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Are breast cancer patients treated with radiotherapy younger now than ten years ago?

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ABSTRACT

Aim: The aim of the present study was to analyze the age of breast cancer patients managed with curative approach at the time of treatment with radiotherapy.
Background: Breast cancer is the most frequent neoplasm in women. Little is known with regard to the age of patients at diagnosis, and some authors have suggested that breast cancer is now affecting women who are younger than before.
Materials and methods: We performed a descriptive study of our series of breast cancer patients from 1998 to 2011. The age of patients, city of residence, year of treatment and uni- or bilateral location were extracted from the administrative database of the Radiation Oncology Department. The demographical and reference populational data were extracted from the Catalan Institute of Statistics.
Results: 3382 patients were obtained. The mean age was 57.79 years. No statistical differences were observed in the mean age during the period of study ($p > 0.05$), nor in patients with bilateral neoplasias with regard to unilateral tumours ($p > 0.5$). Patients aged less than 30, 40, 50 and 65 years were 0.3%, 6.3%, 27.0% and 69.1%, respectively. The proportion of patients aged less, equal or more than 40 and 50 years was not statistically different.
Conclusions: Breast cancer patients treated with adjuvant radiotherapy after radical surgery have not experienced significant changes in their mean age at treatment. The subgroups

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of patients that remain out of the mammographic screening programmes were unchanged as well. The observed differences can be explained by demographical disparities and by a probable increase in the indications for adjuvant radiotherapy.

1. Background

Breast cancer is the most frequent neoplasm in women. It represents 28% of female cancer cases in Catalonia (Spain) with an incidence of 97.3 and 99.3 new cases per 100 000 women, according to the population registries of Tarragona and Girona, respectively (data from 1998 to 2002). In 2002 the estimated incidence was of 3829 cases which is expected to rise to 6482 new cases in 2019.[1] Fortunately, breast cancer deaths declined by 3% per year in Catalonia between 1993 and 2007.[2] A recent analysis of 2023 women with incident invasive breast cancer collected from 1992 to 2005 in an institutional cancer registry in Barcelona (Catalonia, Spain), showed that the 5-year disease-specific survival rate increased from 73.5% to 86.4% (log rank, $p < 0.001$).[3]

However, there is a lack of recent data in describing possible age variations at diagnosis of breast cancer patients. To our knowledge, the only previous study was conducted by the Geneva Cancer Registry (Switzerland), motivated by the feeling of some health professionals that breast cancer incidence was increasing in younger patients. The study showed an 8.7% annual increase in breast cancer incidence for women aged less than 40 years in the period from 2002 to 2004.[4]

While the "Vallès Occidental" region holds the second highest rates of population density in Catalonia, the area lacks a population cancer registry. Cancer incidence estimates in Catalonia come from the population registries of Tarragona and Girona that cover approximately 20% of the whole Catalan population. It is well known that adjuvant radiation therapy (ART) for breast cancer can reduce by half the risk of recurrence and by a sixth the probability of death.[5,6] In addition, ART in breast cancer patients is advisable for approximately 83% of all surgically treated patients.[7] So, as matter of the high percentage of breast cancer patients that receive radiotherapy, the objective of this study was to describe the age distribution of breast cancer patients treated with ART with the aim of defining the possible variations in the age at treatment of breast cancer patients during the last 10 years.

2. Materials and methods

This is a descriptive epidemiological study of a series of breast cancer patients treated with adjuvant radiation therapy in the region of the *Vallès Occidental* (*Catalonia, Spain*) that has a population of about 900 000 inhabitants. The study included patients coming from the following municipalities in the region: *Badia del Vallès*, *Barberà del Vallès*, *Castellar del Vallès*, *Castellbisbal*, *Cerdanyola del Vallès*, *Matadepera*, *Palau-solità i Plegamans*, *Polinyà*, *Ripollet*, *Rubí*, *Sabadell*, *Sant Cugat de Vallès*, *Sant Llorenç de Savall*, *Sant Quirze del Vallès*, *Santa Perpètua de Mogoda*, *Sentmenat*, *Terrassa*, *Ullastrell*, *Vacarisses* and *Viladecavalls*. We extracted the administrative data of the correlative patients treated from 1st January 1998 to 31st December 2011 at the Radiation Oncology Department of the *Institut Oncològic del Vallès*, at *Sant Cugat* headquarters. The patients come referred from the main hospitals in the region: *Corporació Sanitària Parc Taulí* (Sabadell, Barcelona), the *Consorci Sanitari de Terrassa* and *Mutua de Terrassa* (Terrassa, Barcelona). Population accounts were extracted from the Catalonian Statistics Institute website.[8] Due to logistic reasons, some patients meeting the inclusion criteria (135) were referred for treatment to the RT Department of the Parc de Salut Mar (Barcelona). Those patients were counted when calculating the rates of RT treatments performed during the last 10 years.

2.1. Participants, procedures, variables, and measures

We obtained a sample of 3382 patients during 10 years. Due to the administrative nature of the extracted data, neither clinical nor private information was obtained from clinical reports.

Inclusion criteria were: (1) female sex, and (2) first treatment with radiotherapy to the breast or chest wall. Exclusion criteria were: (1) male sex, and (2) palliative approach.

Study variables were: (1) the age of patients when the radiotherapy treatment began, (2) the year of RT administration, (3) laterality (unilateral or bilateral, in spite of a synchronic or metachronic diagnosis), (4) city of residence, and (5) inhabitants per city.

Data were stratified by age groups at thresholds of 40, 50 and 65 years.

2.2. Data analysis

We began with descriptive analyses to characterize the study population. The obtained sample easily led us to obtain a wide 3% of accuracy (e) for an error alpha of 0.05, based on the probability of being diagnosed with breast cancer at an age under 45 years (12.1%[9]). The qualitative variables were characterized by proportions and an interval of confidence (IC) of 95%. Quantitative variables were characterized by means and standard deviation (DE).

Statistical differences were analyzed by the t-Student test, χ^2 or by ANOVA with a signification degree (p) of less than 0.05.

The statistical analysis was performed with the software Stata v10.1[10] and OpenEpi.[11]

3. Results

In the period of study 3382 patients were treated with adjuvant RT after curative surgery. The mean age for all patients was 57.79 years (SD = 12) ranging from 25 to 96 years.

Approximately half of the patients came from both the biggest cities of *Sabadell* and *Terrassa*. The mean age for all patients ranged from 52.87 to 66.30 years. We found statistical differences between cities only when comparing the minimal (from *Barberà del Vallès*, $X = 52.87$; SD = 11.43) with the maximal mean age (from *Sant Llorenç de Savall* $X = 66.3$; SD = 14.69; $p < 0.001$).

The observed mean age of patients per year is shown in Fig. 1. The ANOVA analysis did not reveal significant differences in the mean age of patients treated during the study period ($p > 0.05$).

Fifty-three patients (1.5%) had bilateral tumours either synchronous or metachronous. The *t*-test for independent samples failed to show significant differences in the mean age of these patients ($X = 58.24$ years-old; SD = 10.51) compared to those with unilateral disease ($X = 7.79$ years-old; SD = 14.69; $p > 0.5$).

The region *Vallès Occidental* also experienced a population increase during the last decade.[8] We studied the correlation between the number of patients treated and the female population of the region for the last 10 years, which was found to be strong (coefficient = 0.943). In addition, there was a notable increase in the number of treatments performed since 2002 (Fig. 2).

The proportion of patients under the age of 30, 40, 50 and 65 years was of 0.3% (12 patients), 6.3% (214 patients), 27% (915 patients) and 69.1% (2338 patients), respectively. The number of patients aged less; equal or more than 40 and 50, did not show a significant modification across the period. We only observed a higher number of treated women aged less than 65 years for the periods 2004 and 2007. For the remaining periods, these differences were not statistically significant (Table 1).

Among the women treated with adjuvant RT at ages between 50 and 65 years (target ages for mammographic screening), the ANOVA analysis did not show significant differences either ($p > 0.05$) (Table 2).

Table 2 – Mean age of patients in the group of 50–65 years-old along the period of study. Std. Dev.: standard deviation. Obs: observations.

Year	Mean (age)	Std. Dev.	Obs.
1998	58.19	12.59	118
1999	58.98	12.60	119
2000	56.54	13.20	128
2001	59.84	12.18	129
2002	57.10	12.53	143
2003	57.01	11.97	270
2004	56.12	11.95	243
2005	57.35	13.07	240
2006	57.68	12.48	274
2007	57.43	12.03	283
2008	58.33	12.04	377
2009	58.90	12.15	376
2010	57.17	11.82	367
2011	58.69	12.28	315
Total	57.80	12.27	3382

4. Discussion

Our study describes the age of patients at the time of their first radiotherapy treatment for breast cancer in our region (*Vallès Occidental*) through the last decade. The region experienced a vast industrial transformation during the sixties showing a peak of growth in 2004 in terms of economic output over Catalan mean averages. Cancer is the leading cause of mortality in Catalonia for women aged between 55 and 64 representing more than half of all deaths in this age group. In addition, an increase of breast cancer incidence throughout the last decade has been reported.[15] Hence, some of our patients are worried that these new environmental factors are playing a role in cancer genesis and will translate to more cancers in younger people.

Although this is a descriptive study based on an institutional sample, we did not establish any modification in the proportion of breast cancer patients treated with ART younger than 40 and 50 years. The mean age of treated patients was 57.79 years, which is slightly lower than the mean age at diagnosis observed by the Surveillance, Epidemiology and End Results (SEER) in the United States for the period 2005–2009

Table 1 – Odds ratio (OR), 95%CI confidence interval and level of significance of the number of patients at lower age vs equal or superior to 40, 50 and 60 years-old.

Year	<40 vs ≥40 years-old			<50 vs ≥50 years-old			<65 vs ≥65 years-old		
	OR	CI 95%	*p*	OR	CI 95%	*p*	OR	CI 95%	*p*
1999	1			1			1		
2000	0.51	0.19–1.30	0.16	0.60	0.34–1.04	0.07	0.80	0.45–1.41	0.43
2001	1.95	0.55–7.77	0.31	1.22	0.67–2.22	0.52	1.04	0.60–1.81	0.90
2002	0.75	0.27–2.01	0.58	0.73	0.42–1.26	0.25	0.73	0.42–1.27	0.29
2003	0.78	0.30–1.86	0.61	0.92	0.55–1.51	0.75	0.66	0.40–1.05	0.06
2004	0.66	0.25–1.57	0.37	0.72	0.43–1.19	0.20	0.51	0.31–0.85	0.01
2005	0.88	0.33–2.16	0.80	0.77	0.46–1.26	0.30	0.76	0.47–1.24	0.28
2006	0.75	0.29–1.78	0.55	0.78	0.47–1.27	0.33	0.78	0.49–1.26	0.30
2007	0.98	0.37–2.38	0.98	0.83	0.50–1.36	0.47	0.62	0.38–1.00	0.04
2008	1.32	0.50–3.22	0.54	0.93	0.57–1.49	0.78	0.89	0.57–1.39	0.58
2009	1.06	0.41–2.49	0.88	1.10	0.67–1.78	0.69	0.84	0.53–1.32	0.44
2010	1.03	0.40–2.43	0.92	0.84	0.51–1.34	0.47	0.66	0.41–1.04	0.07

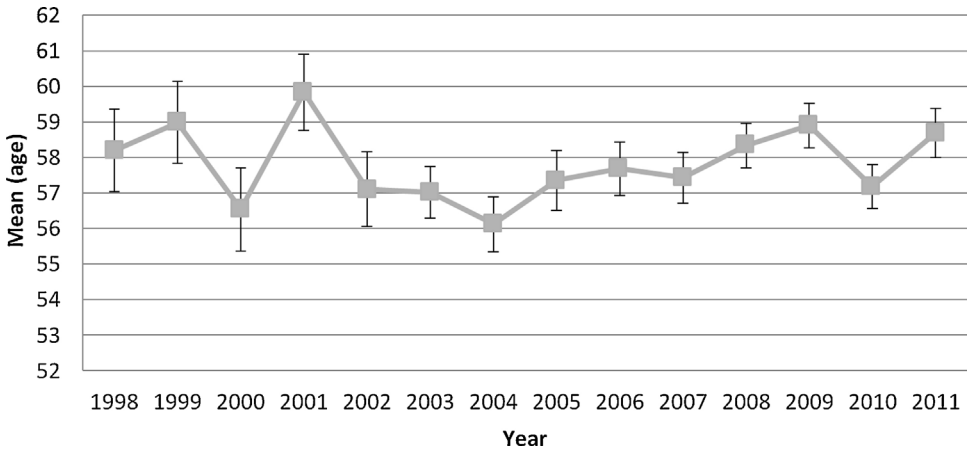

Fig. 1 – Mean age and standard deviation of patients from 1998 to 2011.

(61 years),[12] and the data published by the Tarragona Cancer Registry for the period 1998–2001 (61.5 years). This difference could be explained by the fact that adjuvant RT could be misused in elderly patients, who are more often treated with surgery or hormone therapy alone,[13] that would have biased downward the mean age at treatment found in our patients. Neither did we detect any significant differences in the mean age at treatment of patients between 50 and 65 years-old (the target age for screening programmes in European countries). However, the administrative nature of our data does not allow us to know how many of these patients have been diagnosed via a screening programme that limits us to studying the potential differences in age according to the diagnostic source.

We only observed mean age differences between municipalities, but these were secondary to the demographic disparities for the last 10 years. For example, women living in *Sant Llorenç de Savall* are significantly older than those from *Barberà del Vallès* (30% of females over 60 years compared with 17%, respectively).

Neither did we observe significant differences in the age of patients treated with bilateral tumours compared to unilateral presentation. The proportion of patients treated with bilateral disease (either synchronous or metachronous) was 1.5% of the total treatments, fewer than 3.1% as reported by the breast cancer screening programme from Sabadell-Cerdanyola for the years 1995–2003.[14] This source also reports 18.8% of "in situ" neoplasms and 24.3% of small invasive lesions that also show, in 80% of cases, good positive hormone receptors. So, we consider that for the remaining half of patients not treated with ART, some factors such as age, clinical conditions and/or good prognosis of pathologic findings have probably led to a more conservative approach.

In our study, the percentage of treated patients younger than 40 and 50 years was 6.3% and 27.0%, respectively. These results are consistent with the findings of an EBCTCG meta-analysis[6] that show a 4.99% and 20.87% of patients under 40 and 50 years, respectively. These findings are also in concordance with the reported proportion of patients under the age of 50 years (24.90%) at the population registry of Tarragona.[15]

The cancer registry of Geneva (Switzerland) documented an increase in breast cancer incidence among younger patients, of 8.7% per year in the period 2002–2004 for women younger than 40.[4] Unfortunately, our study cannot answer this question and the results from our sample cannot be inferred to the population. However, the fact that the proportion of patients younger than 40 and 50 did not significantly change over the period of our study, would suggest a stability of the behaviour of breast cancer in the region of the *Vallès Occidental*.

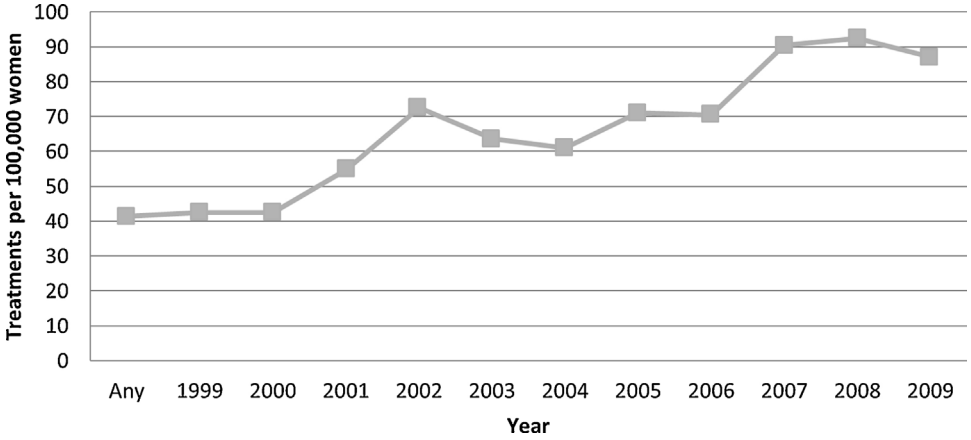

Fig. 2 – Number of curative/adjuvant treatments per 100 000 women along the period of study.

The probability of developing breast cancer in the next 10 years is (excluding cases of family history or genetic disorders) 1.4% starting at the age of 40, and 1.9% above 50.[16] There is a debate about the appropriate age to start screening programmes. While the U.S. advises to start an annual mammography after 40, in most European countries mammograms are biannual and start from the age of 50. In our study, we found that the proportion of patients treated outside age for mammographic screening in Spain (grouped either under 40 or 50 years) has not undergone significant changes. Nevertheless, we found a trend towards a higher proportion of patients younger than 65 years that may translate into a group of patients that have benefited from early diagnosis in a screening programme. The programme for early detection of breast cancer in Catalonia started gradually from the beginning of the nineties and was first offered to women aged 50–64 years. Since 2000, it has been extended to women up to 69 years. The screening programme in our region started at *Sabadell-Cerdanyola* in 1995 with a good public response (57–72%) and the coverage of the target population of 86.8%.[17] The programme extended later, in May 2002, to the cities of *Terrassa les Fonts – Sant Quirze del Vallès*, *Rubí*, *Sant Cugat*, *Matadepera*, *Castellbisbal*, *Ullastrell* and *Viladecavalls*, with an initial uptake of 50% increasing to 73.6% in 2005, and achieving the coverage of 60%.[18] In consequence, this latter implementation would have justified the increase of RT treatments observed from 2002. Moreover, the proportion of conservative surgeries for breast cancer in Catalonia has increased from 60.3% in 2003 to 70.18% in 2009[19] that have also probably been followed by an increase in the use of ART.

5. Conclusions

Although we cannot determine the real incidence of breast cancer in our region from the current data, we can explain some epidemiological features of breast cancer in the *Vallès Occidental*. The patients treated with adjuvant radiotherapy after radical surgery have not experienced significant changes in their mean age at treatment, as well as the age of the subgroups that are currently excluded from mammographic screening programmes. The observed differences can be explained by demographical disparities and also by a probable increase in referrals for adjuvant radiotherapy during the past decade.

Conflict of interest

None declared.

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