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Extent of ductal carcinoma in situ according to breast cancer subtypes: a population-based cohort study

Shusma C. Doebar[1] · Esther C. van den Broek[2] · Linetta B. Koppert[3] · Agnes Jager[4] · Margreet. H. A. Baaijens[5] · Inge-Marie A. M. Obdeijn[6] · Carolien H. M. van Deurzen[1]

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Abstract Ductal carcinoma in situ (DCIS) is a precursor of invasive breast carcinoma (IBC). The DCIS component is often more extensive than the invasive component, which affects local control. The aim of our study was to analyze features of DCIS within different IBC subtypes, which may contribute to the optimization of personalized approaches for patients with IBC. Patients with IBC reported according to the synoptic reporting module in the Netherlands between 2009 and 2015 were included. Data extraction included characteristics of the invasive component and, if present, several features of the DCIS component. Resection margin status analyses were restricted to patients undergoing breast-conserving surgery (BCS). Differences between subtypes were tested by a Chi-square test, spearman's Rho test or a one-way ANOVA test. Overall, 36.937 cases of IBC were included. About half of the IBCs ($n = 16.014$; 43.4 %) were associated with DCIS. Her2+ IBC (irrespective of ER status) was associated with a higher prevalence of adjacent DCIS, a larger extent of DCIS and a higher rate of irradicality of the DCIS component as compared to ER+/Her2− and triple-negative subtypes ($P < 0.0001$ for all variables). The prevalence of DCIS in triple-negative IBC on the other hand was lowest. In this large population-based cohort study, we showed significant differences between the prevalence and extent of DCIS according to IBC subtypes, which is also reflected in the resection margin status in patients treated with BCS. Our data provide important information regarding the optimization of local therapy according to IBC subtypes.

Keywords Breast cancer subtypes · Ductal carcinoma in situ · Prevalence

Introduction

Invasive breast cancer (IBC) is a heterogeneous disease which can be categorized into several histologic or intrinsic subtypes that differ in their biological behavior and clinical outcome [1–3]. Intrinsic subtypes are most precisely categorized based on multigene expression assays, although each subtype has an immunohistochemical surrogate based on ER, PR, Her2, and Ki-67 index [4–7]. Ductal carcinoma in situ (DCIS) is seen as a nonobligate precursor of invasive ductal carcinoma (IDC). In the last decades, the detection rate of DCIS increased markedly in the age group of 50–75 years, as a result of the increased use and improved resolution of mammographic mass screening [8, 9]. Synchronous DCIS and adjacent IDC show a high degree of concordance regarding morphology and genetic profiles [10–15]. The concordance of receptor expression of ER, PR, and Her2 in DCIS and coexisting IDC is high,

✉ Shusma C. Doebar
s.doebar@erasmusmc.nl

1 Department of Pathology, Erasmus MC Cancer Institute, PO Box 2040, 3000 CA Rotterdam, The Netherlands

2 Stichting Palga, Randhoeve 231A, 3995 GA Houten, The Netherlands

3 Department of Oncological Surgery, Erasmus MC Cancer Institute, PO Box 5201, 3008 AE Rotterdam, The Netherlands

4 Department of Medical Oncology, Erasmus MC Cancer Institute, PO Box 5201, 3008 AE Rotterdam, The Netherlands

5 Department of Radiotherapy, Erasmus MC Cancer Institute, PO Box 5201, 3008 AE Rotterdam, The Netherlands

6 Department of Radiology, Erasmus MC Cancer Institute, PO Box 5201, 3008 AE Rotterdam, The Netherlands

with 92 % for ER, 93–97 % for PR, and about 98–100 % for Her2 [10–12].

Data regarding the process of progression of DCIS to IBC is limited. Several studies reported frequencies of pure DCIS subtypes based on immunohistochemical surrogates originally described for IBC [5, 13, 14, 16]. In these pure DCIS studies, the distribution of subtypes differs from studies including IBC. In pure DCIS studies, frequencies of Her2−positive subtypes are higher as compared to reported frequencies in IBC; about 15–32 % of pure DCIS cases are Her2 positive, while this frequency is lower in IBC, about 6–14 % [5, 13, 14, 16–18]. Reported frequencies of triple-negative pure DCIS on the other hand are lower than reported frequencies in IBC, 6–8 % in pure DCIS versus 11–13 % in IBC [5, 13, 14, 16, 17]. Regarding the Luminal A and Luminal B subgroups, the reported frequencies for pure DCIS and IBC are overlapping (38–63 % in pure DCIS versus 38–73 % in IBC for luminal A and 7–28 % in pure DCIS versus 5–26 % in IBC for luminal B) [5, 13, 14, 16, 17, 19]. Based on these prevalences, a mathematical, hypothetical model has been built, suggesting different speeds of progression according to breast cancer subtypes [20]. This model suggests that Her2+ DCIS has the slowest progression to IBC, while triple-negative DCIS has the fastest progression.

Since the last decades, the proportion of patients undergoing mastectomy decreased and the majority of patients with localized DCIS are treated with breast-conserving surgery (BCS), followed by breast irradiation [21]. Overall, the local recurrence rate (LRR) for patients with DCIS treated with BCS followed by breast irradiation is about 10–17 % within the first 15 years after treatment, of which 50 % concerns IBC [22–24]. Recent studies reported that DCIS subtype was an independent predictor for ipsilateral recurrence after treatment by breast surgery alone (BCS or mastectomy) or breast surgery followed by breast irradiation [25–28]. The overall LRR in patients with pure DCIS was the highest in Her2-positive and luminal B subgroups (10–48 % and 25–42 % recurring within 10 years of follow-up, respectively) and the lowest in the luminal A subgroup (9–21 %) [25–27]. Regarding triple-negative DCIS, no firm conclusion could be drawn from the reported LRRs due to limited numbers of patients. Nevertheless, based on LRRs per subtype, Her2-positive DCIS seems to have an increased risk for LR after breast surgery as compared to Her2-negative DCIS. In line with this, the highest LRR was also observed for Her2−positive IBC following breast surgery and irradiation (LRR of 8–21 % within 10 years of follow-up), as compared to Luminal A and Luminal B type IBC (LRR 1–8 % and 2–10 % respectively) [29–31]. These data suggest that adjustment of current treatment guidelines according to breast cancer subtypes, e.g., aggressive local therapy restricted to patients with a high LRR, could result in reduction of complications and costs for low risk patients.

Subtyping of DCIS has the potential to study progression-related features and to identify patients at high risk for LR. However, in daily practice, pure DCIS cases are not routinely analyzed for ER, PR and Her2 status, which limits the opportunity for large-scale retrospective studies. Patients with IBC on the other hand are routinely studied for ER, PR, and Her2 status. This provides the opportunity to indirectly assess adjacent DCIS features, which, as mentioned above, share receptor expression pattern in the vast majority of cases. The aim of this study was to analyze features of DCIS within different IBC subtypes, including the resection margin status in patients treated with BCS, which may contribute to the optimization of personalized approaches for patients with IBC.

Patients and methods

Data acquisition

In the Netherlands, all pathology reports are archived in the Dutch Pathology Registry (PALGA) [32]. Since 2009, synoptic reporting modules for reporting several common tumor types including breast cancer became available. In these modules, the parameters are captured in numerous variables instead of free text fields. This offers the unique opportunity to analyze all reports created with the module simultaneously.

Patient and tumor characteristics

For this study, we included all patients with IBC reported according to the protocol module in the Netherlands between January 1, 2009 and September 1, 2015 ($n = 36.937$ cases). Patients with missing ER, PR, and/or Her2 status; pure DCIS; and patients with IBC after previous treatment (irradical resection, neoadjuvant therapy) were excluded. Patients with bilateral IBC were included as two cases. In case of multiple IBCs in one breast, the largest IBC was included for analysis of tumor characteristics, except for resection margin status, which was assessed for all tumors.

Clinicopathologic characteristics included age, type of surgical procedure (BCS or mastectomy), tumor size ($\leq$2 cm, >2 to $\leq$5 cm or >5 cm), histological type (according to WHO), grade (according to the modified Bloom and Richardson grading system) [33], ER status, PR status, Her2 status, presence of angioinvasion, presence of DCIS, and nodal status. ER status and PR status were defined as positive in case more than 10 % of the cancer cells that showed nuclear staining, irrespective of density, according

to the Dutch Guideline for breast cancer treatment [34]. Her2 status was scored according to the international guidelines [35]. Based on immunohistochemistry, tumors were divided according to the surrogate definitions of intrinsic subtypes as reported in the St Gallen International Expert Consensus 2013 [36]. Low PR expression was defined as ≤20 % [37]. However, the absence of information regarding Ki-67 indexes in our dataset limited the ability to differentiate between Luminal A and Luminal B (Her2−) subtypes, so based on the available information, our cases were subtyped according to the following 5 categories:

1. ER+/PR high/Her2−,
2. ER+/PR− or low/Her2−,
3. ER+/Her2+,
4. ER−/PR−/Her2+, and
5. ER−/PR−/Her2−.

In case DCIS was present, the following features were documented: relation to the invasive component (restricted to invasive component or not), diameter, nuclear grade, and presence of microcalcifications [38]. The overall resection margin status was reported, as well as the margin for both the invasive component and the DCIS component as either free, focally irradical, or more than focally irradical, according to the Dutch Guideline for Breast Cancer Treatment [34]. Focally irradical is defined as tumor (either invasive or DCIS) reaching the ink in a small area (≤4 mm). In case the tumor (either invasive or DCIS) reaches the ink in a larger area or multiple smaller areas, it is defined as more than focally irradical. This distinction has important clinical consequences in the Netherlands, since patients with a focally positive resection margin of IBC or adjacent DCIS do not undergo second surgery (since radiation with a boost dose results in adequate local control), while patients with a more than focally positive resection margin undergo reexcision, according to the Dutch Guideline for Breast Cancer Treatment 2002 [39]. However, these definitions are not applied in most other European and North American countries [40]. Therefore, in this study, we use the term irradicality to describe either focally or more than focally irradical resection margins.

Statistical analysis

Differences between IBC subtypes were tested by means of a Chi-square test (categorical variables) or a one-way ANOVA (continuous variables). Missing values are included in the tables but excluded in the analyses.

Furthermore, the correlation between grade of the invasive component and the DCIS component was tested with Chi-square. The correlation between the extent of the DCIS component and resection margin status of the DCIS component was tested with a spearman's correlation coefficient. All analyses were performed with SAS Enterprise Guide 7.1.

Results

Baseline characteristics

Overall, we included 36.937 consecutive cases of IBC reported between January 1, 2009 and September 1, 2015. The median age of our patient cohort was 62 years (range 18–100). The majority of patients (60.4 %) underwent BCS. Table 1 provides an overview of clinicopathologic data of all patients. About half of the IBCs ($n = 16.014$; 43.4 %) were associated with DCIS, either restricted within or outside the invasive component (45.3 and 54.7 %, respectively).

Table 2 provides details of all patients with IBC and adjacent DCIS. Overall, there was a strong correlation between grade of the DCIS component and grade of the invasive component ($p < 0.0001$, Chi-square test). Both the extent of DCIS and DCIS extending beyond the invasive component correlated with irradicality of the DCIS component (spearman's rho $= 0.3$, $p < 0.0001$ and $P < 0.0001$, Chi-square test, respectively). The frequency of multiple IBCs was significantly higher in IBC cases with adjacent DCIS (10.2 %) as compared to IBC cases without adjacent DCIS (7.4 %) ($p < 0.0001$, Chi-square test).

Clinicopathologic features according to breast cancer subtypes

Based on immunohistochemical stainings, IBCs were categorized into the following 5 categories: ER+/PR high/Her2− ($n = 21315$; 57.7 %), ER+/PR− or low/Her2− ($n = 7541$; 20.4 %), ER+/Her2+ ($n = 2806$; 7.6 %), ER−/PR−/Her2+ ($n = 1334$; 3.6 %), or ER−/PR−/Her2− ($n = 3941$; 10.7 %). Table 3 provides an overview of patient and tumor characteristics according to different IBC subtypes.

Overall, regarding the invasive component, the ER−/Her2+ and triple-negative subgroups showed the most aggressive biological features. The ER+/Her2− subgroups showed the most favorable biological features while the ER+/Her2+ subgroup showed intermediate results. Regarding the ER+/Her2− subgroups, the presence of a high PR expression was associated with more favorable tumor characteristics as compared to those cases with absence or low PR expression.

In general, patients with Her2+ (irrespective of ER status) and triple-negative IBC were younger as compared to patients with ER+/Her2− IBC ($P < 0.0001$). Besides,

Table 1 Baseline characteristics of all patients with IBC ($n = 36937$)

Characteristic	N	(%)
Age at diagnosis, years, mean, median (range)	Mean: 61.0	
	Median: 62.0 (18–100)	
Type of surgery		
Breast-conserving surgery	22,328	60.45
Mastectomy	14,609	39.55
Histologic tumor type		
Ductal	29,630	80.22
Lobular	4703	12.73
Other	2604	7.05
Tumor size		
≤2 cm	24,359	65.95
>2 to ≤5 cm	11,117	30.10
>5 cm	1461	3.96
Tumor grade		
1	8622	27.13
2	14,894	46.86
3	8266	26.01
Missing	5155	–
ER status		
Positive	31,662	85.72
Negative	5275	14.28
PR status		
Positive	25,400	68.77
Negative	11,487	31.10
Her2 status		
Positive	4140	11.21
Negative	32,797	88.79
Multiple invasive tumors		
Yes	2650	8.63
No	28,051	91.37
Missing	6236	
Angioinvasion		
Yes	3715	14.03
No	22,773	85.97
Missing	10,449	–
Presence of DCIS component		
Yes	16,014	43.35
No	20,923	56.65
Overall resection margin status (invasive component and/or DCIS component)[a]		
Free	18,552	83.09
Focally irradical	2286	10.24
More than focally irradical	1490	6.67
Resection margin status of invasive component only[a]		
Free	19,755	88.48
Focally irradical	1621	7.26
More than focally irradical	952	4.26
Nodal status		
Negative	11,428	60.22
Positive	7550	39.78
Missing	17,959	–

[a] Analysis restricted to patients with BCS ($n = 22328$)

Table 2 DCIS characteristics of all patients with IBC and adjacent DCIS ($n = 16014$)

Characteristic	N	(%)
DCIS grade		
1	2598	16.33
2	7896	49.64
3	5414	34.03
Missing	106	–
DCIS restricted to invasive component		
Yes	4452	45.29
No	5377	54.71
Missing	6185	–
Diameter of DCIS, cm, mean, median (range)	Mean: 2.08	–
	Median: 1.50 (0–20)	
Presence of DCIS-associated microcalcifications		
Yes	4400	49.97
No	4406	50.03
Missing	7208	–
Resection margin status of DCIS component only[a]		
Free	8323	83.67
Focally irradical	1168	11.74
More than focally irradical	456	4.58
Missing	34	

[a] Analysis restricted to patients with BCS ($n = 9981$)

median tumor size of these subtypes was larger ($P < 0.0001$), which was in line with the higher proportion of patients undergoing a mastectomy ($P < 0.0001$). Histologically, these tumors were more often of ductal type ($p < 0.0001$) and of higher grade ($P < 0.0001$). The frequency of angioinvasion and nodal involvement was highest in the ER−/Her2+ subgroup ($P < 0.0001$).

There was a strong correlation between the presence of DCIS and breast cancer subtype ($P < 0.0001$). Table 4 provides an overview of all DCIS characteristics according to different subtypes of IBC. DCIS was most often present adjacent to IBCs with overexpression of Her2 (irrespective of ER status) with a frequency of 59.1 % in the ER+/Her2+ subgroup and 57.4 % in the ER−/Her2+ subgroup. The frequency of a DCIS component was lowest in the triple-negative subgroup (34.1 %).

Besides a higher prevalence of DCIS in the Her2+ groups, DCIS was more often located outside the invasive component and the DCIS component was more extensive ($P < 0.0001$ for all variables). DCIS-associated microcalcifications were most often seen adjacent to Her2+ IBC, while the frequency was lowest in the triple-negative group ($p < 0.0001$).

Analysis of resection margin status was restricted to patients treated with BCS. Overall, the frequency of irradicality (of either the invasive or the DCIS component) was highest in the Her2+ subgroups and lowest in the triple-negative subgroup ($P < 0.0001$). Analysis of irradicality of the invasive component separately showed the highest frequency of irradicality in the ER+/Her2− subgroups and the lowest in the triple-negative subgroup ($P < 0.0001$). Analysis of irradicality of the DCIS component however showed another distribution as compared to the irradicality of the invasive component; the frequency of irradicality of the DCIS component was highest in the Her2+ subgroups ($P < 0.0001$).

Discussion

Our national registration system for pathology reporting provided a unique opportunity for this large-scale population-wide cohort study describing the presence and extent of DCIS according to breast cancer subtypes, in relation to other clinicopathologic features.

In our study, we showed substantial differences between immunohistochemical breast cancer subtypes regarding age, type of surgery, histology, tumor grade, and tumor size, which is consistent with literature [41, 42]. Briefly, Her2+ and triple-negative tumors are associated with younger age, larger size, and higher grade compared to luminal subtypes. However, on the other side of the spectrum, ER+/Her2− IBC showed the most favorable tumor

Table 3 Clinicopathologic characteristics according to different subtypes of IBC ($n = 36937$)

Characteristic	ER+, PR high, Her2− ($n = 21315$)		ER+, PR− or low Her2− ($n = 7541$)		ER+, Any PR, Her2+ ($n = 2806$)		ER−, PR−, Her2+ ($n = 1334$)		ER−, PR−, Her2− ($n = 3941$)		P-value
Age at diagnosis, years, mean, median and range	Mean: 61.1 Median: 62 Range: 18–99		Mean: 63.4 Median: 64 Range: 21–97		Mean: 57.6 Median: 57 Range: 19–100		Mean: 59.3 Median: 59 Range: 24–97		Mean: 59.0; Median: 59 Range: 22–98		<0.0001
Type of surgery, no (%)											<0.0001
Breast-conserving surgery	13,507	63.37	4476	59.36	1514	53.96	599	44.90	2232	56.64	
Mastectomy	7808	36.63	3065	40.64	1292	46.04	735	55.10	1709	43.36	
Tumor type, no (%)											<0.0001
Ductal	16,695	78.33	5753	76.29	2548	90.81	1255	94.08	3379	85.74	
Lobular	3130	14.68	1319	17.49	147	5.24	20	1.50	87	2.21	
Other	1490	6.99	469	6.22	111	3.96	59	4.42	475	12.05	
Tumor size, no (%)											<0.0001
≤2 cm	14,849	69.66	4931	65.39	1719	61.26	729	54.65	2131	54.07	
>2 to ≤5 cm	5771	27.07	2267	30.06	964	34.35	528	39.58	1587	40.27	
>5 cm	695	3.26	343	4.55	123	4.38	77	5.77	223	5.66	
Tumor grade, no (%)											<0.0001
1	6513	35.17	1786	27.41	203	8.63	29	2.62	91	2.77	
2	9559	51.62	3379	51.86	1018	43.28	273	24.66	665	20.21	
3	2445	13.20	1351	20.73	1131	48.09	805	72.72	2534	77.02	
Missing	2798	–	1025	–	454	–	227	–	651	–	
Multiple invasive tumors, no (%)											<0.0001
Yes	1624	9.02	510	8.25	216	9.45	106	9.97	194	5.97	
No	16,296	90.94	5671	91.75	2070	90.55	957	90.03	3057	94.03	
Missing	3395	–	1360	–	520	–	271	–	690	–	
Angioinvasion, no (%)											<0.0001
Yes	1734	11.20	727	13.46	427	21.72	267	29.28	560	20.52	
No	13,747	88.80	4673	86.54	1539	78.28	645	70.72	2169	79.48	
Missing	5834	–	2141	–	840	–	422	–	1212	–	
Overall resection margin status (invasive and/or DCIS component)[a]											<0.0001
Free	11,243	83.24	3676	82.13	1205	79.59	459	76.63	1969	88.22	
Focally irradical	1366	10.11	492	10.99	178	11.76	92	15.36	158	7.08	
More than focally irradical	898	6.65	308	6.88	131	8.65	48	8.01	105	4.70	
Resection margin status of invasive component[a], no (%)											<0.0001
Free	11,879	87.95	3910	87.35	1344	88.77	540	90.15	2082	93.28	
Focally irradical	1028	7.61	356	7.95	112	7.40	41	6.84	84	3.76	
More than focally irradical	600	4.44	210	4.69	58	3.83	18	3.01	66	2.96	
Nodal status, no (%)											<0.0001
Negative	6717	62.17	2293	59.19	774	53.20	359	47.61	1285	61.45	
Positive	4087	37.83	1581	40.81	681	46.80	395	52.39	806	38.55	
Missing	10,511	–	3667	–	1351	–	580	–	1850	–	

[a] Analysis restricted to patients with BCS ($n = 22328$)

characteristics, especially in the case of a high PR expression. This is in line with recent work of Prat et al. in which they concluded that the addition of a PR expression of more than 20 % adds prognostic value within the current immunohistochemical-based luminal A definition by improving the identification of IBCs with a good prognosis

Table 4 DCIS characteristics according to different subtypes of IBC ($n = 16014$)

Characteristic	ER+, PR high, Her2− ($n = 21315$)		ER+, PR− or low Her2− ($n = 7541$)		ER+, Any PR, Her2+ ($n = 2806$)		ER−, PR−, Her2+ ($n = 1334$)		ER−, PR−, Her2− ($n = 3941$)		P-value
Presence of DCIS, no (%)											<0.0001
Yes	9168	43.01	3078	40.82	1658	59.09	766	57.42	1344	34.10	
No	12,147	56.99	4463	59.18	1148	40.91	568	42.58	2597	65.90	
DCIS grade, no (%)											<0.0001
1	1983	21.77	512	16.72	61	3.70	4	0.53	38	2.86	
2	5310	58.32	1613	52.66	572	34.73	106	13.93	294	21.11	
3	1813	19.91	938	30.62	1014	61.57	651	85.55	998	75.04	
Missing	61	–	15	–	11	–	5	–	14	–	
Presence of DCIS-associated microcalcifications, no (%)											<0.0001
Yes	2464	48.21	876	52.02	512	59.26	240	60.91	308	40.90	
No	2647	51.79	808	47.98	352	40.74	154	39.09	445	59.10	
Missing	4057	–	1394	–	794	–	372	–	591	–	
DCIS restricted to invasive component, no (%)											<0.0001
Yes	2774	48.52	823	43.82	383	39.24	127	29.13	345	41.97	
No	2943	51.48	1055	56.18	593	60.76	309	70.87	477	58.03	
Missing	3451	–	1200	–	682	–	330	–	522	–	
Diameter of DCIS, cm, mean, median and range	Mean: 1.9; Median: 1.4 Range: 0–20		Mean: 1.9; Median: 1.4 Range: 0–19		Mean: 2.6; Median: 2.0 Range: 0–20		Mean: 3.2; Median: 2.3 Range: 0–20		Mean: 2.1; Median: 1.5 Range: 0–15		<0.0001
Resection margin status of DCIS component[a]											
Free	5103	85.33	1622	83.44	707	78.82	251	71.10	640	82.79	<0.0001
Focally irradical	640	10.70	245	12.60	127	14.16	73	20.68	83	10.74	
More than focally irradical	237	3.96	77	3.96	63	7.02	29	8.22	50	6.47	
Missing	22	–	5	–	2	–	0	–	5	–	

[a] Analysis restricted to patients with BCS and presence of DCIS

[37]. The ER+/Her2+ group seems to be an intermediate subgroup.

Regarding DCIS, we showed that Her2+ IBC is associated with a higher prevalence of adjacent DCIS and a larger extent of DCIS as compared to other IBC subtypes. In line with this, we reported a relatively high rate of irradicality of the DCIS component in Her2+ IBC. These findings are consistent with previous studies reporting a relatively high rate of Her2 positivity in pure DCIS cases, presence of extensive DCIS adjacent to Her2+ IBC, and a high LRR after BCS for Her2+ IBC [13, 29, 30, 42, 43]. Since the risk of an irradical resection is higher for IBCs that are associated with an extensive DCIS component as compared to those with a limited in situ component [41, 44], it seems likely that the DCIS component adjacent to Her2+ IBC is responsible for the high LRR. Therefore, preoperative knowledge regarding the extent of DCIS according to breast cancer subtypes may result in adjustment of local therapy and consequently local control. This may reduce undertreatment in those patients with a large DCIS component, including fewer secondary surgeries and local recurrences. On the other hand, it may result in less overtreatment in those patients with a low prevalence and/or limited extent of DCIS, e.g., by reduction of excision volume which affects cosmetic outcome. In recent years, there is an increased number of pathology laboratories performing the ER, PR, and Her2 status on preoperative needle biopsies on a routine basis, mainly as a result of the increased use of neoadjuvant treatment, which provides a better understanding of tumor growth patterns preoperatively. The presence of DCIS-associated microcalcifications adjacent to the majority of Her2+ IBCs, as shown in this study, may provide important preoperative information regarding imaging by mammography. Besides, since the DCIS component adjacent to Her2+ IBCs is mainly of high grade, a preoperative MRI could be beneficial for these patients, particularly for those without microcalcifications, since this imaging technique is considered to be the most sensitive modality in detecting the presence and extent of intermediate- and high-grade DCIS [45, 46].

According to our knowledge, our study includes the largest series of patients ever published regarding the presence and extent of DCIS adjacent to breast cancer subtypes, thanks to our national protocolled registration of breast cancer pathology reports. However, our study also has several weaknesses including the missing data regarding receptor expression of the DCIS component. However, since several studies reported a very high concordance (90–100 %) of ER, PR, and Her2 expression between DCIS and adjacent IBC, it is highly unlikely that this has affected our results. The second limitation is the lack of information regarding proliferation, because Ki-67 is not routinely performed in our pathology laboratories. This limited an accurate categorization of luminal A versus luminal B subtypes, which is partly based on a low versus a high Ki-67 index. A third limitation of our study is the lack of clinical follow-up regarding local control. In this study, we used data from 2009 (in this year we started registering according to standard pathology protocols) until 2015, resulting in inadequate follow-up time.

In conclusion, in this large population-based cohort study, we showed significant differences between the prevalence and extent of DCIS according to breast cancer subtypes. Her2+ IBC was associated with the highest prevalence and extent of DCIS, while on the other side of the spectrum, triple-negative IBC had the lowest prevalence of DCIS of all IBC subtypes. Since the extent of DCIS was also reflected in the resection margin status in patients treated with BCS, these data provide important information regarding the optimization of local therapy.

Compliance with ethical standards

Conflict of interest None declared.

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