patient from breast cancer, distant metastasis free survival (DMFS) which is the time interval from the date the surgery was performed to the appearance of a distant recurrence of the cancer and local relapse free survival (LRFS) which is the time interval from the date of surgery to local breast relapse.

Factors to be considered



RESULTS AND DISCUSSION

To improve the survival of the patients a good prognosis is required. For that the treatment regimen should be planned and executed as early as the breast cancer is developed. For that several factors must be evaluated for a proper treatment of breast cancer patients and thus increase their survival outcome. The factors as mentioned in the introduction part are the subtypes of breast cancer namely Luminal A (ER+ or PR+ and HER-2–), Luminal B (ER+ or PR+ and HER-2+), and HER-2+. It is highly required to know the subtype of the tumor to plan the treatment. This along with the age of the patients helps to develop the proper treatment. The model below projects a clear idea about the relationship between the factors and the survival of the patients.

Age of Patient

The study evaluated the HER2+ condition is more frequent in young aged patients then older ones. Patients who are < 40 years old had a lower chance of Luminal A [ER(+)/PR(+)/HER2(−)] phenotype of breast cancer from occurring. The chances of occurrence of basal [ER(−)/PR(−)/HER2(−)] phenotype which is also known as "triple negative" remain almost same between younger and older patients. A linear correlation was found when comparing between age and ER(+)/PR(+)/HER2(−) and ER(−)/PR(−)/HER2(−) phenotypes. Younger and older patients both are more likely to have experienced a mastectomy (Sanpaolo *et al*., 2012). Older patients more often undergo an invasive ductal carcinoma, while younger patients received both CT and HT more frequently. On the other hand, older patients did not receive HT. Older patients had a HER2(+)/ER(−)/PR(−) phenotype more frequently (Sanpaolo *et al*., 2012). The distribution of ER(−)/PR(−)/HER2(−) subtype of breast cancer was similar between younger and older patients. Considering the all articles being studied, mean 5-year BCSS, DMFS and LRFS rates showed a great number of people had survived for more than 5 years after the treatment of cancer. It also shows the fact that less amount of people have recurrence of the cancer as a result leading a healthy life. There were no significant differences found among DMFS and LRFS rates stratified by age subgroups. With respect to phenotypes, women with HER2(+)/ER(−)/PR(−) subtype of breast cancer had the lowest 5-year LRFS rate (Sanpaolo *et al*., 2012).

With relation to the facts mentioned above another report showed great agreement. It is verified that predominantly ER(+) tumor i.e. Luminal A or B subtype developed in elderly women (Diab *et al*., 2000; Rosen *et al*., 1985; Molino *et al*., 2006; Daidone *et al*., 2003; Hébert-Croteau *et al*., 2004; Martelli *et al*., 1993; Nixon *et al*., 1994 and Clark *et al*., 1984). Also patients who are greater than 40 years old presented probability of PR(+) tumors occurrence which is also Luminal A or B subtype (Molino *et al*., 2006 and Daidone *et al*., 2003). As a result a higher proportion of ER(+)/PR(+) tumors in these subgroup of age was observed. Nevertheless, a greater proportion of ER(+) but PR(−) tumors in patients, older than 50 years, was reported by the paper presented by Quong *et al*. (2002). These contributes in understanding the fact that breast cancers from women older than 40 years old lost the binding function to SP1DNA which is necessary for PR gene expression Quong *et al*. (2002). Finally, as stated by Molino *et al*. (2006), it can be noted that the percentage of occurrence of ER(−) and PR(−) tumors decreased with increasing age. Also the occurrence of ER(−)/PR(+) tumors is low.

Some authors (Ihemelandu *et al*., 2007) illustrated the fact that triple negative subtype had a shorter BCSS compared with other phenotypes. It also concludes that women of age < 35 years old had a shorter BCSS compared with women of age > 35 years old. It was also reported that patients older than 80 years had a shorter mean survival. Other authors (Parise *et al*., 2009) reported that patients with Luminal A [ER(+)/PR(+)/HER2(−)] subtypes had a statistically better survival (5 years) compared with other subtypes. Lowest BCSS and DMFS was observed in patients having the ER(−)/PR(−)/HER2(−) subgroup. Older patients (>70 years old) had lower BCSS and DMFS compared to other age subgroups, while younger patients (≤40 years old) had lowest BCSS. The most common explanation for this is that patients affected by ER(−)/PR(−)/HER2(−) phenotype cannot receive adjuvant therapies such as trastuzumab or hormone therapy (Daidone *et al*., 2003).

The Different Subtypes

Luminal A subtype shows the receptor status – ER(+)/PR(+)HER2(−). From the studies it can be deduced that patients who are less than 40 years old had a lower chance of Luminal A [ER(+)/PR(+)/HER2(−)] phenotype of breast cancer from occurring. This phenotype is more commonly occurs in elderly patients as they developed predominantly ER(+) breast type cancers i.e. Luminal A or B subtype of breast cancer (Diab *et al*., 2000; Rosen *et al*., 1985; Molino *et al*., 2006; Daidone *et al*., 2003; Hébert-Croteau *et al*., 2004; Martelli *et al*., 1993; Nixon *et al*., 1994 and Clark *et al*., 1984). Also patients > 40 years old presented more probability of

PR(+) tumor occurrence which is also Luminal A or B subtype (Molino *et al*., 2006 and Daidone *et al*., 2003). It can be deduced that a higher proportion of ER(+)/PR(+) tumors occurs in patients who are greater than 40 years old. According to the statistical data present patients with Luminal A [ER(+)/PR(+)/HER2(−)] subtypes have better survival (5 years) compared to other subtypes and also they have better prognosis than the other subtypes. Thus their survival rate is better. In comparison Luminal B subtype had poorer prognosis. It usually occurs to younger patients and the treatment should be started at early age. On the other hand HER2 patients have poorer prognosis with a lower survival rate. The recurrence rate is high meaning that the cancer may occur again or the cancer bed may remain for the cancer to re-grow. More dangerous subtype of cancer is considered to be ER(−)/HER2(−) tumors, which compared to other subtypes of tumors is observed to have poorest prognostic (Nikolic-Vukosavljevic *et al*., 2001; Keshgegian *et al*., 1996).

Contribution and Insight

The need for a better treatment of cancer is a necessity. The requirement of a proper diagnosis is thus required at early stage of the tumor development. For this the factors need to be clarified as much as possible and extensive evaluation of the different receptors involved in the tumor development along with age are some of the factors that affect the survival rate of the patients. The more detailed analysis of the cancer type may produce great improvement in mortality of the patients. Some of the drug related treatment include administering hormonal drugs. Few examples are given below –

Tamoxifen – is recommended to pre or postmenopausal women with ER(+)/PR(+) subtype.
Anastrozole – is recommended to postmenopausal women with early stage of ER(+)/PR(+) subtype.

Different subtypes of breast cancer require a different line of treatment. For Luminal type breast cancer it endocrine therapy is mostly recommended but the response may be different for Lumnal A and B to tamoxifen and aromatase. Luminal B shows a better response on administering chemotherapy then Luminal A. Also it was previously mentioned that prognosis in Luminal A cancer is better than in Luminal B (Schnitt, 2010). HER2 subtype of breast cancer responses to therapy including trastuzumab (Herceptin). Although it generally has poor prognosis, anthracycline-based chemotherapy seems a promising procedure for therapy (Schnitt, 2010). "Prevention is better than cure." Recently it has come to the attention that the effect of taking preventive measures may have a huge impact on the incidence of cancer, its diagnosis and treatment. The principal concept of this effort embeds upon chemoprevention and surgery. However lifestyle issues might also contribute to the prevention of breast cancer occurrence (Lebovic *et al*., 2010).

Conclusion

More and more research needs to be carried out to properly analyze the risk factors and design better treatment procedures for the individual patients. The ultimate goal should be to try to improve the condition of patients even after the treatment.
A limitation of the study done in the literatures reviewed is that, the immunochemistry or FISH tests are being done to know the classification of ER, PR, and HER-2 status. Genotype evaluation is not being done. Hence, it increase the bias-ness in the selection of patients. There are other methods present for gene profiling but immunochemistry or FISH methods are considered to be a valid alternative to classify breast cancer. They are also helpful in making decisions on therapy in daily practice. The study showed that –

- HER2(+) occurrence is more in younger patient and they are less likely to experience ER(+)/PR(+)/HER2(−) phenotype.
- Older patients have a high chance of experiencing an invasive ductal carcinoma. They did not require to receive HT.
- Prognosis in Luminal A cancer is better than in Luminal B. HER2+ and have a poorer prognosis with low LRFS rate.

From this study it can be concluded that all patients showed a relevance between their ages. As a result it can be said that breast cancer occurrence is highly affected by tissue age. Women should be diagnosed at least once a year to be aware of their health and prevent breast cancer. Breast cancer awareness campaign helps identify the breast cancer subtype and the prognosis. Even after treatment of breast cancer the patient should have consecutive follow-up check-ups to prevent recurrence of breast cancer.

Acknowledgment

First of I would like to thank the Almighty Creator, Who has given me the opportunity and privilege to write this article. I would like to thank Prof. Christian Bach for his immense support by supervising me to write this paper. I would also like to thank my parents, family and my friends for their constant support.

REFERENCES

Baranovsky, A. and M.H. Myers, *Cancer incidence and survival in patients 65 years of age and older.* Ca-A Cancer Journal for Clinicians, 1986. 36(1): p. 26-41.

Kroman, N., *et al*., *Factors influencing the effect of age on prognosis in breast cancer: Population based study.* British Medical Journal, 2000. 320(7233): p. 474-478.

Swanson, G.M. and C.S. Lin, *Survival patterns among younger women with breast cancer: the effects of age, race, stage, and treatment.* Journal of the National Cancer Institute. Monographs, 1994(16): p. 69-77.

Colleoni, M., *et al*., *Very young women (<35 years) with operable breast cancer: Features of disease at presentation.* Annals of Oncology, 2002. 13(2): p. 273-279.

Albain, K.S., D.C. Allred, and G.M. Clark, *Breast cancer outcome and predictors of outcome: are there age differentials?* Journal of the National Cancer Institute. Monographs, 1994(16): p. 35-42.

Sotiriou, C., *et al*., *Breast cancer classification and prognosis based on gene expression profiles from a population-based study.* Proceedings of the National Academy of Sciences of the United States of America, 2003. 100(18): p. 10393-10398.

Sørlie, T., *et al*., *Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications.* Proceedings of the National Academy of Sciences of the United States of America, 2001. 98(19): p. 10869-10874.

Sørlie, T., *et al*., *Repeated observation of breast tumor subtypes in independent gene expression data sets.* Proceedings of the National Academy of Sciences of the United States of America, 2003. 100(14): p. 8418-8423.

Perou, C.M., *et al*., *Distinctive gene expression patterns in human mammary epithelial cells and breast cancers.* Proc Natl Acad Sci U S A, 1999. 19: p. 18-27.

Spitale, A., *et al*., *Breast cancer classification according to immunohistochemical markers: clinicopathologic features and short-term survival analysis in a population-based study from the South of Switzerland.* Annals of Oncology, 2009. 20(4): p. 628-635.

Brenton, J.D., *et al*., *Molecular Classification and Molecular Forecasting of Breast Cancer: Ready for Clinical Application?* Journal of Clinical Oncology, 2005. 23(29): p. 7350-7360.

Carey, L.A., *et al*., *RAce, breast cancer subtypes, and survival in the carolina breast cancer study.* JAMA, 2006. 295(21): p. 2492-2502.

Nguyen, P.L., *et al*., *Breast cancer subtype approximated by estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after breast-conserving therapy.* Journal of Clinical Oncology, 2008. 26(14): p. 2373-2378.

Parise, C.A., *et al*., *Breast cancer subtypes as defined by the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2) among women with invasive breast cancer in California, 1999-2004.* Breast Journal, 2009. 15(6): p. 593-602.

Sanpaolo, P., V. Barbieri, and D. Genovesi, *Prognostic value of breast cancer subtypes on breast cancer specific survival, distant metastases and local relapse rates in conservatively managed early stage breast cancer: A retrospective clinical study.* European Journal of Surgical Oncology (EJSO), 2011. 37(10): p. 876-882.

Sanpaolo, P., *et al*., *Patients younger than 40 years old and older than 70 years old affected by ER(−)/PR(−)/HER2(−) breast cancer have low survival rates: Results of a mono-institutional retrospective analysis.* Journal of Geriatric Oncology, 2012. 3(4): p. 312-319.

Daidone, M.G., *et al*., *Primary breast cancer in elderly women: biological profile and relation with clinical outcome.* Critical Reviews in Oncology/Hematology, 2003. 45(3): p. 313-325.

Nikolic-Vukosavljevic, D., *et al*., *Natural history of estrogen receptor-negative, progesterone receptor-positive breast cancer.* The International journal of biological markers, 2001. 17(3): p. 196-200.

Molino, A., *et al*., *Pathological, biological and clinical characteristics, and surgical management, of elderly women with breast cancer.* Critical Reviews in Oncology/Hematology, 2006. 59(3): p. 226-233.

Diab, S.G., R.M. Elledge, and G.M. Clark, *Tumor Characteristics and Clinical Outcome of Elderly Women With Breast Cancer.* Journal of the National Cancer Institute, 2000. 92(7): p. 550-556.

Rosen, P.P., M.L. Lesser, and D.W. Kinne, *Breast carcinoma at the extremes of age: A comparison of patients younger than 35 years and older than 75 years.* Journal of Surgical Oncology, 1985. 28(2): p. 90-96.

Hébert-Croteau, N., *et al*., *Compliance With Consensus Recommendations for Systemic Therapy Is Associated With Improved Survival of Women With Node-Negative Breast Cancer.* Journal of Clinical Oncology, 2004. 22(18): p. 3685-3693.

Martelli, G., *et al*., *Surgical resection plus tamoxifen as treatment of breast cancer in elderly patients: a retrospective study.* European Journal of Cancer, 1993. 29(15): p. 2080-2082.

Nixon, A.J., *et al*., *Relationship of patient age to pathologic features of the tumor and prognosis for patients with stage I or II breast cancer.* Journal of Clinical Oncology, 1994. 12(5): p. 888-94.

Clark, G.M., C.K. Osborne, and W.L. McGuire, *Correlations between estrogen receptor, progesterone receptor, and patient characteristics in human breast cancer.* Journal of Clinical Oncology, 1984. 2(10): p. 1102-9.

Quong, J., *et al*., *Age-dependent changes in breast cancer hormone receptors and oxidant stress markers.* Breast cancer research and treatment, 2002. 76(3): p. 221-236.

Ihemelandu, C.U., *et al*., *Molecular Breast Cancer Subtypes in Premenopausal and Postmenopausal African-American Women: Age-Specific Prevalence and Survival.* Journal of Surgical Research, 2007. 143(1): p. 109-118.

Keshgegian, A.A. and A. Cnaan, *Estrogen receptor-negative, progesterone receptor-positive breast carcinoma: poor clinical outcome.* Archives of pathology & laboratory medicine, 1996. 120(10): p. 970-973.

Schnitt, S.J., *Classification and prognosis of invasive breast cancer: from morphology to molecular taxonomy.* Mod Pathol, 2010. 23(S2): p. S60-S64.

Lebovic, G.S., A. Hollingsworth, and S.A. Feig, *Risk assessment, screening and prevention of breast cancer: A look at cost-effectiveness.* The Breast, 2010. 19(4): p. 260-267.

****