DÉLIO MARQUES CONDE

CÂNCER DE MAMA, MENOPAUSA E QUALIDADE DE VIDA

Tese de Doutorado

ORIENTADOR: Prof. Dr. AARÃO MENDES PINTO-NETO
CO-ORIENTADOR: Prof. Dr. CÉSAR CABELLO DOS SANTOS

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Tese de Doutorado apresentada à Pós-Graduação da Faculdade de Ciências Médicas da Universidade Estadual de Campinas para obtenção do Título de Doutor em Tocoginecologia, área de Tocoginecologia

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Curso de Pós-Graduação em Tocoginecologia da Faculdade de Ciências Médicas da Universidade Estadual de Campinas

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Dedico este trabalho...

*...**Aos meus pais**,*
José Ferreira (in memorian) e Lúcia,
pelo exemplo de amor à família, estímulo constante
e pelas palavras amigas nos momentos de incerteza.

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Sumário

Símbolos, Siglas e Abreviaturas

BCCQ	*Breast Cancer Chemotherapy Questionnaire*
BCT	*Breast-Conserving Therapy*
BMI	*Body Mass Index*
CAISM	Centro de Atenção Integral à Saúde da Mulher
EORTC QLQ-BR23	*European Organization for Research and Treatment of Cancer Breast Cancer-Specific Quality of Life Questionnaire*
FACT-B	*Functional Assessment of Cancer Therapy Breast*
FDA	*Food and Drug Administration*
Kg/m^2	Quilograma(s) por metro(s) quadrado(s)
MCS	*Mental Component Summary*
MENQOL	*Menopause Quality of Life Questionnaire*
MRS	*Menopause Rating Scale*
NHP	*Nottingham Health Profile*
95% CI	*95% Confidence Interval*

OR	*Odds Ratio*
PCS	*Physical Component Summary*
QOL	*Quality of Life*
QV	Qualidade de Vida
QWB	*Quality of Well Being*
SERM	*Selective Estrogen Receptor Modulator*
SF-36	*Short-Form 36*
TH	Terapia Hormonal
UQOL	*Utian Quality of Life*
Unicamp	Universidade Estadual de Campinas
WHQ	*Women's Health Questionnaire*
WHOQOL	*World Health Organization Quality of Life*

Resumo

Objetivos: Comparar a prevalência de sintomas climatéricos, a proporção de mulheres com atividade sexual e a qualidade de vida (QV) em mulheres com e sem câncer de mama e identificar os fatores associados à QV em mulheres com câncer de mama. **Sujeitos e Métodos**: Realizou-se um estudo de corte transversal em mulheres com idade entre 45 e 65 anos, não usuárias de terapia hormonal ou tamoxifeno nos últimos seis meses. As participantes foram selecionadas nos Ambulatórios de Oncologia Mamária e de Menopausa do Centro de Atenção Integral à Saúde da Mulher da Universidade Estadual de Campinas. Foram incluídas 97 mulheres com câncer de mama e 85 sem câncer de mama. As características sociodemográficas, clínicas e a prevalência de sintomas climatéricos foram descritas em cada grupo. A QV foi avaliada através do questionário *Medical Outcomes Study 36-item Short-Form Health Survey (SF-36)*. Para comparar as características sociodemográficas e clínicas entre os grupos foram utilizados os testes t de Student e exato de Fisher. Modelos de regressão logística múltipla e de regressão linear foram aplicados com controle de potenciais variáveis confundidoras. A seguir, o modelo generalizado linear permitiu identificar os possíveis fatores associados à QV de mulheres com câncer de mama. **Resultados**: A média de idade das mulheres com

câncer de mama foi de 53,2±6,2 anos e daquelas sem câncer foi de 57,8±4,9 anos (p<0,01). A média de idade à menopausa foi de 47,2±5,1 anos e de 47,4±4,9 anos para mulheres com e sem câncer de mama (p=0,76), respectivamente. Aproximadamente 25% das mulheres com câncer e 4,7% das participantes sem câncer estavam na pré-menopausa (p<0,01). Não houve diferenças na prevalência de sintomas climatéricos entre os grupos. Dentre os sintomas vasomotores, as ondas de calor foram os mais prevalentes com uma freqüência de 53,6% para mulheres com câncer e de 50,6% para aquelas sem câncer (p=0,70). Mulheres com câncer de mama relataram menos atividade sexual (51,5%) do que mulheres sem câncer (62,4%) (p<0,01). A QV foi boa nos dois grupos. Houve diferença no domínio capacidade funcional, com mediana dos escores de 90 para o grupo com câncer e de 75 para o grupo sem câncer (p<0,01). Os sintomas climatéricos, ser casada, estado de pós-menopausa e a cirurgia conservadora de mama associaram-se negativamente à QV de mulheres com câncer de mama. **Conclusões**: A prevalência de sintomas climatéricos foi similar em mulheres com e sem câncer de mama. A atividade sexual foi menos freqüente em mulheres com câncer de mama. A QV foi boa em mulheres com e sem câncer de mama, porém mulheres com neoplasia maligna de mama apresentaram melhor capacidade funcional. Foram identificados fatores que se associaram negativamente à QV e que representam eventos comuns na vida da mulher (sintomas climatéricos, pós-menopausa e ser casada), devendo ser alvo de futuras intervenções que minimizem suas repercussões sobre a QV. Estes aspectos devem ser discutidos entre os profissionais de saúde e as mulheres com câncer de mama, para que estas, uma vez informadas, possam decidir conjuntamente na escolha da opção terapêutica.

Summary

Objectives: To compare the prevalence of menopausal symptoms, ratio of sexually active women and quality of life (QOL) in women with and without breast cancer and identify factors associated with QOL in breast cancer patients. **Subjects and Methods**: A cross-sectional study was conducted on women aged between 45 and 65 years, who had not received hormone therapy or tamoxifen in the last six months. Participants were selected from the Breast Cancer and Menopause Outpatient Facilities of the Centro de Atenção Integral à Saúde da Mulher at the Universidade Estadual de Campinas. Ninety-seven women with breast cancer and 85 women without breast cancer were included. Sociodemographic and clinical features, and prevalence of menopausal symptoms were described in each group. QOL was assessed by the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) questionnaire. To compare sociodemographic and clinical features between groups, the Student's t test and Fisher's exact test were used. Multiple logistic regression and linear regression models were used to control for potential confounding variables. Then, the generalized linear model allowed identification of the likely factors associated with QOL in women with breast cancer. **Results**: The mean age was 53.2±6.2 years for participants with breast cancer and 57.8±4.9 years for those

without breast cancer (p<0.01). The mean age at menopause was 47.2±5.1 years and 47.4±4.9 years for women with and without breast cancer (p=0.76), respectively. Approximately 25% of women with cancer and 4.7% of participants without cancer were premenopausal (p<0.01). There was no difference between groups on the prevalence of menopausal symptoms. Among vasomotor symptoms, hot flashes were the most prevalent symptoms with a frequency of 53.6% for women with cancer and 50.6% for those without cancer (p=0.70). Women with breast cancer reported having less sexual activity (51.5%) than women without cancer (62.4%) (p<0.01). QOL was good in both groups. There was a significant difference regarding the physical functioning dominion, with a median score of 90 for the cancer group and 75 for the group without cancer (p<0.01). Menopausal symptoms, being married, postmenopausal status and breast-conserving surgery were negatively associated with QOL in women with breast cancer. **Conclusion**: The prevalence of menopausal symptoms was similar in women with and without breast cancer. Sexual activity was less frequent in women with breast cancer. QOL was good in women with and without breast cancer, although women with breast cancer have better physical functioning scores. Factors that were negatively associated with QOL and represented common events in a woman's life (menopausal symptoms, postmenopause and being married) were identified. These factors should be the target for future interventions to minimize their repercussions on QOL. Health care professionals must discuss these issues with breast cancer patients to inform women about the treatment options available and help them decide on the most suitable therapy.

1. Introdução

A melhoria das condições socioeconômicas e de assistência à saúde proporcionou aumento da longevidade da população mundial, estimando-se que em 2050 mais de 20% da população será composta de idosos, fenômeno não restrito às sociedades desenvolvidas (DICZFALUSY, 1986). Verifica-se no Brasil um processo semelhante de envelhecimento populacional. Como reflexo desse processo estima-se que a esperança de vida da mulher brasileira, que era de 66 anos em 1980, seja de 84,5 anos em 2050 (IBGE, 2004). Com o aumento da esperança de vida há um aumento da ocorrência de doenças crônicas como a osteoporose, doenças cardiovasculares e neoplasias malignas. Dentre as neoplasias mais comuns na população feminina, o câncer de mama é a segunda neoplasia maligna mais freqüente no Brasil e no mundo, superada apenas pelo câncer de pele não melanoma (PARKIN, 2001; INCA, 2004).

O diagnóstico da neoplasia de mama pode determinar amplas repercussões na vida da mulher, afetando os domínios físico, psicológico, sexual, social e econômico. Mulheres que recebem esse diagnóstico podem vivenciar reações

emocionais negativas como insônia, perda de apetite, alterações do humor (JAMISON et al., 1978; CARPENTER et al., 2004; SAVARD et al., 2004), medo de ser abandonada pela família e pelos amigos, medo de recidiva e da morte (KORNBLITH e LIGIBEL, 2003). Essas mulheres apresentam maior risco de desenvolver disfunções sexuais, que podem persistir por muitos anos após o diagnóstico. A etiologia dessas disfunções não está totalmente compreendida, porém alguns fatores preditivos da vida sexual dessas mulheres foram descritos, como a secura vaginal, dispareunia, bem-estar emocional, auto-imagem, qualidade do relacionamento com o parceiro e disfunções sexuais no parceiro (GANZ et al., 1998; 1999; MEYEROWITZ et al., 1999; GREENDALE et al., 2001; KORNBLITH e LIGIBEL, 2003).

O diagnóstico do câncer de mama ocorre com freqüência durante os anos climatéricos e na pós-menopausa (GANZ et al., 2000; FOSP, 2004). Nesse período são comuns as queixas de ondas de calor, sudorese, alterações do humor, secura vaginal, insônia, incontinência urinária, que podem comprometer a qualidade de vida (QV) em mulheres com e sem câncer de mama (DALY et al., 1993; COUZI et al., 1995; STEIN et al., 2000; FU et al., 2003). Esses sintomas podem ser agravados em decorrência da terapia antineoplásica, particularmente a quimioterapia e o tamoxifeno, que podem induzir a um estado de deficiência estrogênica, transitório ou permanente, tornando mais grave o quadro clínico.

A importância da quimioterapia no tratamento adjuvante do câncer de mama está estabelecida na literatura, proporcionando um aumento da sobrevida livre

de doença e da sobrevida global (EARLY BREAST CANCER TRIALIST'S COLLABORATIVE GROUP, 1998; BERGH et al., 2001). Porém, a quimioterapia apresenta efeitos adversos como náuseas, vômitos, fadiga e queda de cabelos, que devem ser considerados por médicos e pacientes, quando da decisão por essa terapêutica (ARNDT et al., 2004). Além desses efeitos, ela pode induzir à falência ovariana, com diminuição do número de folículos e fibrose, associando-se ou agravando os sintomas de deficiência estrogênica (SHAPIRO e RECHT, 2001).

O tamoxifeno, por sua vez, é considerado um *Selective Estrogen Receptor Modulator* (SERM), com ação tanto agonista quanto antagonista do estrogênio (OSBORNE, 1998). Nesse sentido ele preserva a densidade mineral óssea em mulheres na pós-menopausa (POWLES et al., 1996) e bloqueia os receptores de estrogênio na mama (OSBORNE, 1998). Porém, o tamoxifeno pode apresentar efeitos adversos como o aumento do risco de eventos tromboembólicos, toxicidade ocular (NAYFIELD e GORIN, 1996) e o aparecimento ou exacerbação dos sintomas climatéricos, determinando um aumento da freqüência e da intensidade das ondas de calor (LOVE et al., 1991; COUZI et al., 1995; CARPENTER et al., 1998; BIGLIA et al., 2003).

Entretanto, não há evidências de que o uso de tamoxifeno associe-se à pior QV. Durante o climatério, as ondas de calor e a sudorese são sintomas que podem relacionar-se ao tamoxifeno; porém outros sintomas como artralgia, ganho de peso, alterações do humor e dificuldades de concentração são mais prováveis

de estar associados ao processo de envelhecimento e à menopausa e não podem ser relacionados diretamente ao uso de tamoxifeno (GANZ, 2001).

A sobrevida livre de doença e a sobrevida global são os objetivos principais do tratamento oncológico, porém tornou-se evidente que são insuficientes para a avaliação de novas terapias antineoplásicas, devendo considerar-se a QV como mais um desses objetivos. Um grande impulso foi dado para a avaliação da QV em ensaios clínicos com a declaração do *Food and Drug Admininstration* (FDA) dos Estados Unidos de que a QV seria um dos critérios para a aprovação de novas drogas anticâncer (JOHNSON e TEMPLE, 1985). Houve o reconhecimento da importância da QV como um resultado que deve ser considerado nos programas de avaliação para a alocação de recursos (VELIKOVA et al., 1999).

O diagnóstico do câncer de mama pode coincidir com a fase do climatério e determinar uma preocupação ainda maior com a saúde da mulher. Nesta fase, muitas mulheres estarão vivenciando os sintomas climatéricos ou estarão em uso de terapia hormonal (TH) para o controle destes sintomas. Após o diagnóstico da neoplasia muitas mulheres interrompem a TH, por iniciativa própria ou sob orientação médica, o que provoca o retorno abrupto dos sintomas climatéricos, podendo influenciar negativamente a QV (GANZ et al., 2000; STEIN et al., 2000).

Diante desse quadro, as mulheres com câncer de mama vivenciam duas condições que podem afetar a QV: os sintomas climatéricos associados à menopausa e/ou ao tratamento antineoplásico e o próprio câncer de mama. Objetivando diminuir a freqüência e a intensidade dos sintomas de deficiência

estrogênica, o tratamento de primeira escolha é a TH, que demonstrou redução em torno de 70% a 90% desses sintomas (LOBO et al., 1984; NAND et al., 1998; NOTELOVITZ et al., 2000). Embora a TH promova uma melhora significativa dos sintomas climatéricos, sua relação com a QV permanece controversa. Alguns estudos observaram melhora dos sintomas de deficiência estrogênica com uma correspondente melhora da QV (WIKLUND et al., 1993; GELFAND et al., 2003), porém em outros não se verificou essa melhora da QV (WILSON et al., 1998; HAYS et al., 2003). HAYS et al. (2003) não observaram melhora da QV em usuárias de TH, porém as participantes deste estudo apresentavam média de idade de 63 anos, altos escores de QV previamente à TH e apenas 12% eram sintomáticas.

Embora seja conhecido o efeito benéfico da TH no alívio dos sintomas climatéricos, ela tem sido contra-indicada para mulheres com história de câncer de mama. Este fato estimulou a investigação de terapias não hormonais para o alívio dos sintomas de deficiência estrogênica, uma vez que estes sintomas podem afetar negativamente a QV, particularmente em mulheres com câncer de mama, nas quais eles tendem a ser mais freqüentes e intensos (CARPENTER et al., 2002). Dentre as alternativas de tratamento não hormonal para os sintomas vasomotores destacam-se os inibidores seletivos da recaptação de serotonina (paroxetina, venlafaxina, fluoxetina), agonistas α-adrenérgicos (clonidina), gabapentina, que demonstraram efeito benéfico no controle desses sintomas (LOPRINZI et al., 2000; 2002; SICAT e BROKAW, 2004).

O uso de lubrificantes vaginais deve ser considerado o tratamento de primeira linha para o alívio dos sintomas urogenitais, uma vez que o uso tópico de hormônio pode apresentar efeito sistêmico (NAESSEN et al., 2001), permanecendo incerto o quanto isto poderia afetar o risco de recidiva ou de um novo câncer de mama (CHLEBOWSKI et al., 2003). Todas essas medidas têm por finalidade diminuir a intensidade e a freqüência dos sintomas climatéricos, bem como melhorar a QV.

O interesse pelo estudo da QV é crescente em várias áreas da atividade humana. O conceito de QV é subjetivo e multidimensional, e é influenciado por vários fatores relacionados à educação, economia e aos aspectos socioculturais, não havendo um consenso quanto à sua definição. Atualmente há uma tendência em reconhecer a importância do ponto de vista do paciente em relação à sua doença e na monitoração da qualidade das medidas terapêuticas empregadas (CICONELLI, 1997). Apesar de não haver consenso quanto à definição de QV, a maioria dos autores concorda que em sua avaliação devem estar contemplados os domínios físico, social, psicológico e espiritual, buscando captar a experiência pessoal de cada indivíduo. Neste contexto questiona-se como transformar informações subjetivas, que envolvem conceitos individuais, em dados objetivos, mensuráveis e também como essas informações podem ser quantificadas e comparadas entre diferentes populações. Objetivando responder a essas questões foram elaborados questionários de QV, que possibilitaram a médicos e a pesquisadores transformar informações subjetivas em medidas quantitativas para que possam ser usadas em ensaios clínicos e em estudos econômicos (FADEN e LEPLÉGE, 1992;

FITZPATRICK et al., 1992; BOWLING e BRAZIER, 1995). Também há sugestões para inclusão destes questionários na prática clínica diária, com a finalidade de melhorar a qualidade da assistência (DETMAR e AARONSON, 1998).

Os questionários ou instrumentos de QV podem ser divididos em genéricos e específicos (CICONELLI, 1997). Os instrumentos genéricos procuram avaliar de forma global os aspectos importantes relacionados à QV (físico, social, psicológico, espiritual); como exemplos destacam-se o *Medical Outcomes Study 36-item Short-Form Health Survey (SF-36), Nottingham Health Profile (NHP), Quality of Well-being (QWB), World Health Organization Quality of Life (WHOQOL)*. Os instrumentos específicos são capazes de avaliar de forma individual e específica alguns aspectos da QV, e são mais sensíveis na detecção de alterações após uma intervenção (CICONELLI, 1997; WIEBE et al., 2003). Os questionários específicos podem ser direcionados para avaliação de determinada função (capacidade funcional, sono, função sexual, aspectos sociais), população (idosos, jovens, mulheres climatéricas) ou doença (câncer de mama, câncer de ovário, diabetes) (GUYATT et al., 1995). Os instrumentos específicos mais citados para o estudo da QV em mulheres com câncer de mama são: *Functional Assessment of Cancer Therapy Breast (FACT-B), Breast Cancer Chemotherapy Questionnaire (BCCQ), European Organization for Research and Treatment of Cancer Breast Cancer-Specific Quality of Life Questionnaire (EORTC QLQ-BR23)*, enquanto no climatério destacam-se a *Utian Quality of Life (UQOL), Menopause Quality of Life Questionnaire (MENQOL), Menopause Rating Scale (MRS), Women's Health Questionnaire (WHQ)*.

Diante de vários instrumentos torna-se difícil a escolha daquele que melhor se aplica aos objetivos de determinada investigação. Como orientação para a decisão correta, o instrumento deve ser simples, de fácil aplicação e compreensão e com tempo de administração apropriado (BELL et al., 1990). Considerando-se esses aspectos, o questionário SF-36 foi aplicado em vários estudos que avaliaram mulheres com câncer de mama (GANZ et al., 1998; BROECKEL et al., 2000; GANZ et al., 2000; 2002). É um instrumento genérico de fácil aplicação e compreensão, sendo atualmente um dos questionários mais conhecidos e difundidos na área de saúde (WOOD-DAUPHINE, 1999), traduzido e validado para a língua portuguesa no Brasil (CICONELLI, 1997).

O SF-36 é um questionário multidimensional, composto por 11 questões e 36 itens, com oito componentes: capacidade funcional (10 itens), aspectos físicos (4 itens), dor (2 itens), estado geral de saúde (5 itens), vitalidade (4 itens), aspectos sociais (2 itens), aspectos emocionais (3 itens), saúde mental (5 itens) e uma questão que compara as condições de saúde atuais com as de um ano atrás (WARE e SHERBOURNE, 1992). Esses componentes podem ser resumidos em: sumário do componente físico e sumário do componente mental (WARE et al., 1994). Cada componente do SF-36 corresponde a um valor, que varia de zero a 100, onde zero corresponde ao pior e 100 ao melhor estado de saúde (WARE et al., 2000). Todavia, o SF-36 apresenta algumas limitações como a não inclusão de questões sobre o sono e a sexualidade.

Além dos sintomas climatéricos (STEIN et al., 2000; CARPENTER et al., 2002), a QV pode ser influenciada por outros fatores relacionados à terapia antineoplásica. Dessa forma, a quimioterapia (BROECKEL et al., 2000; JOLY et al., 2000), radioterapia (WENGSTRÖM et al., 2000), tipo de cirurgia (COHEN et al., 2000; GANZ et al., 2002), idade ao diagnóstico, linfedema do braço (DORVAL et al., 1998; GANZ et al., 2002) e suporte psicossocial (FUKUI et al., 2000; OKAMURA et al., 2003) foram fatores explorados e relacionados à adaptação psicológica e à QV de mulheres com história de câncer de mama em países desenvolvidos.

Não foram identificados estudos avaliando os sintomas climatéricos e a QV de mulheres brasileiras com câncer de mama. Uma vez que fatores socioculturais podem afetar a experiência da transição climatérica, a percepção e a auto-avaliação da QV, realizou-se este estudo, cujos objetivos foram comparar a prevalência de sintomas climatéricos e a QV em mulheres com e sem câncer de mama, e identificar os fatores associados à QV em mulheres com história de câncer de mama.

2. Objetivos

2.1. Objetivo geral

Comparar a prevalência de sintomas climatéricos, a proporção de mulheres com atividade sexual e a qualidade de vida em mulheres com e sem câncer de mama e identificar os fatores associados à qualidade de vida de mulheres com câncer de mama.

2.2. Objetivos específicos

- **Artigo 1**

  1. Comparar a prevalência de sintomas climatéricos em mulheres com e sem câncer de mama.

  2. Comparar a proporção de mulheres com atividade sexual.

  3. Comparar a qualidade de vida dessas mulheres.

– **Artigo 2**

1. Avaliar a qualidade de vida de mulheres com história de câncer de mama.

2. Identificar os fatores associados à qualidade de vida dessas mulheres.

3. Publicações

Artigo 1

Menopausal Symptoms and Quality of Life in Women Aged Between 45 and 65 years with and without Breast Cancer.

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Artigo 2

Quality of Life in Brazilian Breast Cancer Survivors Aged 45 to 65: Associated Factors.

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3.1. Artigo 1

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Dear Dr. Pinto-Neto:

Thank you for submitting your revised manuscript entitled "Menopausal Symptoms and Quality of Life in Women Aged Between 45 and 65 Years with and without Breast Cancer." I am delighted to report that it has been accepted for publication and forwarded on to our publisher slated for inclusion in Volume 12(4) of ***Menopause***.

The journal is adding to the Table of Contents a summary of each article. Because you know the material best, we ask that you write on the accompanying form (enclosed) 1-2 summary sentences about your article to be included on the table of contents page.

Thank you again for all your support of the journal, ***Menopause***.

Sincerely,

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Menopausal Symptoms and Quality of Life in Women Aged Between 45 and 65 years with and without Breast Cancer

Menopausal symptoms, quality of life and breast cancer

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Abstract

Objective: To compare the prevalence of menopausal symptoms, sexual activity and quality of life in women with and without breast cancer. Design: A cross-sectional study with one group for comparison was conducted on women aged between 45 and 65 years, who had not received hormone therapy or tamoxifen during the last six months. Participants were recruited from the Menopause and Breast Cancer Outpatient Facilities. One hundred and eighty-two women were included, 97 with breast cancer and 85 without breast cancer. Sociodemographic and clinical features and prevalence of menopausal symptoms were assessed. The quality of life was assessed by the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) questionnaire. To compare sociodemographic and clinical features between groups, the Student's t test or Fisher's exact test were used. Multiple logistic regression and linear regression models were used to control for potential confounding variables. Results: The mean age of participants with breast cancer was 53.2±6.2 years, the mean age of those without cancer was 57.8±4.9 years ($p<0.01$). Age at menopause was 47.2±5.1 years and 47.4±4.9 years for women with and without breast cancer ($p=0.76$), respectively. Approximately one-fourth of women with breast cancer and 4.7% of women without cancer were premenopausal ($p<0.01$). The prevalence of menopausal symptoms was similar between the groups. Women with breast cancer reported less sexual activity (51.5%) than women without cancer (62.4%) ($p<0.01$). Quality of life scores were good in both groups. There was a significant difference regarding physical functioning, with a median score of 90 for the cancer group and 75 for

the group without cancer ($p<0.01$). Conclusion: The prevalence of menopausal symptoms was similar in women with and without breast cancer. Sexual activity was less frequent in women with breast cancer. Quality of life was good in women from both groups, although women with breast cancer had the highest level of physical functioning.

Key words: Menopause, Breast cancer, Climacteric syndrome, Quality of life, SF-36 questionnaire

Introduction

Breast cancer is the second most common cancer in women worldwide[1]. In the United States, about 215.990 new cases of breast cancer are expected for the year 2004[2], most cases occurring in women over 45 years of age[3]. In Brazil, breast cancer is the second most frequent cancer in women, and about 41.610 new cases had been expected for 2003[4], most cases occurring in women aged between 40 and 60 years[5]. This age range coincides with the mean age of menopause, which is 51.1 in the United States[6], and 51.2 years in Brazil[7].

During the climacteric, hot flashes, sweating, vaginal dryness, dyspareunia, irritability and insomnia are common complaints. Many women will thus present menopausal symptoms at the time of their breast cancer diagnosis[8]. Studies that evaluated the prevalence of climacteric symptoms in women with breast cancer showed rates of 65% of hot flashes[9,10], 44% of night sweats and 48% of vaginal dryness[9]. One of the factors associated with climacteric symptoms in these women is the use of tamoxifen[11,12]. Hot flashes are the main adverse effects of tamoxifen use, occurring in up to 80% of users[12]. It is worth emphasizing that climacteric symptoms vary according to cultural, racial, educational and socioeconomic aspects of the population evaluated[13-15]. These symptoms may have a negative impact on women's quality of life[16,17].

Quality of life is influenced by multiple factors and its evaluation has been increasingly incorporated into the clinical trials and management of breast cancer patients[18,19]. Women diagnosed with breast cancer experience negative emotional responses such as insomnia, loss of appetite[20], fear of recurrence and death[21]. Studies that assessed quality of life in women with breast cancer in different

sociocultural contexts explored aspects such as the administration of adjuvant therapy[22], frequency and intensity of climacteric symptoms[8,9,16], and age at diagnosis[23]. These studies showed that quality of life in these women underwent modifications as a function of time. As the years pass, quality of life in women with breast cancer is comparable to that of women without breast cancer[22,24].

Given the epidemiological features of breast cancer, its diagnosis may coincide with the appearance of climacteric symptoms. Some women will require specific cancer treatment and specialized counseling about menopause and its consequences. To date, few studies have evaluated the climacteric syndrome in women with breast cancer. Such studies have been conducted in developed countries with different socioeconomic and cultural realities, and focused on the occurrence of hot flashes. Unlike the above-mentioned studies, this study aimed at evaluating the climacteric syndrome. Considering that cultural differences may influence the climacteric symptoms and quality of life, the aim of the present study was to compare the prevalence of menopausal symptoms, sexual activity and quality of life in women with and without breast cancer, who were non-users of tamoxifen and hormone replacement therapy.

Methods

Sample size

To estimate sample size, we considered a number that permitted a difference of at least 20% in the prevalence of hot flashes between groups with and without breast cancer[25]. Considering the prevalence of hot flashes to be 77.8% in Brazilian postmenopausal women[26], the sample was calculated in at least 82 women with

breast cancer and 82 women without the disease. The probability of making type I (α) error was 5% and the maximum probability of making type II (β) error was 20%.

Subjects

A cross-sectional study was conducted with one group for comparison. Participants of this study were selected among patients consecutively treated in the Outpatient Facilities of Menopause and Breast Cancer in the Women's Hospital, at Universidade Estadual de Campinas, between August 2002 and June 2003. Women seeking treatment in this institution are underprivileged, with limited education and are referred for the evaluation of different health-related problems. During outpatient consultation, patients who met the inclusion criteria were invited to participate in the study. One hundred and eighty-seven were invited, 100 with breast cancer and 87 without breast cancer. Three women with breast cancer and two without cancer refused to participate, and participation rate was 97.3%. The patients refused to participate in the interview, allegedly due to lack of time.

All women without cancer and 10 women with breast cancer were selected among patients seen at the Menopause Outpatient Facility. The remaining participants of the cancer group were invited to participate in the Breast Cancer Outpatient Facility. If they agreed, these patients were referred for evaluation and interview at the Menopause Outpatient Facility, where about 4% of premenopausal women or breast cancer patients are examined. These women either spontaneously seek assistance or are referred by specialists. The group of premenopausal patients seen in this outpatient setting consisted of women referred for climacteric

evaluation or those who had a history of cancer (breast cancer, endometrial cancer, ovarian cancer and cervical cancer).

Participants were divided into two groups: 97 women with a personal history of breast cancer and 85 women without breast cancer. Inclusion criteria were: age between 45 and 65 years, non-users of hormone replacement therapy or tamoxifen during the last six months, no history of malignant tumors, with the exception of breast cancer. Women were invited to participate, regardless of menopausal status.

All women were interviewed after consultation to assess sociodemographic and clinical features, e.g. age, age at menarche, race (white/non white), body mass index (BMI), smoking habit, ranking as smokers (women who were still smoking or those who had quit the habit less than five years prior to enrollment in the study) and non-smokers (those who had never smoked or had quit smoking more than five years before enrollment), age at menopause (at least 12 months of amenorrhea)[27], menopausal status and tumor stage. These characteristics were compared between groups. This study was approved by the Institutional Review Board and all women signed an informed consent form.

Evaluation of Menopausal Symptoms and Sexual Activity

The prevalence of menopausal symptoms experienced during the four weeks prior to enrollment in the study was assessed by a questionnaire. The symptoms studied were: hot flashes, sweating, palpitations, dizziness (vasomotor symptoms); nervousness, headache, depression, insomnia (psychological symptoms); dyspareunia and vaginal dryness (genital symptoms)[28]. The ratio of sexually active women was also evaluated during the four weeks prior to inclusion in the study.

Assessment of Quality of Life

To assess quality of life, the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) questionnaire was used[29]. The SF-36 is a generic tool for assessment of quality of life. Currently, it is one of the most widely known and used instruments in health[30]. It has already been translated and validated to the Portuguese language in Brazil[31]. It is a multidimensional questionnaire, composed of 11 questions and 36 items, with eight components: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health. These components are summed up in two summaries: the physical component summary (PCS) and the mental component summary (MCS). Each SF-36 component corresponds to a value, ranging from zero to 100, where zero corresponds to the worst score and 100 to the best score for health status[32]. The questionnaires were administered by one of the investigators in the form of an interview.

Statistical analysis

For data analysis, breast cancer (with cancer/without cancer) was the independent variable, while menopausal symptoms and quality of life were the dependent variables. The potentially confounding variables were age, age at menarche, parity, body mass index, menopausal status, smoking habit, race and marital status. Results are presented as means and standard deviations (SD) or as absolute and relative frequencies, according to the type of variable. To compare the sociodemographic and clinical features between groups an unpaired two-sided Student's t-test or a Fisher's exact test were used[33]. Multiple logistic regression models[34] were used to compute odds ratios with 95% confidence intervals as estimates of the strength of association between each climacteric symptom and

groups, adjusting for potential confounding variables. To estimate the prevalence of dyspareunia, only sexually active women were included. Regression models described the association between each SF-36 score output and groups. Control for confounders (age, age at menarche, body mass index, menopausal status, parity, smoking habit, race and marital status) was also considered. The SF-36 scores presented an asymmetrical distribution, explaining why their values were expressed in median and 25% and 75% percentiles. Usual linear models were not used because the distribution shape of SF-36 score outputs was quite skewed and transformation was ineffective. As an alternative, we used the linear least absolute value (LAV) regression models by solving the L_1 norm minimization problem[35]. These models allow comparisons between medians. We used the LAV subroutine implemented in STATA software (IML procedure)[36]. In all hypothesis testing, we set a significance level of 5 per cent.

Results

Sociodemographic and clinical features

Table 1 results demonstrated that there was great inequality between women with and without breast cancer, according to several sociodemographic and clinical features. The mean age was 53.2±6.2 years for women with breast cancer and 57.8±4.9 years for those without breast cancer ($p<0.01$), body mass index was 28.0±5.5 and 29.9±5.6 Kg/m^2 for women with and without breast cancer ($p=0.03$), respectively. Seventy per cent of women with breast cancer and 68.2% of those without cancer lived with a partner ($p=0.87$), 15.5% of women with cancer and

7.1% of those without cancer reported smoking habit (p=0.10). Regarding race, 74.2% of women with cancer and 67.1% of women without cancer were white (p=0.33). Other characteristics are shown in Table 1.

In the breast cancer group, the median time since diagnosis was 35.1 months (range, 2–246.2 months). The types of surgeries performed were mastectomy in 57.7% and quadrantectomy in 42.3% of the women, while invasive carcinoma was present in 90.7% of the participants with cancer. Approximately sixty-two percent of women underwent chemotherapy, 54.6% underwent radiation therapy and 44.3% underwent chemotherapy and radiation therapy. Twenty-two patients were undergoing breast cancer treatment. Percentage distribution according to tumor stage was: 0 (9.3%), I (15.5%), II (48.5%), III (23.7%) and IV (3.0%).

Menopausal symptoms and sexual activity

Hot flashes were the most prevalent vasomotor symptoms, with a frequency of 53.6% in women with breast cancer and 50.6% in the group without cancer (p=0.70). After adjusting for potentially confounding variables, no difference was found between groups regarding the prevalence of vasomotor (Table 2) and psychological symptoms (Table 3). No difference was found regarding the prevalence of genital symptoms. However, in an adjusted analysis, sexual activity was less frequent in women with breast cancer than in women without breast cancer (OR=0.16, p<0.01). About half of the women with breast cancer (51.5%) and 62.4% of the women without breast cancer reported having been sexually active in the four weeks prior to inclusion in the study (Table 4).

Quality of life

The quality of life scores are shown in Table 5. Comparing the median SF-36 scores in an unadjusted analysis, differences between groups were observed regarding the physical functioning (median score of 90 for women with breast cancer and 75 for those without cancer (p=0.04), and bodily pain (median scores were 61 and 51 for women with and without breast cancer [p<0.01], respectively). After adjusting for this set of confounding variables, a significant difference between the median scores on the SF-36 persisted only for the physical functioning domain (p<0.01).

Physical and mental component summaries

When comparing the PCS scores between groups, a slight difference was noted, a median of 50 for women with breast cancer and 44.9 for women without cancer (p=0.05), respectively. However, this difference disappeared after adjusting for this set of confounding variables (p=0.30). The groups had no significant effect on MCS scores, the median was 50 for women with cancer and 47.4 for women without cancer (p=0.35 in an unadjusted analysis and p=0.28 in an adjusted analysis) (Table 6).

Discussion

The aim of this study was to compare the prevalence of menopausal symptoms, sexual activity and quality of life in women with and without breast cancer. The importance of this investigation is based on the fact that breast cancer is diagnosed predominantly during the climacteric years in Brazil and

other countries[8]. Furthermore, certain climacteric symptoms, especially hot flashes, appear to be more severe in these women[17].

The prevalence of menopausal symptoms was similar among women with and without breast cancer and also similar to that observed in a population-based study conducted in Brazilian women[26]. Among vasomotor symptoms, hot flashes were highlighted as the most prevalent symptoms, occurring in premenopausal and postmenopausal women. Oldenhave et al.[37] reported that hot flashes are prevalent in 41.1% of premenopausal women. The prevalence was similar in Brazilian premenopausal women[26]. In the current study, the frequency of hot flashes in women without breast cancer was 50.6%, while in a population-based study carried out in Brazilian postmenopausal women, the prevalence was 77.8%. Perhaps this difference is related to the fact that the present study evaluated women who were users of a public health service. These women had access to medical information and psychological assistance, which could have influenced them to report the symptoms.

Previous studies documented the prevalence of menopausal symptoms in women with breast cancer[9,10,16,38]. Couzi et al.[9], as well as Carpenter et al.[10] in the United States, interviewed postmenopausal women with breast cancer, reporting that the most prevalent symptoms in this group were hot flashes, with a 65% rate. In the current study, hot flashes were frequent symptoms, although the percentage (53.6%) was lower. A possible explanation for this difference is related to cultural and racial influences, which may affect the experience and perception of climacteric symptoms. It is likely that Brazilian women, similar to Asian and Central American women[15,39-41], report less symptoms than North American women. Another possible explanation for this difference could be the lack of tamoxifen users in the present

study, whereas 35% of the women in the study conducted by Couzi et al.[9] and 47% in the study conducted by Carpenter et al.[10] had undergone endocrine therapy with tamoxifen, whose use is associated with climacteric symptoms[42,43]. Another difference is related to the inclusion of women in the analysis who were undergoing breast cancer treatment, perhaps minimizing the impact of climacteric syndrome in this group. More recently, Harris et al.[44] evaluated postmenopausal and premenopausal women with breast cancer and observed that the prevalence of symptoms was 73%. Of symptomatic women, 96% reported hot flashes, however, 56.4% of them were tamoxifen users. In the current case study, tamoxifen users were excluded, permitting us to observe the prevalence of menopausal symptoms, regardless of endocrine therapy use. If we had included a group of tamoxifen users, we could have evaluated the association between this drug and the climacteric symptoms experienced by Brazilian women, as well as differences in the quality of life.

In this case study, the most prevalent psychological symptom was nervousness with a similar percentage among the groups. Women with a history of breast cancer may present psychological alterations such as feeling depressed[9], sexual dysfunction, dependency, and fear of being abandoned by family and friends[45]. We highlight that in a population-based study of Brazilian climacteric women, nervousness was also the most prevalent psychological symptom reported[26]. Avis et al.[15] reported a lower prevalence of tension/nervousness (56.1%) among the Caucasian women in the United States, which might be explained by cultural differences. There is strong evidence that vasomotor symptoms reflect hormonal changes, whereas psychological symptoms may be attributed to hormonal alterations or factors

that coincide with menopause[46]. The actual prevalence of psychological and psychiatric alterations in women with breast cancer remains unknown[45].

In the present case study, there was no difference in the prevalence of dyspareunia and vaginal dryness between women with and without breast cancer, however around 50% of the women with breast cancer reported not being sexually active during the month prior to the interview. The only Brazilian population-based study that assessed data on climacteric women's sexuality reported that 34% of these women had not been sexually active during the last month, primarily due to lack of a partner[26]. We can presume that in the present study that was not the case, since 70% of women with breast cancer were living with a partner. Data presently available suggests that women with breast cancer are at risk of developing sexual dysfunction, which may last for years after cancer diagnosis[45,47]. Barni e Mondin[48] evaluated women with breast cancer, with a median age of 48 years and observed that lack of sexual desire was the main dysfunction. Lack of desire was also the main sexual dysfunction observed in women going through the menopausal transition in Brazil[26] and in other countries[49,50].

The present study confirmed that quality of life was good in both groups. The lowest scores were observed in the bodily pain and vitality domains, with no significant difference between groups. The best scores were observed in the role-emotional (median of 100) and physical functioning (median of 90 for women with cancer and 75 for women without cancer) components. The good scores observed could reflect the multiprofessional care provided to these women by the institution, highlighting psychosocial support and physical therapy. This support may contribute towards a better perception of health status, minimizing

the impact of breast cancer diagnosis and treatment. Results of previous studies reported the importance of providing psychosocial support in the management of breast cancer patients[51,52]. The PCS and MCS scores observed in the current study were similar in women with and without breast cancer. In women with breast cancer, the PCS and MCS scores were 50, a result similar to that observed in North American women with a history of breast cancer[22].

Okamura et al.[52], in a prospective study involving 41 women with breast cancer, after a six-month period, observed that counseling on cancer and its treatment, as well as providing psychosocial support and information on how to cope with the disease contributed towards a significant improvement in quality of life. Ganz et al.[22] prospectively evaluated North American women with a history of breast cancer after a mean time since diagnosis of 6.3 years. Applying the SF-36, these authors confirmed good quality of life scores. There was a slight decline in the following components: physical functioning, role-physical, general health and bodily pain, although the authors highlighted that this finding would be expected for an aging population. However, these women continued to show good quality of life scores, in accordance with the results presented here. In another study, Arndt et al.[53] assessed quality of life in German women (mean age of 58 years) with breast cancer. These authors observed good quality of life scores in the domains evaluated, reporting a global health score that was similar to that of the general population.

This study was the first to evaluate menopausal symptoms and quality of life in Brazilian women with breast cancer. Other aspects of this study that are worth mentioning relate to the existence of one group for comparison and the use of a nationally validated questionnaire on quality of life. The groups assessed

showed distinct characteristics. To minimize these differences, we used logistic regression and linear regression models adjusted for potentially confounding variables. Education and socioeconomic status are factors that may influence the report of climacteric symptoms and sexual behavior. However, we believe that this aspect was minimized, since the women evaluated, with or without breast cancer, were recruited from the same institution (public service). In this institution, women are of a low-income and are less educated. Limitations were related to the study design (cross-sectional) and failure to use an instrument that assessed the intensity of symptoms. Further studies are needed to explain important aspects associated with menopausal symptoms and their impact on quality of life in women with breast cancer. Some of these aspects are related to modifications with time, due to systemic treatment (chemotherapy and endocrine therapy), repercussions on sexuality, and population characteristics (education, social status, employment), among others.

Finally, we believe that this study may contribute to the management of women with breast cancer. We observed that the prevalence of menopausal symptoms was similar in women with and without breast cancer. Perhaps if we had included tamoxifen users, we would have observed a higher prevalence of hot flashes among breast cancer survivors. However, when we designed this study our aim was to gain knowledge about the climacteric syndrome in breast cancer survivors who were not receiving hormone therapy. Therefore, women with breast cancer require interventions that minimize the impact of the climacteric syndrome on their lives as much as those without breast cancer.

Conclusion

The prevalence of menopausal symptoms in women with breast cancer is similar to that found in women without breast cancer. Sexual activity was less frequent in women with breast cancer. Quality of life was good in women with and without breast cancer. Women with breast cancer had higher levels of physical functioning than those without cancer.

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TABLE 1. Sociodemographic and clinical features of women with and without breast cancer (n=182).

Characteristics	With Cancer N=97	Without Cancer N=85	p value
Age (years)*	53.2 (6.2)	57.8 (4.9)	<0.01(1)
Age at menarche (years)*	13.0 (1.7)	13.1 (1.8)	0.78(1)
Age at first childbirth (years)*	22.7 (5.0)	22.2 (4.6)	0.54(1)
Age at menopause (years)* †	47.2 (5.1)	47.4 (4.9)	0.76(1)
Body Mass Index (kg/m^2)*	28.0 (5.5)	29.9 (5.6)	0.03(1)
Parity#			0.03(2)
Nulliparity	13 (13.4)	4 (4.7)	
1-2	38 (39.2)	26 (30.6)	
≥3	46 (47.4)	55 (64.7)	
Menopausal status#			<0.01(2)
Premenopausal	24 (24.7)	4 (4.7)	
Postmenopausal	73 (75.3)	81 (95.3)	

*Values expressed in mean (SD).

#Values expressed in N (%).

†Exclusion of 10 women with unknown date of their last menstruation from each group.

(1)Student's t test.

(2)Fisher's exact test.

TABLE 2. Vasomotor symptoms in women without cancer (n=85) and with breast cancer (n=97).

Variables	Group	%	Adjusted OR[a] (95% CI)	Adjusted p value[a]
Hot flashes	without cancer	50.6	1.00	0.70
	with cancer	53.6	0.85 (0.38-1.89)	
Sweating	without cancer	49.4	1.00	0.10
	with cancer	37.1	0.54 (0.27-1.12)	
Palpitation	without cancer	38.8	1.00	0.27
	with cancer	23.7	0.65 (0.30-1.39)	
Dizziness	without cancer	47.1	1.00	0.07
	with cancer	34.0	0.51 (0.24-1.05)	

[a]Adjusted for age, age at menarche, body mass index, parity, smoking habit, race, marital status and menopausal status, using unconditional logistic regression models.

TABLE 3. Psychological symptoms in women without cancer (n=85) and with breast cancer (n=97).

Variables	Group	%	Adjusted OR[a] (95% CI)	Adjusted p value[a]
Nervousness	without cancer	67.1	1.00	0.77
	with cancer	70.1	0.90 (0.42-1.89)	
Headache	without cancer	49.4	1.00	0.17
	with cancer	43.3	0.60 (0.29-1.24)	
Depression	without cancer	48.2	1.00	0.23
	with cancer	43.3	0.64 (0.31-1.32)	
Insomnia	without cancer	52.9	1.00	0.94
	with cancer	49.5	0.97 (0.48-1.96)	

[a]Adjusted for age, age at menarche, body mass index, parity, smoking habit, race, marital status and menopausal status, using unconditional logistic regression models.

TABLE 4. Genital symptoms and sexual activity in women without cancer (n=85) and with breast cancer (n=97).

Variables	Group	%	Adjusted OR[a] (95% CI)	Adjusted p value[a]
Vaginal dryness	without cancer	37.6	1.00	0.29
	with cancer	39.2	0.67 (0.31-1.41)	
Dyspareunia[b]	without cancer	27.8	1.00	0.39
	with cancer	30.0	0.57 (0.16-2.03)	
Sexual activity	without cancer	62.4	1.00	<0.01
	with cancer	51.5	0.16 (0.05-0.43)	

[a]Adjusted for age, age at menarche, body mass index, parity, smoking habit, race, marital status and menopausal status, using unconditional logistic regression models.

[b]Including sexually active women.

TABLE 5. Comparison between the median scores on the SF-36, considering women with breast cancer (n=97) and without cancer (n=85).

SF-36 domains	Group	Median	Percentile		Crude	Adjusted
			25%	75%	p value	p value[a]
Physical functioning	with cancer	90.0	65.0	95.0	0.04	<0.01
	without cancer	75.0	55.0	90.0		
Role-physical	with cancer	75.0	0	100.0	1.00	0.93
	without cancer	75.0	75.0	100.0		
Bodily pain	with cancer	61.0	42.0	72.0	<0.01	0.28
	without cancer	51.0	41.0	72.0		
General health	with cancer	72.0	57.0	82.0	0.49	0.18
	without cancer	67.0	47.0	77.0		
Vitality	with cancer	65.0	50.0	80.0	0.61	0.61
	without cancer	60.0	45.0	75.0		
Social functioning	with cancer	75.0	50.0	87.5	1.00	1.00
	without cancer	75.0	50.0	100.0		
Role-emotional	with cancer	100.0	33.3	100.0	1.00	1.00
	without cancer	100.0	0	100.0		
Mental health	with cancer	68.0	52.0	80.0	0.50	0.06
	without cancer	64.0	48.0	80.0		

[a]Adjusted for age, age at menarche, body mass index, parity, smoking habit, race, marital status and menopausal status, using linear least absolute value regression models.

TABLE 6. Comparison between the median physical and mental component summaries scores on the SF-36, considering women with breast cancer (n=97) and without cancer (n=85).

Component summary	Group	Median	Percentile		Crude p value	Adjusted p value[a]
			25%	75%		
PCS[b]	with cancer	50.0	37.7	53.8	0.05	0.30
	without cancer	44.9	35.1	51.3		
MCS[c]	with cancer	50.0	38.4	56.1	0.35	0.28
	without cancer	47.4	35.8	55.4		

[a]Adjusted for age, age at menarche, body mass index, parity, smoking habit, race, marital status and menopausal status, using linear least absolute value regression models.

[b]PCS: Physical Component Summary.

[c]MCS: Mental Component Summary.

3.2. Artigo 2

----- Original Message -----

From: <karen.earick@jax.ufl.edu>
To: <aarao@unicamp.br>
Sent: Sunday, February 06, 2005 1:27 AM
Subject: Manuscript submitted - TBJ-00022-2005

Re: Quality of Life in Brazilian Breast Cancer Survivors Aged 45 to 65: Associated Factors

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Sincerely,

Karen Earick
Manager Editor
The Breast Journal

Quality of Life in Brazilian Breast Cancer Survivors Aged 45 to 65: Associated Factors

Quality of life in breast cancer survivors

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Key words: Breast cancer, Menopause, Quality of life, SF-36 questionnaire

Abstract

The objectives of this study were to evaluate quality of life (QOL) and identify its associated factors in climacteric women with a history of breast cancer. A cross-sectional study was performed including 75 breast cancer survivors aged 45 to 65 years, who had undergone complete oncologic treatment and non-users of hormone therapy or tamoxifen in the last six months. Sociodemographic and clinical characteristics, in addition to the prevalence of climacteric symptoms were evaluated. QOL was evaluated by the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) questionnaire. Generalized linear models were used to analyze data, allowing the identification of factors affecting QOL, adjusting for confounding variables. The mean age of the participants was 53.1±5.9 years. Breast cancer survivors reported good QOL. The most prevalent symptoms were nervousness (69%) and hot flashes (56%). Factors negatively associated with the Physical Component Summary were: dizziness, postmenopausal status and breast-conserving therapy (BCT), while radiation therapy was positively related to this component. Insomnia and being married were negatively related to the Mental Component Summary. In conclusion, participants demonstrated good QOL. We identified factors that may influence QOL in women with breast cancer, highlighting being married, climacteric symptoms, postmenopausal status and BCT. Given the impact of these factors, health professionals and patients must discuss choices of alleviating climacteric symptoms and explanations of the potential repercussions of breast cancer treatment.

Introduction

Breast cancer is the second most common malignancy in the world (1) and millions of dollars are spent annually on the disease (2). A significant number of cases occur in women aged 40 to 60 years (3), characterizing the neoplasm as a disease affecting climacteric women (4). With the reduction in mortality due to breast cancer (5), the number of women with a history of the disease during the menopausal transition is increasing.

During the climacteric, complaints associated with estrogen deficiency are common, and may occur in premenopausal and postmenopausal women (6). Previous studies reported a 65% prevalence of hot flashes (7, 8), 48% of vaginal dryness and 26% of dyspareunia in women with breast cancer (7). Tamoxifen use is described as a factor associated with these symptoms, which might be more severe and frequent in these women (7), negatively influencing their quality of life (QOL) (9, 10).

The definition of QOL is subjective because it encompasses the sociocultural aspects of the population studied and the individual's own perception of health status. In research on breast cancer patients, the endpoints are traditionally disease-free survival, tumor response and overall survival. However, it became evident that these endpoints did not provide sufficient basis for making treatment decisions (11). Interest in the QOL of cancer patients has increased, and there are suggestions for assessing QOL in daily clinical oncology practice (12).

Studies on QOL and climacteric symptoms in women with breast cancer were performed in developed countries (6-8), where cultural and economic realities are different from those of developing countries. Few investigations evaluated middle-aged women with breast cancer, at a time marked by hormonal and emotional changes. Given

these aspects, we conducted the current study to evaluate QOL and identify its associated factors in climacteric women with a history of breast cancer.

Patients and Methods

Selection of the participants was previously described in detail (13). Briefly, the current sample was derived from a study comparing the prevalence of menopausal symptoms, sexual activity and QOL in women with and without breast cancer. However, factors associated with QOL were not investigated (13).

Between August 2002 and June 2003 a cross-sectional study was conducted at the Women's Hospital, School of Medicine, Universidade Estadual de Campinas, Brazil. This institute serves usually women of low income and little education. Participants had been undergoing routine follow-up. Inclusion criteria were: age between 45 and 65 years, non-users of hormone replacement therapy or tamoxifen in the last six months, no history of other malignant tumors. After outpatient consultation, one hundred patients with breast cancer were consecutively invited to participate in the study. Three patients refused to participate in the interview, allegedly due to lack of time. Twenty-two patients were undergoing oncologic treatment. Therefore, 75 women with a history of breast cancer constituted the present study sample.

Participants responded to an interview that evaluated sociodemographic characteristics, including age, parity, marital status, race, body mass index (BMI), smoking, menopausal status (postmenopause: at least 12 months of amenorrhea). Clinical characteristics included time since breast cancer diagnosis, type of surgery, tumor stage, chemotherapy, radiation therapy, diabetes mellitus and arterial hypertension. The prevalence of climacteric symptoms (present/absent) experienced during the four weeks prior to enrollment in the study was investigated using a checklist. Hot flashes, sweating, palpitations, dizziness (vasomotor

symptoms), nervousness, headache, depression, insomnia (psychological symptoms), dyspareunia and vaginal dryness (genital symptoms) were studied. The ratio of sexually active women was also evaluated during the four weeks prior to inclusion in the study.

QOL was assessed by the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) questionnaire (14), a generic tool for evaluating QOL. SF-36 is currently one of the best known and widespread instruments in the health field, translated and validated to the Portuguese language in Brazil (15). It is a multidimensional questionnaire, with eight components: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. These components may be summed up in two summaries: physical component summary (PCS) and mental component summary (MCS). Each component corresponds to a value, varying from zero to 100, zero corresponding to the worse and 100 to the best health status (16). An interview was conducted by one of the investigators who applied the questionnaires. Institutional Review Board approval was obtained for the study and all women signed an informed consent form.

Generalized linear models (GLM) (17) were used to analyze data. These statistical models aimed at identifying factors that affected QOL with adjustments for confounding variables (age, BMI, menopausal status). These models allowed estimation of PCS and MCS least square means for each variable level of interest. Least square means are means corrected for imbalances in other variables. Continuous independent variables (age, BMI and time since diagnosis) were categorized into four levels and converted to a set of 0/1 variables defining ordinal categories (often known as dummy variables). The significance of each factor's effect on QOL was expressed using two-sided *p* values, where a *p* value of 0.05 or less was considered statistically significant. Analyses were performed using PROC GENMOD, SAS version 8.02 software (SAS Institute Inc.; Cary, NC).

Results

The mean age of the participants was 53.1±5.9 years. Time since diagnosis ranged from 4.0 to 246.2 months (mean: 66.0±54.9 months). Among study participants, 81% were postmenopausal, 73% were white and 70% were married. Fifty-six per cent had undergone mastectomy, 35% had been diagnosed 12 months or less before entering the study, most had undergone chemotherapy (75%) and radiation therapy (69%). Diabetes mellitus and arterial hypertension occurred in 11% and 27% of participants, respectively.

The best QOL scores were seen in the physical functioning components (82.7) and social functioning (75.8), while bodily pain (58.5) and vitality (61.9) scored lowest. Mean PCS and MCS scores were 47.1 and 46.7, respectively (Table 1). We observed that mean PCS scores were significantly lower for participants with BMI equal to or higher than 35 kg/m^2 ($p<0.01$). We observed that mean MCS scores of married or separated women were significantly lower than those of single women, $p=0.01$ and $p=0.04$, respectively. Mean PCS scale scores were significantly lower for those who had given birth to 1 or 2 children ($p=0.02$) (Table 2). Time since diagnosis ranging from 12 to 36 months was associated with lower MCS scale scores ($p<0.01$) (Table 3).

Nervousness and hot flashes were the most prevalent symptoms, 69% and 56%, respectively. Sexual activity was reported by 52% of the sample, with 31% of these women reporting dyspareunia. Statistical comparisons of PCS and MCS scores were made by the least square means within symptom groups, considering age, BMI and menopausal status as confounding variables. We noted that most PCS and MCS mean scores were lower in women presenting each specific symptom, but statistically significant differences between MCS means were observed in women who reported

palpitations, dizziness, nervousness, depression and insomnia (all respective *p* values lower or equal to 0.01). A statistically significant difference between PCS means was only observed for dizziness, means of 39.6 and 48.7 ($p<0.01$), for those with and without dizziness, respectively (Table 4).

Multiple GLM regression analysis was performed to simultaneously identify significant associations of PCS and MCS with all independent variables. Dyspareunia was not included in this model because several sampled women were not sexually active (48%), thus the missing information on this symptom could not be incorporated into the statistical model. We noted that postmenopausal status ($p<0.01$), a history of breast-conserving therapy (BCT) ($p=0.02$) and dizziness ($p<0.01$) were negatively associated with the physical component, whereas radiation therapy was positively associated with the PCS scale ($p<0.01$). Insomnia ($p<0.01$) and being married ($p=0.02$) were negatively related to the MCS scale (Table 5).

Discussion

In this cross-sectional study, we evaluated QOL and identified its associated factors in climacteric women with a history of breast cancer. Although some authors have assessed these aspects in middle-aged women with breast cancer, their studies were conducted in developed countries (7, 18-20).

Overall, our study participants had a good QOL. Physical functioning and social functioning had the best scores. These findings are consistent with those of previously published studies on different populations of breast cancer survivors (18-20). Good scores in the present cohort were likely attributed to the multiprofessional care offered by this institute, highlighting psychosocial support and physical therapy. Both treatments may contribute towards a better perception of health status, minimizing the impact of cancer

diagnosis and treatment. Other researchers have reported the importance of psychosocial support in the management of breast cancer patients (21).

In a prospective study of breast cancer survivors, Ganz et al. (19) observed good QOL scores after an average of 6.3 years since diagnosis. These authors reported a slight decrease in physical functioning, role-physical, general health and bodily pain, emphasizing that for an aging population this result was to be expected. Casso et al. (20) also observed good scores in the physical functioning and social functioning scales after an average of 7.3 years since diagnosis. The lowest score in the vitality dominion was also confirmed by other investigators (20). PCS and MCS scores were slightly lower than those reported in North American women with breast cancer (19, 20).

PCS scale scores were significantly lower in women with a higher BMI, a result confirmed in previous studies. Obesity is associated with a worse QOL in patients with (22) and without breast cancer (23). Difficulty in walking and performing daily activities may account for these results. Parity showed a non-linear association with QOL. Women with no children had better PCS scale scores, compared to women with one or two children, however there was no difference when they had three or more children. Negative associations between parity and QOL were described in middle-aged women without breast cancer (24).

Time since diagnosis also showed a non-linear relation to QOL scores. Other investigators reported that cancer had a minimum impact on QOL in long-term breast cancer survivors (25). In the current study, the period between 12 and 36 months since diagnosis was associated with the lowest MCS scale scores. During that period women were likely to experience greater psychological distress, since oncologic treatment had ended and psychosocial support was no longer available as frequently as in the

beginning of therapy. Patients suffered with the expectation of returning to normal activities, doubts about the future and fear of disease recurrence. These concerns lessened over time.

In the present study, a history of chemotherapy was not associated with QOL. Joly et al. (18) compared two groups of women with breast cancer (chemotherapy vs. no chemotherapy) after a mean period of 9.6 years since the beginning of treatment. These authors observed no differences in QOL. However, Broeckel et al. (26) evaluating women during a mean period of two years since diagnosis, reported a worse QOL in those undergoing chemotherapy. Ganz et al. (19) also reported QOL impairment in women receiving chemotherapy, emphasizing that these results needed further studies designed specifically to address this issue. Analysis of these studies suggests that the influence of chemotherapy on QOL changes with time, its association or influence remains uncertain and may be explained by future prospective studies.

Hot flashes were the most common vasomotor symptoms, affecting 56% of women but not influencing QOL. However, palpitations which affected 28% of the participants was negatively associated with MCS, likely indicating anxiety and fear, which may affect these women and negatively influence their QOL. The most prevalent psychological symptom was nervousness (69%), similar to that observed in a population-based study conducted among climacteric women in Brazil (27). Women with a history of breast cancer may present psychological alterations such as depression (7), fear of recurrence and fear of abandonment by family and friends (28). In the present case study, depression was reported by 40% of the participants, similar to that reported in breast cancer survivors in the United States (7). Interpretation of the depression prevalence reported in both studies must consider that formal tools were not

used to assess depression. The actual prevalence of psychological and psychiatric changes in women with breast cancer remains unknown (28).

Previous investigations observed that middle-aged women with climacteric symptoms have severely impaired QOL (29, 30). In the current study, after multivariate analysis, dizziness and insomnia remained negatively associated with QOL. Our findings indicate that dizziness was negatively associated with the physical component, perhaps due to difficulties in performing daily chores. According to several studies, insomnia is correlated with fatigue and mood swings (31), negatively affecting QOL (32), as our results have shown. The higher prevalence of climacteric symptoms and other changes associated with postmenopause estrogen deficiency could explain the worse QOL during this period.

We observed that being married was negatively associated with QOL. Published studies reported that partner relationship is important to QOL in women with breast cancer (33). It may be a source of stress or support, depending on the quality of the relationship between the couple. Women who are satisfied with their partners report feeling psychologically better (33). Married women in this study might not have enjoyed a good relationship, perhaps explaining their compromised MCS, although the quality of the relationship was not studied.

A positive association between radiation therapy and QOL is counter-intuitive. According to a previous study, the critical period for breast cancer patients is the interval between the second week of treatment and two weeks following the end of radiation therapy, improving after this period (34). A likely explanation for these findings is that our study participants had been diagnosed an average of 66 months previously. After facing cancer, these women may have changed their expectations and assessed life in a

more positive way. However, we highlight that these findings represent an association and not causality and should be explored in future investigations including larger samples.

The relationship between type of surgery, psychological adjustment and QOL is controversial in the literature. Some studies reported that patients undergoing BCT had a better self-image (35), however, others described better psychological adjustment in women submitted to mastectomy (36, 37), despite the similar QOL results observed (37). A negative association between BCT and QOL may have occurred because women submitted to BCT frequently reported pain, changing their perception of physical well-being, limiting their adjustment and reducing the benefits of BCT (38). Another explanation is that breast tissue was partly preserved in women undergoing BCT, a likely source of growing anxiety over disease recurrence (37).

Interpretation of our data must consider some limitations, e.g. sample size and study design. The cross-sectional design allowed identification of several factors associated with QOL, although causal inferences could not be made. Another limitation was failure to evaluate the intensity of climacteric symptoms and to correlate it with QOL.

In the current study, we emphasized the use of a standardized and internationally validated QOL questionnaire. We believe that it was the first study conducted in Latin America to describe an association between climacteric symptoms and QOL in women with breast cancer. It was probably one of the first studies to report a negative association between postmenopause and QOL in middle-aged women with breast cancer, suggesting the need to conduct new research on the subject.

In conclusion, we believe that our results are of interest to all health professionals and healthcare providers involved in the management of women with breast cancer. Our

study indicated that women with a history of breast cancer had a good QOL. Factors causing QOL impairment were identified, e.g. postmenopause, climacteric symptoms, BCT and being married. The findings of this study should be the target of further research, emphasizing the need for interventional studies that minimize the negative impact of the climacteric symptoms and menopause on the QOL in women with breast cancer. Psychological support for couples who experience breast cancer diagnosis may improve QOL. Prospective studies are needed to evaluate the influence of other factors (school education, socioeconomic status, job, quality of partner relationship) on QOL and climacteric symptoms with time.

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Table 1. Summary characteristics of all SF-36 scales and summary scale scores of breast cancer patients (n=75).

Scale	Mean	SD	Quartile 25%	Quartile 75%	Minimum	Maximum
Physical functioning	82.7	18.8	70.0	100	25.0	100
Role-physical	64.3	44.1	0	100	0	100
Bodily pain	58.5	25.4	41.0	72.0	0	100
General health	69.6	17.8	62.0	82.0	15.0	95.0
Vitality	61.9	27.8	50.0	85.0	0	100
Social functioning	75.8	23.6	62.5	100	12.5	100
Role-emotional	69.3	42.4	33.3	100	0	100
Mental health	66.0	22.3	52.0	80.0	12.0	100
Physical Component Summary	47.1	9.6	39.0	54.3	20.9	64.7
Mental Component Summary	46.7	12.6	38.4	56.7	17.3	64.6

SD: standard deviation.

Table 2. Mean values of the physical and mental component summary scales, according to the sociodemographic characteristics of women with a history of breast cancer (n=75).

Characteristic	N	%	PCS scale Adjusted mean	PCS scale p-value	MCS scale Adjusted mean	MCS scale p-value
Age (years)						
≤49	10	13	48.7	ref.	48.5	ref.
50-54	19	25	45.1	0.19	42.3	0.08
55-59	21	28	47.0	0.54	46.6	0.61
>60	25	34	47.4	0.70	51.7	0.48
Smoking habit[a]						
Smoker	9	12	44.7	ref.	48.0	ref.
Non-smoker	66	88	49.3	0.14	49.4	0.76
Body mass index (kg/m^2)[b]						
<25	25	33	47.7	ref.	49.3	ref.
25-30	31	42	49.2	0.51	45.3	0.21
30-35	15	20	46.5	0.68	47.4	0.63
≥35	4	5	31.0	<0.01	51.0	0.80
Menopausal status[c]						
Premenopause	14	19	47.1	ref.	47.9	ref.
Postmenopause	61	81	42.8	0.16	48.3	0.91
Race[a]						
White	55	73	45.3	ref.	48.5	ref.
Non-white	20	27	44.0	0.58	47.2	0.68
Marital Status[a]						
Single	7	9	49.9	ref.	59.0	ref.
Married	52	70	43.9	0.10	46.9	0.01
Separated	6	8	48.8	0.82	45.6	0.04
Widow	10	13	46.9	0.52	49.2	0.12
Parity[a]						
Nullipara	12	16	49.3	ref.	49.8	ref.
1-2	39	39	42.6	0.02	46.7	0.45
≥3	34	45	44.9	0.13	48.5	0.76

ref: reference category for comparisons.

[a]Least square means adjusted for age, body mass index and menopausal status.

[b]Least square means adjusted for age and menopausal status.

[c]Least square means adjusted for age and body mass index.

Table 3. Mean values of the physical and mental component summary scales, according to the clinical characteristics of women with a history of breast cancer (n=75).

Characteristic	N	%	PCS scale		MCS scale	
			Adjusted Mean[a]	p-value	Adjusted Mean[a]	p-value
Type of surgery						
Mastectomy	42	56	45.9	ref.	47.6	ref.
Breast-conserving therapy	33	44	44.0	0.40	48.9	0.73
Time since diagnosis (months)						
≤12	26	35	42.6	ref.	54.4	ref.
12-36	20	27	45.6	0.41	40.8	<0.01
36-72	20	27	44.2	0.66	49.6	0.31
>72	9	12	47.0	0.21	46.2	0.08
Stage						
0	14	19	48.4	0.40	41.3	0.28
I	41	55	45.1	0.99	45.5	0.75
II	12	16	43.8	0.64	51.0	0.32
III	8	10	45.1	ref.	47.0	ref.
Chemotherapy						
Yes	56	75	44.0	ref.	48.6	ref.
No	19	25	47.9	0.08	46.7	0.56
Radiation therapy						
Yes	52	69	44.4	ref.	48.4	ref.
No	23	31	45.6	0.60	47.8	0.84
Diabetes						
Yes	8	11	43.1	ref.	46.6	ref.
No	67	89	45.3	0.55	48.4	0.73
Hypertension						
Yes	20	27	44.4	ref.	49.8	ref.
No	55	73	45.4	0.68	46.6	0.37

ref: reference category for comparisons.

[a]Least square means adjusted for age, body mass index and menopausal status.

Table 4. Mean values of the physical and mental component summary scales, according to climacteric symptoms and sexual activity in women with a history of breast cancer (n=75).

Variables		N	%	PCS scale		MCS scale	
				Adjusted Mean[a]	p-value	Adjusted Mean[a]	p-value
Hot flashes	yes	42	56	44.0	0.48	46.8	0.45
	no	33	44	45.6		49.1	
Sweating	yes	31	41	44.2	0.52	45.7	0.12
	no	44	59	45.5		50.0	
Palpitations	yes	21	28	43.3	0.40	41.8	0.01
	no	54	72	45.3		49.6	
Dizziness	yes	28	37	39.6	<0.01	42.8	<0.01
	no	47	63	48.7		51.9	
Nervousness	yes	52	69	43.6	0.18	43.7	<0.01
	no	23	31	46.9		54.7	
Headache	yes	33	44	43.3	0.14	45.6	0.10
	no	42	56	46.4		50.4	
Depression	yes	30	40	44.6	0.83	38.7	<0.01
	no	45	60	45.1		52.0	
Insomnia	yes	39	52	50.0	0.09	41.0	<0.01
	no	36	48	46.3		51.9	
Sexual activity	yes	39	52	44.3	0.48	48.9	0.53
	no	36	48	45.7		47.2	
Vaginal dryness	yes	30	40	45.2	0.86	47.1	0.60
	no	45	60	44.8		48.6	
Dyspareunia[b]	yes	12	31	45.4	0.81	41.3	0.06
	no	27	69	46.1		47.8	

[a]Least square means adjusted for age, body mass index and menopausal status

[b]Includes only women with sexual activity.

Table 5. Multivariate model, variables associated with physical and mental component summary scales in women with a history of breast cancer (n=75).

	PCS scale			MCS scale		
Parameter	Estimate	SE	p-value	Estimate	SE	p-value
Intercept	0.3995	0.3169	0.21	0.6952	0.4019	0.08
Menopausal status						
Premenopause	ref.	-	-	ref.	-	-
Postmenopause	-0.4235	0.1194	<0.01	-0.0822	0.1483	0.58
Marital status						
Single	ref.	-	-	ref.	-	-
Married	0.0051	0.2182	0.98	-0.6309	0.2767	0.02
Separated	0.0851	0.2310	0.71	-0.3037	0.2965	0.31
Widow	0.1424	0.2337	0.54	-0.3457	0.2990	0.25
Type of surgery						
Mastectomy	ref.	-	-	ref.	-	-
Breast-conserving therapy	-0.2401	0.1060	0.02	0.1871	0.1368	0.17
Radiation therapy	0.2978	0.1127	<0.01	-0.1391	0.1427	0.33
Dizziness	-0.4599	0.1005	<0.01	-0.2273	0.1257	0.07
Insomnia	0.0734	0.1206	0.54	-0.5155	0.1534	<0.01

ref.: Reference category for multiple comparisons.

SE: Standard error of parameter estimates.

4. Discussão

Os objetivos deste estudo foram comparar a prevalência de sintomas climatéricos, a proporção de mulheres com atividade sexual e a QV em mulheres com e sem câncer de mama e identificar os fatores associados à QV de mulheres com câncer de mama. Na prática clínica diária no Ambulatório de Oncologia Mamária e no Ambulatório de Menopausa do Centro de Atenção Integral à Saúde da Mulher (CAISM) da Universidade Estadual de Campinas (Unicamp) observa-se que são comuns as queixas de sintomas climatéricos de pacientes com história de câncer de mama. Habitualmente essas pacientes questionam acerca das opções de tratamento para o alívio destes sintomas, após serem informadas da contra-indicação à TH. Dessa forma, profissionais de saúde e pacientes vivenciam as dúvidas nem sempre esclarecidas sobre a atenção ao climatério em mulheres com câncer de mama.

Essas observações estimularam a realização deste estudo, a partir do qual foram elaborados dois artigos que se complementam e auxiliam na compreensão e na interpretação da experiência da transição climatérica e da QV em mulheres com e sem câncer de mama. No primeiro artigo os dois grupos foram incluídos

para comparação da prevalência dos sintomas climatéricos e da QV, enquanto no segundo artigo procurou-se identificar os fatores associados à QV de mulheres com história de câncer de mama e tratamento oncológico completo.

Os sintomas climatéricos em mulheres com câncer de mama podem ser conseqüência do tratamento oncológico ou coincidir com esse diagnóstico. No presente estudo a prevalência de sintomas climatéricos (vasomotores, psicológicos, genitais) foi semelhante em mulheres com e sem câncer de mama. Dentre os sintomas vasomotores, as ondas de calor foram os mais freqüentes, porém com prevalência menor que a relatada por outros autores (COUZI et al., 1995; CARPENTER et al., 1998; BIGLIA et al., 2003). A diferença de prevalência com outros estudos possivelmente relacionou-se à exclusão de usuárias de tamoxifeno, às diferenças socioculturais entre as diferentes populações estudadas, uma vez que estes autores avaliaram mulheres de outros países. Estudos prévios destacaram a importância dessas diferenças na vivência da menopausa e no relato dos sintomas climatéricos (FU et al., 2003). As ondas de calor podem ter um impacto negativo na QV por causarem insônia, que resulta em fadiga, irritabilidade, esquecimento, desconforto físico e efeitos negativos no trabalho (OLDENHAVE et al., 1993). A insônia pode estar relacionada às ondas de calor, porém apresenta origem multifatorial, incluindo fatores emocionais, físicos e cognitivos (CARPENTER et al., 2004; SAVARD et al., 2004), podendo comprometer a QV, como observado no presente estudo.

O sintoma psicológico mais prevalente foi o nervosismo, semelhante ao reportado em estudo de base populacional entre mulheres climatéricas no Brasil

(PEDRO et al., 2003b). Embora seja sabido que o diagnóstico e a terapia anticâncer induzam repostas emocionais negativas, o estado de incerteza prévio ao diagnóstico pode gerar mais ansiedade do que o evento adverso (diagnóstico do câncer) em si (NOSARTI et al., 2002).

Vale destacar que uma proporção significativamente menor de mulheres com câncer de mama referiu atividade sexual quando comparada ao grupo-controle, formado por mulheres sem câncer de mama, não usuárias de TH nos últimos seis meses e freqüentadoras da mesma instituição. Embora a etiologia das disfunções sexuais não seja bem compreendida, SCHULTZ et al. (1992) sugerem que reações psicológicas ao câncer também podem servir de base para as disfunções sexuais em algumas mulheres. Vale lembrar que as mulheres avaliadas no presente estudo apresentavam idade entre 45 e 65 anos, fase em que pode haver uma diminuição da atividade sexual conseqüente às influências sociais e às alterações decorrentes do hipoestrogenismo como a secura vaginal, levando à dispareunia.

Em estudo de base populacional conduzido entre mulheres brasileiras no climatério observou-se como principal queixa sexual a diminuição do interesse, fato semelhante ao relatado em outros países (UTIAN e SCHIFF, 1994; PEDRO et al., 2003b; BLÜMEL et al., 2004). Porém, o presente estudo limitou-se a relatar a proporção de mulheres com e sem atividade sexual. Não explorou aspectos como o prazer e o interesse sexuais, que podem estar comprometidos em mulheres com câncer de mama (BUKOVIC et al., 2005). A relação entre sexualidade e QV deverá ser avaliada em futuros estudos, uma vez que a autopercepção do estado de saúde como excelente/boa relaciona-se com a obtenção do prazer (TADINI, 2000).

No presente estudo, a QV, avaliada através do SF-36, foi considerada boa em mulheres com e sem câncer de mama. Quando comparados os dois grupos, as mulheres com câncer de mama apresentaram significativamente melhor capacidade funcional. A análise apenas das mulheres tratadas de câncer de mama também demonstrou o melhor escore no domínio capacidade funcional, sugerindo que a terapia antineoplásica não interferiu na realização de tarefas diárias.

Estudos prévios relataram bons escores de QV em mulheres com câncer de mama, aplicando-se diferentes questionários (GANZ et al., 1998; 2002; ARNDT et al., 2004). GANZ et al. (2002), em estudo prospectivo, avaliaram 763 mulheres norte-americanas e observaram bons escores de QV. Os autores referiram que houve uma pequena diminuição dos escores nos componentes aspectos físicos, capacidade funcional, estado geral de saúde e dor, porém ressaltaram que isto seria o esperado para uma população que está envelhecendo. Contrariamente, essas mulheres apresentaram melhora dos sintomas depressivos e aspectos emocionais, o que provavelmente relacionou-se ao amadurecimento emocional que se segue ao processo de envelhecimento.

Os bons escores de QV observados no presente estudo podem ser reflexo da assistência multiprofissional prestada nesta instituição, ressaltando-se o suporte psicossocial. Este suporte contribui para uma melhor percepção do estado de saúde, minimizando os impactos do diagnóstico e do tratamento do câncer de mama (FUKUI et al., 2000; GANZ et al., 2002; OKAMURA et al., 2003). O acesso a informações sobre a neoplasia de mama, bem como sobre as modificações que

ocorrem durante a transição climatérica, também contribuem para uma melhor auto-avaliação do estado de saúde e da QV.

Na presente casuística a quimioterapia não se associou à QV. GANZ et al. (2002), observaram que mulheres com antecedente de quimioterapia apresentaram menores escores de QV, à semelhança dos resultados de outros autores (SCHAGEN et al., 1999; BROECKEL et al., 2000). Porém, outros pesquisadores não observaram diferenças na QV entre mulheres com e sem o antecedente de quimioterapia (JOLY et al., 2000). Além da quimioterapia, outros fatores podem influenciar a QV de mulheres com câncer de mama. Dentre estes fatores citam-se estado marital, tipo de cirurgia, radioterapia e os sintomas climatéricos. No presente estudo, alguns fatores que podem determinar prejuízos à QV de mulheres com câncer de mama foram identificados: ser casada, sintomas climatéricos, estado de pós-menopausa e cirurgia conservadora de mama.

Outros pesquisadores reportaram alguns desses fatores como preditivos da QV em mulheres com e sem câncer de mama (BLÜMEL et al., 2000; STEIN et al., 2000; FUH et al., 2003). Porém, algumas associações permanecem controversas e necessitam de novos estudos para serem esclarecidas. A relação entre tipo de cirurgia e QV apresenta resultados conflitantes na literatura. Embora a cirurgia conservadora de mama associe-se a uma melhor percepção da auto-imagem (SCHOVER, 1991), este fato parece não determinar diferenças significativas na QV a longo prazo (COHEN et al., 2000; GANZ et al., 2002). Estudos prospectivos poderão esclarecer associações que permanecem controversas, pois os estudos realizados até o momento são, em sua maioria, de corte transversal.

Este estudo, até onde se sabe, foi o primeiro no Brasil a avaliar a síndrome climatérica e a QV em mulheres com câncer de mama. Não se limitou à avaliação da prevalência das ondas de calor, porém incluiu sintomas genitais, psicológicos e outros sintomas vasomotores. Outros aspectos que merecem referência são a existência de um grupo-controle e o uso de um questionário de QV com confiabilidade e validade comprovadas. A investigação dos sintomas climatéricos acrescentou aspectos não avaliados pelo SF-36 como o sono e a atividade sexual, contribuindo para uma melhor compreensão dos diversos domínios da QV. Vale ressaltar a identificação de eventos naturais na vida da mulher (menopausa, sintomas climatéricos) como fatores associados negativamente à QV.

O desenho do estudo, um corte transversal, possibilitou conhecer a prevalência de sintomas climatéricos e identificar fatores associados à QV, porém sem estabelecer relações de causalidade. Outro fator limitante foi a não aplicação de um instrumento validado que permitisse estudar a intensidade desses sintomas. Se tivéssemos incluído um grupo de usuárias de tamoxifeno poderíamos avaliar a associação desta droga com os sintomas climatéricos e com a QV.

Futuras investigações deverão contemplar outros fatores associados à síndrome climatérica e à QV de mulheres com câncer de mama. Aspectos como escolaridade, nível socioeconômico, emprego, qualidade do relacionamento com o parceiro, entre outros, deverão ser avaliados. Estudos prospectivos poderão contribuir para o esclarecimento de questões relacionadas às modificações da QV ao longo do tempo e ao real impacto da terapia adjuvante sobre a QV, os

sintomas climatéricos e a sexualidade. Nesse sentido, a aplicação de questionários genéricos e específicos será útil.

O reconhecimento da ocorrência de sintomas climatéricos em mulheres com câncer de mama e, mais ainda, a identificação destes sintomas como fatores que contribuem para a deterioração da QV são importantes aspectos relacionados à assistência dessas mulheres. Esses dados suportam a necessidade de intervenções que minimizem o impacto da síndrome climatérica na vida dessas mulheres, tanto quanto na daquelas sem câncer.

5. Conclusões

- **Artigo 1**

  1. A prevalência de sintomas climatéricos foi semelhante em mulheres com e sem câncer de mama.

  2. Mulheres com câncer de mama referiram menos atividade sexual, quando comparadas às mulheres sem câncer de mama.

  3. A qualidade de vida foi boa em mulheres com e sem câncer de mama, porém mulheres com câncer de mama apresentaram melhor capacidade funcional.

- **Artigo 2**

  1. Mulheres com câncer de mama apresentaram boa qualidade de vida.

  2. Sintomas climatéricos, cirurgia conservadora de mama, ser casada e pós-menopausa associaram-se negativamente à qualidade de vida de mulheres com câncer de mama.

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7. Bibliografia de Normatizações

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8. Anexos

8.1. Anexo 1 – Lista de Verificação

CÂNCER DE MAMA, MENOPAUSA E QUALIDADE DE VIDA

Grupo: |____| 1. Com câncer de mama 2. Sem câncer de mama Nº estudo_____

	Aceita	Rejeita
1. Quantos anos a Sra. tem?	| 1 | ≥45 e ≤65	| 2 | <45 ou >65
2. Nos últimos seis meses, a Sra. tomou algum hormônio para a menopausa?	| 1 | Não	| 2 | Sim
3. Nos últimos seis meses, a Sra. tomou tamoxifeno? (Somente para mulheres com câncer de mama).	| 1 | Não	| 2 | Sim
4. A Sra. teve algum tipo de câncer? (Somente para mulheres sem câncer de mama).	| 1 | Não	| 2 | Sim
5. A Sra. teve algum outro tipo de câncer, além do câncer de mama? (Somente para mulheres com câncer de mama)	| 1 | Não	| 2 | Sim
Selecionada	**| | Sim**	**| | Não**

Se a resposta for | 2 | em alguma das questões,
a mulher não será aceita para o estudo.

8.2. Anexo 2 - Termo de Consentimento Livre e Esclarecido

CÂNCER DE MAMA, MENOPAUSA E QUALIDADE DE VIDA

Eu, _____,
RG nº_____, fui informada de que está sendo realizada uma pesquisa no CAISM – UNICAMP com mulheres na menopausa, um grupo com câncer de mama e outro sem essa doença. O objetivo da pesquisa é estudar o que ocorre com a vida dessas mulheres quando estão próximas da menopausa. Com esse conhecimento poderá ser dado um melhor atendimento médico a essas mulheres. Se eu concordar em participar da pesquisa responderei a um questionário, com a liberdade para deixar de responder as questões que não desejar. Terei que realizar dois exames que fazem parte do atendimento às mulheres na menopausa.

Um exame serve para ver a taxa de colesterol no sangue. Será colhida uma pequena quantidade de sangue (10ml) na veia com a utilização de seringa descartável, após um período de jejum de 12 horas. A coleta será realizada no Serviço de Patologia Clínica do Hospital das Clínicas – UNICAMP, onde também o sangue será analisado. O outro exame serve para avaliar se já há desgaste no osso, medindo a quantidade de osso, e se chama densitometria óssea. Ele é parecido com raios-x, não causa dor, durando aproximadamente 20 minutos. É realizado no Serviço de Medicina Nuclear do Hospital das Clínicas – UNICAMP.

Retornarei após três meses para ver os resultados dos exames. Foi esclarecido que se algum dos exames apresentar resultado alterado, receberei o tratamento e o seguimento, que forem necessários. Terei acesso às informações que solicitar no início e durante o andamento do estudo, podendo entrar em contato com o pesquisador principal Délio Marques Conde pelo telefone 3788-93-06 ou pessoalmente no Ambulatório de Menopausa CAISM - UNICAMP às terças e quartas-feiras das 08:00h às 13:00h. Poderei recusar-me a participar ou retirar-me da pesquisa a qualquer momento, sem nenhum prejuízo ao meu atendimento. Também fui informada que meu nome ou

qualquer dado que possa me identificar não serão divulgados, sendo do conhecimento apenas dos pesquisadores.

Se eu achar necessário, poderei pedir esclarecimentos ou informações a respeito das questões éticas desta pesquisa ao Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP pelo telefone 3788-8936.

Declaro que estou ciente da todas as informações prestadas e que concordo em participar deste estudo.

Campinas, _____, de _____ de _____

_____

Assinatura da participante

_____

Assinatura do pesquisador principal

8.3. Anexo 3 - Ficha de Coleta de Dados

CÂNCER DE MAMA, MENOPAUSA E QUALIDADE DE VIDA

Identificação da participante (a ser destacada da FICHA DE COLETA DE DADOS):

Grupo: |___| 1. Com câncer 2. Sem câncer		Nº no estudo |___|___|___|
Nome:		
HC: |___|___|___|___|___|___|___|		
Data 1ª consulta: |___|___|_____|		
Rua:		Nº
Bairro:	Cidade:	Est.:
Tel:		
Obs.:		

FICHA DE COLETA DE DADOS

Grupo: |___| 1. Com câncer de mama 2. Sem câncer de mama Nº estudo |__||__||__|

SEÇÃO I – CARACTERÍSTICAS PESSOAIS

“Gostaria de fazer algumas perguntas sobre a senhora”:

1.1a Qual a sua idade? |___|___| anos 1.1b Qual sua data de nascimento? |___|___|_____|

1.2 Entre estas que eu vou ler, qual a Sra. considera que é a sua cor ou raça: branca, preta, parda, amarela ou indígena?

(1) Branca
(2) Preta
(3) Parda
(4) Amarela
(5) Indígena
(6) Outra. Qual? _____

1.3 Atualmente a Sra. é solteira, casada, vive junto, separada/divorciada ou viúva?

(1) Solteira
(2) Casada
(3) Vive junto
(4) Separada/Divorciada
(5) Viúva

1.4 A Sra. fuma atualmente, já fumou no passado ou nunca fumou?

(1) Fuma atualmente >>>>>>>> Passe a 1.6
(2) Fumou no passado
(3) Nunca fumou >>>>>>>> Passe à Seção II

1.5 Há quanto tempo a Sra. parou de fumar?

|___|___| meses ou |___|___| anos

1.6 Quantos cigarros a Sra. fuma/fumava por dia? |___|___| cigarros

1.7 Há quanto tempo a Sra. fuma/Por quanto tempo a Sra.fumou? |___|___|___| meses

SEÇÃO II – ASPECTOS REPRODUTIVOS

“Agora vou fazer algumas perguntas sobre sua menstruação e seus partos”:

2.1 Quantos anos a Sra. tinha quando teve sua primeira menstruação? |___|___| anos

2.2 A Sra. já ficou grávida?
(1) Sim
(2) Não >>>>>>>> Passe a 2.5

2.3 Quantos anos a Sra.tinha quando teve seu primeiro filho? |___|___| anos
|_8_|_8_| Nunca teve parto >>>>>>>> Passe a 2.5

2.4 Quantos partos a Sra. teve? |___|___| partos

2.5 A Sra. fez alguma das cirurgias ginecológicas que eu vou ler?
a. Retirada do útero? (1) Sim (2) Não
b. Retirada dos dois ovários? (1) Sim (2) Não

Se: a e b= 2	>>>>>>>>	Passe a 2.8

2.6 Quantos anos a Sra. tinha quando fez a cirurgia? |___|___| anos

2.7 Quando a Sra. fez a cirurgia, a menstruação estava como sempre foi, estava irregular, ou já não estava menstruando?
(1) Estava como sempre foi
(2) Estava irregular >>>>>>>> Passe à Seção III
(3) Já não estava menstruando

2.8 A Sra. ainda tem menstruações?
(1) Sim
(2) Não >>>>>>>> Passe a 2.13

2.9 A sua menstruação está como sempre foi ou mudou de algum tempo para cá?
(1) Está como sempre foi >>>>>>>> Passe a 2.11
(2) Mudou

2.10 Há quanto tempo mudou? |___|___| meses

2.11 A Sra. já tomou remédio para regular a menstruação?
(1) Sim
(2) Não >>>>>>>> Passe a 2.13

2.12 Há quanto tempo tomou o remédio?
|___|___| meses ou |__|__| anos

2.13 Há quanto tempo foi sua última menstruação natural (sem que precisasse tomar remédios para menstruar?)
|___|___| meses ou |___|___| anos

SEÇÃO III – SOBRE A MENOPAUSA

“Agora, gostaria de fazer algumas perguntas sobre a menopausa”:

3.1 Vou ler alguns sintomas e gostaria de saber se a Sra. sentiu algum deles no último mês:

a. Ondas de calor? (fogacho)	(1) Sim	(2) Não
b. Suor intenso? (sudorese)	(1) Sim	(2) Não
c. Batedeira? (palpitação)	(1) Sim	(2) Não
d. Tontura?	(1) Sim	(2) Não
e. Nervosismo/ansiedade?	(1) Sim	(2) Não
f. Dor de cabeça?	(1) Sim	(2) Não
g. Depressão? (tristeza, melancolia)	(1) Sim	(2) Não
h. Insônia? (dificuldade para dormir)	(1) Sim	(2) Não
i. Atividade Sexual	(1) Sim	(2) Não
j. Dor durante a relação sexual?	(1) Sim	(2) Não
l. Sensação de secura vaginal?	(1) Sim	(2) Não

“Gostaria de agradecê-la pela atenção e pelo tempo dedicado para responder às perguntas”.

SEÇÃO IV – CO-MORBIDADES

41. PA	4.1a PAS: _____	4.1b PAD: _____
4.2 HAS	(1) SIM	(2) NÃO
4.3 Diabetes	(1) SIM	(2) NÃO

SEÇÃO V – SOMENTE PARA AS MULHERES COM CÂNCER DE MAMA

5.1 Estádio:
- (1) 0
- (2) I
- (3) II
- (4) III
- (5) IV

5.2 Data da biópsia: |___|___|___|

5.3 Tipo histológico
- (1) Carcinoma Ductal *in situ*
- (2) Carcinoma Ductal Invasivo
- (3) Carcinoma Lobular Invasivo
- (4) Outros. Qual? _____

5.4 Cirurgia
- (1) Sim➔Data: |___|___|___|
- (2) Não➔Passe a 5.5

5.5 Tipo de cirurgia
(1) Mastectomia Radical Modificada
(2) Mastectomia Radical Halsted
(3) Mastectomia Simples
(4) Quadrantectomia
(5) Tumorectomia

5.6 Radioterapia
(1) Sim
(2) Não

5.7 Quimioterapia
(1) Sim
(2) Não➔Passe a 5.9

5.8 Início da quimioterapia: |___|___|___|

5.9 Último ciclo da quimioterapia: |___|___|___|

5.10 Estado atual:
(1) Com Doença
(2) Sem Doença

SEÇÃO VI - MEDIDAS

6.1 Peso: |___|___|___|___| Kg

6.2 Altura: |___|___|___| m

6.3 Índice de massa corpórea: |___|___| Kg/m^2

6.4 Colesterol total: |___|___|___| mg/dl

6.5 HDL colesterol: |___|___|___| mg/dl

6.6 LDL colesterol: |___|___|___| mg/dl

6.7 Triglicérides: |___|___|___| mg/dl

6.8 Densitometria óssea:

	BMD	Young adult		Age matched	
	g/cm^2	%	T	%	Z
Fêmur					
• Colo	|__|.|__|__|__|	|__|__|__|	|__|__|.|__|__|	|__|__|__|	|__|__|.|__|__|
• Wards	|__|.|__|__|__|	|__|__|__|	|__|__|.|__|__|	|__|__|__|	|__|__|.|__|__|
• Trocânter	|__|.|__|__|__|	|__|__|__|	|__|__|.|__|__|	|__|__|__|	|__|__|.|__|__|
C. lombar					
• (L2-L4)	|__|.|__|__|__|	|__|__|__|	|__|__|.|__|__|	|__|__|__|	|__|__|.|__|__|

Observações:_____

_____

8.4. Anexo 4 - Questionário SF – 36

CÂNCER DE MAMA, MENOPAUSA E QUALIDADE DE VIDA

Grupo: |___| 1. Com câncer de mama 2. Sem câncer de mama Nº estudo |__||__||__|

Instruções: Esta pesquisa questiona você sobre sua saúde. Estas informações nos manterão informados de como você se sente e quão bem você é capaz de fazer suas atividades de vida diária. Caso você esteja insegura em como responder, por favor, tente responder o melhor que puder.

1. Em geral, você diria que sua saúde é: (circule uma)
   - Excelente..... 1
   - Muito boa..... 2
   - Boa..... 3
   - Ruim..... 4
   - Muito ruim..... 5

2. Comparada há um ano atrás, como você classificaria sua saúde em geral, agora? (circule uma)
   - Muito melhor agora do que há um ano atrás..... 1
   - Um pouco melhor agora do que há um ano atrás..... 2
   - Quase a mesma de um ano atrás..... 3
   - Um pouco pior agora do que há um ano atrás..... 4
   - Muito pior agora do que há um ano atrás..... 5

3. Os seguintes itens são sobre atividades que você poderia fazer atualmente durante um dia comum. **Devido à sua saúde**, você tem dificuldade para fazer essas atividades? Neste caso, quanto?

(circule um número em cada linha)

Atividades	**SIM.** Dificulta muito	**SIM.** Dificulta um pouco	**NAO.** Não dificulta de modo algum
a. **Atividades vigorosas**, que exigem muito esforço, tais como correr, levantar objetos pesados, participar em esportes árduos	1	2	3
b. **Atividades moderadas**, tais como mover uma mesa, passar aspirador de pó, jogar bola, varrer a casa	1	2	3
c. Levantar ou carregar mantimentos	1	2	3
d. Subir **vários lances** de escada	1	2	3
e. Subir **um lance** de escada	1	2	3
f. Curvar-se, ajoelhar-se ou dobrar-se	1	2	3
g. Andar **mais de 1 quilômetro**	1	2	3
h. Andar **vários quarteirões**	1	2	3
i. Andar **um** quarteirão	1	2	3
j. Tomar banho ou vestir-se	1	2	3

4. Durante as **últimas 4 semanas**, você teve algum dos seguintes problemas com o seu trabalho ou com alguma atividade diária regular, **como conseqüência da sua saúde física**?

(circule um número em cada linha)

Atividades	SIM	NAO
a. Você diminuiu **a quantidade de tempo** que se dedicava ao seu trabalho ou a outras atividades?	1	2
b. Realizou **menos tarefas** do que você gostaria?	1	2
c. Esteve **limitado** no seu tipo trabalho ou em outras atividades?	1	2
d. Teve **dificuldade** de fazer seu trabalho ou outras atividades (p.ex.: necessitou de um esforço extra)?	1	2

5. Durante as **últimas 4 semanas**, você teve algum dos seguintes problemas com o seu trabalho ou outra atividade regular diária, **como conseqüência de algum problema emocional (como sentir-se deprimido ou ansioso)**?

(circule um número em cada linha)

	SIM	NAO
a. Você diminuiu a quantidade de tempo que se dedicava ao seu trabalho ou a outras atividades?	1	2
b. Realizou **menos tarefas** do que você gostaria?	1	2
c. Não trabalhou ou não fez qualquer das atividades com tanto cuidado como geralmente faz?	1	2

6. Durante as **últimas 4 semanas**, de que maneira sua saúde física ou problemas emocionais interferiram nas suas atividades sociais normais, em relação à família, vizinhos, amigos ou em grupo? (circule uma)

- De forma nenhuma..... 1
- Ligeiramente..... 2
- Moderadamente..... 3
- Bastante..... 4
- Extremamente..... 5

7. Quanta **dor no corpo** você teve durante as **últimas 4 semanas**? (circule uma)

- Nenhuma..... 1
- Muito leve..... 2
- Leve..... 3
- Moderada..... 4
- Grave..... 5
- Muito grave..... 6

8. Durante as **últimas 4 semanas**, quanto a dor interferiu com o seu trabalho normal (incluindo tanto o trabalho fora de casa e dentro de casa)? (circule uma)

- De maneira alguma..... 1
- Um pouco..... 2
- Moderadamente..... 3
- Bastante..... 4
- Extremamente..... 5

9. Estas questões são sobre como você se sente e como tudo tem acontecido com você durante as **últimas 4 semanas**. Para cada questão, por favor, dê uma resposta que mais se aproxime da maneira como você se sente. Em relação às **últimas 4 semanas.**

(circule um número em cada linha)

	Todo tempo	A maior parte do tempo	Uma boa parte do tempo	Alguma parte do tempo	Uma pequena parte do tempo	Nunca
a. Quanto tempo você tem se sentido cheio de vigor, cheio de vontade, cheio de força?	1	2	3	4	5	6
b. Quanto tempo você tem se sentido uma pessoa muito nervosa?	1	2	3	4	5	6
c. Quanto tempo você tem se sentido tão deprimido que nada pode animá-lo?	1	2	3	4	5	6
d. Quanto tempo você tem se sentido calmo ou tranqüilo?	1	2	3	4	5	6
e. Quanto tempo você tem se sentido com muita energia?	1	2	3	4	5	6
f. Quanto tempo você tem se sentido desanimado e abatido?	1	2	3	4	5	6
g. Quanto tempo você tem se sentido esgotado?	1	2	3	4	5	6
h. Quanto tempo você tem se sentido uma pessoa feliz?	1	2	3	4	5	6
i. Quanto tempo você tem se sentido cansado?	1	2	3	4	5	6

10. Durante as **últimas 4 semanas**, quanto do seu tempo a sua saúde física ou problemas emocionais interferiram com as suas atividades sociais (como visitar amigos, parentes, etc) (circule uma)

- Todo o tempo..... 1
- A maior parte do tempo..... 2
- Alguma parte do tempo..... 3
- Uma pequena parte do tempo..... 4
- Nenhuma parte do tempo..... 5

11. O quanto **verdadeiro ou falso** é cada uma das afirmações para você?

(circule um número em cada linha)

	Definitivamente verdadeira	A maioria das vezes verdadeira	Não sei	Definitivamente falsa	A maioria das vezes falsa
a. Eu costumo adoecer um pouco mais facilmente que as outras pessoas.	1	2	3	4	5
b. Eu sou tão saudável quanto qualquer pessoa que eu conheço.	1	2	3	4	5
c. Eu acho que a minha saúde vai piorar.	1	2	3	4	5
d. Minha saúde é excelente.	1	2	3	4	5