Multimorbidity clusters among long-term breast cancer survivors in Spain: Results from the SURBCAN Study

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Goal

Multimorbidity, the co-occurrence of multiple diseases, is associated with an increased mortality and use of health services, especially primary care. The scarce knowledge of multimorbidity patterns among breast cancer survivors (BCS) hampers the long-term disease management and challenges health providers. Here we identify multimorbidity clusters among long-term BCS by means of hierarchical cluster analysis and assess the impact of those clusters on mortality and use of health services.

Methods

Retrospective study using electronic health records from 6512 women diagnosed with breast cancer between 2000 and 2006 and a survival period of at least 5 years during the follow-up period (2012-2016) from 5 Spanish regions. Chronic diagnoses were extracted using 290 clinical blocks from the Clinical Classification Software as of ICD-9 and ICD-10 codes. Multimorbidity patterns were identified through hierarchical clustering and Observed/Expected ratios were used to identify associated-comorbidities. Adjusted Cox regression and negative binomial models by age, survival time, tumor behavior, Charlson Index and visits to healthcare services were fitted in order to estimate the impact of clusters on mortality and use of primary care and hospital.

Results

6512 long-term BCS were included in the analysis (mean age: 66.0, SD: 12.6). Five multimorbidity clusters were identified: C1-Unspecific (29.9%), C2-Metabolic and degenerative (28.3%), C3-Anxiety and fractures (9.7%), C4-Musculoskeletal and cardiovascular (9.6%), C5-Thyroid disorders (5.3%) plus the group of long-term BCS without comorbidities (17.3%). %). All clusters except the C5-Thyroid disorders were associated with increased mortality compared to BCS without comorbidities, being the highest risk in C4 (HR=1.88, 95%CI 1.68-2.33). Women in cluster C3 presented the highest health services use both for primary care (RR=2.01, 95%CI: 1.90-2.12) and for hospital-based services (RR=2.75, 95%CI: 2.60-2.92) compared with BCS without comorbidity. BCS in C4-Muskuloskeletaland cardiovascular showed the highest risk of mortality, while BCS in C3-Anxiety and fractures the highest risk of health services use when compared to BCS without comorbidity.

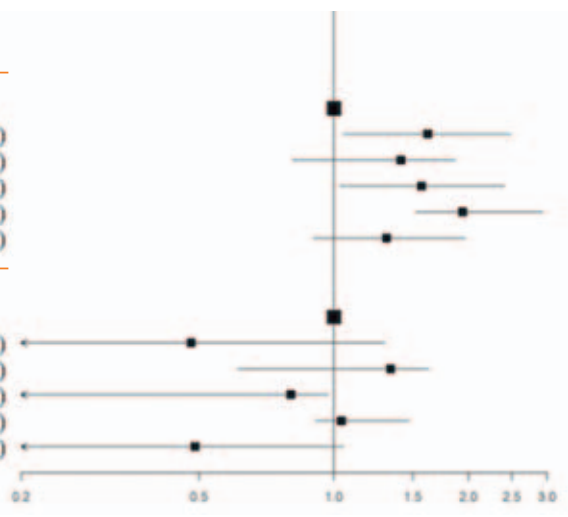
Figure 1. Association between clusters and mortality stratified by survival time (n=6512)

Characteristics	Long-term BCS N=6512
Age, mean (SD)	66.0 (12.6)
Age groups, n (%)	
18-49 years	562 (8.7)
50-69 years	3395 (52.1)
≥70 years	2555 (39.2)
Survival time, n (%)	
5-10 years	4719 (74.8)
≥10 years	1590 (25.2)
BCS without CCS-CD comorbidities, n (%)	1125 (17.3)
Multimorbidity, n (%)	3563 (54.7)
Mean number of chronic diseases (SD)	2.35 (2.06)
Charlson Index, n (%)	
0-1	1397 (24.6)
≥2	4279 (75.4)
Tumor behaviour, n (%)	
In situ	517 (12.7)
Invasive	3544 (87.3)
Surgery, n (%)	
No	126 (3.1)
Yes	3930 (96.9)
Annual visits to PC, mean (median)	25.4 (14)
Annual visits to hospital-based services, mean (median)	5.4 (3)
Vital status, n (%)	
Alive	5662 (87.4)
Exitus	819 (12.6)

BCS: breast cancer survivors; SD: standard deviation; CCS-CD: chronic diseases from the Clinical Classifications Software list; PC: primary care.

Table 1. Baseline characteristics of included long-term BCS

	N (cluster)	N (exitus)	aHR (95% CI)
5-10 years			
BCS without comorbidities*	813	108	Ref
C1-Unspecific	1,480	155	1.62 (1.05 - 2.49)
C2-Metabolic and degenerative	1,303	174	1.41 (0.81 - 1.87)
C3-Anxiety and fractures	453	36	1.57 (1.03 - 2.40)
C4-MSK and cardiovascular	430	80	1.94 (1.53 - 2.93)
C5-Thyroid disorders	240	28	1.31 (0.90 - 1.97)
> 10 years			
BCS without comorbidities*	263	14	Ref
C1-Unspecific	440	6	0.48 (0.11 - 1.30)
C2-Metabolic and degenerative	455	11	1.34 (0.61 - 1.63)
C3-Anxiety and fractures	146	2	0.80 (0.10 - 0.97)
C4-MSK and cardiovascular	192	3	1.04 (0.91 - 1.47)
C5-Thyroid disorders	94	2	0.49 (0.10 - 1.05)



aHR: adjusted hazard ratio for age, tumor behavior, primary and hospital care contacts and Charlson Index. CI: confidence interval. MSK: musculoskeletal. Mortality was assessed through vital status at the end of follow-up (31st December 2016).
**BCS without comorbidities were defined as those BCS without CD from the Clinical Classification Software list and those without any comorbidity reported in the EHR.*

Table 2. Association between clusters and both mortality and healthcare services use in long-term BCS at baseline follow-up (n=6512).

	Mortality		Primary Care		Hospital-based services	
	aHR	95% CI	aRR	95% CI	aRR	95% CI
Multimorbidity clusters						
BCS without CCS-CD comorbidities	Ref.		Ref.		Ref.	
C1-Unspecific	**1.43**	**1.39-3.10**	**1.59**	**1.52-1.67**	**1.70**	**1.62-1.79**
C2-Metabolic and degenerative	**1.41**	**1.37-3.03**	**1.83**	**1.71-1.97**	**1.93**	**1.87-2.02**
C3-Anxiety and fractures	**1.55**	**1.52-2.62**	**2.01**	**1.90-2.12**	**2.75**	**2.60-2.92**
C4-MSK and cardiovascular	**1.88**	**1.68-2.33**	**1.50**	**1.41-1.59**	**2.15**	**2.02-2.30**
C5-Thyroid disorders	**0.74**	**0.31-0.96**	**1.72**	**1.59-1.86**	**2.11**	**1.95-2.28**
Age	**1.10**	**1.08-1.10**	**1.01**	**1.01-1.01**	**0.98**	**0.98-0.99**
Charlson Index (≥2)	1.25	0.95-1.75	1.17	0.95-1.23	**1.23**	**1.18-1.26**
Tumour behavior(invasive)	**2.72**	**1.49-3.78**	**1.20**	**1.15-1.28**	1.04	0.99-1.08
Survival time (>10 years survival)	**0.14**	**0.09-0.22**	-		-	
Primary care visits	0.98	0.98-1.04	-		-	
Hospital-based services visits	0.99	0.99-1.00	-		-	
Vital Status (exitus)	-		0.95	0.86-1.07	**1.12**	**1.08-1.17**

aHR: adjusted hazard ratio by age, survival time, tumor behavior, primary and hospital care visits and Charlson Index.CI: confidence interval. aRR: adjusted relative risk by age, vital status, tumor behavior and Charlson Index. CCS-CD: chronic diseases from the Clinical Classification Software list. MSK: musculoskeletal.Reference categories: cluster (women without CCS-CD comorbidities); Charlson Index (0-1); tumor behavior (in situ); survival time (5-10 years survival); vital status (alive)

Conclusions

Multimorbidity clusters have a different impact on mortality and healthcare services use. These results help to identify sub-groups of long-term breast cancer survivors with specific needs and mortality risks and to orientate BCS clinical practice to multimorbidity.

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