Cancer Epidemiology 50 (2017) 268–271

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

Characteristics of invasive breast cancer and overall survival of patients eligible for mass breast cancer screening in Guadeloupe compared to those of the preceding age group

Philippe Kadhel[a,b,*], Daphné Borja De Mozota[a], Stéphanie Gaumond[c], Jacqueline Deloumeaux[d]

[a] Service de Gynécologie-Obstétrique Centre Hospitalier Universitaire de Guadeloupe, Guadeloupe F.W.I. Route de Chauvel, 97159 Pointe-à-Pitre Cedex, France
[b] Institut National de la Santé et de la Recherche Médicale Inserm U1085–IRSET, Campus Universitaire de Fouillole, Pointe à Pitre 97157, Guadeloupe, France
[c] Service d'Anatomopathologie, Centre Hospitalier Universitaire de Guadeloupe, Guadeloupe F.W. I. Route de Chauvel, 97159 Pointe-à-Pitre Cedex, France
[d] Registre Général des Cancers de Guadeloupe, Centre Hospitalier Universitaire de Guadeloupe, Guadeloupe F.W. I. Route de Chauvel, 97159 Pointe-à-Pitre Cedex, France

ARTICLE INFO

Article history:
Received 17 March 2017
Received in revised form 30 July 2017
Accepted 5 August 2017

Keywords:
Breast cancer mass screening
Invasive breast cancer
Prognostic factors
French west indies (FWI)
People of african descent

ABSTRACT

Background: Mass breast cancer screening is offered to French women between the ages of 50 and 74. In the French overseas department of Guadeloupe, where the population is of mostly African ancestry, a low age at diagnosis of breast cancer has been reported, as for African-Americans. This raises the question of whether breast cancer is more aggressive in the age group preceding that eligible for mass screening (40–49) in Guadeloupe.
Methods: We compared the tumor-related prognostic factors, first line therapy and overall survival rates of breast cancer cases diagnosed between the 40–49 and 50–74 age groups, based on reports of the cancer registry of Guadeloupe for the period 2008–2013.
Results: The characteristics studied, risk of death after breast cancer (HR 0.84 [95% CI: 0.58-1.22] and overall survival, did not differ significantly between the two groups, except for higher tumor size (28.8 vs 24.0; p = 0.004) in the younger group.
Conclusion: These results do not show a pattern of more aggressive breast cancer in the age group preceding that eligible for mass screening in Guadeloupe.

1. Introduction

Geographical disparities in breast cancer incidence, outcomes, and mortality have been reported worldwide [1]. Women of Guadeloupe, where most of the population is of African descent, are diagnosed for invasive breast cancer (BC) at a lower age than those in mainland France, which has a mostly Caucasian population [2]. In this previous study, we examined the distribution of BC by age, frequency distributions, the world age-standardized incidence, and the expected number of BC cases in a standard population. The results link the Guadeloupian population to African-Americans, rather than to the mainland French or Caucasian-American populations.

The French national mass BC screening program is offered to women between the ages of 50 and 74 years in mainland France and Guadeloupe, as it is an French overseas department with an equivalent health care system. According to a previous study [2], almost 28% of BC cases were diagnosed between 40 and 49. Younger women with BC have been reported to have a poorer prognosis than older patients [3]. These findings raised the question of whether BC is more aggressive in the population preceding the age group eligible for BC mass screening in Guadeloupe. To address this issue, we analyzed the characteristics of BC cases diagnosed before the age of 50.

2. Materials and methods

We recently published a report on the incidence, mortality, tumor-related factors, and first line therapy according to subtype, based on hormone receptors and HER2 status, of BC in Guadeloupe using data from the population-based cancer registry of Guadeloupe for the period spanning 2008–2013 [4].

* Corresponding author at: Centre Hospitalier Universitaire de Pointe–à–Pitre/Abymes, Pôle Parent–Enfant, Service de Gynécologie et Obstétrique. Route de Chauvel, BP 465. 97159 Pointe–à–Pitre cedex. Guadeloupe, France.
E-mail address: philippe.kadhel@orange.fr (P. Kadhel).

http://dx.doi.org/10.1016/j.canep.2017.08.004
1877-7821/

This registry records all incident cases of cancer since 2008. Cases are identified from multiples sources: pathology and hospital discharge records, registration of long-term illness by the health insurance system, and medical files. The data collected include demographic data (date and place of birth, gender, place of residence), tumor characteristics (date of diagnosis, tumor size, histological type, staging and hormonal markers), and first treatment (date and type of treatment). Given that French legislation does not allow ethnic classification, no information on race/ethnicity were available. It is commonly known that more that 80% of the Guadeloupean population is of African descent. The registry uses the rules of the International Agency of Cancer Registries (IACR). Data on death from breast cancer for resident patients from Guadeloupe were obtained from the French epidemiological center on medical causes of death from the French National Institute of Health and Medical Research (CépiDc, Inserm: www.cepidc.inserm.fr).

Here, we analyzed the data of the population-based cancer registry of Guadeloupe considering the age groups for BC mass screening. We restricted the analysis to a comparison between the 40–49 (G40) and 50–74 (G50) age groups, as breast cancer before the age of 40 is often associated with genetic syndromes [3].

Among the 1275 confirmed cases of BC from the population-based general cancer registry of Guadeloupe spanning the period 2008–2013 [4],1009 were diagnosed between the ages of 40 and 74 and comprised the study population. Among these cases, 308 (24,2%) were in G40 and 701(55%) in G50. In mainland France, in 2012, the percentage of new cases was 17.6% for G40 and 53.8% for G50." These data were extracted from the Globocan database [5].

The BC subtypes were defined based on hormone receptor (HR) and HER2 gene expression status at diagnosis determined by immunohistochemistry. Patients were coded HR+ when the tumors were positive for both estrogen and progesterone receptors and HR- when the tumor was negative for both receptors. We considered four main groups of patients: HR+/HER2+, HR+/HER2-, HR-/HER2+, and HR-/HER2- as triple negative breast cancer (TNBC) [6]. Patients not classified within these four groups (missing data) were classified as unknown [6]. We used the simplified cancer staging (localized/local spread, regional spread, metastatic/non-resectable) from the European Network Cancer Registries (ENCR) [7] because of missing data for TNM. Tumor grade was classified using the modified Scarff and Bloom-Richardson (MSBR) grading system. We also considered first line treatment. Cases with missing data for tumor size, cancer stage, MSBR grade, and first treatment were included in the unknown group. The unknown group was included in the analyses. Descriptive analyses were performed according to the two age groups using the nonparametric equality-of-medians test to compare numerical variables and Pearson's Chi-square test for categorical variables.

Overall survival was computed by Kaplan-Meier analysis [8] for the two age groups with the endpoint set to December 31, 2015. Death certificates were obtained from the French epidemiological center on medical causes of death from the French National Institute of Health and Medical Research (CépiDc, Inserm: http://www.cepidc.inserm.fr/site4/).

Patients lost to follow-up were censored on the date of their last visit (recorded hospitalization or medical consultation). Cox's proportional hazards model [9] was used to determine hazard ratios for death with the associated 95% confidence interval (CI). The age group was our main variable of interest and was forced into the model. All variables with a $p < 0.2$ in the univariate model, and for which the proportional-hazards assumption was respected, were used. We therefore built models by adding each variable (tumor size, cancer stage, receptor status, and fist line of treatment) to adjust the two-variable models with age group. The assumption of proportional hazards for the Cox model was tested using Schoenfeld residuals [10].

All analyses were performed using Stata statistical software release 14.0 (Stata Corp LP, College Station, TX, USA) and a p value of 0.05 was considered to be statistically significant.

3. Results

Breast cancer tumor-related prognostic factors at diagnosis for the whole population (1275) and for the age groups (G40 and G50) defined above are presented along with the comparison tests in Table 1. The tumors were significantly larger in G40 than G50; all other recorded prognostic factors did not differ significantly.

The Kaplan-Meier survival curves for the two age groups, adjusted to tumor size, are presented in Fig. 1.

The crude and adjusted Cox proportional Hazard ratios for death are presented in Table 2. The hazard ratios of death for the age group 50–74 were not statistically different in the bivariate models that included the age group with tumor size, receptors status, cancer stage, or first line of treatment (the last not shown). The hazard ratio of death was also not statistically different in the complete model that included all variables.

4. Discussion

Taking into account our small sample size as a limitation, there was no significant difference between G40 and G50 in this

Table 1
Breast cancer prognostic factors at diagnosis in Guadeloupian women according to the age group of those eligible for mass breast cancer screening (50–74) and the preceding age group (40–49).

		Age groups		
n(%)	Total [a] 1275	40–49 308 (30.5)	50–74 701 (69.5)	P [b]
Tumor size (mm), median [IQR]	20 [15–30]	25 [15–35]	20 [13–30]	0.004[b]
Cancer subtype, n(%)				0.1 [c]
HR+/Her2-	534 (41.9)	112 (36.4)	310 (44.2)	
HR+/Her2+	299 (23.4)	86 (27.9)	150 (21.4)	
HR-/Her2+	74 (5.8)	22 (7.1)	46 (6.6)	
TNBC	180 (14.1)	39 (12.7)	95 (13.5)	
Unknown	188 (14.8)	49 (15.9)	100 (14.3)	
MSBR grading, n(%)				0.8 [c]
Grade 1	222 (17.4)	54 (17.5)	128 (18.3)	
Grade 2	585 (45.9)	139 (45.1)	325 (46.4)	
Grade 3	307 (24.1)	70 (22.7)	163 (23.2)	
Missing data	161 (12.6)	45 (14.6)	85 (12.1)	
ENCR condensed Staging, n(%)				0.1 [c]
Localized/local spread	660 (51.8)	154 (50.0)	368 (52.5)	
Regional	332 (26.0)	92 (29.9)	179 (25.5)	
Extended	47 (3.7)	15 (4.9)	22 (3.1)	
Unknown	236 (18.5)	47 (15.2)	132 (18.8)	
Morphology, n(%)				0.8
Duct carcinoma	1059 (83.1)	260 (84.4)	586 (83.6)	
Lobular carcinoma	68 (5.3)	18 (5.8)	38 (5.4)	
Other carcinoma	148 (11.6)	30 (9.7)	77 (11.0)	
First line therapy, n(%)				0.6
Surgery	941 (73.8)	223 (72.4)	522 (74.5)	
Radio/Chemotherapy	107 (8.4)	30 (9.7)	55 (7.8)	
Unknown	227 (17.8)	55 (17.9)	124 (17.7)	

IQR: Interquartile range of the median. HR: hormone receptors. Her2: Human Epidermal Growth Factor Receptor 2. TNBC: triple negative breast cancer. MSBR: modified Scarff Bloom Richardson grading system. ENCR: European Network of Cancer Registries.

[a] Whole study population data irrespective of age [4].

[b] Median test for numerical variables.

[c] Pearson chi2 test for categorical variables.

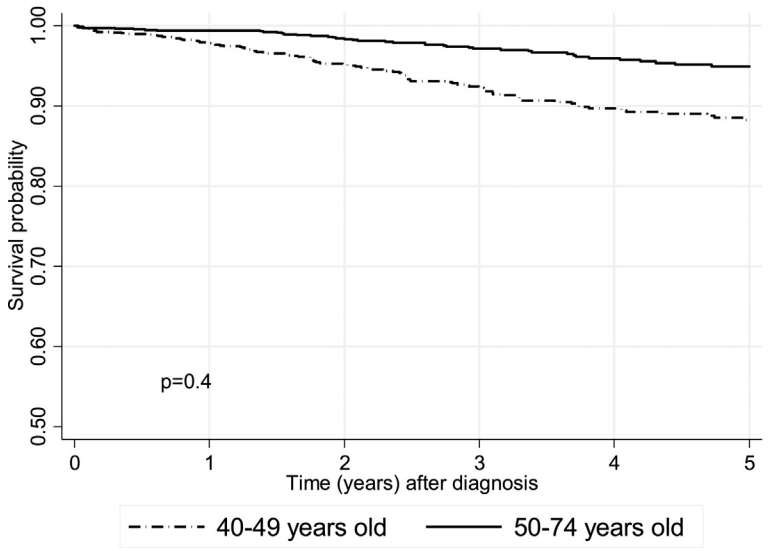

Fig. 1. Kaplan-Meier survival curves for the age group eligible for mass screening for breast cancer (50–74) vs the preceding age group (40–49). Please refer to Table 2 for crude and adjusted hazard ratios and P values comparing the two age groups.
P = 0.4 for Stratified Wilcoxon (Breslow) test for equality of survivor functions (50–74 versus 40–49 age groups).

comparison of breast cancer cases between patients eligible for mass BC screening in Guadeloupe and those in the preceding 10-year age group, except tumor size which was greater in the younger group (G40).

The tumor related factors we studied are classic prognostic and predictive markers for several indicators, such as recurrence, disease-free and overall survival, and response to therapy [11]. We were concerned that the characteristics of G40 would be more closely related to the group under 40 than G50. BC cases in patients under 40 are known to have more aggressive features and to be more frequently association with genetic syndromes [3]. Our results do not support this concern of cancer in G40 related to characteristics of cancer in patients under 40.

The differences in tumor size can be explained by the fact that cancer is more frequently diagnosed based on clinical signs in G40, usually by the palpation of the tumor. In contrast, cases in G50 are more frequently diagnosed by mass screening at the subclinical size. The overall survival rate in G40 does not support our previous concerns fueled by reports of a poorer prognosis in the African-American population [12]. Nevertheless, greater tumor size is a classic factor for a poor prognosis. There appears to be no significant difference in the survival between G40 and G50, despite a greater tumor size, was likely linked to the efficiency of the treatment.

The curves in Fig. 1 tend to steadily move apart with time but the hazard ratio of death between the age groups showed no significant difference for the different adjusted Cox models (Table 2). However, we cannot exclude the lack of power. In the sub-population of cases for patients above 74, the overall survival rate was significantly lower (data not show). We also cannot exclude that the absence of a significant difference in the overall survival rate between G40 and G50 is linked to a higher burden of BC cases in the oldest women of G50.

5. Conclusion

Our study took place in Guadeloupe. French laws do not allow the gathering of ethnic information, but it is commonly acknowledged that over 80% of the population is of African descent. It is reasonable to assume that at least 80% of the inhabitants are of African ancestry, as for the other West Indies islands, which share a comparable history of slave trade [13]. It did not compare data with populations that would be considered to be Caucasian.

Although our study is limited by the small sample size, our results do not show a more aggressive pattern and no lower overall patient survival for breast cancer cases in women in the 10-year age group preceding eligibility for mass screening in the Guadeloupian population than those who were eligible. It is possible that this result is due to free access to efficient medical care in Guadeloupe. This finding may add to the debate surrounding several issues linked to breast cancer screening in the Guadeloupean population. These include lowering the recommended screening age for the population of African ancestry because of their higher rate of BC under the age of 50, the risks related to mammography screening, the lower sensitivity and specificity of mammography for those under 50, and the increasing

Table 2
Cox proportional Hazard ratio (HR [95% CI]) of death after breast cancer for the age group eligible for mass breast cancer screening (50–74) versus the preceding age group (40–49).

Age group	Crude	Adjusted		
		tumor size	receptors	Model 1
50–74	1	1	1	1
40–49	0.93 [0.65–1.35]	0.90 [0.63–1.31]	0.93 [0.64–1.34]	0.43 [0.16–1.15]

Model 1: Adjusted for receptor status, tumor size, cancer stage, and first line of treatment. Significant interaction terms between the covariates were included in the model.

efficiency of treatment, especially when full access to treatment is available.

Authorship contribution statement

P. Kadhel: conception and design, interpretation of the data, drafting the article, and final approval of the version to be published.

D Borja de Mozota: interpretation of the data, participation in drafting the article and approval of the version to be published..

S Gaumond: data acquisition and final approval of the version of the article to be published.

J. Deloumeaux: acquisition, analysis, and interpretation of data, final approval of the version of the article to be published.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

We wish to thank B. Bhakkan, Manip Nsome M'Ebobisse, W. Lafrance, P Lancelot, D. Vacqué, Y. Negesse, and A. Diedhiou for their participation in the data collection, and Luc Multigner for advice on writing the manuscript.

The cancer registry of Guadeloupe is granted financial support from the Institut National du Cancer (INCa) and Santé Publique France.

References

[1] I. Ferlay, R. Soerjomataram, S. Dikshit, C. Eser, M. Mathers, D.M. Rebelo, D. Parkin, F. Forman, Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012, Int. J. Cancer 136 (5) (2015) E359–E386.

[2] P. Kadhel, L. Multigner, Age at breast cancer diagnosis in populations of African and European ancestry, Breast J. 20 (2) (2014) 180–184.

[3] C.K. Anders, R. Johnson, J. Litton, M. Phillips, A. Bleyer, Breast cancer before age 40 years, Semin. Oncol. 36 (3) (2009) 237–249.

[4] J. Deloumeaux, S. Gaumond, B. Bhakkan, N. Manip M'Ebobisse, W. Lafrance, P. Lancelot, D. Vacque, Y. Negesse, A. Diedhiou, P. Kadhel, Incidence, mortality and receptor status of breast cancer in African Caribbean women: data from the cancer registry of Guadeloupe, Cancer Epidemiol. 47 (2017) 42–47.

[5] J. Ferlay, I. Soerjomataram, M. Ervik, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, D. Parkin, D. Forman, F. Bray, GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet], International Agency for Research on Cancer, Lyon France, 2013.

[6] N. Howlader, S.F. Altekruse, C.I. Li, V.W. Chen, C.A. Clarke, L.A. Ries, K.A. Cronin, US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status, J. Natl. Cancer Inst. 106 (5) (2014).

[7] J.E. Tyczynski, E. Démaret, D.M. Parkin (Eds.), Standards and Guidelines for Cancer Registration in Europe: the ENCR Recommendations, International Agency for Research on Cancer, Lyon, 2003.

[8] E.L. Kaplan, P. Meier, Nonparametric estimation from incomplete observations, J. Am. Stat. Assoc. 53 (282) (1958) 457–481.

[9] D.R. Cox, Partial likelihood, Biometrika 62 (2) (1975) 269–276.

[10] D. Schoenfeld, Partial residuals for the proportional hazards regression model, Biometrika 69 (1) (1982) 239–241.

[11] R. Mehta, R.K. Jain, S. Badve, Personalized medicine: the road ahead, Clin. Breast Cancer 11 (1) (2011) 20–26.

[12] R.T. Chlebowski, Z. Chen, G.L. Anderson, T. Rohan, A. Aragaki, D. Lane, N.C. Dolan, E.D. Paskett, A. McTiernan, F.A. Hubbell, L.L. Adams-Campbell, R. Prentice, Ethnicity and Breast cancer factors influencing differences in incidence and outcome, J. Natl. Cancer Inst. 97 (6) (2005) 439–448.

[13] Barbados Statistical Service, Barbados Population and Housing Census, (2010), pp. 2010 (available at: http://www.barstats.gov.bb/files/documents/PHC_2010_Census_Volume_1.pdf Accessed October 2, 2016).