Influence of Surgical Treatment on Complications, Readmissions and Clinical Progress of Breast Cancer in Women Participating in Breast Cancer Screening Programs

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Abstract

Background

Complications and readmissions derived from surgical treatment of breast cancer have been scarcely evaluated. The studies that compare mastectomy with conservative, usually focus only in recurrence and/or mortality and sometimes the results are discordant in some aspects. The aim of this study was to analyze complications and readmissions, recurrence and mortality, according to the surgical treatment received in the mammary gland.

Methods

This multicenter study included 1086 women diagnosed with breast cancer from the CaMISS cohort study of women aged between 50 and 69 years participating in 4 breast cancer screening programs in Spain between 2000 and 2009 with a follow up until 2014. Multivariate models were used to estimate the adjusted odds ratio of breast surgery (mastectomy vs conservative treatment) for complications and readmissions and hazard ratios for recurrences and mortality.

Results

Primary breast surgical treatment consisted of conservative treatment in 821 women (80.1%) and mastectomy in 204 (19.9%). Mastectomy was associated with readmissions, recurrences and mortality but this association was not statistically significant on multivariate adjusted analysis (ORa=1.51 [95%CI 0.89-2.57], HRa=1.37 [95%CI 0.85-2.19] and HRa=1.52 [95%CI 0.95-2.43] respectively). In our sample, the variables with greatest impact on complications, recurrences and mortality were stages III and IV (ORa=4.4 [95%CI 1.22-16.16], HRa=7.96 [95%CI 3.32-19.06] and HRa=3.92 [95%CI 1.77-8.67]).

Conclusion

Complications, readmissions, recurrence and mortality were similar in both surgical techniques. These results support that surgical treatment for breast cancer can be adapted to professional and health system circumstances, and to the surgical needs and desires of each patient.

Introduction

Breast cancer treatment is constantly changing due to ongoing advances and the need to adapt to new knowledge. It has evolved rapidly since the beginning of the 20th century, when the treatment was based solely on the extensive radical Halsted mastectomy[1]. Nowadays, international clinical practice guidelines include multiple chemotherapeutic, hormonal and immunotherapeutic treatments, as well as radiotherapy and several accepted surgical techniques[2] [3]. Depending on the characteristics of the patient (comorbidities, family history, genetic alterations, patient preferences), the tumor (tumor-node-metastases stage, histology, phenotype), and the size of the mammary gland, the patient receives the appropriate treatment following breast cancer treatment protocols and international guidelines[2] [3].

Survival has greatly improved due to all advances in multidisciplinary treatments[4] [5] and the early detection through screening[6] [7] [8]. However, breast cancer is still a potentially serious disease and is the most frequent form of cancer in women, with 1,671,149 new cases estimated per year worldwide, with an annual mortality of 521,907 patients[9]

Surgery plays a fundamental role in the cure of breast cancer and both mastectomy and breast conservative surgery are accepted as validated techniques. When the evidence on the effectiveness and safety of a given treatment is high, low variability in medical practice is expected[10]. However, variability in surgical practice may be a problem to face today[11] [12], with moderate-to-high variability in the performance of surgical treatment of breast cancer [10] [13] [14] [15]. After the two seminal randomized trials for breast conservation surgery, NSAPB-B06 trial[16] and Veronesi's Italian trial[17], were published, several studies have compared mastectomy with conservative surgery for the treatment of breast cancer. In some of them, no difference in mortality has been observed, although in others, the results on mortality and recurrence are discordant in some aspects. Furthermore, there are fewer studies on the impact of surgical variability on complications and readmissions. Also, studies on readmissions have focused on short-term readmissions after surgery[18] [19] [20], showing an association with postoperative complications. Only a few studies have evaluated readmissions in the long term[21] [22].

Women participating in breast cancer screening programs are more likely to be diagnosed at earlier stages and requiring less aggressive treatment modalities, having higher percentages of breast-conserving surgery and showing better survival than women diagnosed symptomatically [10] [23]. However, less attention has been paid to the impact on readmissions and treatment-related complications derived from surgical variability. A high surgical variability (mastectomy vs conservative surgery) was observed in women with the same characteristics and type of tumor in different hospitals from the CaMISS cohort study performed in Spain among women participating in breast cancer screening program[13], in agreement with other studies [10] [14] [15].

On this basis, with patients of the same age and tumor characteristics who received different surgical treatments, the aim of this current study has been to analyse complications, readmissions, recurrence and mortality according to the surgical treatment received in the mammary gland in women participating in a homogenous cohort from screening breast cancer program population.

Methods

Study population

This study included 1086 women diagnosed with breast cancer included in the CaMISS cohort. The CaMISS retrospective cohort included women aged between 50 and 69 years participating in 4 breast cancer screening programs in Spain between 2000 and 2009. This multicenter study included eight hospitals from Barcelona, Girona, Sabadell and Canary islands screening programs, and the cohort contains information on the diagnostic process, treatment, complications and follow-up until 2014[24].

Of the 1086 women included in the CaMISS cohort, 29 were excluded because they received only medical treatment without surgery and 32 were excluded because of missing information. The total target population included in the final analysis was 1025 patients (94.4%) (Fig. 1).

Diagnosis

Breast cancer was detected through screening mammography or emerged as an interval cancer. In Spain, women aged between 50 and 69 years are invited to participate in a population-based screening program by a postal letter every 2 years to undergo a screening mammogram following the European guidelines for Quality Assurance in Mammographic Screening Recommendations[25]. The definition of interval cancer used was that proposed in the European guidelines as “primary breast cancer arising after a negative screening episode, with or without further assessment, and before the next screening invitation, or within 24 months for women who reached the upper age limit”[26].

The final diagnosis was obtained by biopsy of the lesion detected through an imaging test and successive histopathological study in all cases. After diagnosis, each woman was treated at the referral hospital of their screening program.

Variables and data sources

Information on patient age and detection method (screening or interval) was obtained from the databases of the population and hospital-based screening programs. Information on tumor characteristics (TNM, histology, phenotype) and treatment was obtained from medical records and from hospital-based cancer registries.

Treatment was decided in a multidisciplinary committee in each hospital. Surgical treatment was classified in two categories: conservative treatment or mastectomy. In conservative surgery, the tumor is excised with a concentric margin of healthy tissue with negative excision margins and preservation of the rest of the breast gland. Almost all patients who undergo conservative surgery receive radiotherapy. Regarding mastectomy, it consists of complete surgical resection of the breast tissue and includes all the non- conservative surgeries: modified radical mastectomy, simple mastectomy, skin-sparing mastectomy, and nipple-areolar sparing mastectomy. Mastectomy is indicated for patients who are not candidates for breast-conserving therapy, for rescue after conservative surgery that does not meet the criteria for new conservative surgery or by patient preference.

ALND was included for a better understanding of the surgical approach in each woman and because of its known relationship with complications and cancer recurrences[27]. In axillary surgery, the performance of the sentinel node biopsy (SNB) in N0 or the performance of axillary lymph node dissection (ALND) in N1/N2/N3 was recorded.

Outcome variables consisted of complications after surgical treatment, hospital readmissions, cancer recurrences and mortality. All these data were obtained from clinical records cataloged on specific annual time points from hospital-based cancer registries since the date of surgery until the end of follow-up in June 2014.

Complications included were systemic complications, surgery-related (seroma, wound infection), pain[28] and psychological events (anxiety and/or depression).

Readmissions have been considered a complication and a loss of quality of life for patients and they were included from the surgical intervention until the end of the follow-up. The causes of readmission included surgical causes (surgery due to margin enlargement, the need to perform an ALND or mastectomy), complications of the surgical site requiring admission (infection, abscess drainage, sepsis) and complications related to systemic causes (disease progression, decompensation of concomitant diseases).

Cancer recurrence was classified in three sections: local recurrence when there was a reappearance of cancer in the ipsilateral breast, regional recurrence when the tumor involved the ipsilateral regional lymph nodes (axillar or clavicular) and metastatic when the recurrence was remote. All-cause mortality was also included.

Data were collected through a protocol approved by the clinical research ethics committee of Parc de Salut Mar (Barcelona), and the rest of the participating institutions.

Statistical analysis

A descriptive analysis including all the study variables was performed. Women's and tumor characteristics were compared by surgical treatment (conservative surgery or mastectomy) through the chi-squared test as all the study variables were categorical.

Multivariate logistic regression models were used to estimate crude and adjusted odds ratios (OR) according to complications and readmissions. Cox models were used for cancer recurrence and mortality after surgical treatment to take into account the time between the treatment and these outcomes.

The adjusted analysis included the following variables: age, diagnostic method, screening program, TNM stage, histology, phenotype, surgical treatment and performance of ALND.

Statistical significance was set at $p < 0.05$. Statistical analyses were performed through the SPSS statistical package (version 23.0).

Results

Descriptive analysis of the CaMISS cohort according to the received surgical treatment

The results of the descriptive analysis are shown in Table 1. Primary breast surgical treatment included conservative treatment in 821 women (80.1%) and mastectomy in 204 (19.9%). The mean age of the patients at the time of diagnosis was 58.5 ± 5.45 years (49–69) with no statistically significant differences according to surgical treatment. Breast cancer was detected through screening mammograms in 713 women (69.6%). The percentage breast cancer detected by screening mammography that underwent conservative surgery was higher than that among women with interval cancer (73.9 and 52%, respectively, $p < 0.001$).

Conservative treatment was more frequent in stage I tumors than mastectomy (51.4% vs 15.7%, $p < 0.001$). Mastectomy was more frequent in women with advanced stage tumors (stage III: 19.6% vs. 6.3%, $p < 0.001$). The percentages of B luminal and HER2 were higher in the mastectomy group than in the conservative surgery group (luminal B: 19.6% vs 23%, HER2: 4.8% vs 12.3%, $p = 0.002$).

ALND was more frequent in the mastectomy group than in the conservative surgery group (78.4% vs. 58.9%, $p < 0.001$). There were differences in the surgical treatment received according to the screening program ($p < 0.001$)[13].

Table 1
CAMISS cohort descriptive analysis according to the surgical treatment received

	Treatment						
	Conservative n = 821	%	Mastectomy n = 204	%	Total n = 1025	%	p-value
Age (years)							
Median (IQR)	57 (49–69)		58 (50–69)		58 (49–69)		
Age groups (years)							
50–54	230	28.0	65	32.2	295	28.8	0.27
55–59	219	26.7	57	27.9	276	26.9	
60–64	228	27.8	43	21.1	271	26.4	
65–69	144	17.5	39	19.1	183	17.9	
Diagnostic method							
Screening	607	73.9	106	52.0	713	69.6	**< 0.001**
Interval	214	26.1	98	48.0	312	30.4	
TNM							
In situ	85	10.4	17	8.3	102	9.9	**< 0.001**
I	422	51.4	32	15.7	454	44.3	
II	250	30.5	76	37.3	326	31.8	
III	52	6.3	70	19.6	122	11.9	
IV	2	0.2	5	2.5	7	0.7	
Histology							
Invasive ductal carcinoma	605	73.7	138	64.6	743	72.5	**0.001**
Ductal carcinoma in situ	77	9.4	16	7.8	93	8.3	
Invasive lobular carcinoma	63	7.7	34	16.7	97	9.6	
Others	72	8.8	13	6.4	85	8.3	
Phenotype							
Luminal A	323	39.3	72	35.3	395	38.5	**0.002**
Luminal B	161	19.6	47	23.0	208	20.3	

ALND: Axillary lymph node dissection

	Treatment						
	Conservative n = 821	%	Mastectomy n = 204	%	Total n = 1025	%	p-value
HER2	39	4.8	25	12.3	64	6.2	
Triple negative	66	8.0	17	6.9	83	8.1	
ALND							
Yes	484	58.9	160	78.4	644	62.8	**< 0.001**
No	337	41.1	44	21.6	381	37.2	
Program							
1	303	36.9	84	41.2	387	37.8	**< 0.001**
2	254	30.9	38	18.6	292	28.5	
3	86	10.5	17	8.3	103	10.0	
4	178	21.7	65	31.9	243	23.7	
ALND: Axillary lymph node dissection							

Descriptive analysis of complications, readmissions, recurrence and mortality

Complications, readmissions, recurrences and mortality outcomes by surgical treatment are shown in Table 2. A total of 292 women (28.3%) experienced at least one complication with no differences according to surgical treatment (p value 0,744).

A total of 223 women (21.8%) were readmitted after surgical treatment until the end of the follow-up. Readmissions were slightly more frequent in the mastectomy group than in the conservative treatment group (27% and 20.5%, respectively, $p = 0.04$). They predominated during the first year after surgery in patients undergoing conservative surgery (75.6%) but were more evenly distributed during follow-up in patients undergoing mastectomy (54.4% during the first year) ($p = 0.004$).

Regarding cancer recurrence, it affected 146 women (14.2%) and was more frequent in the mastectomy group than in the conservative surgery group (27.9% vs. 10.8%, $p < 0.001$). The most frequent type of recurrence was the local one in conservative treatment (3.8%).

The mortality rate for this cohort with a follow-up period of 13 years was 13.8% (n = 141), and was higher in the mastectomy group than in the conservative surgery group (26.5% vs. 10.6%, $p < 0.001$).

Table 2
Descriptive analysis of complications, readmissions, recurrence and mortality

	Treatment						
	Conservative n = 821	%	Mastectomy n = 204	%	Total n = 1025	%	p-value
Complications							
No	589	71.7	144	70.6	733	71.5	0.744
Yes	232	28.3	60	29.4	292	28.5	
Type of complication							
Systemic complications	30	12.9	5	8.3	35	12.0	0.744
Surgery-related complications	17	7.3	7	11.7	24	8.2	
Pain	87	37.5	19	31.7	106	36.3	
Psychological events	72	31.0	23	38.3	95	32.5	
Others	26	11.3	6	10.0	32	11.0	
Readmissions							
No	653	79.5	149	73.0	802	78.2	**0.044**
Yes	168	20.5	55	27.0	223	21.8	
Time of readmission							
≤ 1 year after treatment	127	75.6	30	54.5	157	70.4	**0.004**
> year after treatment	41	24.4	25	45.5	66	29.6	
Recurrences							
No	732	89.2	147	72.1	879	85.8	**<0.001**
Yes	89	10.8	57	27.9	146	14.2	
Type of recurrence							
Local	31	3.8	7	3.4	38	3.7	**0.023**
Regional	9	1.1	9	4.4	18	1.6	

	Treatment							
Metastatic or remote	49	6	41	20	90	8.9		
Mortality								
No	734	89.4	150	73.5	884	86.2	**<0.001**	
Yes	87	10.6	54	26.5	141	13.8		

Univariate and multivariate adjusted analysis of complications, readmissions, recurrence and mortality

In the unadjusted and adjusted OR analysis (Table 3), surgical treatment was not associated with complications (ORa = 0.71 [95%CI 0.40–1.32]) nor with readmissions in the adjusted analysis (ORa = 1.51 [95%CI 0.89–2.57]). The presence of ALND and stage III and IV tumors were associated with the presence of complications (OR a (ALND) = 3.3 [95%CI 2.0-5.4] and OR a (TNM) = 4.4 [95%CI 1.22–16.16]) but not with readmissions.

Table 3
Unadjusted and adjusted OR of complications and readmissions after surgical treatment (logistic regression)

	Complications				Readmissions			
	Unadjusted OR	**95% CI**	**Adjusted OR**	**95% CI**	**Unadjusted OR**	**95% CI**	**Adjusted OR**	**95% CI**
Treatment								
Conservative surgery	1	1	1	1	1	1	1	1
Mastectomy	1.37	0.91–1.99	0.71	0.40–1.32	1.44	1.01–2.04	1.51	0.89–2.57
ALND								
No	1	1	1	1	1	1	1	1
Yes	1.20	0.89–1.69	**3.3**	**2.0-5.4**	1.19	0.79–1.79	1.4	0.86–2.24
Age groups (years)								
50–54	1	1	1	1	1	1	1	1
55–59	1.03	0.70–1.50	1.17	0.67–2.02	0.92	0.63–1.34	0.94	0.57–1.56
60–64	0.78	0.53–1.16	0.72	0.40–1.31	0.73	0.49–1.07	0.51	0.29–0.91
65–70	0.67	0.43–1.05	0.77	0.40–1.46	0.35	0.35–0.88	0.57	0.30–1.05
Diagnostic method								
Screening	1	1	1	1	1	1	1	1
Interval	1.13	0.82–1.56	1.50	0.94–2.39	1.17	0.86–1.59	1.00	0.09–0.30
TNM								
In situ	0.19	0.08–0.45	0.35	0.09–1.26	0.85	0.48–1.48	1.04	0.47–2.32
I	1	1	1	1	1	1	1	1
II	1.67	1.15–2.40	1.19	0.69–2.06	1.41	0.85–2.35	1.15	0.68–1.96
III + IV	1.88	1.02–3.47	**4.44**	**1.22–16.16**	1.47	0.83–2.61	1.07	0.26–4.40

Adjusted by: treatment, ALND, age, TNM, phenotype, histology, diagnostic method and program. ALND: Axillary lymph node dissection.

	Complications				Readmissions			
	Unadjusted OR	95% CI	Adjusted OR	95% CI	Unadjusted OR	95% CI	Adjusted OR	95% CI
Histology								
Invasive ductal carcinoma	1	1	1	1	1	1	1	1
Ductal carcinoma in situ	0.13	0.05–0.33	0.11	0.01–2.12	0.59	0.33–1.07	0.11	0.01-1.00
Invasive lobular carcinoma	1.01	0.61–1.67	1.31	0.63–2.74	0.55	0.61–0.99	0.55	0.24–1.28
Others	0.80	0.49–1.33	0.84	0.36–1.93	1.49	0.92–2.39	1.12	0.52–2.43
Phenotype								
Luminal A	1	1	1	1	1	1	1	1
Luminal B	0.99	0.65–1.53	1.03	0.62–1.71	1.45	0.93–2.27	0.73	0.45–1.20
HER2	0.88	0.43–1.79	0.92	0.40–2.10	1.89	0.97–3.67	1.17	0.55–2.36
Triple negative	1.4	0.74–2.63	1.13	0.54–2.33	1.45	0.77–2.76	0.87	0.44–1.73

Adjusted by: treatment, ALND, age, TNM, phenotype, histology, diagnostic method and program. ALND: Axillary lymph node dissection.

The HR analysis (Table 4) showed that mastectomy was associated with recurrences and mortality in the unadjusted analysis but the association did not remain significant after adjustment (HRa = 1.37 [95%CI 0.85–2.19] and HRa = 1.52 [95%CI 0.95–2.43]) respectively). Among the other variables, only stage III/IV and HER2 phenotype had a statistically significant association with recurrences and mortality in the adjusted analysis, with the highest HRa found for stages III and IV and the risk of recurrences (HRa = 7.96 [95%CI 3.32–19.06]).

Table 4
Unadjusted and adjusted HR of recurrences and mortality (COX)

	Recurrences				Mortality			
	Unadjusted HR	**95% CI**	**Adjusted HR**	**95% CI**	**Unadjusted HR**	**95% CI**	**Adjusted HR**	**95% CI**
Treatment								
Conservative surgery	1	1	1	1	1	1	1	1
Mastectomy	**2.86**	**2.05–3.99**	1.37	0.85–2.19	**2.73**	**1.94–3.83**	1.52	0.95–2.43
ALND								
No	1	1	1	1	1	1	1	1
Yes	1.20	0.82–1.74	0.92	0.51–1.65	0.99	0.69–1.43	0.76	0.45–1.35
Age groups (years)								
50–54	1	1	1	1	1	1	1	1
55–59	0.69	0.46–1.04	0.56	0.33–0.93	0.67	0.43–1.07	0.62	0.36–1.08
60–64	0.81	0.54–1.20	0.71	0.41–1.22	0.94	0.62–1.43	0.86	0.48–1.52
65–70	0.56	0.34–0.93	0.49	0.26–0.92	1.33	0.87–2.04	1.37	0.78–2.35
Diagnostic method								
Screening	1	1	1	1	1	1	1	1
Interval	1.91	1.39–2.61	0.98	0.63–1.53	2.18	0.59–2.98	1.33	0.85–2.07
TNM								
In situ	1.10	0.49–2.27	0.88	0.32–2.42	0.19	0.05–0.77	0.28	0.07–1.20
I	1	1	1	1	1	1	1	1
II	1.28	0.77–2.15	1.27	0.65–2.48	0.81	0.50–1.34	0.79	0.43–1.45
III + IV	**5.04**	**3.01–8.44**	**7.96**	**3.32–19.06**	**4.07**	**2.26–7.35**	**3.92**	**1.77–8.67**

Adjusted by: treatment, ANLD, age, TNM, histology, phenotype, diagnostic method, program and diagnosis date. ALND: Axillary lymph node dissection

	Recurrences				Mortality			
	Unadjusted HR	**95% CI**	**Adjusted HR**	**95% CI**	**Unadjusted HR**	**95% CI**	**Adjusted HR**	**95% CI**
Histology								
Invasive ductal carcinoma	1	1	1	1	1	1	1	1
Ductal carcinoma in situ	0.47	0.22–1.01	0.02	0.00-0.28	0.14	0.03–0.55	-	-
Invasive lobular carcinoma	1.07	0.65–1.75	0.97	0.37–2.57	0.88	0.52–1.51	1.32	0.60–2.92
Others	0.71	0.37–1.35	0.26	0.06–1.11	1.07	0.62–1.83	1.04	0.44–3.47
Phenotype								
Luminal A	1	1	1	1	1	1	1	1
Luminal B	1.38	0.88–2.17	1.33	0.80–2.20	1.10	0.70–1.74	1.27	0.77–2.09
HER2	**3.62**	**2.17–6.03**	**3.39**	**1.92–5.98**	**2.83**	**1.70–4.70**	**3.01**	**1.68–5.38**
Triple negative	**2.05**	**1.18–3.53**	1.63	0.86–3.10	**1.95**	**1.15–3.30**	1.60	0.85–2.07

Adjusted by: treatment, ANLD, age, TNM, histology, phenotype, diagnostic method, program and diagnosis date. ALND: Axillary lymph node dissection

Discussion

In our study population of women participating in breast cancer screening programs diagnosed with breast cancer, 80.1% patients received breast-conservative surgery and 19.9% underwent mastectomy. Mastectomy presented more readmissions, recurrences and mortality. However, after adjusting for possible confounders there was no statistically significant difference on the overall risk of complications, readmissions, recurrence and mortality between performing a conservative surgery or a mastectomy. TNM (stages III-IV) and phenotype were the factors that had a greater impact on recurrence and mortality and TNM and ALND on complications.

Complications

In our study, no differences were found in the frequency of complications depending on the type of surgical treatment. Our results showed that 28,5% of women presented complications after surgical treatment, being

pain and psychological events the most frequent ones. This results are in line with other studies [30–34] that have shown that up to 50% of women diagnosed with breast cancer suffer from pain.

We also found that seroma was present in 8.2% of women. Seroma is a common complication after breast cancer surgery [29] [30], occurring at rates ranging from 3–85%[31] [32] although breast surgery is categorized as a low-morbidity procedure[33] and has been described as a clean operation[34]. Some studies have reported that seromas are more likely to occur after mastectomy than after breast conservation[35] [29], while others have reported a higher rate of infection in patients undergoing mastectomy[34] [35].

As expected, statistically significant differences were found in the stage-adjusted analysis: Stages III and IV had a strong relationship with the presence of complications in adjusted analysis and the performance of an ALND involved a higher risk of complications, probably because seroma and wound infection are increased when the surgery involved lymph node dissection[34] [36]. This finding is particularly of interest in an era where the tendency is to avoid unnecessary ALND, with new protocols following the publications of Dr Guliano et al[37], However, in our cohort including all stages and all histologic/phenotypic kind of tumors, mortality and recurrences were equivalent between N0 patients who received SNB versus N1/N2/N3 patients who underwent ANLD.

Readmisions

Readmissions after surgical treatment occurred in 21.8% of women, being slightly higher in the mastectomy group (27%) than in the conservative treatment group (20.5%) but without finding statistically significant differences. Similar percentages were reported by a study performed in the United States where breast-conservative surgery had a readmission rate due to reoperation of 21.6% [18]. In previous study from the same population[38] readmissions risk was not increased by surgical aproche but rather by the complications themselves. The percentage of readmissions is an official quality and hospital safety indicator in USA, Europe and other countries [39] [40] [41] and to understand and to avoid causes of readmissions is an important strategy for improving health outcomes and controlling healthcare costs[40]. In addition, admission to hospital is undoubtedly one of the most disabling situations a patient can face, both in the physical and psychological spheres[42]

Recurrences

Previous reports indicate that about 10% of women have a recurrence in the first 5 years after surgical treatment[43] [44] [45]. In our study, with a longer follow-up until 13 years (mean of 8.5 years), breast cancer recurrence affected 14.2% of women. In this study, we included women with all stages of the disease and women in stages III and IV had the highest risk of recurrences, as expected and consistent with the evidence[46] [44] [45] [47], along with patients with HER2-positive tumors[47] [48]. Women included in our study were diagnosed between 2000 and 2006 and treatment for HER2 was introduced in 2004–2005, which could explain this result, as observed in other studies where women not receiving chemotherapy or trastuzumab for HER2-postitive tumors had a significantly higher risk of recurrence[48]. As it was observed in another study[46], recurrence was more frequent in patients who underwent a mastectomy, but after the

adjusted analysis it lose the statistical significance, probably due to the tumor characteristics and higher stages associated to this surgical technique.

The percentage of local recurrences was similar in the two surgical techniques but was slightly higher in conservative surgery (3.7%) than in mastectomy (3.4%). Although some studies show much higher local recurrence after conservative surgery than after mastectomy[49] [50] [51], our data agree with those in the literature, with percentages of local recurrence in patients undergoing conservative surgery of 2%-3.5% at 10 years, due to improvements in imaging techniques, attention to surgical margins and advances in systemic therapy[46] [52], with recurrence being equivalent to that in patients with mastectomy[53] [46].

For regional recurrences (local and nodes), our results showed a higher percentage of recurrences in women with mastectomy (7.8%) than in those with conservative surgery (4.8%). This result is in agreement with studies reporting regional recurrence of around 5%-10%[46] after surgery and with this type of recurrence being similar for the two techniques[54] [45].

Metastatic recurrences were clearly higher in women with mastectomy (20%), as observed in another study[55]. However, a meta-analysis of nine articles on different types of mastectomies[56] found a percentage of distant recurrence after mastectomy of around 10%-12%, even other studies described a similar metastatic recurrence in patients undergoing mastectomy and conservative surgery[50] [54].

Mortality

No difference in the adjusted risk of mortality was observed according surgical procedure.

The mortality rate in this cohort with a follow-up of up to 13 years was 13.8%, which is within the range described in other studies[44] [57]. Mortality was higher in the group of women receiving mastectomy, which are the group with a less favorable prognosis, a fact that has been widely described in previous studies[58] [59] [60] [61]. Evidence in the literature is inconclusive for mortality according to the surgical technique: some studies comparing mastectomy and conservative surgery plus radiotherapy have reported similar results in terms of survival[49] [53] [50] [54] [62], even in patients with tumors > 5cm[63] [64]. However, other studies suggested better survival among women treated with conservative surgery compared with mastectomy[5] [58] [59] [60] [61] [65]. In contrast, a meta-analysis published in 2016[66] indicated that mastectomy might provide a slightly overall survival benefit compared with breast-conservative therapy in early breast cancer patients with larger tumor size.

As with the most recurrent phenotypes, mortality is higher in HER2-positive and triple negative tumors, but only the statistical significance for HER2-positive tumors was maintained in the adjusted model. This study was conducted at a time when the use of monoclonal antibodies was not standardised. A recent study[67] has shown that early-stage tumors (T1N0) have the same risk of mortality regardless of phenotypic subtype, including HER2-positivity. Having estrogen and progesterone receptor-negative tumors plays a stronger role in survival than HER2 positivity for tumors of all sizes[67].

Limitations And Strength

This study has some limitations. It is based in a cohort of women participating in a population breast cancer screening program, and consequently all participants were aged between 50 and 70 years at diagnosis. This hampers comparisons with studies including women of all ages, but also lends homogeneity to the sample. The women were diagnosed between 2000 and 2009 and since then, treatment improvements have been introduced, the most important being the introduction of sentinel node biopsy and treatment for HER2-positive tumors[68] [69]. Moreover, information on complications and readmissions were obtained from the medical history, which might have introduced information bias, either due to some misinformation or to variability in the quality of the information in the clinical records in the distinct hospitals. However, the clinical records review was done by trained professionals, following a common protocol, and the final models were adjusted by different screening programs. This study did not evaluate either monetary costs or patients' quality of life after surgical treatment, which are also important factors for decision making. However, few studies have analysed complications, readmissions, recurrence and mortality in the same multicenter work, with a fairly long follow-up period, taking into account tumor characteristics (including all TNM stages), diagnostic method and type of treatment in more than 1000 patients.

Conclusion

Surgeons are concerned about surgical variability in breast cancer and its related long-term outcomes. To contribute to make decisions about surgical treatment, taking into account long-term effects, it is important to have complete information about all possible outcomes.

This study supports current evidence that the results of different surgical treatment are similar: as long as safe oncological surgery is performed, breast-conserving surgery and mastectomy are equally effective in terms of complications, readmissions, recurrence and mortality adjusted by individual tumor and patients characteristics. This finding allows freer adaptation to professional and health system circumstances, and the needs and desires of each patient with the certainty that personalized surgery will not influence the prognosis of the disease, allowing us to focus on life quality of the patients.

Abbreviations

aHR
Adjusted Hazard ratio
ALND
axillary lymph node dissection
aOR
Adjusted odds ratio
CI
Confidence intervals
ER
Estrogen receptor
HR
Hazard ratio

Her2
Human epidermal growth factor receptor 2
OR
Odds ratio
PR
Progesterone receptor
SNB
sentinel node biopsy
TNM
Tumor-node-metastasis

Declarations

Ethics approval and consent to participate

Study data were collected using a protocol approved by the ethics committee of Parc de Salut Mar (CEIC-Parc de Salut MAR), Barcelona. Specific patient consent was not required because we used retrospective data from screening participants who had previously signed information release documents. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are not publicly available due to privacy regulations, but are available from the corresponding author on reasonable request

Competing interest

The authors declare that they have no conflict of interest.

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Authors' contribution

LB, XC and MS designed the study. LB, AJ and MS wrote the manuscript. AJ and JL performed the statistical analyses and LB, AJ and MS contributed to the analyses and interpreted the data. JB, TB, MB, and LD were involved in data acquisition. JJ, XC and MS review and edit the manuscript and all authors read and approved the final manuscript.

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Figures

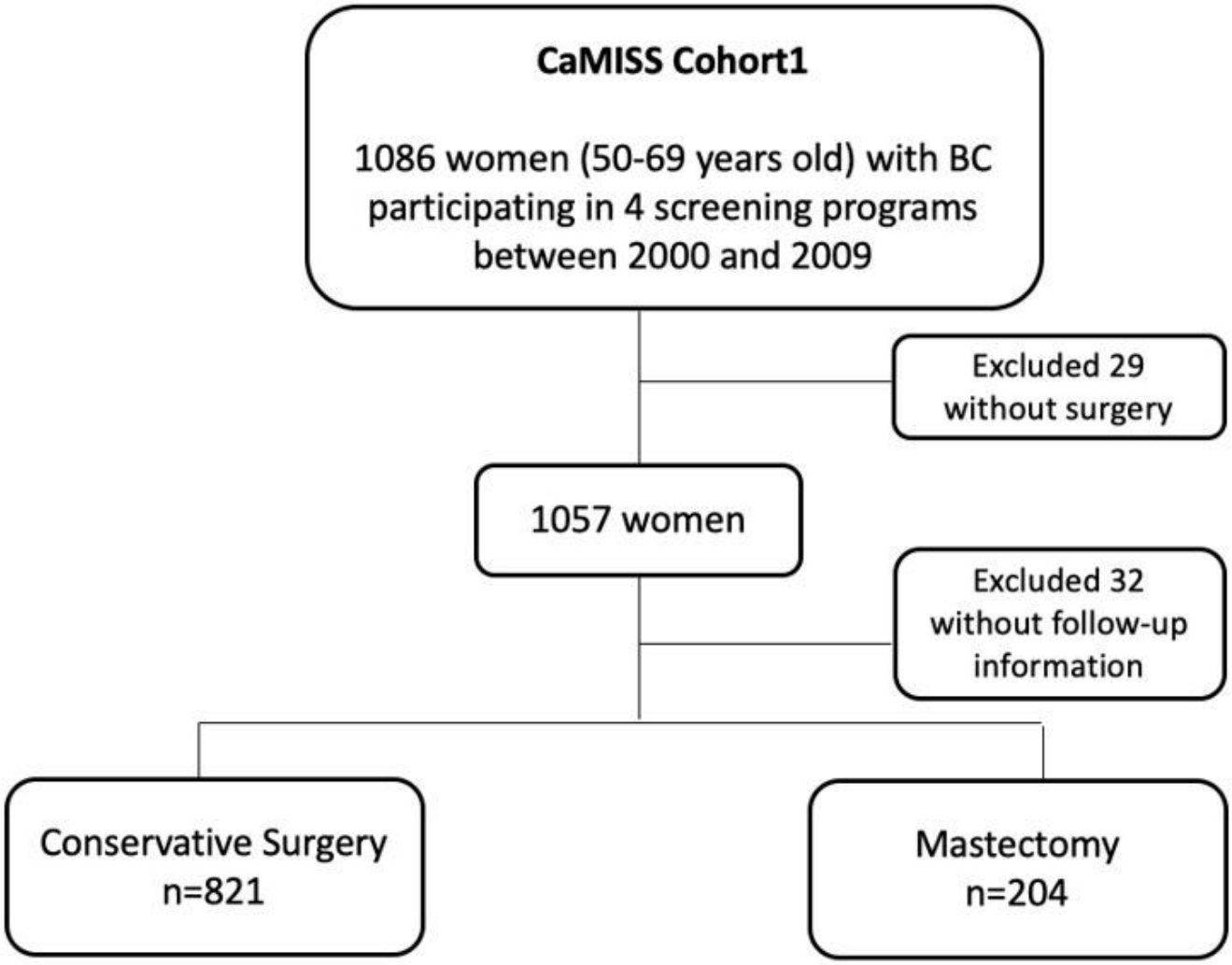

Figure 1

Study population