Association between clinical staging and molecular subtypes of breast cancer according to age

Karen de Souza Abrahão, Anke Bergmann, Suzana Sales de Aguiar, Eduardo Camargo Millen, Marcelo Aldeodato Bello, Luiz Claudio Santos ThulerBrazilian National Cancer Institute (INCA), Rio de Janeiro - Brazil.

PURPOSE

Breast cancer is the cancer type that affects most women around the world (1). The classification of the tumors in different molecular subtypes has been associated not only to the clinical pathological features of the disease, but also to its own prognosis (2).

The current study has the goal to identify the frequency of the molecular subtypes according to the age group, and to estimate its association with the clinical staging of the breast cancer

METHODS

Study design: cross-sectional study

Population: 1921 women identified from the Hospital Cancer Registry (HCR)

Inclusion criteria: women with breast cancer, aged 18 or over, with information about immunohistochemical markers and who were diagnosed and treated in a reference center for cancer treatment between 2008 and 2009.

Exclusion criteria: 52 women were excluded for the following reasons: previous cancer (30), DCIS (ductal carcinoma in situ) (16), simultaneous primary cancer (5) and lobular carcinoma in situ diagnosis (1).

Coleta de dados: Data were collected from electronic medical records.

Outcome: Molecular subtypes and clinical staging

Independent variables: clinical, surgical and socioeconomic variables

Statistical analysis: A descriptive analysis was performed. The chi-square test was used to compare the clinical and demographic characteristics according to the age group. The association between independent variables and the outcome was performed by using Odds Ratio (OR). The data considered clinically and statistically relevant ($p < 0.20$) in the univariate analysis were included in the logistic regression analysis by the stepwise forward method. For all the analysis, $p<0.05$ was considered statistically significant.

Ethycal issues: This study was approved by the Committee of Ethics in Research of the National Cancer Institute according to the CNS number 466/12 resolution under the number 128/11.

SUMMARY AND RESULTS

A total of 1869 women remained at the end of the study with a mean age of 55.7 years (±13.0). Out of these, 196 (10.5%) were young (= 40 years old). The socioeconomic variables associated with young age at diagnosis were: having studied for at least 8 years, living in the capital of the state of Rio de Janeiro, and the absence of a smoking habit. In addition, young women had a greater chance of diagnosis at advanced staging and triple negative tumors.

Among the young women, there was a greater risk of diagnosis at an advanced stage (>IIA) in the cases classified as triple negative (OR=5.4; CI95%=1.88-15.84), having the luminal subtype as a reference. Among the non-young women, the risk was increased in the triple negatives cases (OR=2.3; CI95%=1.63-3.26), HER2 (OR=1.8; IC95%=1.24-2.73) and luminal B (OR=1.5; CI95%=1.05-2.14).

CONCLUSION

The triple negative molecular subtype was associated with diagnosis at an advanced stage, regardless of the age of the patient. Luminal B and HER2 subtypes were associated with diagnosis in an advanced stage only in women over 40 years of age

REFERENCES

1.Brasil, Ministério da saúde. Instituto Nacional de Câncer José Alencar Gomes da Silva (Brasil). Estimativa 2016: Incidência de Câncer no Brasil. Rio de Janeiro, Brazil. 2015. http://www.inca.gov.br/dncc (accessed november 27, 2015)

2.Perou CM, Sørlie T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature 2000; 406(6797):747-52.

Table 1 - Sociodemographic and clinical characteristics of women with breast cancer enrolled in the study, 2008-2009, by age group

Characteristics	Age group ≤ 40 years N (%)	Age group > 40 years N (%)	Total N (%)	p-value *
Race/skin color				
White	98 (50.0)	922 (55.2)	1020 (54.6)	0.378
Mulatto	68 (34.7)	481 (28.8)	549 (29.4)	
Black	30 (15.3)	265 (15.9)	295 (15.8)	
Asian Brazilians	0	1 (0.1)	1 (0.1)	
Indigenous	0	4 (0.2)	4 (0.2)	
Educational level (years)				
Illiterate	3 (1.5)	81 (4.8)	84 (4.5)	**<0.001**
1 to 7 years	55 (28.1)	725 (43.3)	780 (41.7)	
8 years	31 (15.8)	282 (16.9)	313 (16.7)	
9 to 11 years	81 (41.3)	407 (24.3)	488 (26.1)	
≥ 12 years	25 (12.8)	174 (10.4)	199 (10.6)	
Missing	1 (0.5)	4 (0.2)	5 (0.3)	
Place of residence				
Capital	104 (53.1)	1045 (62.5)	1149 (61.5)	**0.013**
Other municipalities	92 (46.9)	628 (37.5)	720 (38.5)	
Marital status				
No partner	73 (37.2)	329 (19.7)	402 (21.5)	**<0.001**
Married or in stable union	106 (54.1)	770 (46.1)	876 (46.9)	
Widow	3 (1.5)	324 (20.5)	345 (18.5)	
Legally separated	14 (7.1)	229 (13.7)	243 (13.0)	
Missing	0	1 (0.1)	1 (0.1)	
Histological type				
Invasive ductal carcinoma	180 (91.8)	1437 (85.9)	1617 (86.5)	0.053
Invasive lobular carcinoma	5 (2.6)	102 (6.1)	107 (5.7)	
Others	11 (5.6)	134 (8.0)	145 (7.8)	
Histological grade				
Grade 1	15 (7.7)	179 (10.7)	194 (10.4)	0.244
Grade 2	62 (31.6)	509 (30.4)	571 (30.6)	
Grade 3	87 (44.4)	640 (38.3)	727 (38.9)	
Not applicable/Missing	32 (16.1)	345 (20.6)	377 (20.1)	
Clinical staging				
≤ IIA	67 (34.2)	754 (45.1)	821 (43.9)	**0.007**
> IIA	124 (63.3)	904 (54.0)	1028 (55.0)	
Missing	5 (2.6)	15 (0.9)	20 (1.1)	
Type of surgery				
Mastectomy	137 (69.9)	1091 (65.2)	1228 (65.7)	**0.004**
Breast-conserving surgery	22 (11.2)	346 (20.7)	368 (19.7)	
No surgery	37 (18.9)	236 (14.1)	273 (14.6)	
Axillary approach				
Sentinel lymph node biopsy	28 (14.3)	392 (23.4)	420 (22.5)	**0.010**
Lymphadenectomy	130 (66.3)	1029 (61.5)	1159 (62.0)	
No axillary approach	38 (19.4)	252 (15.1)	290 (15.5)	
Molecular Subtypes				
Triple negative	51 (26.0)	250 (14.9)	301 (16.1)	**<0.001**
HER2	17 (8.7)	172 (10.3)	189 (10.1)	
Luminal B	28 (14.3)	189 (11.3)	217 (11.6)	
Luminal A	100 (51.0)	1062 (63.5)	1162 (62.2)	

*The differences correspond to missing values; In bold statistically significant p-values

Table 2 – Multiple analysis of the association between molecular subtypes and clinical stage by age group

Molecular subtypes	Advanced Stage (> IIA) N (%)	Initial Stage (< IIA) N (%)	Crude OR	95%CI	p-value	Adjusted OR	95%CI	p-value
= 40 years*	**111 (64.9)**	**60 (35.1)**						
Triple negative	41 (33.1)	7 (10.4)	5.2	2.13-12.68	**<0.001**	5.4	1.88-15.84	**0.002**
HER2	12 (9.7)	5 (7.5)	2.1	0.70-6.48	0.184	2.0	0.58-7.22	0.266
Luminal B	18 (14.5)	8 (11.9)	2.0	0.79-5.01	0.141	2.3	0.86-6.09	0.097
Luminal A	53 (42.7)	47 (70.1)		Reference			Reference	
> 40 years**	**917 (54.6)**	**761 (45.4)**						
Triple negative	174 (19.2)	76 (10.1)	2.5	1.83-3.31	**<0.001**	2.3	1.63-3.26	**<0.001**
HER2	113 (12.5)	58 (7.7)	2.1	1.49-2.95	**<0.001**	1.8	1.24-2.73	**0.002**
Luminal B	112 (12.4)	76 (10.1)	1.6	1.16-2.18	**0.004**	1.5	1.05-2.14	**0.026**
Luminal A	505 (55.9)	544 (72.1)		Reference			Reference	
Total***	**1028 (55.6)**	**821 (44.4)**						
Triple negative	215 (20.9)	83 (10.1)	2.7	2.08-3.62	**<0.001**	2.6	1.85-3.57	**<0.001**
HER2	125 (12.2)	63 (7.7)	2.1	1.52-2.91	**<0.001**	1.8	1.25-2.66	**0.002**
Luminal B	130 (12.6)	84 (10.2)	1.6	1.22-2.21	**0.001**	1.6	1.15-2.24	**0.005**
Luminal A	558 (54.3)	591 (72.0)		Reference			Reference	

* Adjusted by educational level and histological grade
** Adjusted by educational level, race/skin color and histological grade
***Adjusted by race/skin color, histological grade, educational level, histological grade and place of residence
In bold statistically significant p-values

Projeto Gráfico: Serviço de Edição e Informação Técnico-Científica / INCA