

SURVIVAL RATES TO WOMAN WITH BREAST CANCER: REVIEW

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ABSTRACT: Integrative research that aimed to identify results in the publications available through the databases LILACS, SciELO and PubMed, period 2004-2009, the contributing factors to the increment of the survival rates in five years and the disease-free survival rate in five years in women with breast cancer. The results in 40 publications showed a higher incidence of the disease for the age groups between 50-60 years and 40-49 years. Screening programs, genetic, immunohistochemical and cytological diagnostic methods, increment of the education and socioeconomic patterns, associations of conventional therapies with new therapies contribute to the increase of survival rates, quality of life and care for women with breast cancer.

DESCRIPTORS: Survival rate. Breast cancer. Early diagnosis.

TAXA DE SOBREVIDA NA MULHER COM CÂNCER DE MAMA: ESTUDO DE REVISÃO

RESUMO: Revisão integrativa que identificou nas publicações da LILACS, SciELO e PubMed, período 2004-2009, fatores contribuintes para a elevação das taxas de sobrevida em cinco anos e sobrevida livre de doenças em cinco anos das mulheres com câncer de mama. Os resultados, 40 publicações, demonstraram maior incidência da doença nas idades 50-60 e 40-49 anos. Programas de rastreamento, elevação da escolaridade, do padrão socioeconômico, métodos diagnósticos genéticos, imuno-histoquímicos e citológicos, associação das novas terapêuticas com as convencionais são fatores contribuintes para elevação das taxas de sobrevidas, da qualidade de vida e do cuidado à mulher com câncer de mama.

DESCRIPTORIOS: Taxa de sobrevida. Neoplasias da mama. Diagnóstico precoce.

TASA DE SUPERVIVENCIA EN MUJER CON CÁNCER DE MAMA: ESTUDIO DE REVISIÓN

RESUMEN: Investigación integrativa que identificó en las publicaciones de LILACS, SciELO y PubMed en el período 2004-2009, los factores contribuyentes para la elevación de las tasas de supervivencia en cinco años y supervivencia libre de enfermedades en cinco años de las mujeres con cáncer de mama. Los resultados de 40 publicaciones, demuestran que la mayor incidencia de la enfermedad se dio entre los 50-60 años y 40-49 años. Programas de rastreo, elevación de la escolaridad, del patrón socioeconómico, estudios genéticos, inmunohistoquímicos y citológicos además de las terapéuticas convencionales favorecen a la elevación de las tasas de supervivencia, la calidad de vida y de los cuidados de la mujer con cáncer de mama.

DESCRIPTORIOS: Tasa de supervivencia. Neoplasias de la mama. Diagnóstico precoz.

INTRODUCTION

Each year approximately 1.3 million women are affected by breast cancer worldwide, making it the most common malignancy in females. Some risk factors are related to breast cancer. The increasing age of the woman is one of these factors, with the incidence doubling every ten years until the menopause.¹⁻⁴ Geographic variations, ethnicity and race are also influential. In the West, the number of cases of breast cancer is higher than in the East. Early menarche and late menopause increase the risk for breast cancer, as well as nulliparity and an increased age at the first birth.^{2,4}

A family history of breast cancer before the age of 40, bilateral breast cancer, ovarian cancer, male breast cancer (first degree parent), among other factors, demonstrate that the genetic predisposition accounts for 10% of breast cancer cases. The genes breast cancer 1 (BRCA1) and breast cancer 2 (BRCA2) are associated with the onset of the disease.^{2,4} Benign breast diseases are also other indications for breast cancer. For example, women with atypical epithelial hyperplasia have a four to five times higher risk of developing breast cancer than women who do not show proliferative alterations in their breast.^{2,4} Exposure to ionizing radiation, particularly during the mammary development period, doubles the risk. A high-fat diet does not seem to be a really strong indication for breast cancer. Being overweight, however, is associated with increased risk in the postmenopausal period and the intake of alcohol contributes as a risk factor. Smoking does not directly influence the onset of disease.² During the period of oral contraceptive use and for ten years after its disuse, there is a small increased risk of developing breast cancer. The users of hormone replacement therapy also have an increased risk, especially if using the combination of progesterone and estrogen.²

Many of these factors can not be prevented. Furthermore, little is known today about the factors that may prevent the incidence of breast cancer. Therefore, early screening is still the best way to control the disease and configures one of the strategies to increase the survival rate of the women.² Survival refers to the occurrence of a specific event of interest, starting from an initial time until a final time, for example, from the diagnosis of breast cancer to the death.⁵

The main parameters of the analysis of survival are constituted by the probability of survival over each interval of time considered and the probability of accumulated survival. Thus, the analysis of survival means the likelihood of survival from zero time until the final time considered.⁶ Knowing the factors that contribute to increased survival rates among women with breast cancer may help define early detection actions, and improve treatment and care proposals, in the nursing area as well as in all the areas of health. Therefore, this study aims to identify, in the publications of the Latin American and Caribbean Health Science Literature (LILACS), Scientific Electronic Library Online (SciELO) and United States National Library of Medicine - PubMed, for the period 2004-2009, factors contributing to the higher rates of survival at five years and disease-free survival at five years for women with breast cancer.

METHOD

This is an integrative review, developed using publications indexed in the LILACS, SciELO and PubMed databases. These databases were chosen due to their scientific coverage of the areas of healthcare and nursing. The integrative review makes it possible to deduce generalizations about substantive issues from a set of study results. It therefore contributes to the synthesis, analysis and development of a body of knowledge from the studies investigated.⁷ The research question that gave rise to the study was: which factors contribute to increased survival rates among women with breast cancer?

The terms used to search the databases were: In the LILACS database, *câncer de mama* AND *taxa de sobrevivida*; in SciELO *câncer de mama* OR breast cancer, *taxa de sobrevivida* OR survival rate; in PubMed, breast cancer AND survival rate. Note: *câncer de mama* = breast cancer; *taxa de sobrevivida* = survival rate. The limits adopted were, publications from July 2004 to July 2009, which considered females and were published in English, Spanish or Portuguese. For the PubMed database, only articles available in full were included.

The inclusion criterion established was that the publications should present the survival rate of women with breast cancer at five years or the disease-free survival rate at five years. For the application of the inclusion criteria all

the abstracts were read. For articles in which the abstracts did not present criteria for inclusion and exclusion clearly, the full text was read. The search for publications using the established terms provided 317 articles, 5 in LILACS, 22 in SciELO and 290 in PubMed and of these 40 met the inclusion criteria. The publications included in the study were read in full.

The study designs of the 40 publications included in this investigation were: one case-control study, three randomized studies, five clinical trials, five historical and/or retrospective cohort studies, nine survival analysis studies and 17 transversal epidemiological studies. The publications originated from 20 countries: Korea (six studies),⁸⁻¹³ Japan (five studies),¹⁴⁻¹⁸ Brazil (four studies),^{3,19-21} Canada (three studies),²²⁻²⁴ United States (three studies),²⁵⁻²⁷ Italy (three studies),²⁸⁻³⁰ Switzerland (three studies),³¹⁻³³ France (two studies),^{34,35} China (one study),³⁶ Singapore and Sweden (one study, study performed in both countries),³⁷ Scotland (one study),³⁸ Spain (one study),³⁹ Finland (one study),⁴⁰ India (one study),⁴¹ England (two studies),^{42,45} Mexico (one study),⁴³ Poland (one study),⁴⁴ and the Netherlands (one study).⁴⁶

From the aim established for this study, the variables to be investigated were defined: the study design, study site/country, number of subjects, age of the subjects, five year survival rate, disease-free five year survival rate, factors that contribute to the increase in survival rates. For the data collection an investigation form was developed. The data were entered into Microsoft Excel spreadsheets.

RESULTS AND DISCUSSION

The total number of subjects, as regards the 40 publications, was 1,152,521, with the minimum number of subjects being seven (clinical trial)²⁶ and the maximum 1,000,000.⁴⁶ The study that included 1,000,000 subjects was conducted in the Netherlands and evaluated the impact on survival according to the socioeconomic status, after the implementation of a mammography breast cancer screening program. The study highlighted that, despite the high participation of women with lower socioeconomic status, the survival rates arising from the implementation of the screening program were higher in

the women with higher socioeconomic status. This result is justified due to the prevalence of comorbidities and treatments that did not cover diseases concomitant to the cancer in more underprivileged women.⁴⁶

The epidemiological data encountered indicated that the highest incidence for breast cancer is in the age group of 50 and 60 years, followed by the age group 40 to 49.^{3,20,39,43} Thus, this reaffirms the necessity of conducting mammography examinations from the age of 50, as established by the International Consensus for the Control of Breast Cancer,⁴⁷ and the Brazilian initiative, which instituted mammography for all women from the age of 40 approaching this reality. This initiative was enacted by Law 11.664/08, which made effective healthcare actions that ensure the prevention, detection, treatment and monitoring of the cancers of the cervix and breast, in the context of the Brazilian National Health System (SUS), with this initiative, anticipation mammography for 40 year olds, being contrary to the international consensus.⁴⁸

Relating the survival rate to education, studies have shown that women with higher education had overall five-year survival rates equivalent to 92.2%, for women with education up to the high school level the rate drops to 84%; elementary education to 73.6%; and illiterate to 56%. The illiterate women are about seven times more likely to die than those with higher education. The increased level of education indicates a tendency for the risk of death to decrease.^{3,21,34}

Socio-economic status is an important factor in the survival of women with breast cancer. A population based study developed with French women with breast cancer showed that survival was higher in the women with higher socioeconomic standards, with higher education, and with more children. The greater number of children contributes because these women visit the gynecologist more often,³⁴ which facilitates the health monitoring and evaluation by the nurse. More than the absolute differential of the socioeconomic level, the influence of the access to healthcare services may explain the inverse relationship between the decrease in late diagnosis and increasing educational levels.⁴⁹ Neither can the cultural differences be disregarded, because with them there is the issue of the heterogeneity

of access to healthcare and quality treatment.³³ Women of higher socioeconomic status benefit more from the therapy, regardless of the disease stage. The uneven ratio relative to the lowest socioeconomic class can be explained by lifestyle, by higher rates of obesity and smoking, which contribute to worsen the general health during the treatment and include the association of smoking related diseases. Comorbidities are more common in individuals with lower socioeconomic status, reducing the survival rates.⁴⁶ Nurses should pay attention to these contributing factors in the data collection for the nursing history, as this may indicate specific interventions.

Given these findings, it is relevant to develop healthcare and education policies that facilitate access to information and the possibility of an education that contributes to professional and socioeconomic development, facilitating the adoption of care that encourages healthier living.

Screening programs for the early detection of breast cancer, increased schooling and higher socioeconomic levels represent factors which contribute to increase the survival rates and to decrease the emergence of the disease in its advanced stages. A study conducted with 27,377 women from Singapore and Sweden showed that the white race is predominant in the diagnosis of breast cancer and presents higher survival (76.9%) than women of black, brown, yellow and indigenous races when grouped (62.2%).²¹ Among Mexican women the most frequent diagnosis is in stages II (55.6%) and III (34.8%), with the five-year survival being higher among women diagnosed in stage I (82%) and reduced to 59.9% when associating all stages. The lowest survival corresponds to stages IIIB (47.5%), IIIA (44.2%) and IV (15%).⁴³ A similar result was found in the Spanish study, in which the diagnosis of breast cancer was more frequent in stage II (42%) and the survival at five years was 95%. Women diagnosed at early stages have higher percentages of survival. In the *in situ* stage 100% of the women survived, in stage I and II 99.3% survived, in stage III 92.9% survived and in stage IV 63.9% survive.³⁹

A Brazilian study conducted in the state of Minas Gerais, described the predominance of stage II and III (86%), where among patients with stage III, 27.9% died.²⁰ In the state of Santa Catarina, only 18.1% of women were diagnosed with stage

I, with them having the best overall survival at five years (93.6%), whereas the women diagnosed with stage IV had the worst overall survival at five years (27.3%). The risk of death for women with stage III was 7.18 times that of those with stage I, and those with stage IV at diagnosis were 19.49 times more likely to die.²¹

Regardless of the survival rate and of the staging, physical and psychosocial implications arising from the illness are usually present, which require the healthcare and nursing team to provide a care plan aimed at the rehabilitation of the women. This is a global and dynamic process directed toward the physical and psychological recovery of women affected by cancer, aiming to treat or alleviate the disability caused by the disease and treatment, to support the social reintegration and to maintain the quality of the survival. In this context, the rehabilitation is associated with an expanded concept of health, which incorporates the biopsychosocial and spiritual well-being that all individuals have the right to.⁵⁰

Considering the size of the tumor, the diagnosis of breast cancer tends to be performed by self-examination with the tumor greater than 2.0 cm, varying between 2.0 and 5.0 cm.^{8,14,20,38,43} This result demonstrates the difficulty for the healthcare systems to diagnose breast cancer in the early stages, especially with the absence of metastasis, when the disease is easy to control and potentially curable.

Regarding the survival rate at five years, this was investigated by 36 studies (90%), and the results showed a variation in the rate from 49% to 100%. The rate of disease-free survival at five years was investigated by four studies (10%), and the results showed a variation from 24% to 95.3%. Survival presents a significant decrease with increasing tumor size (up to 2.0 cm: 87.2%, greater than 2.0 cm: 78.9%) and with the disease stage (I: 90%; II: 89%; III: 68.7%).¹¹ The presence of lymph node metastases in the breast cancer is a predictive factor for the survival and recurrence of the disease in the women, reducing survival by 40% when compared to the survival of women with non-metastatic disease.⁴³ In Italy, between 1996 and 2000, the five-year survival rate was 94% in the group detected by the screening program. In the unscreened group the rate was 84%. The rate of disease-free survival at five years

was 89% for the screened group and 75% for the unscreened group.³⁰

The survival of Canadian women with invasive breast cancer (between 50 and 70 years of age) diagnosed from mammographic screening before 1997 with annual mammography, was 95.2% at five years and 90.4% at ten years. For the diagnoses that took place after 1997 with biannual mammography this percentage was 94.6% at five years and 89.2% at ten years. Thus, there was no significant increase in survival for the women screened annually. However, comparing the results of annual and biannual screening over ten years, it was observed that there was an decrease of 1.2% in the specific survival of the women screened biannually.²³ It is noteworthy that this integrative review investigated five-year survival, during which there is a higher tendency for survival. The investigation of survival at ten years or more would probably demonstrate lower rates. It is also evident that the screening programs contribute to the control and early detection of breast cancer.

Of the predictive factors, the most important for a better prognosis are the absence of metastatic lymph node involvement and the presence of estrogen receptors. This strengthens the importance of the diagnosis and treatment in the initial stages, increasing the chance that the disease has not yet invaded the axillary lymph nodes, which increases the survival, the possibilities of a cure and permits the adoption of less aggressive treatments.^{3,13,19} Among the women with tumors greater than 2.0 cm, 71.1% of them presented lymph node involvement. The majority of the women presented more than ten compromised lymph nodes.²⁰

Only early diagnosis can alter this reality and consequently increase the survival rate of women with breast cancer, especially when the screening is associated with the development of effective therapy after the early detection of the disease. The prioritization of the early diagnosis, primarily in the nursing and medical care, with guidance, information and consistent care practices, can significantly alter the sad reality of delayed breast cancer diagnosis, as well as quick access to health-care services and resolvability from the planning in the diagnostic and therapeutic steps.

With respect to the therapies, currently, less mutilating surgery is a trend and some stud-

ies evaluate the survival from this new form of therapy. The five-year survival for women who underwent surgical breast conservation treatment was 92% and for women who underwent total mastectomy was 93%. However, in both the total mastectomy and the breast conserving surgery, when there is axillary involvement, axillary dissection is essential to avoid the risk of local recurrence and spread of the disease. Breast conservation is contraindicated when there is already a predictive factor for skin invasion.^{15,33}

Adjuvant radiotherapy was identified by the studies as a therapy with a good prognosis after surgical treatment. The result is favorable for younger women, for those with advanced stage tumors and when there is lymph node involvement. Locoregional radiation is also indicated in cases where adjuvant chemotherapy is indicated, since the addition of this therapy is important for achieving a higher cure and survival rate.⁴¹⁻⁴²

Regarding the use of hormone therapy, a Swiss study showed that in postmenopausal, hormone receptor positive women with breast cancer, adjuvant therapy with letrozole reduces the risk of disease recurrence, particularly metastasis, when compared with tamoxifen.³² A Canadian study concluded that radiotherapy combined with tamoxifen reduces the risk of axillary recurrence of breast cancer and axillary recurrence after quadrantectomy in axilla negative and hormone receptor positive women with small tumors.²⁴ These and other current indications, favor the individualized therapy plan, contributing to increased survival.

The survival rate for the patients with mutations in BRCA2 is lower (81%) than for those negative for mutations in BRCA2 (91%).²⁸ Women with breast cancer who are Human Epidermal Growth Factor Receptor 2 (HER2) positive have a 30% to 50% risk of disease recurrence, using conventional therapies. The combined use of doxorubicin, cyclophosphamide, and paclitaxel, with one additional year of trastuzumab, demonstrates a 52% reduction in the recurrence of the disease and a 33% reduction in the mortality risk compared with women who did not receive trastuzumab.²⁶ Positive cyclin E expression, detected by immunohistochemical analysis is indicative of a poor prognosis regarding invasive ductal breast cancer, especially in women with positive lymph nodes,

as is Maspin expression, which plays an important role in the tumor invasion and metastases.^{10,44}

The identification of FOXA1 expression (a member of the family of transcription factors associated with estrogen receptors) is useful in the therapeutic decision. The positive expression is related to better survival.²² High levels of protein Erβ2 also improve relapse free survival.⁴⁵ Vascular endothelial growth factor is an important regulator of angiogenesis and vascular permeability and has been associated with advanced stages and survival of several cancers. A Chinese study evaluated the association of functional polymorphisms of the gene for vascular endothelial growth factor with breast cancer survival. The results suggest that it is a significant genetic marker for determining the breast cancer prognosis.¹⁸ These results demonstrate the importance of the diagnostic methods that currently exist, as they support the professionals in the comprehension and treatment of breast cancer.

CONCLUSION

The publications that make up this integrative review present contributing factors that increase the survival rate of women with breast cancer. Thus, the research question was answered and the proposed aim achieved. The results reaffirm that detection through screening programs represents an alternative that favors the diagnosis of the disease in the initial stages, which in turn contributes to curative treatment and/or higher survival rates. It is emphasized that the diagnosis in the initial stages, with tumors identified by imaging examinations while they are still small, absence of lymph node compromise, women with higher socioeconomic standards and with higher levels of education, are contributing factors directly related to higher survival rates and to the reduction of the discovery of the disease in its advanced stages.

Therapeutic radiotherapy being cited as a contributing factor in the treatment of women with breast cancer reaffirms the need for the expansion of Radiotherapy Services in Brazil, performed by only 191 services (services registered with the National Nuclear Energy Commission). Considering the territorial area of Brazil and the incidence of the cancer, it is necessary to expand this form of

therapy and the access to it, as well as to increase the number of specialist professional nurses that work in this area.

The newly discovered therapies, including monoclonal antibodies such as *trastuzumab*, the use of taxanes and the definitions of the best indications for hormonal therapies need to be available for all women. The best therapeutic response, made possible by these treatment alternatives, increases the survival and consequently reduces the governmental costs and the general damage to society caused by breast cancer. The new diagnostic and therapeutic discoveries are not yet accessible to all health services, however, they configure new routes to be followed that can lead to greater cancer control and to the reduction of cases of advanced disease, poor prognosis, low survival and high rates of mortality.

The studies favor the comprehension of the manifestations and the establishment of more effective actions, from the various therapeutic indications provided by scientific advances in the treatment of breast cancer. However, early diagnosis still remains the best option for disease control and to minimize its consequences. Therefore, it is necessary to implement health policies that include the current scientific results and that are primarily aimed at women from the age of 40. It is also necessary to streamline the flow of care in the low, medium and high complexity healthcare services. Speed in the treatment and referral is essential to support the early diagnosis. Social inequalities and access to the public healthcare services should be urgently modified. In this context, nursing should participate in the political struggles, in the organization of the work processes and in the competent care to the woman, only then can we contribute to increase the survival rates of women with breast cancer. To know and use the scientific results presented here, in the care of women with breast cancer, can enable the cure and control of the disease, increasing the quality and the hope for life of the women and their families.

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