# Health-Related Quality of Life and Cardiovascular Comorbidity Risk for Breast Cancer Diagnosis

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*Qualidade de Vida Relacionada à Saúde e Risco de Comorbidade Cardiovascular ao Diagnóstico de Câncer de Mama* Calidad de Vida Relacionada con la Salud y Riesgo de Comorbilidad Cardiovascular al Diagnóstico de Cáncer de Mama

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#### Abstract

**Introduction:** The literature suggests that women with cardiovascular diseases have worse quality of life when diagnosed with breast cancer. **Objective**: To evaluate the association between health-related quality of life (HRQoL) and cardiovascular disease at diagnosis of breast cancer. **Method**: Cross-sectional study with women diagnosed with breast cancer. HRQoL was assessed by the questionnaires of the European Organization for Research and Treatment of Cancer Quality of Life Questionnarie (EORTC QLQ-C30) and Breast Cancer Module (QLQ-BR23) and comorbidity was assessed by the Cumulative Illness Rating Scale Geriatric (CIRS-G). It were calculated the differences between mean HRQoL values and comorbidity. Logistic multiple regression was used to evaluate the association. **Results**: 953 women with a mean age of 54 years (SD±11.7) were included. Comorbidity was presented at diagnosis of breast cancer in 84.1% of the women. The heart system was affected in 10.8% and the vascular system in 48.2%. After adjustment, an association between physical and sexual function scores and heart and vascular system problems was observed. An association between worse pain and dyspnea scores and the heart system was also noticed. Regarding the presence of diseases in the vascular system, this was associated with better sexual satisfaction, better future outcome and worse breast symptoms. **Conclusion**: HRQoL was associated with cardiovascular disease in breast cancer patients, in relation to physical and sexual function, sexual satisfaction, future perspectives and symptom scales (pain, dyspnea and breast symptoms).

Key words: Cardiovascular Diseases; Breast Neoplasms; Comorbidity; Quality of Life.

#### Resumo

Introdução: A literatura sugere que mulheres com doenças cardiovasculares apresentam pior qualidade de vida ao diagnóstico de câncer de mama. Objetivo: Avaliar a associação entre a qualidade de vida relacionada à saúde (QVRS) e as doenças cardiovasculares ao diagnóstico de câncer de mama. Método: Estudo transversal com mulheres diagnosticadas com câncer de mama. A QVRS foi avaliada pelos questionários European Organization for Research and Treatment of Cancer Quality of Life Questionnarie (EORTC QLQ-C30) and Breast Câncer Module (QLQ-BR23) e a comorbidade por meio da Cumulative Illness Rating Scale Geriatric (CIRS-G). Foram calculadas as diferenças entre as médias dos escores de QVRS e comorbidade. A associação foi avaliada por regressão logística múltipla. Resultados: Foram incluídas 953 mulheres com média de idade de 54 anos (DP±11,7). Apresentavam alguma comorbidade ao diagnóstico de câncer de mama 84,1% das mulheres. O sistema coração foi afetado em 10,8% e o sistema vascular em 48,2%. Após ajuste, observou-se associação entre os escores das funções física e sexual e problemas nos sistemas coração e vascular. Foi ainda observada associação entre os piores escores de dor e dispneia e o sistema coração. Em relação à presença de doenças no sistema vascular, este esteve associado à melhor satisfação sexual, melhor perspectiva futura e piores sintomas na mama. Conclusão: A QVRS se mostrou associada a doenças cardiovasculares em pacientes com câncer de mama em relação à função física, sexual, satisfação sexual, a perspectivas futuras e às escalas de sintomas (dor, dispneia e sintomas na mama).

Palavras-chave: Doenças Cardiovasculares; Neoplasias da Mama; Comorbidade; Qualidade de Vida.

#### Resumen

Introducción: La literatura sugiere que las mujeres con enfermedad cardiovascular tienen una peor calidad de vida cuando se les diagnostica cáncer de la mama. Objetivo: Evaluar la asociación entre la calidad de vida relacionada con la salud (CVRS) y la enfermedad cardiovascular en el diagnóstico de cáncer de mama. Método: Estudio transversal con mujeres diagnosticadas con cáncer de mama. La CVRS se evaluó mediante los cuestionarios European Organization for Research and Treatment of Cancer Quality of Life Questionnarie (EORTC QLQ-C30) and Breast Câncer Module (QLQ-BR23) y la comorbilidad se evaluó mediante Cumulative Illness Rating Scale Geriatric (CIRS-G). Se calcularon las diferencias entre las puntuaciones medias de CVRS y la comorbilidad. La asociación se evaluó mediante regresión logística múltiple. Resultados: Se incluyeron 953 mujeres con una edad media de 54 años (DP±11,7). Algunas tenían comorbilidad en el diagnóstico de cáncer de mama 84,1% de las mujeres. El sistema cardíaco se vio afectado en 10,8% y el sistema vascular en 48,2%. Después del ajuste, se observó una asociación entre las puntuaciones de la función física y sexual y los problemas del corazón y del sistema vascular. También se observó una asociación entre puntajes de dolor y disnea peores y el sistema cardíaco. Con respecto a la presencia de enfermedades en el sistema vascular, esto se asoció con una mejor satisfacción sexual, una mejor perspectiva futura y peores síntomas mamarios. Conclusión: La CVRS se asoció con la enfermedad cardiovascular en pacientes con cáncer de mama, con respecto a la función física, la función sexual, la satisfacción sexual, las perspectivas futuras y las escalas de síntomas (dolor, disnea y síntomas de mama).

**Palabras clave:** Enfermedades Cardiovasculares; Neoplasias de la Mama; Comorbilidad; Calidad de Vida.

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# INTRODUCTION

Breast cancer is the most incident tumor among women in the world and is responsible for 24.2% of the cases of cancer<sup>1</sup>. In Brazil, for each year of 2018-2019, 59,700 cases of breast cancer were estimated, the greatest incidence occurring in the Southern and Southeast regions<sup>2</sup>.

Age is an important risk factor for the development of breast cancer; women older than 50 years have higher incidence<sup>3</sup>. With the increase of life expectancy, other non-communicable chronic diseases (NCD) from population ageing are found. Consequently, many patients at the diagnosis of the disease have already some type of comorbidity and/or some previous NCD, among them the most incident are the cardiovascular, which according with the World Health Organization (WHO), are considered the main causes of death in the world<sup>4</sup>.

According to Patnaik et al.<sup>5</sup>, patients with breast cancer above 65 years old have bigger risk of death by cardiovascular disease than by cancer, even if diagnosed with neoplasm in initial staging. The cardiac events after antineoplastic therapy are well documented in the scientific literature<sup>6-8</sup> as the cardiovascular deaths associated to the diagnosis and the breast cancer treatment<sup>9</sup>.

During all the phases of the treatment since the moment of the diagnosis, the patients go through emotional and physical experiences that directly impact the health-related quality of life (HRQoL)<sup>10,11</sup>. Studies conducted with those who present comorbidities report worse score in the scale of quality of life at the diagnosis of breast cancer<sup>12-14</sup>.

Therefore, at the breast cancer diagnosis, women who already present comorbidities appear to present worst HRQoL also. In this context, this study has the objective of evaluating the association between HRQoL and cardiovascular changes at the diagnosis of breast cancer.

### **METHOD**

Cross-sectional study with women enrolled at "Hospital do Câncer III" at "Instituto Nacional de Câncer José Alencar Gomes da Silva (HC III/INCA)" with diagnosis of breast cancer.

Women  $\geq$ 18 years diagnosed with breast cancer were included according to the 3<sup>rd</sup>. edition of the International Classification of Diseases (ICD-O) (C50)<sup>15</sup>, with indication of curative treatment from April 2016 to October 2018. Women using auxiliary walking equipment with previous history of cancer without clinical, psychological or emotional conditions of responding to the questionnaire and who did not agree in signing the Informed Consent Form (ICF) were excluded. Previously to the beginning of the oncologic treatment the patients were interviewed. Through direct search, the physical and/or electronic charts provided information on comorbidities and medical exams.

The 3<sup>rd</sup>. version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) was used to evaluate HRQoL with 30 questions divided by scale, five of them functional (physical, cognitive, emotional, social and role) and three of symptoms (fatigue, pain, nausea and vomit), in addition to a scale that evaluates the quality of life and general health. The specific module about breast cancer, Breast Cancer Module (QLQ-BR23), has 23 questions divided in two dimensions, the functional scale (body image, sexual functioning, sexual enjoyment and future perspective) and the symptoms scale (systemic therapy side effects, arm symptoms, breast symptoms and upset hair loss). Both questionnaires were translated and validated for the Brazilian population<sup>16</sup>.

The outcomes heart and vascular systems were obtained through the Cumulative Illness Rating Scale Geriatric (CIRS-G)<sup>17</sup>, which evaluated the presence and severity of the previous diseases to the diagnosis in different organs and systems through a score of severity. CIRS-G is an adaptation of the scale for adults called CIRS<sup>18</sup> with the inclusion of some diseases related to older adults, which made it more complete. Further, CIRS-G is used extensively in oncogeriatrics<sup>19-22</sup>. There is no study of validation of CIRS or CIRS-G for the Brazilian population, as the diseases, addressed in each organic system are in the 10<sup>th</sup> edition of the International Classification of Diseases and Related Health Problems (ICD-10)<sup>23</sup> and are universal.

Sociodemographic information (age at diagnosis, income, race/skin color, marital status, education, occupation at diagnosis and use of alcohol and tobacco at diagnosis) and clinic (clinical condition, histological type, menopausal status, Body Mass Index and level of physical activity) were collected.

Descriptive analysis of the population was performed through mean and standard deviation for continuous variables and determination of the distribution of frequency for categorical variables. The differences calculated between the means of the scores obtained and tested through analysis of variance to evaluate the association between HRQoL and cardiovascular comorbidity, considering p value of <0.20 with statistically significant. Multiple logistic regression by the method enter (stepwise forward), considering the confidence interval of 95%. All analyzes were made with statistical package SPSS, version 23.0 (IBM).

The Institutional Review Board of INCA reviewed and approved the study, report number 1.400.320, in compliance with Resolution CNS (National Health Council) n.º 466/12 that disposes about Ruling Guidelines and Norms involving human beings.

### RESULTS

It were enrolled 953 women with diagnosis of breast cancer in the study period. The mean age was 54 years (SD±11.7), the majority non-Caucasian (65.0%) with more than eight years of education (68.8%) and income higher than one minimum wage (82.9%) (Table 1).

The highest frequency encountered for clinical characteristics was advanced staging (54.5%) with histological type invasive ductal carcinoma (83.8%).

Table 1. Sociodemographic characteristics of the study population  $\left(n{=}953\right)$ 

Age Mean (±SD) $54.05 (11.72)$ Income in minimum wages** Mean (±SD) $2.65 (2.65)$ Age group $2.65 (2.65)$ $< 50$ years $343$ $36.0$ $\geq 50$ years $610$ $64.0$ Race/skin color $Caucasian$ $334$ $35.0$ Non-Caucasian* $619$ $65.0$ Marital Status $Warried/Living with partner48050.4Divorced or separated/single/widowed47349.6Education (years of study)<8 years29731.2\geq 8 years65668.81ncome**<< 1 minimum wage79082.9No information111.2Occupation at diagnosisS9362.2Not working36037.8Alcohol use in the last 30 dagsZ47725.9NoNo70373.8No information30.3Use of tobacco at diagnosisWarringS247725.9No information30.30.3Use of tobacco at diagnosisWarringS247725.9No information30.3Use of tobacco at diagnosisWarringS247725.9No information30.3Use of tobacco at diagnosisWarringS36S777No information30.3Use of tobacco at diagnosisWarringS5S.9No information20.20.2$	Variables	N	%
Income in minimum wages**Mean ( $\pm$ SD)2.65 (2.65)Age group $< 50$ years< 50 years	Age		
Mean (±SD) 2.65 (2.65)   Age group 343 36.0   < 50 years	Mean (±SD)	54.05 (11.72)	
Age group< 50 years	Income in minimum wages	5**	
< 50 years	Mean (±SD)	2.65 (2.65)	
≥ 50 years61064.0Race/skin color33435.0Caucasian33435.0Non-Caucasian*61965.0Marital StatusMarried/Living with partner48050.4Divorced or separated/ single/widowed47349.6Education (years of study)<	Age group		
Race/skin colorSineCaucasian33435.0Non-Caucasian*61965.0Marital StatusMarried/Living with partner48050.4Divorced or separated/ single/widowed47349.6Education (years of study) $<$ 8 years29731.2 $\geq$ 8 years65668.8Income** $<$ 11.2 $<$ 1 minimum wage15215.9 $\geq$ 1 minimum wage79082.9No information111.2Occupation at diagnosis $<$ Working59362.2Not working36037.8Alcohol use in the last 30 days $<$ Yes24725.9No70373,8No information30.3Use of tobacco at diagnosis $<$ Non-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	< 50 years	343	36.0
Caucasian33435.0Non-Caucasian* $619$ $65.0$ Marital StatusMarried/Living with partner $480$ $50.4$ Divorced or separated/ single/widowed $473$ $49.6$ Education (years of study) $<$ < 8 years	≥ 50 years	610	64.0
Non-Caucasian* $619$ $65.0$ Marital Status $4173$ $619$ $65.0$ Married/Living with partner $480$ $50.4$ Divorced or separated/ single/widowed $473$ $49.6$ Education (years of study) $<$ $8$ years $297$ $31.2$ $\geq 8$ years $656$ $68.8$ $1$ Income** $<$ $<$ $1$ $1.2$ $< 1$ minimum wage $152$ $15.9$ $2$ $\geq 1$ minimum wage $790$ $82.9$ No information $11$ $1.2$ Occupation at diagnosis $<$ Working $593$ $62.2$ Not working $360$ $37.8$ Alcohol use in the last 30 days $<$ Yes $247$ $25.9$ No $703$ $73.8$ No information $3$ $0.3$ Use of tobacco at diagnosis $<$ Non-smoker $645$ $67.7$ Ex-smoker $221$ $23.2$ Current tobacco user $85$ $8.9$	Race/skin color		
Marital StatusMarried/Living with partner48050.4Divorced or separated/ single/widowed47349.6Education (years of study) $<$ < 8 years	Caucasian	334	35.0
Married/Living with partner48050.4Divorced or separated/ single/widowed47349.6Education (years of study)< 8 years	Non-Caucasian*	619	65.0
Divorced or separated/ single/widowed $473$ $49.6$ Education (years of study)< 8 years	Marital Status		
single/widowed $473$ $49.6$ Education (years of study)< 8 years	Married/Living with partner	480	50.4
single/widowedAndEducation (years of study)< 8 years	Divorced or separated/	472	40.4
< 8 years	single/widowed	4/3	49.0
≥ 8 years65668.8Income**15215.9< 1 minimum wage	Education (years of study)		
Income**< 1 minimum wage	< 8 years	297	31.2
< 1 minimum wage	≥ 8 years	656	68.8
≥ 1 minimum wage79082.9No information111.2Occupation at diagnosis $V$ Working59362.2Not working36037.8Alcohol use in the last 30 days $V$ Yes24725.9No70373,8No information30.3Use of tobacco at diagnosis $V$ Non-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	Income**		
No information   11   1.2     Occupation at diagnosis	< 1 minimum wage	152	15.9
Occupation at diagnosisWorking59362.2Not working36037.8Alcohol use in the last 30 daysVesYes24725.9No70373,8No information30.3Use of tobacco at diagnosisNon-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	≥ 1 minimum wage	790	82.9
Working   593   62.2     Not working   360   37.8     Alcohol use in the last 30 days   703   73.8     Yes   247   25.9     No   703   73,8     No information   3   0.3     Use of tobacco at diagnosis   703   73,8     Non-smoker   645   67.7     Ex-smoker   221   23.2     Current tobacco user   85   8.9	No information	11	1.2
Not working36037.8Alcohol use in the last 30 days70325.9Yes24725.9No70373,8No information30.3Use of tobacco at diagnosis70350.3Non-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	Occupation at diagnosis		
Alcohol use in the last 30 daysYes247No703No information3Use of tobacco at diagnosisNon-smoker645Ex-smoker221Current tobacco user85	Working	593	62.2
Yes   247   25.9     No   703   73,8     No information   3   0.3     Use of tobacco at diagnosis   Use   645   67.7     Non-smoker   645   67.7   23.2     Current tobacco user   85   8.9	Not working	360	37.8
No70373,8No information30.3Use of tobacco at diagnosisNon-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	Alcohol use in the last 30 a	days	
No information30.3Use of tobacco at diagnosis0Non-smoker64567.7Ex-smoker22123.2Current tobacco user858.9	Yes	247	25.9
Use of tobacco at diagnosisNon-smoker64564567.7Ex-smoker22123.2Current tobacco user858.9	No	703	73,8
Non-smoker   645   67.7     Ex-smoker   221   23.2     Current tobacco user   85   8.9	No information	3	0.3
Ex-smoker22123.2Current tobacco user858.9	Use of tobacco at diagnosi	s	
Current tobacco user 85 8.9	Non-smoker	645	67.7
	Ex-smoker	221	23.2
No information 2 0.2	Current tobacco user	85	8.9
	No information	2	0.2

Women in postmenopause found in 62.7% of the cases, in its majority with overweight (36.8%) and obesity (35.9%) (Table 2).

The comorbidities evaluated at the cancer diagnosis by the scale CIRS-G, indicated that 84.1% of the women had some comorbidity, 29.8% classified as mild, 50.9% moderate and 3.4%, severe. The heart and vascular system were affected in 10.8% and 48.2% respectively (Table 2). The main diseases found in the heart system were diastolic dysfunction grade 1 (7.03%); mitral insufficiency (1.36%) and arrhythmia (0.95%); and in the vascular system, arterial hypertension (46.1%), dyslipidemia (2.83%) and varices (1.78%).

At the diagnosis of breast cancer, there were higher scores of the scales of physical and social function (EORTC C-30). Women with heart (p=0.008) and vascular (p<0.001) problems had worse score for physical function. In the scale of symptoms, worse scores occurred

Table 2. Clinical characteristics and comorbidities of the study population (n=953)  $\,$ 

Variables	Ν	%
Clinical staging		
<iib< td=""><td>418</td><td>43.9</td></iib<>	418	43.9
≥IIB	520	54.5
No information	15	1.6
Histological type		
IDC	798	83.8
Other	148	15.5
No information	7	0.7
Menopausal status		
Postmenopause	597	62.7
Premenopause	329	34.5
No information	27	2.8
Body Mass Index		
Underweight	11	1.2
Normal weight	219	23.0
Overweight	351	36.8
Obesity	342	35.9
No information	30	3.1
Scale CIRS-G categorical		
No comorbidity	152	15.9
Mild comorbidity	284	29.8
Moderate comorbidity	485	50.9
Severe comorbidity	32	3.4
Affected Heart System		
Yes	103	10.8
No	850	89.2
Affected Vascular System		
Yes*	459	48.2
No	494	51.8

**Captions:** SD=Standard Deviation; \* Non Caucasian=Brown, black, indigenous or Asian; \*\*Mean of the number of minimum wages from 2016 to 2018 = 924 reais.

**Captions:** IDC=Invasive Ductal Carcinoma; CIRS-G= *Cumulative illness rating scale geriatric*; \*439 cases presented systemic arterial hypertension

1-7

for insomnia and pain. Those with heart system problems had worse scores of the symptoms of pain (p=0.031) and dyspnea (p=0.007) (Table 3).

After assessing the HRQoL by EORTC BR-23, there was worse function of the domain sexual functions and worse symptom of the arm. When comparing the scores according to the comorbidities, there was worse sexual function among those with problems in the heart (p=0.001) and vascular (p<0.001) system. In addition, those with problems in the vascular system also presented worse score of sexual satisfaction (p=0.026) and better score of future perspective (p=0.037) and hair loss (p=0.005) (Table 4).

After adjustment, while assessing the associations between the scores of the scales of function of HRQoL by EORTC QLQ C-30 and comorbidity at the diagnosis of breast cancer, at each increase of one figure in the score of physical function, there was a 1.1% drop of risk to the heart system (OR=0.989 CI 95% 0.979 to 0.999; p=0.025) and of 1.4% of risk of problems in the vascular system (OR=0.986 CI 95% 0.986 to 0.994; p<0.001). In the scales of EORTC QLQ BR-23, at each raise of one figure of the score of sexual function, there was a drop of 1.2% of the risk of problems to the heart (OR=0.988 CI 95% 0.980 to 0.996; p=0.003) and vascular (OR=0.988 CI 95% 0.983 to 0.993; p<0.001) system. It was also

Table 3. Health Related Quality of Life (EORTC QLQ C-30) and comorbidities of the diagnosis of breast cancer (n=953)

		Heart	system affe	cted	Vascula	ected	
EORTC QLQ C-30	Total	Νο	Yes		Νο	Yes	
		850 (89.2%)	103 (10.8%)	1	494 (51.8)	459 (48.2)	
Functional scales*	Mean (SD)	Mean (SD)	Mean (SD)	p value	Mean (SD)	Mean (SD)	p value
Global Quality of Life	69.5 (23.3)	69.9 (23.1)	65.6 (24.7)	0.074	69.7 (22.5)	69.2 (24.1)	0.729
Physical Functioning	83.0 (19.8)	83.6 (19.6)	78.0 (21.0)	0.008	85.6 (19.1)	80.2 (20.3)	<0.001
Role Functioning	78.7 (30.3)	79.2 (30.0)	74.5 (32.9)	0.144	80.4 (28.7)	76.8 (32.0)	0.068
Cognitive Functioning	74.4 (28.8)	74.2 (29.1)	75.9 (26.3)	0.570	75.6 (29.0)	73.1 (28.4)	0.186
Emotional Functioning	56.1 (31.4)	55.8 (31.5)	59.0 (30.8)	0.330	55.8 (31.0)	56.5 (31.8)	0.713
Social Functioning	81.1 (29.7)	81.4 (29.8)	78.4 (29.1	0.340	80.3 (29.7)	81.9 (29.7)	0.388
Symptom scales**	Mean (SD)	Mean (SD)	Mean (SD)	p value	Mean (SD)	Mean (SD)	p value
Fatigue	22.6 (26.1)	22.6 (26.1)	23.1 (25.7)	0.842	22.5 (26.5)	22.7 (25.7)	0.888
Pain	31.3 (32.8)	30.5 (32.8)	37.9 (32.1)	0.031	30.0 (32.0)	32.6 (33.6)	0.225
Dyspnea	11.4 (24.8)	10.6 (23.9)	17.6 (30.3)	0.007	10.8 (24.2)	12.0 (25.4)	0.460
Insomnia	37.4 (41.8)	37.4 (41.9)	37.0 (41.2)	0.932	36.9 (41.4)	37.9 (42.3)	0.724
Appetite loss	14.2 (29.1)	14.1 (28.7)	14.7 (31.7)	0.841	12.7 (26.8)	15.7 (31.3)	0.111
Nausea and vomiting	7.3 (15.9)	7.0 (15.3)	9.9 (19.9)	0.077	7.1 (14.9)	7.5 (16.8)	0.723
Constipation	18.7 (32.7)	18.7 (32.8)	18.9 (31.9)	0.938	18.9 (33.0)	18.5 (32.4)	0.834
Diarrhea	6.7 (19.3)	6.4 (18.7)	9.1 (23.5)	0.174	6.2 (18.2)	7.2 (20.4)	0.432
Financial difficulties	28.7 (39.9)	28.6 (39.9)	30.1 (39.7)	0.721	28.3 (39.6)	29.2 (40.3)	0.742

**Captions:**\*Higher scores, better HRQoL; \*\*Higher scores, worse HRQoL; SD=Standard deviation. **Note:** The statistically significant values are highlighted in bold.

	<b>T</b> 1	Heart	system affec	ted	Vascular system affected		
EORTC BR-23	Total	No	Yes	P value	Νο	r system affe Yes Mean (SD) 83.2 (24.9) 25.4 (29.2) 67.8 (30.8) 38.3 (40.2) Mean (SD) 20.2 (18.7) 26.0 (28.9) 19.4 (24.5)	P value
Functional scales*	Mean ( SD)	Mean (SD)	Mean (SD)	P value	Mean (SD)	Mean (SD)	P value
Body image	83.1 (24.9)	82.8 (25.3)	85.9 (21.0)	0.244	83.1 (24.9)	83.2 (24.9)	0.946
Sexual functioning	33.1 (31.5)	34.3 (31.8)	22.7 (27.3)	0.001	40.3 (31.9)	25.4 (29.2)	<0.001
Sexual enjoyment	71.8 (29.1)	72.3 (29.0)	64.5 (29.7)	0.149	74.1 (27.8)	67.8 (30.8)	0.026
Future perspective	35.5 (39.1)	36.0 (39.2)	31.7 (38.5)	0.294	33.0 (38.0)	38.3 (40.2)	0.037
Symptom scales**	Mean (SD)	Mean (SD)	Mean (SD)	P value	Mean (SD)	Mean (SD)	P value
Systemic therapy side effects	19.2 (17.5)	19.1 (17.7)	19.5 (16.5)	0.867	18.2 (16.3)	20.2 (18.7)	0.075
Upset by hair loss	28.8 (29.8)	36.2 (42.3)	22.7 (40.3)	0.155	31.4 (30.3)	26.0 (28.9)	0.005
Breast symptoms	18.2 (24.3)	28.7 (29.8)	29.7 (29.1)	0.745	16.9 (24.0)	19.4 (24.5)	0.119
Arm symptoms	34.9 (42.2)	17.8 (24.2)	21.2 (24.2)	0.177	32.7 (40.0)	37.2 (44.5)	0.429

Table 4. Health-related quality of life (EORTC QLQ BR-23) and comorbidities of the diagnosis of breast cancer (n=953)

**Captions:**\*Higher scores, better HRQoL; \*\*Higher scores, worse HRQoL; SD=Standard deviation.

Note: The statistically significant values are highlighted in bold.

verified that, at each raise of one figure in the score of sexual satisfaction, there was a drop of 0.7% in the risk of problems in the vascular system (OR=0,993 CI 95% 0.986 to 0.999; p=0.030). In relation to the score of future perspective, a raise of one figure caused a raise of 0.4% of the risk of problems in the vascular system (OR=1.004 CI 95% 1.000 to 1.007; p=0.042) (Table 5).

While assessing the scales of symptoms of EORTC C-30, at each raise of one figure of the scale of pain, there was an increase of 0.8% in the risk of problems in the heart system (OR=1.008 CI 95% 1.001 to 1.014; p=0.020) and of 1% of the risk for the scale of dyspnea (OR=1.010 CI 95% 1.002 to 1.017; p=0.009). In the scale of symptoms of QLQ-BR23, at each raise of one figure in the symptoms of breast, the risk of problems in the vascular system dropped 0.8% (OR=0.992 CI 95% 0.988 to 0.997; p=0.001) (Table 5).

## DISCUSSION

In this study, the majority of the women was diagnosed at an advanced staging of breast cancer (≥IIB) and with some comorbidity, being 10.8% with problems in the heart system and 48.2% in the vascular system. There was major risk of disease of the heart system in women with worse physical and sexual conditions and those with worse symptom of pain and dyspnea. For vascular system, there was higher risk for those with worse sexual and physical functions and worse sexual satisfaction. In relation to breast symptoms and future perspective, those with best scores had lower risk of problems in the vascular system.

Breast cancer is associated to the increase of cardiovascular problems resulting mainly from oncologic treatment and, as advanced the diagnosis of breast cancer is, more aggressive will be the treatments and consequently, greater is the risk of cardiovascular complications. In that line, it is essential to know the prevalence of cardiovascular diseases and its risk factors at the diagnosis of breast cancer to guide the oncologic treatments<sup>24-26</sup>.

The prevalence of cardiovascular diseases at the diagnosis of breast cancer varies according to the characteristics of the population studied. In a study with 12,127 Canadian women diagnosed with breast cancer, the majority (80%) older than 50 years, the most prevalent comorbidities at the diagnosis were cardiovascular alterations (39%) measured by the Rx-Risk-V model<sup>27</sup>. Another study conducted in Germany included 3,496 women with breast cancer, in initial staging in its majority, and in age range between 40 and 79 years old. After age standardization, global prevalence of coronary diseases was 3.96% and 2.06% for myocardial acute infarction<sup>28</sup>. In our population, the prevalence of cardiac diseases was 10.8% and vascular, 48.2%. However, the instruments utilized to measure the comorbidities were different of the tumor characteristics of the populations studied, which hampers the comparison of the prevalence.

In relation to HRQoL at the diagnosis of breast cancer in the study population, there were better scores for the physical and social functions and worse symptoms for insomnia and pain. Those with worse scores of HRQoL presented higher risk of diseases in the heart and vascular systems. Similar results were obtained in other populations<sup>12,14</sup>.

In a cohort study with 542 Danish women at the diagnosis of breast cancer, in its majority staging I (31%) or II (41%), 10% presented one comorbidity and 10%,  $\geq 2$  comorbidities (measured by Charlson Comorbidity Index (CCI). Better HRQoL scores (measured by SF-36) were observed for social (92±16.6) and emotional (90.7±17.7) functions. Women with one or more comorbidities

EORTC QLQ C-30		Hear	t System		Vascular system			
Functional scales	Crude OR	P value	Adjusted OR	p value	Crude OR	p value	Adjusted OR	p value
Physical functioning	0.987 (0.978-0.997)	0.008	0.989 (0.979-0.999)ª	0.025	0.986 (0.980 – 0.993)	< 0.001	0.986 (0.978-0.994) <sup>c</sup>	< 0.001
Symptom scales								
Pain	1.007 (1.001-1.013)	0.032	1.008 (1.001-1.014)º	0.020				
Dyspnea	1.009 (1.002-1.016)	0.008	1.010 (1.002-1.017)	0.009				
EORTC BR-23								
Functional scales								
Sexual functioning	0.987 (0.980-0.994)	0.001	0.988 (0.980-0.996) <sup>b</sup>	0.003	0.984 (0.980-0.989)	< 0.001	0.988 (0.983-0.993) <sup>d</sup>	< 0.001
Sexual enjoyment					0.993 (0.986-0.999)	0.027	0.993 (0.986-0.999)°	0.030
Future perspective					1.003 (1.000-1.007)	0.038	1.004 (1.000-1.007) <sup>f</sup>	0.042
Symptom scales								
Breast symptoms					0.994 (0.989-0.998)	< 0.001	0.992 (0.988-0.997) <sup>g</sup>	0.001

Table 5. Raw and adjusted association between the HRQoL scores and comorbidity of the cardiovascular system

**Captions:** <sup>a</sup>adjusted per age and clinical staging; <sup>b</sup>adjusted per clinical staging and occupation; <sup>c</sup>adjusted by age, BMI, education and tobacco addiction; <sup>d</sup>adjusted per education, occupation, BMI and tobacco addiction; <sup>c</sup>adjusted by tobacco addiction; <sup>f</sup>adjusted by BMI and education; <sup>s</sup>adjusted by BMI, education and tobacco addiction.

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presented worse scores of HRQoL in physical function (-4.1 CI 95 % -6.0 to -2.2) and global health (-7.9 CI 95% -12.0 to -3.5)<sup>12</sup>.

In a study with 339 Spanish women diagnosed with breast cancer, most of them staging I (44.3%) and II (38.1%), the global health mean score was 69.2% ( $\pm$  21.1) and better scores were obtained in the scales of physical function (92,3 $\pm$ 12,4) and general function (93.3 $\pm$ 14.3) and worse scores of the symptoms of insomnia (31.7 $\pm$ 29.8) and fatigue (15.8 $\pm$ 17.5). Women with worse global health score had 2.07 higher risk of presenting comorbidities measured by CCI (OR=2.07 CI 95% 1.29-3.30)<sup>14</sup>.

The article has some limitations. The inclusion of a high number of women may have caused borderlines results; this study was conducted with women diagnosed with breast cancer in only one public institution of reference in oncologic treatment and because of this, some caution must be taken while generalizing its results (external validation). In addition, it was not possible the comparison of the study's results with other studies because the instruments utilized to obtain the HRQoL scores and cardiovascular comorbidities were different across the studies.

However, this study presents a theme of great relevance in the evaluation of women at the diagnosis of breast cancer: the relation between the presence of cardiovascular comorbidity and HRQoL. Both aspects are predictors of worse mortality by breast cancer<sup>5,29</sup> and must be incorporated as tools for therapeutic decision taking.

### CONCLUSION

At the breast cancer diagnosis, 10.8% of the women presented heart problems and 48.2%, in the vascular system. There was major risk of heart system illnesses in the women with worse physical and sexual functions and those with worse symptoms of pain and dyspnea. For the vascular system, there was major risk for the women with worse physical and sexual functions and worse sexual satisfaction. For breast symptoms and future perspective, those with better scores had less risk of problems in the vascular system.

#### CONTRIBUTIONS

All the authors contributed for the conception and planning of the study, data collection, analysis and interpretation, wording of the manuscript and approved the final version to be published.

## **DECLARATION OF CONFLICT OF INTERESTS**

The author Anke Bergmann declares conflict of interest because of her capacity as Scientific Editor of "Revista Brasileira de Cancerologia" of INCA. The other authors do have no conflict of interests to declare.

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