

Age and its Impact in Breast Ductal Carcinoma In Situ: An Egyptian Tertiary Cancer Center Retrospective Experience

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ABSTRACT

Introduction: Ductal carcinoma in situ (DCIS) is rarely diagnosed in young female patients; moreover, most studies view age as a poor prognostic factor.

Patient and Methods: We included female patients who underwent surgery for DCIS of the breast (with or without microinvasion) in our department from February 2007 to February 2022. We divided patients into two groups: group I (under 40 years old) and group II (40 years old and above). Our aim was to evaluate and compare clinical-epidemiological, pathological, radiological, operative, and outcome data between the two groups. We sought to test the idea that young age in DCIS patients is a poor prognostic factor that may require more aggressive treatment.

Results: One hundred sixty-two patients were included in the current study. The mean age was 51.8 years. 20.1% of patients were younger than 40 years. The commonest symptom, reported in 79.3% of cases, was a breast lump. The final pathology was pure DCIS in two-thirds of patients. Microinvasion was present in the remaining third. Recurrence occurred in 11 patients (6.7%). Tumor size, grade, histologic subtype, ER status, pathological multicentricity, type of surgery, and recurrence were not statistically significant (p-values = .223, .097, .68, .41, .37, 1, .23, respectively). Disease-free survival was not significantly different between the two groups (p-value = 0.3). However, the use of magnetic resonance imaging and breast reconstruction was more common in the younger age group (p-values = .039 and <.001, respectively).

Conclusion: One-fifth of our patients with DCIS were less than 40 years old, and recurrence was quite uncommon. The use of breast-conserving surgery is increasing in our community, but it is still underutilized. Notably, MRI and breast reconstruction were more common in the younger group. As the outcomes were similar between groups, more aggressive treatment for younger DCIS patients is not justified.

Keywords: ductal carcinoma in situ, young, micro invasion, breast-conserving surgery, outcomes

INTRODUCTION

Ductal carcinoma in situ (DCIS) is a noninvasive pre-cancerous breast lesion that accounts for 20-25 % of annual breast cancer diagnoses (1,2). Recently, there has been a dramatic increase in its incidence from 5% to

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around 25% due to improved and widely used screening mammography and other imaging modalities (3).

However, DCIS is not commonly diagnosed in patients < 40 years (4), as it is mostly detected through screening mammography which is not generally applied for such a population. In previous studies, one of the poor prognosticators for both recurrence or progression and cancer mortality was young age at diagnosis (5-7). As a result, younger patients tend to receive more intensive treatment in terms of surgical extent and radiotherapy (RT) (8,9).

A complex set of biological and psychosocial factors, as well as unique disease characteristics, influences DCIS in younger women. Studies on this topic remain sparse. The absence of age-specific guidelines underscores the importance of research on the characteristics, management, and outcomes of DCIS in younger women compared to older women.

This study evaluates clinical, pathological, radiological, operative, and outcome data in patients with DCIS who are under 40 years old ("younger group") and compares these findings to patients 40 years and older ("older group"). The objective is to test whether being in the younger group is an adverse prognostic factor warranting more aggressive treatment.

PATIENT AND METHODS

Type of Study

This is a retrospective, single-center study approved by the IRB of the Faculty of Medicine, Mansoura University (number R.22.09.1834).

Patient and Variables

We included all patients who were operated on for DCIS of the breast at the surgical oncology department, Oncology Center–Mansoura University (OCMU), between February 2007 and February 2022. Patients were divided into two groups based on age at diagnosis: Group I (patients younger than 40 years) and Group II (patients 40 years of age or older).

Inclusion criteria

The patients with DCIS (with or without micro-invasion) who underwent surgical management and subsequent follow-up at our center.

Exclusion criteria

- Invasive breast carcinoma even with intraductal

component;

- Lobular carcinoma in situ;
- Intracystic papillary carcinoma;
- Non-epithelial pathology;
- Nodal positive disease;
- Missed the patient's data or lost follow-up.

Variables

We retrieved the following data for analysis: age at diagnosis, BMI, family history, symptoms, calcification pattern, and breast density (ACR). Additionally, we recorded the type of surgery, the type of axillary assessment, and the method of breast reconstruction. Morphological pattern of DCIS, tumor size, presence or absence of microinvasion, and lymphovascular emboli (LVE) were noted. Further, ER status, adjuvant therapies, recurrence status/pattern/date, management of recurrence, new non-breast primary cancer, and contralateral breast cancer were also collected.

To minimize data loss, a portion of missing data was collected by two investigators through phone calls with the included patients or their families.

Statistics

Data were analyzed on a personal computer using SPSS® for Windows (Release 26). For qualitative variables, descriptive statistics included counts and percentages. For quantitative variables, the mean, median, range, and standard deviation describe central tendency and dispersion. A p-value of <0.05 was considered statistically significant.

RESULTS

One hundred sixty-two patients were recruited, with two patients having bilateral breast DCIS, thus representing 164 cases. All patients were females. Twenty-one patients (13%) had a family history of breast cancer (6 in the young group versus 15 in the old group). Additionally, 4 patients had a history of uterine cancers (3 in the old and 1 in the young group).

Clinico-epidemiologic, pathologic, and treatment data (table 1)

The mean age was 51.8 years (SD ± 12.9). About 20.4% of patients were younger than 40 years. The median BMI was 35 Kg/m² (range: 17.9-56.2).

Only one case was detected through screening mammography. The most common symptom was a breast lump, reported in 130 cases (79.3%). Nipple

Table 1 - Basic epidemiologic, pathologic and outcomes data of the entire series (162 patients presented as 164 cases)

Variable	Value
Age mean \pm SD (range)	51.8 \pm 12.9 (21-87) years
BMI median (range)	35 (17.9-56.2) Kg/m ²
Presentation*	
• Screening	1 (0.6%)
• Palpable mass	130 (79.3%)
• Nipple discharge	37 (22.6%)
• Nipple erosion	14 (8.5%)
Mammography***	
• Not done	44 (28.2%)
• Done	112 (71.8%)
Mammographic calcifications**	
• No	58 (51.8%)
• Yes	53 (47.3%)
Type of calcifications (n=51) [†]	
• Microcalcifications	43 (84.3%)
• Macrocalcifications	8 (15.7%)
MRI***	
• Not done	127 (81.4%)
• Done	29 (18.6%)
Trial of CBS	
• No	113 (68.9%)
• Yes	51 (31.1%)
Type of surgery	
• CBS	29 (17.7%)
• Mastectomy	135 (82.3%)
Reconstruction	
• No	135 (82.3%)
• Yes 29 (17.7%)	
o Autologous	• 21
o Synthetic	• 7
o Combined	• 1
ALND**	
• No	53 (32.3%)
• Yes	111 (67.7%)
Trial of SLNB	
• No	123 (75%)
• Yes	41 (25%)
Final pathology	
• Pure DCIS	109 (66.5%)
• DCIS with microinvasion	55 (33.5%)
Pathologic size median (range)	5 (1-14) cm
Final grade	
• 1	21 (12.8%)
• 2	27 (16.5%)
• 3	99 (60.4%)
Lymphovascular emboli**	
• No	133 (81.1%)
• Yes	9 (5.5%)
Histologic subtype [†]	
• Non-comedo	59 (40.1%)
• Comedo	88 (59.9%)
Pathologic multicentricity [†]	
• No	113 (83.7%)
• Yes	22 (16.3%)
ER status	
• Negative	61 (37.2%)
• Positive	93 (56.7%)
Adjuvant radiation therapy	
• No	127 (77.4%)
• Yes	30 (18.3%)
Adjuvant hormonal therapy	
• No	54 (32.9%)
• Yes	100 (61%)
Recurrence	
• No	153 (93.3%)
• Yes	11 (6.7%)
Pattern of recurrence [†]	
• Local	2 (18.2%)
• Regional	1 (9.1%)
• Locoregional	1 (9.1%)
• Distant	4 (36.4%)
• Locoregional & distant	3 (27.3%)
Recurrence pathology [†]	
• DCIS	1 (10%)
• DCIS with microinvasion	2 (20%)
• Invasive carcinoma	7 (70%)

*Some patients may have more than one presenting symptom

** Some data is missing; [†] Valid percent

discharge was reported in 37 cases (22.6%), with 51.5% of these being bloody. The median clinical mass size was 3 cm (range: 1-12).

All cases were assessed with ultrasound; 112 cases (71.8%) also underwent mammography. MRI was used in only 29 cases (18.6%).

Preoperative ultrasound showed that BIRADS 4 was reported in 46 cases (28%), BIRADS 5 in 18 cases (11%), and BIRADS 6 in 10 cases (6.1%). The median mass size was 2.5 cm (range: 0.5-19.5).

Various biopsy techniques were used: Fine needle aspiration cytology (FNAC) in 8 cases (4.9%), Tru-cut biopsy in 85 cases (51.8%), incisional biopsy in 15 cases (9.1%), and excisional biopsy in 56 cases (34.1%). Among these, 50 cases (30.5%) were unplanned excisional biopsies done without safety margins outside our center.

Preoperative pathology showed grade 1 DCIS in 24 cases (14.6%), grade 2 in 26 cases (15.9%), and grade 3 in 42 cases (25.6%). Comedo necrosis was observed in 44 cases (26.8%).

Only 29 cases (17.7%) underwent successful breast conserving surgery (BCS) out of 51 attempts (31.1%) to avoid mastectomy. The remainder had persistent positive margins. Another 29 cases (17.7%) received breast reconstruction, mostly using autologous flaps.

One hundred fifty cases (91.5%) underwent axillary surgery. Among them, 109 cases underwent upfront ALND, and 41 underwent SLNB; 2 failed and were converted to ALND. All axillary specimens were pathologically negative.

The final pathology showed pure DCIS in 109 cases (66.5%) and microinvasion in 55 cases (33.5%). ER status was positive in 93 cases (56.7%).

Adjuvant hormonal treatment was given to 100 cases (61%). Of the 30 cases (18.3%) with BCS, 18.3% received adjuvant radiation therapy.

Recurrences (table 1)

The median follow-up period was 50.5 months (range: 0.5 - 195), with recurrence occurring in only 11 cases (6.7%). Of these, 2 were local, 1 was regional, 1 was locoregional, 4 were distant, and 3 were combined locoregional and distant recurrence. Bone is the most common site of distant recurrence (in 4 patients), followed by the lung, distant lymph nodes, and combined bone and liver in 1 patient each.

We report regional nodal recurrence in 5 cases (3%) in our series, of which 4 were initially diagnosed with microinvasion (valid percent: 7.3%) and 1 with pure DCIS (valid percent: 0.9%).

In patients with recurrence, 8 out of 11 (72.7%) had a microinvasive component in the primary lesion, and 8 of them (72.7%) were Grade 3 initially. The histopathology of the recurrence was confirmed as in situ carcinoma in 1 case, micro-invasive carcinoma in 2 cases, and invasive carcinoma in 4 cases. However, biopsy was not feasible at 3 distant metastatic sites; they were considered invasive by definition.

Comparison of Young to Old Groups (table 2)

Family history of breast cancer showed a higher, albeit non-significant, difference in favor of the older patient group (p-value = .38). Diagnostic mammography was more frequently used in the older group, with no statistical significance (p-value = .12). In contrast, MRI was significantly more commonly used in the younger group (p-value = .039).

Both groups were offered the same type of surgery (mastectomy or BCS) (p-value = 1); however, breast reconstruction was significantly more frequently used in the younger group (p-value = <.001).

The pathologic subtype (comedo vs. non-comedo), incidence of microinvasion, final tumor grade, and ER status were similar in both groups (p-values = .68, .1, .097, and .41, respectively).

The incidence of multicentricity in the pathologic specimens was also similar between younger and older patients (p-value=.37). The young age group showed a slightly higher, though not statistically significant, median pathological tumor size (5.5 vs. 5 cm, p-value = .223).

Both groups received similar adjuvant treatments, including radiotherapy and hormonal therapy (p-values = .81 and 1, respectively).

In addition, recurrence rate, its pattern, and recurrence pathology (in situ vs. invasive) were similar in both groups (p-values = .23, .606, and .4, respectively). However, in older patients, all distant recurrences were bony in contrast to visceral +/- bone metastasis in the younger group (p-value = .072).

Four patients developed contralateral breast cancer; all were invasive. Additionally, one case each of uterine cancer, HCC, pancreatic head cancer, ovarian dysgerminoma (in a patient with Cowden syndrome), and appendiceal mucinous neoplasm were reported. All of them were > 40 years apart from the patient with Cowden syndrome. While being lower in the young age group (155.7 vs. 177.5 months), disease-free survival (DFS) was not significant between the two groups (p-value = 0.3) (fig. 1).

Subgroup analysis (table 3)

In the subgroup analysis, comparisons between the two (young vs. old) groups in patients with pure DCIS only and in those with DCIS with microinvasion showed significant differences in both BMI (p-value = .008 and .005) and reconstruction (p-value = .002 and .003), where younger patients were slimmer and opted for more reconstructive procedures, respectively.

DISCUSSION

In the USA, Female patients < 40 years old showed a nearly 4-fold increase in the incidence of DCIS from 1975 to 2015 (10); however, in 2017, Nguyen et al. (11) reported an incidence of 2.9% from 2004 to 2014. In 2019, this patient category represented only 2% of newly diagnosed cases, making this population particularly challenging to study due to the low number of cases (12).

Over 15 years of our practice, young female patients represented only one-fifth of the cases diagnosed with DCIS. However, Alvarado et al. (13) reported an incidence of 6.5%, Jhingran et al. (14) reporting 13%, and Vicini et al. (5) reported 21% of patients were < 45 years old.

Presentations of DCIS vary between clinical and radiological, or both, with different orders among publications. For example, Fisher et al. (15) reported that the most common presentation was imaging-only calcifications without a mass in 77.7% of patients, followed by breast mass ± calcifications in 15.6%. Jhingran et al. (14) reported mass lumps in

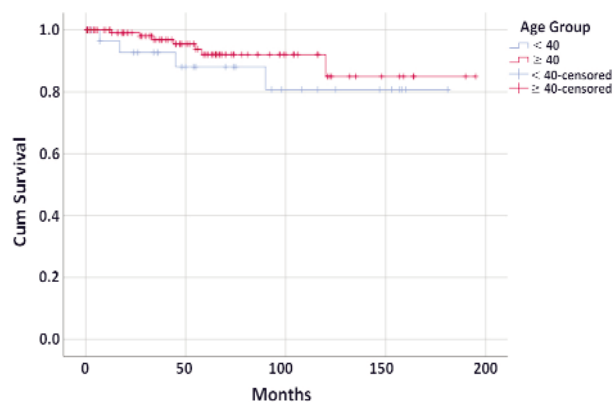


Figure 1 - Kaplan-Meier curve for disease-free survival among the two groups.

Table 2 - Comparison of DCIS cases based on age as young (n = 33) versus old (n = 131)

	Group I (<40 years) 33 cases	Group II (>40 years) 131 cases	Significance
Presentation*			
• Screening	0	1 (0.8%)	
• Palpable mass	27 (81.8%)	103 (78.6%)	
• Nipple discharge	7 (21.2%)	30 (22.9%)	
• Nipple erosion	3 (9.1%)	11 (8.4%)	
Breast density (ACR)			.47
• A	1 (3%)	13 (9.9%)	
• B	4 (12.1%)	24 (18.3%)	
• C	5 (15.1%)	31 (23.4%)	
• D	3 (9.1%)	7 (5.3%)	
Diagnostic Mammography			.12
• No	13 (39.4%)	31 (23.4%)	
• Yes	19 (57.6%)	93 (71%)	
Type of calcifications [†]			.572
• Microcalcifications	6 (31.6%)	37 (39.8%)	
• Macrocalcifications	0	8 (8.6%)	
MRI			.039
• No	21 (63.6%)	106 (80.9%)	
• Yes	10 (30.3%)	19 (14.5%)	
Type of surgery			1
• CBS	6 (18.2%)	23 (17.6%)	
• Mastectomy	27 (81.8%)	108 (82.4%)	
Reconstruction			<.001
• No	17 (51.5%)	118 (90.1%)	
• Yes	16 (48.5%)	13 (9.9%)	
Histologic subtype			.68
• Non-comedo	11 (33.3%)	48 (36.6%)	
• Comedo	20 (60.6%)	68 (51.9%)	
Final pathology			.1
• Pure DCIS	18 (54.5%)	91 (69.5%)	
• With microinvasion	15 (45.5%)	40 (30.5%)	
Pathologic size median (range)	5.5 (2-14) cm	5 (1-14) cm	.223
Final grade			.097
• 1	1 (3%)	20 (15.3%)	
• 2	4 (12.1%)	23 (17.6%)	
• 3	24 (72.7%)	75 (57.3%)	
ER status			.41
• Negative	14 (42.4%)	47 (35.9%)	
• Positive	16 (48.5%)	77 (58.8%)	
Pathologic multicentricity			.37
• No	23 (69.7%)	90 (68.7%)	
• Yes	2 (6.1%)	20 (15.3%)	
Adjuvant radiation			.81
• No	26 (78.8%)	101 (77.1%)	
• Yes	7 (21.2%)	23 (17.6%)	
Adjuvant hormonal**			1
• No	11 (33.3%)	43 (32.8%)	
• Yes	20 (60.6%)	80 (61.1%)	
Recurrence			.23
• No	29 (87.9%)	124 (94.7%)	
• Yes	4 (12.1%)	7 (5.3%)	
Pattern of recurrence***			.606
• Local	1 (25%)	1 (14.3%)	
• Regional	0 (0%)	1 (14.3%)	
• Locoregional	0 (0%)	1 (14.3%)	
• Distant	1 (25%)	3 (42.8%)	
• Locoregional & distant	2 (50%)	1 (14.3%)	
Recurrence pathology			.4
• In-situ	1 (25%)	0	
• Invasive	3 (75%)	6 (85.7%)	
Disease Free Survival median (95%CI) months	155.7 (133.1-178.4)	177.5 (164-191.1)	.3

*Some patients may have more than one presenting symptom

**Minority of patients received hormonal therapy, albeit ER negative depending on PR positivity

***valid percent; †percent regarding the valid cases of diagnostic mammography

Table 3 - Subgroup analysis (the two groups compared according to the result of the final pathology)

Variable	Pure DCIS (N: 109)		p - value	DCIS with microinvasion (N: 55)		p - value
	Young (< 40 years)	Old (≥ 40 years)		Young (< 40 years)	Old (≥ 40 years)	
Number of cases (%)	18 (16.5%)	91 (83.5%)		15 (27.3%)	40 (72.7%)	
Age mean ± SD years	34.4 ± 4	57.4 ± 10.3	<.001	33.2 ± 4.5	54.3 ± 9.6	<.001
BMI median (range)	30 (17.9-37.1)	35.7 (23.8-56.2)	.008	27.6 (25-31.1)	35 (28.7-46.7)	.005
Presentation*						
• Screening	0	1		0	0	
• Palpable mass	14 (77.8%)	68(78.2%)	.96	13(86.7%)	35(87.5%)	1
• Nipple discharge	4(23.5%)	21(23.3%)		3(20%)	9(22.5%)	
• Nipple erosion	2 (11.8%)	8(9.4%)		1(7.7%)	3(7.5%)	
Breast density (ACR)*						
• A	1(12.5%)	11(18.3%)		0	2(13.3%)	
• B	3(37.5%)	19(31.7%)	.97	1(20%)	5(33.3%)	.29
• C	3(37.5%)	24(40%)		2(40%)	7(46.7%)	
• D	1(12.5%)	6(10%)		2(40%)	1(6.7%)	
Diagnostic Mammography*						
• No	6(35.3%)	18(20.9%)	.22	7(46.7%)	13(34.2%)	.53
• Yes	11(64.7%)	68(79.1%)		8(53.3%)	25(65.8%)	
Type of calcifications*						
• Microcalcifications	4(100%)	31(81.6%)	1	2(100%)	6(85.7%)	1
• Macrocalcifications	0	7(18.4%)		0	1(14.3%)	
MRI*						
• No	10(58.8%)	70(81.4%)	.05	11(78.6%)	36(92.3%)	.32
• Yes	7(41.2%)	16(18.6%)		3(21.4%)	3(7.7%)	
Type of surgery						
• CBS	5(27.8%)	17(18.7%)	.36	1(6.7%)	6(15%)	.66
• Mastectomy	13(72.2%)	74(81.3%)		14(93.3%)	34(85%)	
Reconstruction						
• No	12(66.7%)	86(94.5%)	.002	5(33.3%)	32(80%)	.003
• Yes	6(33.3%)	5(5.5%)		10(66.7%)	8(20%)	
Histologic subtype*						
• Non - comedo	6(37.5%)	35(43.75%)	.78	5(33.3%)	13(36.1%)	1
• Comedo	10(62.5%)	45(56.25%)		10(66.7%)	23(63.9%)	
Pathologic size median (range) mm	5.2 (2 - 14)	5 (1 - 14)	.41	5.5 (2 - 9)	5.5 (1 - 12)	.63
Final grade*						
• 1	1(6.7%)	14(16.9%)	.37	0	6(17.1%)	.25
• 2	2(13.3%)	18(21.7%)		2(14.3%)	5(14.3%)	
• 3	12(80%)	51(61.4%)		12(85.7%)	24(68.6%)	
ER status*						
• Negative	8(50%)	28(32.6%)	.25	6(42.9%)	19(50%)	.76
• Positive	8(50%)	58(67.4%)		8(57.1%)	19(50%)	
Pathologic multicentricity#						
• No	12(85.7%)	59(78.7%)	.73	11(100%)	31(88.6%)	.56
• Yes	2(14.3%)	16(21.3%)		0	4(11.4%)	
Adjuvant radiation*						
• No	13(72.2%)	74(85.1%)	.19	13(86.7%)	27(73%)	.47
• Yes	5(27.8%)	13(14.9%)		2(13.3%)	10(27%)	
Adjuvant hormonal***/						
• No	5(29.4%)	25(29.1%)	1	6(42.9%)	18(48.6%)	.76
• Yes	12(70.6%)	61(70.9%)		8(57.1%)	19(51.4%)	
Recurrence						
• No	18(100%)	88(96.7%)	1	11(73.3%)	36(90%)	.19
• Yes	0	3(3.3%)		4(26.4%)	4(10%)	
Pattern of recurrence*						
• Local	0	1(33.3%)		1(25%)	0	
• Regional	0	1(33.3%)		0	0	
• Locoregional	0	0	NA	0	1(25%)	.71
• Distant	0	1(33.3%)		1(25%)	2(50%)	
• Locoregional & distant	0	0		2(50%)	1(25%)	
Recurrence pathology*						
• In - situ	0	0	NA	1(25%)	0	1
• Invasive	0	2(100%)		3(75%)	4(100%)	

*Some patients may have more than one presenting symptom

**A minority of patients received hormonal therapy, albeit ER - negative, depending on PR positivity; # valid percent

only 25% of their patients. In 2013, Vicini et al. (5) reported on 30 cases < 45 years old compared with 115 cases > 45 years old, showing that screening mammography was the most common mode of detection and was used nearly equally in both groups (83.3% in young vs. 90.4% in older patients). Mammographic calcifications were reported in 84.8% of cases (86.7% in the young vs. 84.3% in the old), with the young group showing a higher rate of clinical signs than the old (16.7% vs. 9.6%), although the difference was not statistically significant.

Tesch et al. (4) reported that only 36.8% of their 98 cases showed symptoms at diagnosis, with palpable breast lump observed in 22.4% and radiologic-only features in 52%.

On the other hand, Alvarado et al. (13) reported different patterns of presentation, with statistically significant differences between groups: higher clinical than radiological presentation (56.1% vs. 43.9%) in <40 years old, with breast mass being the most common finding. Conversely, radiological presentation was higher in the older age group (86% vs. 14%).

Regarding our cohort, a breast lump was reported in more than three-quarters of patients, with only one patient detected through screening. This can be explained by the fact that screening mammography is generally not applied to <40 years old females, (4) resulting in most young age patients showing more clinically advanced DCIS. (13) Additionally, the delayed implementation of the breast screening mammography campaign in Egypt until 2019 could be the culprit. However, diagnostic mammography was performed in 71.8% of our cohort and in 57.6% of our younger group, with no statistically significant difference compared with the older group (p -value = .12). All our young patients presented with symptoms, and a breast lump was reported in 81.8% of them. Mammographic calcifications were reported in 47.3% of cases, with the majority (84.3%) being microcalcifications, again with no significant difference among groups (p -value = .572).

Similarly, the same differences among publications can be found regarding tumor biological characteristics. Alvarado et al. (13) reported significantly higher tumor grade, ER-positive status, multicentricity, and multifocality, with no statistically significant difference in size either, mammographically or pathologically, between young and old patients. These unfavorable tumor characteristics in the younger group may be explained by either genetic predisposition or the more advanced clinical presentation, given the fact that this group is generally

below the age threshold for mammographic breast cancer screening, as previously mentioned. Also, Halasz et al. (16) reported significantly larger size and higher grade tumors in young patients <30 years old. In contrast, Vicini et al. (5) reported no statistically significant differences in pathologic calcifications, histologic subtype, or nuclear grade. Similarly, our study showed no significant differences between groups in such parameters, which may be explained, as in Vicini et al. (5), by the relatively low number of young patients in our cohort.

Most patients in both age groups in all of these publications (5,13,16), as well as in our study, there was a trend toward a higher percentage of grade 3 tumors. However, Tesch et al. (4) reported a higher proportion of grade 2 tumors. In fact, it is well known that only 9–12% of DCIS are low grade (17-21).

The comedo architectural subtype was the commonest in our cohort, reported in 59.9% of cases, with no significant difference between groups (60.6% in young vs. 51.9% in old, p -value=.68). Vicini et al. (5) reported a lower incidence of the comedo pattern in 23.6% of cases, with the cribriform pattern being the commonest subtype in 51.4% of cases. The comedo pattern was more frequent at the young age group (30% vs. 20.9%); in contrast, the cribriform pattern was higher at the old age group (53.9% vs. 33.3%). However, no statistically significant difference was reported between groups regarding the pattern. Regarding central necrosis, it was reported in 57.2% of cases, with a higher, though nonstatistically significant, rate in younger than in older patients (73.3% vs. 61%). Alvarado et al (13) also reported the same trend regarding necrosis (44.7% in young vs. 37.2% in old patients).

However, Tesch et al. (4) reported a much lower rate of the comedo pattern in only 3.1% of patients, with the commonest pattern being solid (54.1%), followed by cribriform (25.5%). Comedo necrosis was observed in 35.7 % of patients.

Tesch et al. (4) reported multifocality in 10.2% of their cohort, while Alvarado et al. (13) found that women <40 years had significantly higher rates of both multicentric and multifocal disease than older women (29.3% and 30.1%, respectively). In our study, multicentricity was reported in 16.3% of cases, with no statistically significant difference between the groups (p -value=.37).

DCIS is characterized by its heterogeneous nature and the potential for both recurrence and/or progression to invasive cancer (4), reported in up to 20-30% of patients if not being treated (22). It also carries a

higher risk for breast cancer-related mortality (23,24).

Given the longer life expectancy of younger patients and the greater benefit of risk reduction, multimodality therapy is being pursued, including surgery, adjuvant radiotherapy, and hormonal therapy (25,26). Additionally, the active surveillance strategy is another option that is being investigated through many trials questioning both its validity and the qualified cohort of patients for such an approach (27-31).

The younger population shows some unique considerations in the management of breast cancer, such as increased concerns for possible lower ipsilateral breast cosmesis, overall bilateral breast symmetry, post-treatment quality of life, and the side effects of long periods of hormonal therapy on both fertility and pregnancy (32-34). Also, the high levels of anxiety and the false notion of lower survival benefit following breast conserving surgery (BCS) lead many patients to opt for mastectomy instead (35,36).

However, with the superior cosmetic results, BCS has become the standard of care for DCIS treatment (25,37).

M. Worni et al. (22) found a significant shift in locoregional therapies for DCIS, with the use of lumpectomy combined with adjuvant radiotherapy increased in their cohort by almost 100%, whereas the use of unilateral mastectomy dropped nearly by two-thirds in comparison with past cohorts.

However, Byun et al. (38) reported an increased frequency of bilateral mastectomy in female patients < 40 years old with larger and higher grade pure DCIS tumors from 2004 to 2016, even surpassing BCS since 2010, despite showing no OS benefit. The same trend of increasing bilateral mastectomy use in younger patients was also reported by Halasz et al. (16).

No significant difference was observed among our patients regarding the type of surgery (p -value=1), with fewer than a fifth (17.7%) having a successful BCS. This may be attributed to an increased number of cases referred from rural hospitals, where 30.5% of patients presented after unplanned excisional biopsies without adequate safety margins. Also, the high percentage (79.3%) of patients presented with palpable breast lumps makes it sometimes difficult to preserve the breast. Most tumors were high grade, and another possible cause, until a few years ago, was the concern of a substantial percentage of patients about the safety of BCS in terms of recurrence and survival outcomes, and added to that was the fear of undergoing another surgical intervention (39).

Over-treatment in the form of axillary lymph node

dissection (ALND) was performed in the majority of our patients, which was a common practice in our department until recent years, when a shift towards sentinel lymph node biopsy (SLNB) was commenced (40).

Regarding adjuvant hormonal therapy, it acts as chemoprophylaxis, resulting in reduced risk of both ipsilateral recurrence and contralateral invasive or in situ breast cancer (18,41-45). Therefore, the National Comprehensive Cancer Network (NCCN) guidelines recommend that it can be considered for risk reduction in cases of ER-positive DCIS. (46) In our cohort, nearly two-thirds of patients received adjuvant hormonal therapy; however, no significant difference was noted among the age groups (p -value = 1).

Many clinical trials have confirmed the local control benefit of adjuvant radiotherapy (RT) use after BCS for DCIS, despite showing no effect on overall survival (15,18,47-52). In our cohort, all of our patients who underwent successful BCS, regardless of age group (p -value = .81), received adjuvant RT.

It is worth noting that both the proportional and absolute risk reductions in ipsilateral breast recurrence following adjuvant RT were lower in younger than in older patients, highlighting the influence of age at DCIS diagnosis, an effect that was not confounded by known prognostic factors (37,53). Moreover, there is evidence that adjuvant RT is more likely to reduce the mortality rate in younger than in older women (8,54).

In previous studies, young age at diagnosis, mostly proposed as <40 or <50 years old, was one of the negative risk factors for disease recurrence or progression (5,6). For example, Kong et al. (55) found significantly higher local recurrence (LR) rates in Women <45 years, with significantly lower 5- and 10-year actuarial LRFS 84 vs. 90% and 79% vs. 86%, respectively, compared to those 45-50 years. However, there was no statistically significant difference in invasive local recurrence among groups. Similarly, Alvarado et al. (13) reported 5-year LR rates of 10.1% in women <40 years compared to 3.2% in older women. The 10-year breast tumor recurrence risk was reported as 11.2–31% versus 3–9%. (5,14,56,57).

In our study, recurrence was observed in 6.7% of the entire cohort, with distant recurrence being the most common pattern, followed by combined locoregional-distant, and then local recurrence. Between the two groups, recurrence was more frequent in the young age group (12.1% vs. 5.3%); however, this difference was not statistically significant (p -value = .23). Moreover, there was no

statistically significant difference in the recurrence pattern (p -value = .606). Also, DFS was not significant between the two groups (p -value = 0.3) (fig. 1).

The low incidence of local recurrence in our cohort may be attributed to the high percentage (82.3%) of mastectomies performed. Stuart et al. (25) reported in a meta-analysis of 9,404 DCIS cases with 10-year follow-up that the adjusted meta-regression local recurrence rates were 2.6% for mastectomy, 13.6% for BCS with RT, 25.5% for BCS without RT, and 27.8% for biopsy-only (residual predominantly low-grade DCIS following inadequate excision).

Even after BCS, <45 years women diagnosed with DCIS have a greater risk of local recurrence with different patterns of failure, which is independent of other previously defined risk factors, that are most notable within 10 years of diagnosis (5,58).

Tunon-de-Lara et al. (59) showed that comedo-carcinoma subtype, histological size >10 mm, necrosis, and a positive safety margin were statistically significant predictors of recurrence after BCS in young patients.

Young age has also been associated with a higher breast cancer-specific mortality at 20 years, with the hazard ratio of 2.58 for < 35 years patients (7).

The 20-year risk of breast cancer-related death following diagnosis of DCIS was reported to be 3-fold higher than the general population of the same age, with the standardized mortality ratio for women aged < 40 years being 11.95, which was higher than that for older age groups. (26) It is worth noting that not all women who die of cancer following DCIS experience a local recurrence, suggesting that the current treatment focus on preventing invasive recurrence may be insufficient to eliminate all deaths from breast cancer after DCIS.

As a result of the previously discussed data, young DCIS patients tended to receive more intensive treatment, especially in terms of surgical extent and RT (8,9).

Still, there is a paucity of published articles describing treatment options and outcomes in young patients with DCIS (58,60).

In our study, although some parameters were higher in one group than the other, no statistically significant differences were detected, except for MRI use and breast reconstruction, which were significant among young patients who were more motivated to preserve their breasts.

Strengths and Limitations

Our study has frequent limitations. As a retrospec-

tive study conducted in a single tertiary center with a relatively small number of cases, mainly in the younger group, over an extended period, there is a possibility of missed important data, heterogeneity in assessment and treatment approaches, possible over-treatment, and loss to follow-up. These limitations may have reduced the statistical power of some of our results; therefore, they may not reflect the true impact of age in the larger population. Moreover, our results slightly contradict those of other publications, so caution is warranted when interpreting them in the context of the existing literature. However, this is the first publication from our locality to address this rare issue with such a thorough analysis. Despite limitations, our results stand against pursuing more aggressive treatment in younger patients, such as mastectomy in patients who are candidates for BCS or ALND instead of SLNB. We recommend adherence to the current guidelines with an individualized treatment approach for DCIS patients, regardless of age.

CONCLUSION

One-fifth of our patients with DCIS were less than 40 years old, with recurrence being quite uncommon. The use of Breast-conserving surgery is increasing in our community; however, it is still underutilized. Additionally, MRI and breast reconstruction were more widely used in the younger group. Outcomes were similar, not justifying the use of more aggressive treatment in younger DCIS patients.

Competing Interests

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