Characteristics of women with breast cancer seen at reference services in the North of Minas Gerais

Características das mulheres com câncer de mama assistidas em serviços de referência do Norte de Minas Gerais

Priscila Bernardina M. Soares[I]
Sidinei Quirino Filho[II]
William Pereira de Souza[II]
Renata Cristina R. Gonçalves[III]
Daniella Reis B. Martelli[IV]
Marise Fagundes Silveira[IV]
Hercílio Martelli Júnior[IV]

[I] Departamento de Oncologia da Santa Casa de Misericórdia de Montes Claros, MG.

[II] Iniciação Científica do Curso de Medicina da Universidade Estadual de Montes Claros – Unimontes, MG.

[III] Departamento de Oncologia da Santa Casa de Misericórdia de Montes Claros, MG.

[IV] Centro de Ciências Biológicas e da Saúde da Universidade Estadual de Montes Claros – Unimontes, MG.

Correspondência: Priscila Bernardina Miranda Soares. Avenida Mestra Fininha, 1.951, CEP 39403-222 Montes Claros, MG. E-mail: priscilamirandasoares@yahoo.com.br

Abstract

Objective: To describe the main characteristics, including stage of disease and local treatment of patients admitted to two reference services for the treatment of breast cancer in the North of Minas Gerais. **Methods:** We conducted a cross-sectional descriptive study. We evaluated medical records of 288 female patients with breast cancer admitted between January 2006 and December 2009, referred from a public hospital and a private clinic. Variables were analyzed using the chi-square test and multinomial logistic regression. **Results:** 68.1% of patients were referred from the public hospital. There was a predominance of patients over 50 years old (54.5%), married (59%) and with children (87.8%). The mean age of the population studied was 63 years old. Time between suspected cancer and confirmation of diagnosis was over six months in 42.7% of patients. Cancer diagnosis was late (stage III and IV) in 47.6% of patients. Family history of breast cancer was present in 20.1%, 20.8% of them had performed self-breast examination, and 41% had been submitted to a mammogram. **Conclusion:** There was a higher prevalence of stage III/IV patients from the public service when compared to the private sector. We found that the major factors associated with the late diagnosis of breast cancer were the delay between suspected and confirmed diagnosis, the absence of family history of breast cancer and not having a mammogram.

Keywords: Breast cancer. Epidemiology. Late diagnosis. Health services. Risk Factors.

Resumo

Objetivos: Descrever as principais características de pacientes com câncer de mama admitidas em dois serviços de referência para o tratamento desse tipo de câncer no norte de Minas Gerais, incluindo estágio da doença ao diagnóstico e local de tratamento. **Métodos:** Realizou-se estudo transversal e descritivo, avaliando 288 prontuários de pacientes do gênero feminino com câncer de mama, admitidas entre janeiro de 2006 a dezembro de 2009, oriundas de um serviço público e de um privado. As variáveis analisadas foram submetidas a tratamento estatístico por meio dos testes qui-quadrado e regressão logística multinomial. **Resultados:** Observou-se que 68,1% da população analisada procediam do serviço público. Predominaram pacientes com mais de 50 anos (54,5%), casadas (59%) e com filhos (87,8%). Dentre a população estudada, a média de idade foi de 63 anos, sendo que em 42,7% dos casos prevaleceu o intervalo de tempo acima de 6 meses entre a suspeita clínica e a confirmação diagnóstica. Em 47,6% das mulheres o diagnóstico foi tardio (estágios III e IV). 20,1% tinham histórico familiar de câncer de mama; 20,8% faziam autoexame das mamas e 41% faziam mamografia. **Conclusão:** Verificou-se maior prevalência de pacientes nos estágios III e IV no serviço público quando comparado ao privado. O tempo prolongado entre a suspeita clínica e a confirmação diagnóstica, a ausência de história familiar de câncer de mama e a não realização de mamografia de rastreamento são observados, neste estudo, como os principais fatores associados ao diagnóstico tardio.

Palavras-Chave: Câncer de mama. Epidemiologia. Diagnóstico tardio. Serviços de saúde. Fatores de risco.

Introduction

Cancer is a relevant public health problem worldwide, accounting for 7 million deaths annually[1]. Tumors in the following organs are associated with the highest mortality rates: lungs, stomach, colon and breasts. It is estimated that by 2020 there will be 15 million new cancer cases annually, of which 60% will occur in developing countries[1].

Breast cancer is a malignant neoplasm more frequently found in women, totaling 23% of all cancer cases worldwide[2]. Annually, more than one million women are diagnosed with this disease in the world and more than 410,000 will die from it[3]. This neoplasm is more frequent in developed countries and the highest incidences are found in the United Kingdom, Australia, the USA and Canada[1]. Although the mortality of patients with breast cancer has still shown an increasing trend in several countries for several years, developed countries such as the USA, United Kingdom and Australia have already recorded a reduction in mortality[4], which is attributed to the increasing use of mammography and early disease treatment[5]. In general, the mean survival rate of patients with breast cancer is higher than five years in developed countries such as the USA, Canada, Japan and certain Western European countries and lower in developing countries such as Algeria, Brazil and Eastern European countries[6,7]. Such differences in survival rate can be explained by the greater development in diagnosis in developing countries[8].

In Brazil, it was estimated that by 2010 there would be 49,240 new cases of breast cancer and an estimated risk of 49 cases per 100,000 women. In the Southeast region, breast cancer is more frequent among women, with an estimated risk of 65 new cases per 100,000 women[9]. In the state of Minas Gerais in particular, between 1998 and 2007, approximately 85,000 new cancer cases occurred, of which 14,363 were breast cancer, nearly 17% of the total[10]. In addition, it is the most important cause of death from cancer

in the Brazilian female population and it is likely that diagnosing this disease in a more advanced stage is the main responsible for the continuing high mortality rates[9].

Studies have suggested that factors such as lack of access to health services and delays in the investigation of suspicious breast lesions and in disease treatment implementation have contributed to late diagnosis and, consequently, to a high mortality from breast cancer[11-17]. Thus, the present study aimed to describe the main characteristics of patients with breast cancer admitted to two cancer referral services, one public and the other private.

Methods

A cross-sectional descriptive study was conducted. Researchers assessed a total of 288 medical records of patients admitted to two cancer referral services, one public and the other private, located in the city of Montes Claros, north of Minas Gerais, Brazil. The services mentioned used the same medical reports and therapeutic protocol. All patients with a histopathological diagnosis of breast carcinoma were included in this study, regardless of the clinical variables. Cases with a diagnosis of histological types of malignant breast neoplasm other than carcinomas and cases of breast cancer in males were excluded.

General and clinical information about patients were collected. General characteristics were as follows: age (categorized into three age groups), place of origin (Montes Claros and other cities), marital status (single, married, widowed, divorced/separated), professional activity (employed/self-employed, housewife/retired), religion (Catholic, Evangelical and others), number of children, smoking habit (yes or no), alcohol drinking (yes or no), and place of collection (public or private health service). With regard to clinical characteristics, the following variables were investigated: clinical stage of tumor (stage I, stage II, stages III/IV), length of time between clinical suspicion and diagnostic confirmation (zero to five months and more than five months), menopausal status (premenopausal and postmenopausal), presence of metastasis upon diagnosis (yes or no), mammogram performed (yes or no), breast self-exam performed (yes or no), surgical treatment (conservative surgery or mastectomy), family history of breast cancer (yes or no), chemotherapy performed (yes or no), radiotherapy performed (yes or no), hormone therapy performed (yes or no) and immunohistochemical profile of lesions (ER, PR, HER2 and triple-negative).

A descriptive analysis of general and clinical characteristics was performed using frequency distributions. Chi-square test was used to compare the frequency of clinical stage of the disease between the two health services.

In addition, bivariate and multiple analyses were performed and crude and adjusted prevalence ratios were estimated to assess the association between the "clinical stage" and the remaining characteristics of patients. To achieve this, stages III and IV were grouped, so that the outcome variable was categorized into three levels (stage I, stage II and stages III/IV). Consequently, the multinomial logistic model was adopted, whose reference category was Stage I. The significance level was set at $p<0.05$. The database was constructed using SPSS® 17.0 (Statistical Package for Social Science for Windows, Inc., USA).

The present study was approved by the Research Ethics Committee of the *Universidade Estadual de Montes Claros*, Minas Gerais, Brazil, and both cancer referral services agreed to participate.

Results

A total of 288 women with breast carcinomas, admitted to the public and private cancer referral services between 2006 and 2009, were included in this study. Table 1 shows the general characteristics of the population studied, whereas clinical characteristics are shown in Table 2. The majority of cases (68.1%) originated from the public

health service; women aged more than 50 years (54.5%), married (59%), with children (87.8%) and postmenopausal (53.5%) predominated. The interval of time between the clinical suspicion and diagnostic confirmation was longer than six months in 42.7% of women; a late diagnosis (stages III and IV) was made in 47.6% and the percentages recorded in the public health service were higher than those found in the private service; 20.8% performed a breast self-exam; 41% had a mammogram; and 40.6% had a mastectomy. With regard to the immunohistochemical profile of lesions, 69.4% were

Table 1 - General characteristics of women with breast cancer admitted to oncology reference services in Montes Claros, North of Minas Gerais, between 2006 and 2009.
Tabela 1 - *Características gerais de mulheres com câncer de mama admitidas em Serviços de referência em Montes Claros, Norte de Minas Gerais, entre 2006 e 2009.*

General characteristics of patients	n	%
Age (years)		
27 to 39	34	11.8
40 to 49	97	33.7
>50	157	54.5
Place of origin		
Montes Claros	138	47.9
Other cities	150	52.1
Marital status		
Single	40	13.9
Married	170	59.0
Widowed	38	13.2
Separated/Divorced	40	13.9
Profession		
Employed with a formal employment contract/Self-employed	160	55.6
Housewife/Retired	128	44.4
Number of children		
0	35	12.2
1	22	7.6
2	78	27.1
3	63	21.9
4	30	10.4
>4	60	10.8
Smoking habit		
No	256	88.9
Yes	32	11.1
Alcohol drinking		
No	274	95.1
Yes	14	4.9
Place of collection		
Private health service	92	31.9
Public health service	196	68.1
Religion		
Catholic	158	54.9
Evangelical	33	11.5
Others	15	5.2
Not informed	82	28.5
Total	288	100

Table 2 - Clinical characteristics of women with breast cancer admitted to oncology reference services in Montes Claros, North of Minas Gerais, between 2006 and 2009.
Tabela 2 - *Características clínicas de mulheres com câncer de mama admitidas em Serviços de referência em oncologia em Montes Claros, Norte de Minas Gerais, entre 2006 e 2009.*

Clinical characteristics of patients	n	%
Disease stage		
Stage I	69	24
Stage II	82	28.5
Stages III and IV	137	47.6
Length of time between clinical suspicion and diagnostic confirmation (months)		
0 to 5	165	57.3
≥ 6	123	42.7
Menopausal status		
Postmenopausal	154	53.5
Premenopausal	134	46.5
Metastasis upon diagnosis		
No	267	92.7
Yes	21	7.3
Mammogram performed		
No	170	59
Yes	118	41
Breast self-exam performed		
No	228	79.2
Yes	60	20.8
Surgical treatment		
Conservative surgery	116	46.2
Mastectomy	101	40.6
Family history of breast cancer		
No	230	79.9
Yes	58	20.1
Chemotherapy performed		
No	67	23.3
Yes	221	76.7
Radiotherapy performed		
No	34	11.8
Yes	254	88.2
Hormone therapy performed		
No	125	43.4
Yes	163	56.6
Total	288	100

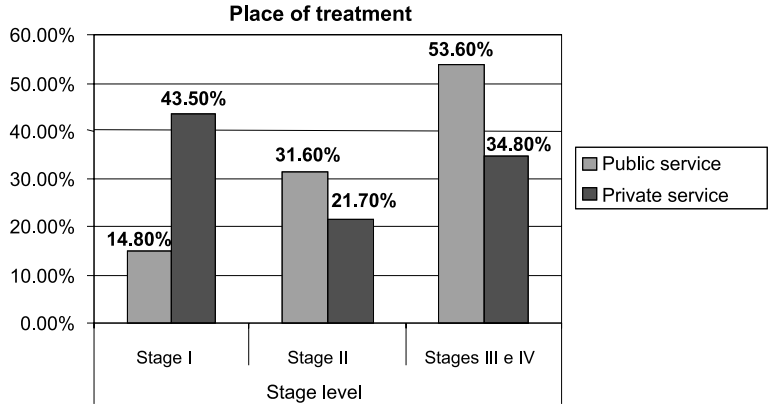
positive ER, 26% had an overexpression of HER-2 and 18.4% were triple-negative.

In terms of disease stages, the public health service was compared to the private one and a higher frequency of patients in clinical stages III and IV was observed in the public service (53.6% versus 34.8%). On the other hand, when the initial diagnosis was analyzed (stage in situ/I), there was a higher frequency in the private service than in the public one (43.5% versus 14.8%), as shown in Graph 1. Table 3 shows an absence of association of age, menopausal status, occupation, immunohistochemical profile and breast self-exam with disease stages, using multinomial logistic regression and comparing stages

II, III and IV with the initial stage (in situ/I). In a distinctive way, not having a mammogram ($PR_{adjusted}$=5.10), the absence of a family history of breast cancer ($PR_{adjusted}$=2.23 and 2.43) and the length of time between the clinical suspicion and diagnostic confirmation ≥ 6 months ($PR_{adjusted}$=2.97 and 3.04) were associated with the more advanced clinical stages of disease.

Discussion

Differently from several developed countries, Brazil has had an increase in the mortality rate from breast cancer in recent years, mainly because of late diagnosis and the delay in the implementation of adequate treatment, as this neoplasm is considered to be curable if diagnosed and treated early[5-9]. The present study enabled researchers to know the profile of women with breast cancer admitted to public and private referral centers located in the city of Montes Claros, north of Minas Gerais, to receive cancer treatment. The mean age of these women was 63 years. The youngest one was 27 years and the oldest one was 100 years, while the majority (54.5%) were aged



*Chi-square test (p < 0.001)
*Teste qui-quadrado (p<0,001)

Graph 1 - Stage of breast cancer in women according to treatment site (public or private service).
Gráfico 1 - *Estadiamento das pacientes com câncer de mama admitidas conforme local de tratamento (serviços público e privado).*

Table 3 - Multinomial logistic regression for the association between mammogram, family history of breast cancer and time between suspected and confirmed diagnosis and clinical staging in women with breast cancer.
Tabela 3 - *Regressão logística multinomial para associação entre mamografia, história familiar de câncer de mama e tempo entre suspeita e confirmação diagnóstica e estadiamento clínico em mulheres com câncer de mama.*

Variable		Stage II*		Stages III and IV*	
		PR_{crude} (95%CI)	$PR_{adjusted}$ (95%CI)	PR_{crude} (95%CI)	$PR_{adjusted}$ (95%CI)
Mammography	Não	2.65 (1.35-5.18)	1.91 (0.87-4.18)	7.52 (3.92-14.20)	5.10 (2.39-10.87)
	Sim	1	1	1	1
Family history of breast cancer	Não	2.56 (1.22-5.56)	2.23 (1.02-4.89)	3.13 (1.56-6.25)	2.43 (1.14-5.19)
	Sim	1	1	1	1
Length of time between clinical suspicion	≥ 6 meses	3.71 (1.7-7.81)	2.97 (1.37-6.45)	4.76(2.39-9.52)	3.04 (1.46-6.37)
and diagnostic confirmation	< 6 meses	1	1	1	1

*Regressão logística multinomial (referência = Estágio in situ/I) (*p<0,05*)
**Multinomial logistic regression (reference = Stage in situ/I) (p <0.05)*
RP_{bruta}=razão de prevalência bruta *(crude prevalence ratio)*
$RP_{ajustada}$=razão de prevalência ajustada *(adjusted prevalence ratio)*
IC-95% = intervalo de confiança de 95% *(95% CI = 95% confidence interval)*

50 years and 53.5% were postmenopausal. Although age is a recognized risk factor for the development of breast cancer, this variable did not show an association between clinical stages of disease and diagnosis according to the results obtained. However, other studies suggest that breast cancer in younger women has a more aggressive physiopathology, contributing to late diagnosis, and the prognosis is worse when compared to breast tumors in older women[18-23].

There was a predominance of married women (59%) and those with children (87.8%). In addition, marital status and the number of children did not interfere with the disease stages, although nulliparity is one of the risk factors associated with breast cancer[24,25]. Similarly, in a survival study conducted with 1,022 women with breast neoplasm, marital status was not considered to be an important factor[26], which confirms the results from a systematic literature review performed by Ramirez et al[13]. Controversially, another study with 540 American female patients revealed that the fact of having never been married increased the risk of having the advanced stage of this disease by almost three times[27].

Family history of breast cancer, reported by 20.1% of women in the present study, was associated with the stage of the disease upon diagnosis, confirming the findings of Hoskins et al[28], which stated that up to 20% of women with breast cancer had a positive family history. According to cross-sectional studies conducted with a population of adult women in the United States, from 5% to 10% had a family history of stage I of breast cancer, suggesting that these women inherited a genetic mutation that puts them at an increased risk of developing breast and ovarian cancer[28]. A systematic review of 14 selected studies on risk factors for breast cancer in Brazilian women concluded that little is known about the prevalence of family history of breast cancer in the Brazilian population and found prevalence rates varying between 3.7% and 13.10%[29]. Another review of family history of breast cancer[30] identified 74 published studies in which authors revealed an estimated relative risk (RR) associated with such family history of 2.0 (CI = 1.8-2.1) for a mother, 2.3 (CI = 2.1-2.4) for a sister and 3.6 (CI = 2.5-5) for a mother and sister. The risks increased when a first degree relative had been diagnosed before the age of 50 years[31].

With regard to immunohistochemistry, the present study found a 26% of overexpression of HER-2 protein according to the medical records analyzed, whereas other studies[32,33] confirmed the overproduction of this protein between 25 and 30% of breast tumors. This protein is associated with worse prognosis, high histological grade, and the reduction in time without disease and overall survival. The estrogen receptor (ER) is expressed in approximately 65% of cases diagnosed before menopause and in nearly 80% of those diagnosed after menopause, and it is usually associated with more favorable prognoses[34]. Likewise, 69.4% of all patients investigated in this study are ER positive. In addition, with regard to immunohistochemistry, Rakha et al[35] identified triple-negative tumors, defined by the absence of expression of hormonal receptors and by the non-positivity of HER-2. It is believed that triple-negative breast cancer corresponds to approximately15% of cases, with a higher frequency in black women, those with BRCA1 mutations, and younger women[36]. Of all women analyzed in this study, 18.4% were triple-negative. However, although hormonal receptors and the expression of the HER-2 protein are related to the prognosis[33,34], these variables were not associated with the stage level upon diagnosis in the present study.

A bivariate analysis of data was performed and found a higher percentage of women in stages III and IV, which was statistically more expressive in the public service than in the private one (53.6% versus 34.8%). In contrast, while 43.5% of women admitted to the private sector were considered to be in stage I, this group totaled 14.8% in the public sector, confirming the results of Rezende et al[16], who identified 51% of women diagnosed between stages II and IV.

Gonçalves et al[37] emphasized that stage III was present in one third of Brazilian women admitted to breast cancer services. Likewise, another study[38] analyzed 43,442 cases of breast cancer between 1995 and 2002 and revealed that 87.7% of women diagnosed with breast cancer were between stages II and IV (stage II=42.8%, stage III=32.6% and stage IV=12.3%). Whereas the standard mortality rates of breast cancer in developed countries decreased, Brazil had an increase in these rates during the same period (from 8.57 to 11.18/100,000 women). The median of percentage of patients between stages II and IV was 45.3% in Brazil and 12.1% in the United States[38].

The monitoring method of breast self-examination, although not an appropriate technique for the early diagnosis of breast cancer, has been considered as an auxiliary method[39]. Several studies[40-42] affirm that there has not been scientific evidence that such practice contributes to the reduction in mortality from this type of cancer. In the present study, not performing a breast self-exam was not associated with more advanced stages upon diagnosis. In contrast, having a mammogram as a more efficient method to monitor breast cancer had a positive impact on the mortality rate[43], which could be reduced by 30% in the 40 to 69 year age group[44]. Types of cancer identified in asymptomatic women are likely to have smaller sizes and to be in the first stages[45]. Although there has been no consensus on guidance on breast cancer monitoring in the age groups of less than 50 years and more than 70 years[46,47], since April 2009, the Brazilian *Sistema Único de Saúde* (SUS – Unified Health System) has guaranteed that mammograms for all women aged 40 years and more will be performed[9]. Similarly, this study pointed to mammography being more frequently performed in the private health service than in the public one and to not having a mammogram being associated with more advanced stages of breast cancer. Marchi et al[48] conducted a cross-sectional study in which 643 women submitted to mammography were interviewed and observed that 472 of them were cared for in public health services and 171 in private health services. Among other characteristics, they assessed the use of mammography among users of public and private health services and concluded that the way they accessed these services influenced the proportion of women previously monitored by mammography, which was higher in the private health network[48].

The present study showed a strong association of the interval of time between the clinical suspicion and diagnostic confirmation with the stage level upon diagnosis of cancer ($PR_{adjusted}$=2.97 and 3.04). This interval was longer than six months in almost half of the women (42.7%), indicating the slowness of the city's health system in the period studied. These results confirm the conclusions of Rezende et al[16], who conducted a study aimed at identifying the causes of delay in caring for women diagnosed with breast cancer in a tertiary hospital of the city of Rio de Janeiro, between January and July 2004, obtaining a median time of one month between the first sign or symptom of disease and the first consultation and of 6.5 months between this consultation and the diagnostic confirmation[16]. Similarly, while studying a cancer service of a public hospital of the city of São Paulo, Trufelli et al[17] emphasized that the delay in the treatment of breast cancer cases was primarily associated with the length of time until the patient sought a health service to have a mammogram and biopsy of suspected lesions performed.

The epidemiological studies conducted showed that there are still important indicators of advanced breast cancer upon diagnosis in Brazil, a fact confirmed in the present study (47.6%). Not having a mammogram performed, the absence of a family history of breast cancer and the long interval of time between clinical suspicion and diagnostic confirmation were emphasized in this study as relevant factors associated with late diagnosis. Researchers observed the need to implement plans and actions aimed at reducing the delay in the treatment of breast cancer cases in public health services to increase the frequency of early detection and, consequently, the cure for this disease in Brazil.

References

1. World Health Organization. International Agency for Research on Cancer. *World Cancer Report*. Lyon: IARC Press; 2008.

2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA *Cancer J Clin* 2011; 61: 69-90.

3. Coughlin SS, Ekwueme DU. Breast cancer as a global health concern**.** *Cancer Epidemiol* 2009; 33: 315-18.

4. Garcia M, Jemal A, Ward E.M et al. *Global Cancer Facts @ Figures 2007*. Atlanta, GA: American Cancer Society; 2007.

5. Berry D.A; Cronin K.A; Plevritis S.K et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005; 353: 1784-92.

6. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R et al. CONCORD Working Group. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008; 9: 730-56.

7. Coleman MP, Gatta G, Verdecchia A, Estève J, Sant M, Storm H et al. and the EUROCARE Working Group. EUROCARE-3 summary: cancer survival in Europe at the end of the 20th century. *Annals of Oncology* 2003; 14: 128-49.

8. Sant M, Allemani C, Capocaccia R et al. Stage at diagnosis is a key explanation of differences in breast cancer survival across Europe. *Int J Cancer* 2003; 106: 416-22.

9. Instituto Nacional Do Câncer – Inca (Brasil). *Estimativa 2010: Incidência de Câncer no Brasil*. Rio de Janeiro; 2009.

10. SisRHC. Sistema de Registro Hospitalar de Câncer (SisRHC). Disponível em http://irhc.inca. gov.br/visualizaTabNetExterno.action [Acessado em 29 de Julho de 2010]

11. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999; 353: 1119-26.

12. Gullatte MM, Phillips JM, Gibson LM. Factors associated with delays in screening of self-detected breast changes in African-American women. *J Natl Black Nurses Assoc* 2006; 17: 45-50.

13. Ramirez AJ, Westcombe AM, Burgess CC. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. *Lancet* 1999; 353: 1127-31.

14. Olivotto IA, Gomi A, Bancej C, Brisson J, Tonita J, Kan L et al. Influence of delay to diagnosis on prognostic indicators of screen-detected breast carcinoma. *Cancer* 2002; 94: 2143-50.

15. Gebrim LH, Quadros LGA. Rastreamento do câncer de mama no Brasil. *Rev Bras Ginecol Obstet* 2006; 28: 319-23.

16. Rezende, MCR; Koch, HA; Figueiredo, JA; Thuler, LCS. Causas do retardo na confirmação diagnóstica de lesões mamárias em mulheres atendidas em um centro de referência do sistema único de saúde no Rio de Janeiro. *Rev Bras Ginecol Obstet* 2009; 31: 75-81.

17. Trufelli DC, Miranda VC, Santos MBB, Fraile NMP, Pecoroni PG, Gonzaga SFR et al. Análise do atraso no diagnóstico e tratamento do câncer de mama em um hospital público. *Rev Assoc Med Bras* 2008; 54: 72-6.

18. Castiglione M, Aebi S. The enigma of young age. *Ann Oncol* 2006; 17: 1475-7.

19. Nixon AJ, Neuberg D, Hayes DF, Gelman R, Connolly JL, Schnitt S et al. Relationship of patient age to pathological features of the tumor and prognosis for patients with stage I or II breast cancer. *J Clin Oncol* 1994; 12: 888-94.

20. Dubsky PC, Gnant MF, Taucher S, Roka S, Kandioler D, Pichler-Gebhard B et al. Young age as an independent adverse prognostic factor in premenopausal patients with breast cancer. *Clin Breast Cancer* 2002; 3: 65-72.

21. Aebi S, De Ridder M, Vlastos G, Vinh-Hung V, Storme G. Young age is a poor prognostic factor in women with stage I breast cancer. *Eur J Cancer* 2006; 4: 121.

22. Bonnier P, Romain S, Charpin C, Lejeune C, Tubiana N, Martin P et al. Age as a prognostic factor in breast cancer: relationship to pathological and biologic features. *Int J Cancer* 2006; 62: 138-44.

23. Chung M, Chang HR, Bland KI, Wanebo HJ. Younger women with breast carcinoma have a poorer prognosis than older women. *Cancer* 1996; 77: 97-103.

24. Lambe M, Hsieh CC, Chan HW, Ekbom A, Trichopoulos D, Adami HO. Parity, age at first and last birth, and risk of breast cancer: a population-based study in Sweden. *Breast Cancer Res Treat* 1996; 38: 305-11.

25. Hulka BS, Stark AT. Breast cancer: cause and prevention. *Lancet* 1995; 346: 883-7.

26. Palmer MK, Lythgoe JP, Smith A. Prognostic factors in breast cancer. *Br J Surg* 1982; 69: 697-8.

27. Lannin DR, Mathews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. *JAMA* 1998; 279: 1801-7.

28. Hoskins KF, Stopfer JE, Calzone KA, Merajver SD, Rebbeck TR, Garber JE et al. Assessment and counseling for women with a family history of breast cancer: a guide for clinicians. *JAMA* 1995; 273: 577-85.

29. Pinho VF, Coutinho ES. Risk factors for breast cancer: a systematic review of studies with female samples among the general population in Brazil. *Cad Saude Publica* 2005; 21: 351-60.

30. Pharoah PD, Day NE, Duffy S et al.: Family history and the risk of breast cancer: a systematic review and meta-analysis. *Int J Cancer* 1997; 71: 800-9.

31. Meiser B, Butow P, Barratt A, Friedlander M, Kirk J, Gaff C et al. Breast cancer screening uptake in women at increased risk of developing hereditary breast cancer. *Breast Cancer Res Treat* 2000; 59: 101-11.

32. Yaziji H, Goldstein LC, Barry TS et al. Her-2 testing using parallel tissue based methods. *JAMA* 2004; 291: 1972-7.

33. Wolff AC, Hammond ME, Schwartz JN et al. American Society of Clinical Oncology/college of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol* 2007; 25: 118-45.

34. Anderson WF, Chatterjee N, Ershler WB, Brawley OW. Estrogen receptor breast cancer phenotypes in the surveillance, Epidemiology, and End Results database. *Breast Cancer Res Treat* 2002; 76: 27-36.

35. Rakha EA, Reis-Filho JS, Ellis IO. Basal-like breast cancer: a critical review. *J Clin Oncol* 2008; 26: 2568-81.

36. Anders C, Carey LA. Understanding and treating triple-negative breast cancer. *Oncology* 2008; 22: 1233-9.

37. Gonçalves PHB, Gaui MF, Martins RG, Bines J. *Padrão de tratamento cirúrgico do câncer de mama de acordo com a idade – Análise de 5 anos do Instituto Nacional do Câncer (INCA)*. Trabalho apresentado no XVI Congresso Brasileiro de Cancerologia e XIII Congresso Brasileiro de Oncologia Clínica, São Paulo, 26 a 30 de novembro de 2003.

38. Thuler LC, Mendonça GA. Estadiamento inicial dos casos de câncer de mama e colo do útero em mulheres brasileiras. *Rev Bras Ginecol Obstet* 2005; 27: 656-60.

39. World Health Organization. *National cancer control programmes: policies and managerial Guidelines.* 2nd ed. Geneva: WHO; 2002.

40. Ellman R, Moss SM, Coleman D, Chamberlain J. Breast self- examination programmes in the trial of early detection of breast cancer: ten year findings. *Br J Cancer* 1993; 68: 208-12.

41. Semiglazov VF, Moiseenko VM, Manikhas AG, Protsenko SA, Kharikova RS, Seleznev IK et al. A prospective randomized trial (St-Petersburg, WHO) of the role of self examination in early detection of breast cancer. *Russ J Oncol* 2000; 2: 4-9.

42. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL et al. Randomized trial of breast self-examination in Shanghai: final results. *J Natl Cancer Inst* 2002; 94: 1445-57.

43. Greenwald P, Kramer B, Weed D. Expanding horizons in breast and prostate cancer prevention and early detection. The 1992 Samuel C. Harvey Lecture. *J Cancer Educ* 1993; 8: 91-107.

44. Tabar L, Yen M, Vitak B, Chen HT, Smith RA, Duffy S. Mammography service screening and mortality in breast cancer patients: 20-year follow-up before and after introduction of screening. *Lancet* 2003; 361: 1405–10.

45. Jackson VP. Screening mammography: controversies and headlines. *Radiology* 2002; 225: 323-6.

46. Smith RA, Mettlin CJ, Davis KJ, Eyre H. American Cancer Society guidelines for the early detection of cancer. *CA Cancer J Clin* 2000; 50: 34-49.

47. Morrison BJ; Canadian Task Force on Preventive Health Care. 1998 recommendation rewording: screening for breast cancer [Internet]. 1998. Disponível em http://www.ctfphc. org/Tables/Ch65tab2.htm [Acessado em 10 de outubro de 2008]

48. Marchi AA, Gurgel MSC, Fonsechi-Carvasan GA. Rastreamento mamográfico em serviços de saúde público e privado. *Rev Bras Ginecol Obstet* 2006; 28: 214-9.

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