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RESEARCH ARTICLE

TRENDS, CLINICOPATHOLOGIC FEATURES, AND MANAGEMENT OF *IN SITU* BREAST CANCER: INSIGHTS FROM THE NORTH ITALY CANCER REGISTRY, 2000-2023

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ABSTRACT: *In situ* breast cancer represents an important subset of breast neoplasms and is frequently detected through organized screening programs. We analyzed incidence trends, clinicopathologic characteristics, and treatment patterns of *in situ* breast tumors registered in the Reggio Emilia Cancer Registry from 2000 to 2023. A total of 1,543 *in situ* breast tumors were identified, representing 13.3% of all registered breast cancers during the study period. Age-adjusted incidence rates per 100,000 were calculated using the 2013 European Standard Population, and the annual percentage change (APC) was estimated to assess temporal trends. Clinicopathologic features, including histology and hormone receptor status, were collected. Surgical management and demographic characteristics were also analyzed. Overall, *in situ* breast tumors showed a modest upward trend over the study period; however, this increase was not statistically significant (APC 0.7; 95%CI -0.6 to 2.2). A modest decline was observed in 2022–2023 following the COVID-19 pandemic, which significantly affected screening uptake in 2020–2021. Age distribution revealed that 8.5% of cases occurred in women under 45 years and 8.5% in women over 75 years. The majority (83%) were diagnosed in women aged 45-74, the primary target of screening programs, including 19.7% in women aged 45-49 years, 69% aged 50-69, and 11.3% aged 70-74. Histologically, the vast majority (93.5%) were ductal in origin. Hormone receptor analysis showed that 36.5% were estrogen receptor-positive (ER+) and 25.9% progesterone receptor-positive (PR+). Breast-conserving surgery was performed in 74.7%, while 19.1% underwent mastectomy. Sentinel lymph node biopsy (SLNB) was performed in 46.2% of cases, whereas axillary lymph node dissection was uncommon (3.3%). Women of foreign nationality represented 6.6% of the cohort. *In situ* breast tumors in our Cancer Registry demonstrated a modest, non-significant increase in incidence over time and predominantly affected women within the screening age range. Most cases were ductal and managed with breast-conserving surgery, reflecting current clinical practice. These findings highlight the sustained impact of screening programs and the importance of ongoing surveillance of early breast cancer, especially in the context of healthcare disruptions such as the COVID-19 pandemic.

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Impact statement: From 2000 to 2023, ***in situ*** breast cancers in the Reggio Emilia Cancer Registry showed a modest, non-significant increase, predominantly ductal and mainly treated with breast-conserving surgery within screening ages.

Key words: *In situ breast cancer; incidence trends; screening; breast-conserving surgery.*

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INTRODUCTION

Ductal carcinoma *in situ* (DCIS) is a non-invasive breast neoplasm characterized by the proliferation of malignant epithelial cells confined to the mammary ducts, without invasion through the basement membrane. DCIS is considered a precursor lesion of many invasive breast carcinomas, although the risk of progression is variable and not fully predictable (1).
The incidence of DCIS increases with age, with the highest rates observed after 50-60 years of age (2). Over the past decades, a marked increase in DCIS incidence has been reported in Western countries, largely attributable to the widespread implementation of population-based mammographic screening programs. The introduction of screening has led to an increase in DCIS diagnoses, reaching approximately 10-11 cases per 100,000 women-years in some populations, with the greatest increases observed among women aged 50-69 years, the primary target group for screening (3).
Some studies also suggest a modest increase in incidence may also be attributable to factors independent of screening, possibly reflecting changes in underlying risk or diagnostic practices (4). Despite the growing number of diagnosed cases, it remains unclear to what extent this trend represents a true increase in clinically relevant disease *versus* improved detection resulting from screening and advances in diagnostic techniques (2). DCIS frequently expresses estrogen (ER) and progesterone (PR) receptors, with implications for the potential use of endocrine therapy in selected cases, similarly to invasive breast carcinoma (5).
DCIS is frequently asymptomatic and is most commonly detected through mammographic screening, with microcalcifications representing the most frequent radiologic finding (6).
Primary surgical treatment options include breast-conserving surgery (lumpectomy), with or without adjuvant radiotherapy, aimed at excising the lesion while preserving the breast (7), and mastectomy, which is recommended in cases of extensive disease, multicentric involvement, or when clear surgical margins cannot be achieved (8).
The use of SLNB has increased over time and may be considered in selected DCIS cases, particularly when mastectomy is planned or when there is a high suspicion of occult invasive disease (7). Endocrine therapy (*e.g.*, tamoxifen) has been shown to reduce the risk of subsequent invasive breast cancer and recurrent DCIS in patients with ER-positive disease, as demonstrated in randomized trials and reflected in international and Italian (AIOM) clinical guidelines (9, 10).
The present study aims to describe a population-based cancer registry case series of *in situ* breast tumors over a long observation period (2000-2023).

MATERIALS AND METHODS

Reggio Emilia Cancer Registry

This study used data from the Reggio Emilia Cancer Registry (RE-CR), a population-based registry covering the Province of Reggio Emilia, Italy, and dedicated to descriptive epidemiological surveillance. Cancer

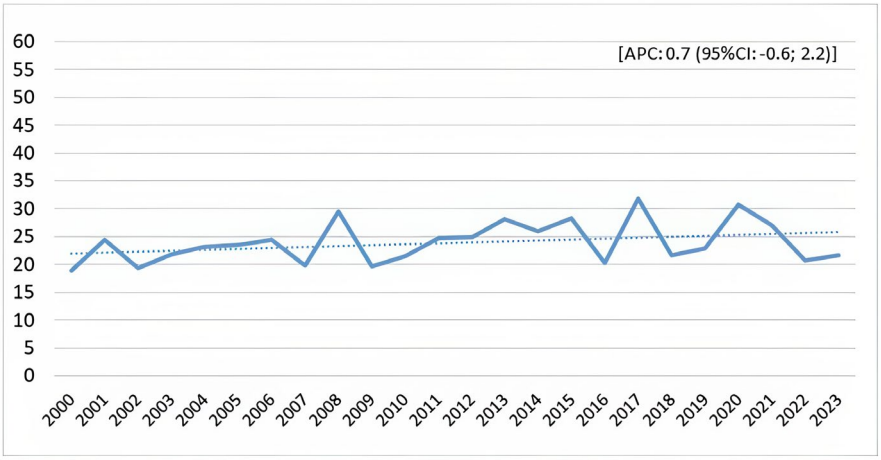

Figure 1. *Reggio Emilia Cancer Registry, 2000-2023. Number of in situ tumors per year of incidence. Agestandarded rate, per 100,000. APC: Annual Percentage Change.*

Registry operates with ethical approval from the Provincial Ethics Committee of Reggio Emilia (Protocol no. 2014/0019740; August 4, 2014). Case ascertainment is achieved through systematic linkage of multiple data sources, including pathology databases, hospital discharge records, mortality registries, laboratory datasets, diagnostic and therapeutic procedure records, and information provided by general practitioners.

The RE-CR covers approximately 532,000 residents and is recognized for the high quality and completeness of its data. Previous analyses reported histological confirmation rates exceeding 90% and a proportion of Death Certificate Only (DCO) cases of 0.2%. For breast cancer specifically, the proportion of microscopically verified cases currently reaches 99.5% (11). Reggio Emilia Cancer Registry is among the few in Italy with incidence data updated through 2023 and has contributed substantially to the epidemiological characterization of cancer burden at national and international levels.

Data analysis

The study included all DCIS of the breast diagnosed between 2000 and 2023. Tumors were classified by topography according to the International Classification of Diseases for Oncology (ICD-O) (12) and grouped by year of diagnosis. Age at diagnosis was categorized as < 45, 45-74 (the organized screening age group in our region since 2010), and ≥ 75 years. For descriptive purposes, the 45-74 age group was further subdivided into 45-49, 50-69, and 70-74 years. Information on receptor status was obtained through careful review of clinical records. Estrogen receptor (ER) and progesterone receptor (PR) were considered positive when expression exceeded 20%. Age-standardized incidence rates were calculated using the resident population of the Province of Reggio Emilia (as of 1 January of each year) as denominators. Rates were standardized by the direct method using the 2013 European Standard Population as a reference. Temporal trends were analyzed by estimating the annual percent change (APC) in age-standardized rates using Joinpoint Regression analysis. The APC represents the average annual percentage change in incidence over a specified time interval, assuming that rates change at a constant percentage of the previous year. The joinpoint model identifies points in time at which statistically significant changes in trend occur, based on predefined statistical criteria. For these analyses, the maximum number of joinpoints was set at four (13).

RESULTS

The study included 1,543 *in situ* breast tumors, representing 13.3% of all breast cancers registered between 2000 and 2023 (**Table 1**). Overall, the incidence of *in situ* tumors showed a slight upward trend over time, with age-adjusted incidence rates per 100,000 women showing a modest increase (**Figure 1**). However, this trend was not statistically significant (APC 0.7; 95%CI -0.6 to 2.2). A modest decline in the number of situ cases was observed in 2022-2023, following the COVID-19 pandemic period, which had as substantial impact on our province during 2020-2021.

In our cohort, 190 patients with an initial diagnosis of *in situ* breast cancer subsequently developed an invasive breast tumor. This is in line with the long-

Table 1. *Distribution of in situ cancers compared with infiltrating tumors, by year of incidence. Reggio Emilia Cancer Registry, 2000-2023.*

YEAR	*IN SITU*	INFILTRATING	% *IN SITU**
2000	42	407	10.3
2001	54	415	13.0
2002	43	398	10.8
2003	49	422	11.6
2004	53	444	11.9
2005	57	439	13.0
2006	59	436	13.5
2007	47	451	10.4
2008	73	440	16.6
2009	53	437	12.1
2010	56	499	11.2
2011	66	502	13.1
2012	67	479	14.0
2013	76	497	15.3
2014	76	465	16.3
2015	82	522	15.7
2016	59	485	12.2
2017	95	522	18.2
2018	64	502	12.7
2019	67	522	12.8
2020	92	551	16.7
2021	83	579	14.3
2022	64	589	10.9
2023	66	577	11.4
Total	**1,543**	**11,580**	**13.3**

** "In situ" refers to non-invasive cancers; "Infiltrating" refers to invasive tumors. Percentages are calculated as the proportion of in situ cases relative to total cases per year.*

term natural history of DCIS documented in NSABP B-17/B-24, the 20-year SweDCIS update, EORTC 10853 at 15 years and the UK Sloane Project, which consistently identify high grade, ER-negativity, comedonecrosis and young age (< 40 years) as predictors of late invasive recurrence.

In our institution, women treated for DCIS undergo oncology-led follow-up with annual mammography for 10 years, after which they re-enter the organized regional screening program. Although our registry spans 24 years, the median follow-up of cases diagnosed after 2010 is still below 15 years, and events beyond 20 years are currently too few to support robust pattern-specific stratification (now stated as a limitation and as a prospective registry objective). Regarding age at diagnosis, 8.5% of cases were recorded in women younger than 45 years, and a similar proportion was observed among women aged 75 years or older (**Table 2**). The 45-74 age group, corresponding to the target population for organized screening programs, accounted for the majority of *in situ* tumors (83%). Within this group, 19.7% of cases occurred in women aged 45-49 years, 69% in those aged 50-69 years, and 11.3% in those aged 70-74 years.

Histologically, 93.5% of tumors were classified as DCIS. Regarding hormone receptor status, 36.5% of tumors were estrogen receptor-positive (ER+) and 25.9% were progesterone receptor-positive (PR+).

Concerning surgical treatment, 74.7% of patients underwent breast-conserving surgery (lumpectomy), while 19.1% underwent mastectomy. SLNB was performed in 46.2% of cases, while axillary lymph node dissection was carried out in 3.3%. Finally, women of foreign nationality represented 6.6% of the overall *in situ* breast cancer cohort.

Table 2. *Characteristics of in situ breast cancers (n = 1,543). Reggio Emilia Cancer Registry, 2000-2023.*

CHARACTERISTIC	N	%
Age at diagnosis		
<45	131	8.5
45–74	1,281	83.0
45–49	*252*	*19.7*
50–69	*884*	*69.0*
70–74	*145*	*11.3*
75+	131	8.5
Morphology		
Ductal	1,442	93.5
Lobular	90	5.8
Other	11	0.7
ER positive	563	36.5
PR positive	400	25.9
Surgery		
None	53	3.4
Quadrantectomy	1,153	74.7
Mastectomy	294	19.1
Tumorectomy/Lumpectomy	41	2.7
NOS	2	0.1
Sentinel lymph node biopsy		
No	830	53.8
Yes	713	46.2
Axillary lymph node dissection		
No	1,492	96.7
Yes	51	3.3
Nationality		
Italian	1,441	93.4
Foreign	102	6.6

Percentages calculated among available cases.

DISCUSSION

Our population-based registry study of 1,543 *in situ* breast tumors (13.3% of all breast cancers, diagnosed between 2000 and 2023) confirms several epidemiologic and clinical patterns consistently reported in the literature.

Incidence and age distribution

Consistent with historical evidence indicating that DCIS incidence increased markedly following the implementation of screening mammography – particularly among women aged 50 and older – our data showed a modest upward trend in age-adjusted DCIS rates over time, followed by a slight decline in 2022-2023. This recent decrease likely reflects pandemic-related disruptions in screening activities and healthcare access. Screening mammography remains one of the strongest determinants of DCIS detection, accounting for a substantial proportion of diagnoses in screened populations (14). The age distribution observed in our cohort mirrors established epidemiologic patterns: the majority of cases occurred in women aged 45-74 years, corresponding to the target population of organized screening programs. These findings further support the central role of screening practices in shaping both the incidence and age distribution of detected DCIS cases (15).

Surgical management and axillary evaluation

Breast-conserving surgery (BCS) was the predominant surgical approach, consistent with contemporary management strategies that favor conservative treatment when appropriate (16). Over time, the use of SLNB in DCIS has increased, particularly in patients undergoing mastectomy, due to the risk of occult invasive disease not detectable preoperatively (17). Large retrospective analyses have demonstrated that SLNB positivity in DCIS is rare, and the likelihood of detecting nodal micrometastases is low. These findings underscore that routine SLNB is not indicated for all DCIS patients, especially those treated with BCS. However, in selected cases – such as patients undergoing mastectomy or those presenting high-risk clinicopathologic features – SLNB may be appropriate to avoid the need for axillary staging after mastectomy. In our cohort, SLNB was performed in 46.2% of cases and axillary dissection in 3.3%, reflecting a tailored application of axillary staging in line with current evidence and guidelines. This approach supports selective rather than routine axillary evaluation in DCIS management (18).

Clinical implications

Screening and detection

The strong association between screening participation and DCIS detection reinforces the need to balance early detection with the risk of overdiagnosis (14, 15). Risk stratification tools incorporating age, imaging characteristics, and biomarkers remain essential to inform individualized screening strategies and follow-up protocols.

Axillary management

The low incidence of axillary metastasis in DCIS argues against routine SLNB in all patients, particularly those undergoing BCS. Decisions regarding axillary staging should be individualized and based on the planned surgical procedure (*e.g.*, mastectomy) and clinicopathologic features suggestive of occult invasion (17, 18).

Surgical decision-making

The high rate of breast-conservative surgery in our cohort underscores the continued emphasis on breast preservation when oncologically appropriate. However, increasing mastectomy rates reported in some settings highlight the importance of shared decision-making that integrates patient preferences with evidence regarding recurrence risk, cosmetic outcomes, and long-term prognosis (18).

Strengths and limitations

A major strength of this study is its population-based design with a long observation period and complete case capture. The analysis included all women diagnosed with *in situ* breast tumors in the Province of Reggio Emilia between 2000 and 2023, without selection criteria. This real-world setting reinforces the external validity of the findings and provides a valuable opportunity to assess the impact of screening programs, evolving clinical guidelines, and advancements in surgical and pathological practice on routine care. The observed trends are consistent with findings reported in the literature, but derive from an unselected, non-trial population, thereby reflecting the translation of evidence into everyday clinical practice. Moreover, the study provides detailed information on molecular characteristics, surgical management, and axillary staging, variables that are not always comprehensively captured in population-based registries.

However, some limitations should be acknowledged. First, this is a single-province study, which may limit generalizability beyond northern Italy, despite the use of standardized diagnostic and therapeutic protocols.

Second, long-term outcome data, such as local recurrence or progression to invasive carcinoma, were not uniformly available, limiting the ability to correlate molecular and clinical characteristics with prognosis. Finally, temporal changes in screening coverage, diagnostic techniques, and healthcare access over the study period may have influenced incidence patterns and treatment choices, potentially introducing residual confounding in trend interpretation.

CONCLUSIONS

In conclusion, this population-based study provides a comprehensive overview of *in situ* breast tumors diagnosed over 23 years period in the Province of Reggio Emilia. The findings indicate a modest increase in DCIS incidence over time, together with a predominant use of breast-conserving surgery and selective approach to sentinel lymph node evaluation. These results reflect real-world practice and are consistent with existing literature. They underscore the value of high-quality population-based cancer registry data in informing screening policies, improving risk stratification, and supporting personalized management strategies for DCIS.

COMPLIANCE WITH ETHICAL STANDARDS

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Conflicts of interest

The authors declare no competing interests.

Availability of data and materials

Data are available under reasonable request to the corresponding author.

Authors' contributions

MBB: conceptualization, investigation, writing – original draft, visualization, supervision. FM: formal analysis. IB: writing – review & editing, visualization, investigation, supervision. AC: investigation, supervision. CP, FG: supervision. MGS: investigation, visualization. LM: conceptualization, writing – original draft, investigation, supervision.

Ethical approval

Human studies and subjects

This population-based cohort study uses data from the Reggio Emilia Cancer Registry, approved by the Provincial Ethics Committee of Reggio Emilia (ref. no. 2014/0019740 of 4 August 2014). The Ethics Committee authorized, even in the absence of consent, the processing of personal data, including those suitable for revealing the state of health of patients who are deceased or untraceable for the execution of the study.

Publications ethics

Plagiarism

We hereby declare that this manuscript is an original work and has not been published or submitted for publication elsewhere. All appropriate references have been cited wherever required. This manuscript does not contain plagiarism.

Data falsification and fabrication

The authors declare that no data fabrication, falsification, or manipulation has been carried out in the preparation of this work.

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