



Benefits of Organized Mammographic Screening Programs in Women Aged 50 to 69 years: A Surgical Perspective

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Abstract

The role of organized mammography screening has been questioned by some authors. We evaluated the benefits of mammographic screening from a surgical point of view through a comparative study. Patients belonging to an organized screening program had a higher probability to receive less invasive treatment, such as breast-conserving surgery and sentinel node biopsy, and to have a shorter hospital stay. Our results support the use of campaigns aimed at increasing adhesion to mammography screening.

Background: The benefits of organized mammographic screening programs (OMSPs) in reducing breast cancer mortality have been addressed by several studies. This study was designed to specifically evaluate the advantages of OMSPs in terms of surgical management of patients with breast cancer. **Materials and Methods:** Surgical treatment of 201 patients with breast cancer aged 50 to 69 years coming from OMSPs was compared with that of 532 non-OMSP patients in same age group. The likelihood of receiving BCS was analyzed through a multivariable regression model. **Results:** The mean tumor size was smaller in the OMSP patients (14 mm vs. 18 mm; $P < .01$). The proportion of patients having metastatic lymph nodes was higher in the non-OMSP group (33.3% vs. 17.9%; $P < .01$). Rates of breast-conserving surgery (BCS) were significantly higher in the OMSP group (89.1% vs. 59.1%; $P < .01$). Sentinel node biopsy was carried out in 84.1% and 62.5% of patients in the OMSP and non-OMSP groups, respectively ($P < .01$). Rates of axillary lymph node dissection were significantly different (24.9% in the OMSP group and 35.8% in the non-OMSP group; $P = .02$). Re-excisions for infiltrated margins after BCS were lower in the OMSP group (4.8% vs. 12.7%; $P < .01$). Hospital stay was shorter in the OMSP group (2.13 vs. 3.02 days; $P < .01$). OMSP women had a 3-fold higher probability of receiving BCS. **Conclusions:** Patients with breast cancer belonging to OMSPs had a higher probability to receive less invasive surgery and to have shorter hospital stay. Our results support the use of campaigns aimed at increasing adhesion to mammography screening.

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Introduction

Breast cancer represents an important public health concern, with an estimated new cases of 1.67 million and more than 500,000 deaths occurring worldwide in 2012.^{1,2} Mortality rates for that disease are expected to further decline over the next years, given the

improvement of multidisciplinary management, early diagnosis, and adhesion to mammographic screening.³ Since the second half of the past century, information campaigns have spread to promote awareness of importance of mammographic screenings, whose primary goal is to reduce the mortality for breast cancer.³⁻⁶ In this

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regard, although some aspects of cancer screening remain controversial, robust evidence exists that deaths from breast cancer have decreased substantially since the implementation of widespread mammography screening and have constantly declined during the past 40 years.⁴⁻⁹ According to the International Agency for Research on Cancer, mammographic screening for women aged between 50 and 74 years can reduce the risk of breast cancer death by 20% to 25%.¹⁰

In Italy, about 53,000 new cases of female breast cancer were recorded in 2018, and about 12,000 deaths caused by that disease were reported in 2015.¹¹ The current extension of mammographic screening is around 73%, whereas participation rates stay at around 56% for the crude rate and 60% for the adjusted rate, with substantial differences between the northern and southern regions.^{7,12} In the region of Sardinia, where nearly 1600 new cases occur every year, an organized screening mammographic program (OMSP) was launched for women aged 50 to 69 years in 2005.¹³

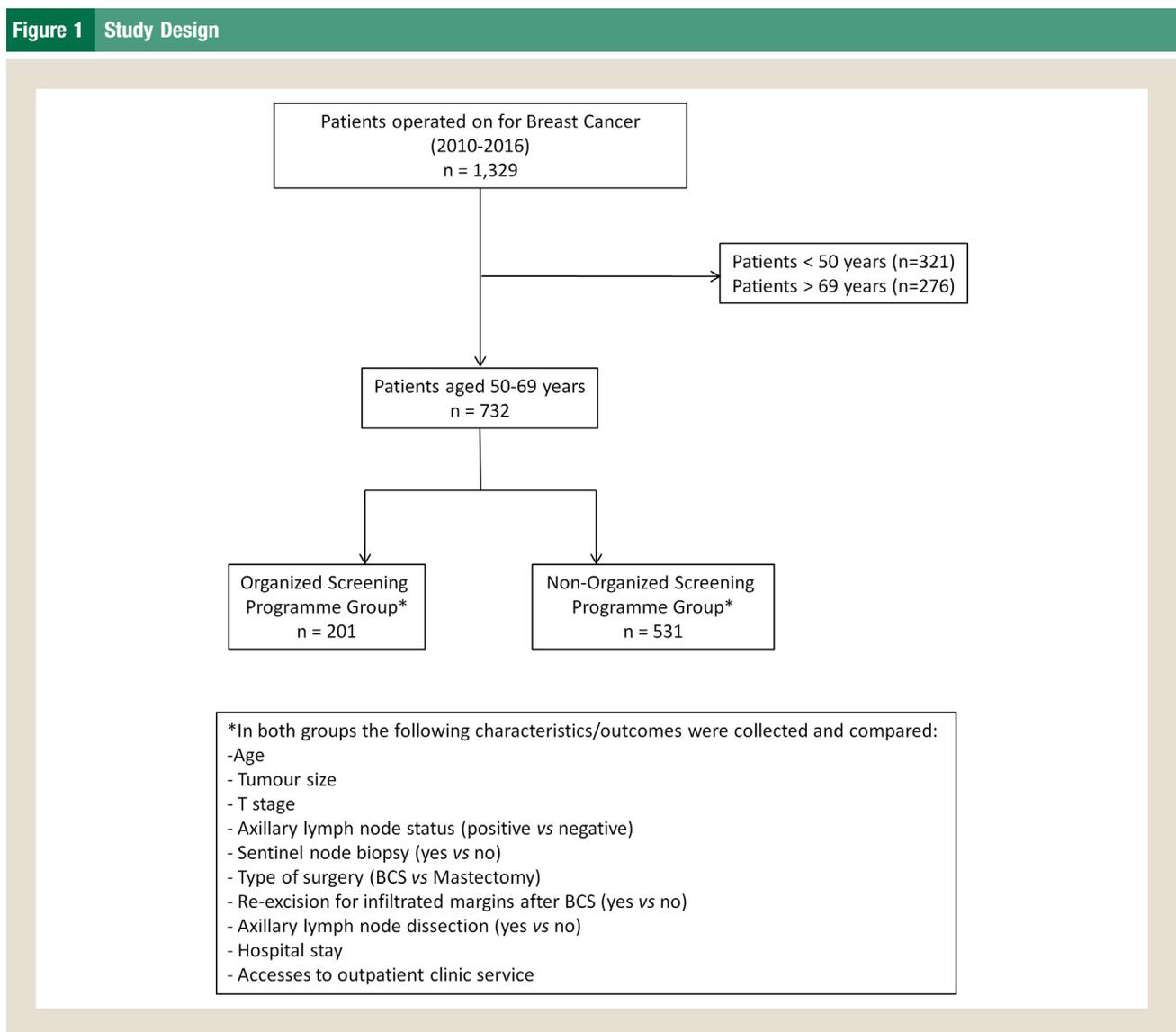
Patients with breast cancer adhering to OMSPs are commonly diagnosed as having small tumors. A logical consequence is that patients with screen-detected breast cancer may have significant advantages in terms of surgical management when compared with their symptomatic counterpart. However, few studies have addressed the advantages of organized screening programs in the aspect of surgical treatment of breast cancer.

The aim of this study was to compare different aspects of surgical management of breast cancer between patients who came from the OMSP and those who did not (non-OMSP). The study was conducted in an academic institution of Northern Sardinia that fulfills the requirements of a Breast Center as described by the European Society of Breast Cancer Specialists (EUSOMA).¹⁴

Materials and Methods

Data of every patient consecutively operated on for breast cancer at the Unit of General Surgery 2 – Clinica Chirurgica of the University of Sassari (Italy) has been prospectively collected in an

Figure 1 Study Design



Abbreviation: BCS = breast-conserving surgery.

institutional review board-approved database since January 1998. For the present study, we queried our institutional database for any patient aged 50 to 69 years who underwent surgical intervention for either invasive breast cancer or ductal carcinoma in situ (DCIS) in the period from 2010 to 2016. Patients who received surgery for lobular carcinoma in situ were excluded. Demographic and tumor characteristics (age, histologic subtypes, pathologic tumor size, sentinel node biopsy, lymph node status), information on initial surgical treatment (breast-conserving surgery [BCS] or mastectomy), and reoperation for infiltrated margins after BCS, were extrapolated for the entire study population. Every patient underwent physical exam, mammography, and ultrasound (US). Breast MRI was carried out in selected cases according to the current guidelines, after multidisciplinary team discussion. Preoperative diagnosis of breast cancer was obtained by means of either US-guided core biopsy or stereotactic vacuum-assisted biopsy. BCS was planned in patients with unifocal cancer and in selected cases of multifocal breast cancer (ie, cancer foci in same quadrant). Wire-guided localization under x-ray or US guidance was carried out in non-palpable tumors. All operations have been performed by 3 surgeons (A.F., P.C., and G.G.) with more than 15 years of experience in breast practice. Patients with invasive carcinoma and clinically negative axilla underwent intraoperative sentinel node biopsy using the radiotracer technique, as described elsewhere,¹⁵ whereas those diagnosed as having pure DCIS underwent sentinel node biopsy only when mastectomy was planned. Patients were divided into 2 groups: namely, the OMSP group and the control group (non-OMSP); the latter included symptomatic patients and those undergoing opportunistic screening. The study design is illustrated in Figure 1.

Statistical Analysis

Demographic and tumor characteristics, type of surgical intervention, and surgical outcomes were summarized with descriptive statistics. Continuous variables were assessed as means \pm standard deviations and compared using the *t* test or the Fisher exact test where appropriate. Differences in proportions between the groups were evaluated using the χ^2 test. All *P* values lower than .05 were considered statistically significant. The likelihood of receiving BCS as upfront treatment was analyzed through a multivariable logistic regression model. Covariates were chosen according on clinical significance, and they were dichotomized to a binary variable (OMSP vs. non-OMSP group; age, ≤ 60 years vs. > 60 years; histotype, invasive vs. in situ; tumor size, ≤ 2 cm vs. > 2 cm). For each variable, a reference category was chosen, generally the no-exposure or majority category, and the other category was compared with the reference one. The odds ratio in each category versus the odds in the reference category were estimated. Statistical analyses were performed using SPSS Statistics 20 (IBM Corporation).

Results

Among 1329 patients operated on for breast cancer during the period from 2010 to 2016, 732 women aged 50 to 69 years were included in the study, 201 in the OMSP group and 531 in the non-OMSP group. Demographic and clinicopathologic characteristics are summarized in Table 1. The mean age was similar between the cohorts (60.4 vs. 59.2 years; *P* < .01), although the percentage of women aged 50 to 59 was significantly higher in the non-OMSP group (50.8% vs. 39.8%; *P* = .008). The mean tumor size was smaller in the OMSP patients (14 mm vs.

Table 1 Characteristics of the Study Population

Characteristic	Total (n = 732), n (%)	Organized Screening Program Group (n = 201), n (%)	Non-organized Screening Program Group (n = 531), n (%)	<i>P</i> Value
Mean age \pm SD, y	59.5 \pm 5.8	60.4 \pm 5.7	59.2 \pm 5.8	.01
Age Group Distribution, y				.008
≤ 60	350 (47.8)	80 (39.8)	270 (50.8)	
> 60	382 (52.2)	121 (60.2)	261 (49.2)	
Mean tumor size \pm SD, mm	16.9 \pm 10.8	14.0 \pm 8.3	18.0 \pm 11.4	<.01
T Stage				<.01
Tis	89 (12.1)	30 (14.9)	59 (11.1)	
T1a	35 (4.8)	15 (7.5)	20 (3.8)	
T1b	129 (17.6)	59 (29.4)	70 (13.2)	
T1c	338 (46.2)	71 (35.3)	267 (50.3)	
T2	131 (17.9)	26 (12.9)	105 (19.7)	
T3	8 (1.1)	0 (0)	8 (1.5)	
T4	2 (0.3)	0 (0)	2 (0.4)	
Histology				.16
Invasive carcinoma	643 (87.9)	171 (85.1)	472 (88.9)	
DCIS	89 (12.1)	30 (14.9)	59 (11.1)	
Axillary Lymph Node Status				<.01
Negative	519 (70.9)	165 (82.1)	354 (66.7)	
Positive	213 (29.1)	36 (17.9)	177 (33.3)	

Abbreviations: DCIS = ductal carcinoma in situ; SD = standard deviation.

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18 mm; $P < .01$). The T stage distribution was significantly different ($P < .01$), although in both groups, the T1c tumors corresponded to the more frequent category. As for histologic type, although invasive carcinoma was the more represented in both groups, there was not a statistically difference in rates of DCIS (14.9% and 11.1% in the OMSP and non-OMSP patients, respectively; $P = .16$). The proportion of patients having metastatic axillary lymph nodes was 17.9% in the OMSP group and 33.3% in the non-OMSP group ($P < .01$).

Surgical Treatment and Outcomes

Surgical treatment and outcomes are shown in Figure 2. The rates of BCS as upfront surgery were significantly higher in the OMSP group (82.1% vs. 59.1%; $P < .01$). Conversely, mastectomy rates were higher in the non-OMSP group (17.9% vs. 40.9%). Sentinel node biopsy was carried out in 84.1% and 62.5% of patients in the OMSP and non-OMSP groups, respectively ($P < .01$). In addition, the rates of axillary lymph node dissection were significantly different (24.9% in the OMSP group and 35.8% in the non-OMSP group; $P = .02$). Rates of re-excisions for infiltrated margins after primary BCS were lower in the OMSP group (4.8% vs. 12.7%; $P < .01$). The hospital stay was shorter in the OMSP group (2.13 vs. 3.02 days; $P < .01$), as well as the number of accesses to outpatient clinical service for wound care or seroma aspiration (4.02 vs. 5.00; $P < .01$).

Factors Associated With Breast Conservation as Upfront Surgery

At multivariate analysis, women were more likely to undergo BCS if they belonged to the OMSP cohort, or had tumors smaller than 2 cm (Table 2). We did not find any association between type of surgical treatment and either age younger or older than 60 years, or histologic type (invasive carcinoma vs. DCIS). The strongest predictor of receiving BCS was belonging to the OMSP cohort (odds ratio, 3.01; 95% confidence interval [CI], 2.00-4.54).

Table 2 Multivariate Logistic Regression for Factors Associated With Breast Conservation as Upfront Surgery

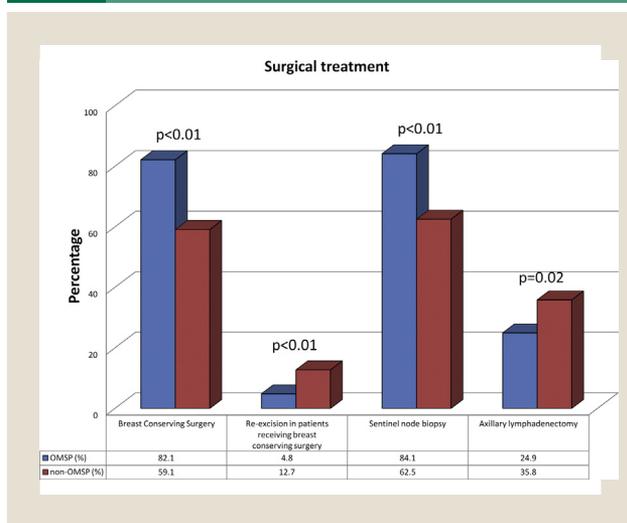
Variables	Odds Ratio	Standard Error	P Value	95% CI
Age, y				
>60	1.03	0.19	.85	0.74-1.42
≤60	Ref			
Histotype				
In situ	1.40	0.27	.19	0.84-2.37
Invasive	Ref			
Tumor Size, cm				
>2	2.68	0.19	<.01 ^a	1.84-3.89
≤2	Ref			
Group				
OMSP	3.01	0.20	<.01 ^a	2.00-4.54
Non-OMSP	Ref			

Abbreviations: CI = confidence interval; OMSP = organized mammographic screening program; Ref = reference.
^aStatistically significant.

Discussion

The main result of the present study is that women with breast cancer coming from OMSP had benefits in many aspects of surgical treatment. In particular, they were more likely to receive a less extensive surgery, such as BCS as upfront treatment. To note, we observed that OMSP women had a 3-fold higher probability of receiving BCS. Breast conservation has several benefits over mastectomy, because it permits sparing the nipple-areola complex in the majority of cases, and in general, it is better accepted from a psychological point of view. In addition, several studies have also showed advantages in sexual health and lifestyle.¹⁶⁻¹⁹ The possibility of removing only a part of the diseased breast somehow represents an implication of 'less severity' of the disease.^{17,20} Moreover, the operative time for BCS is usually shorter, because many patients undergoing mastectomy require an immediate reconstruction with consequent prolongation of operative times. The results of the present study may appear conflicting with some studies that showed that rates of radical mastectomies in the United States and some European countries such as the United Kingdom and the Netherlands were highest among women invited to screening.²¹⁻²⁴ However, it should be taken into account that increasing rates of mastectomy at some institutions recognize multiple and complex factors, and cannot be attributable simply to mammographic screening. As a general rule, we consider BCS as the option of choice for patients with early breast cancer when good esthetical results are preventable. A clear and open discussion about the pros and cons of mastectomy is of paramount importance in the decision-making process of patients suitable for BCS.²⁵ In addition, the use of pre-operative magnetic resonance imaging, which has been related to the rise of mastectomy rates, should be reserved for selected cases according to current guidelines.²⁰ We showed in a previous article that the rates of mastectomy at our institution did not rise in the past 15 years, whereas the percentages of immediate reconstruction did.¹⁸ In the present research, we noticed that rates of re-excision for

Figure 2 Surgical Treatment in the Study Population



Abbreviation: OMSP = organized mammographic screening program.

infiltrated margins after BCS were significantly lower in among OMSP patients. A possible explanation may be that tumor size was smaller (14.0 vs. 18.0 mm; $P < .01$) in that group.

As for histologic type, we observed that the percentage of patients with DCIS was slightly higher among patients belonging to the OMSP group, although there was not a statistically significant difference. It is known that DCIS nowadays accounts for 15% to 20% of screen-detected breast cancers.^{16,26,27} This figure has raised some issues regarding the risk of over-diagnosis related to screening; in fact, one can argue that many DCIS would probably stay indolent and asymptomatic over the lifetime of the patient.^{8,26,28} Although to date it is not clear which DCIS lesions will evolve into invasive carcinoma, current guidelines suggest appropriate treatment for every subtype of DCIS. In our cohorts, all women with DCIS received surgery, mostly BCS and postoperative radiotherapy as completion of the locoregional treatment.

Another aspect to be considered is that patients with invasive carcinoma in the OMSP group were more likely to receive sentinel node biopsy for assessment of axillary lymph node status. As a consequence, they were less likely to receive lymph node dissection for metastatic axillary metastases. The benefits of avoiding axillary lymph node removal cannot be underemphasized, because the possible consequences in terms of arm motility, risk of lymphedema, and worse quality of life are well known. In general, the patients of the screening program group received a less invasive surgery compared with their counterparts because they more often had BCS and avoidance of axillary lymph node dissection. These findings are consistent with the few studies in the literature addressing the effects of screening on surgical management of breast cancer. In a study from Australia comparing 224 patients from a screening program with a control group of 657 women, mostly with symptomatic breast cancer, women in the screening group had significantly higher percentages of BCS (64% vs. 51%).²⁹ In another study on 1449 patients from the Vermont Cancer Registry, in which 979 patients with screen-detected breast cancer were compared with 470 patients with non-screened cancer, the authors reported that rates of BCS, use of sentinel node biopsy, and rates of lymph node dissection were significantly lower in the screening group.¹⁶

We observed that hospital stay was significantly shorter in the OMSP group. We also noticed a reduction in the number of accesses to outpatient clinical service for wound care or seroma aspiration. The latter features, other than being of benefit to the patients, might also be considered advantageous in respect of health care expenditures, although we did not assess the related costs. This issue is of paramount importance in the current climate of spending review.¹⁶

In the last decade of the past century, nationwide population-based organized cancer screening programs were launched in many high-income countries.^{3,4,6} However, screening programs for breast cancer have been criticized for bearing the risk of over-diagnosis and overtreatment, and the mortality reduction owing to mammographic screening has been questioned by some.^{6,8,30} This is a common topic of discussion between epidemiologists and health care givers. Although it is possible that some forms of DCIS as well as some small invasive cancers detected by mammography (especially in older patients) would stay clinically indolent during the patient's lifetime if left untreated, on the other

hand, a large amount of studies have highlighted the reduction of breast cancer mortality after the introduction of mammographic screening.^{3,4,31,32} We believe that the data of the present work may serve as a surrogate of prognostic advantages associated with screening, although the study was focused on the surgical aspects of breast cancer treatment and did not address the survival outcomes. Many authors have highlighted that screening impacts cancer mortality through decreasing the incidence of advanced cancers^{3,8}; in this regard, the percentage of patients in our study having a tumor size smaller than 2 cm and metastatic lymph nodes were significantly lower in the OMSP group.

Interestingly, in our study, we observed that there was a substantial difference in the number of patients in the OMSP and non-OMSP groups (201 vs. 532). This means that there has been a low adherence rate to the screening invitation. In fact, in Italy, the percentages of participation in mammographic screenings are around 57%, with considerable differences between the northern, central, and southern regions. In the northern part of Sardinia, where our institution is located, the rates of adherence are about 41% to 43%. There is no doubt that adherence needs to be improved by increasing the awareness of the advantages of organized screening, although many women in Italy traditionally perform opportunistic screening with similar rates throughout the country.^{7,33} However, we believe that well-structured OMSPs may enable the ability to reach higher levels of coverage among the female population, as well as to reduce possible inequalities in the access to early diagnosis of breast cancer.

This study has some limits: first of all, the retrospective design of the study and the fact that it does not report survival data; however, it was specifically designed to focus on the aspect of surgical treatment of patients with breast cancer. Furthermore, our database did not differentiate in the non-OMSP group between patients with symptomatic breast cancer and those performing opportunistic screening. However, as a point of strength, it is one of the few comparative studies addressing the topic of surgical treatment and outcomes of patients with breast cancer detected with organized mammographic screening.

Conclusion

In summary, in our experience, patients with breast cancer belonging to the screening program had a higher probability of receiving less invasive surgery, such as breast conservative surgery and sentinel node biopsy, and to have a shorter hospital stay. Our results support the use of campaigns aimed at enhancing women's adherence to organized mammography screening.

Clinical Practice Points

- Few studies have addressed the topic of the benefits of organized mammographic screening on the surgical treatment of breast cancer.
- The surgical outcomes of 201 patients with breast cancer coming from the OMSP were compared with a control group of 531 patients of the same age.
- Patients of the OMSP group had significantly higher rates of BCS, sentinel node biopsy, and avoidance of axillary clearance.

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- These results support the use of campaigns aimed at increasing adherence to mammography screening.

Disclosure

The authors have stated that they have no conflicts of interest.

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