



Pure Ductal Carcinoma in Situ: Clinicopathological Experience from a Single Tertiary Care Center

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Abstract Objectives: In this study, we aimed to assess the clinicopathological characteristics and treatment outcomes of pure Ductal Carcinoma *In Situ* (DCIS) at King Abdulaziz University Hospital, in order to better understand its presentation, treatment approaches and rates of recurrence and progression. **Methods:** We conducted a retrospective analysis of 50 female patients diagnosed with pure DCIS from 2010 to 2020. Data on demographics, DCIS characteristics, treatment and outcomes were collected. Statistical analysis involved frequency distribution and descriptive statistics. **Results:** The median age at diagnosis for pure DCIS was 54 years. The median DCIS size was 16 mm and the most common morphological pattern was solid (26%). Grade II was the most frequent nuclear grade (40%), followed by grade III at 34% and grade I at 26%. Central (comedo) necrosis was present in 52% of cases. Regarding hormonal receptor status, 58% of cases were estrogen receptor positive and 44% progesterone receptor positive. Of the 23 cases tested for human epidermal growth factor receptor 2, 20% had positive results and 26% negative results. Negative surgical margins were achieved in 88% of cases. Adjuvant treatment included radiotherapy in 22% of patients and hormonal therapy in 34%. On follow-up, one recurrence and one progression to invasive ductal carcinoma were observed, with no DCIS-related mortality recorded. **Conclusion:** The findings show a low recurrence/progression rate for pure DCIS, consistent with global data indicating that many cases follow an indolent course. The study underscores the need for individualized treatment strategies to balance prevention of progression and avoidance of overtreatment.

Key Words Central (comedo) Necrosis, DCIS Size, ER/PR/HER2, Morphological Pattern, Pure DCIS

INTRODUCTION

Ductal Carcinoma *In Situ* (DCIS) of the breast is a noninvasive breast cancer characterized by the proliferation of malignant ductal epithelial cells that remain constrained inside the ductal-lobular unit, without penetrating the surrounding intact myoepithelial cell layer and basement membrane. DCIS is a diverse disease that exhibits considerable complexity regarding its biological behavior, molecular traits and histopathological features. It serves as a non-obligate precursor to invasive carcinoma, reflecting a range from low to high grades, with varying risks of progression to invasive disease [1].

In the past, DCIS was identified via physical examination, typically manifesting as a palpable mass accounting for 1%-2% of cases [2]. The introduction of breast screening mammograms in the 1990s, however, led to an increase in the prevalence of DCIS, which now represents 20-25% of all breast cancer diagnoses [3,4]. This approach has resulted in the identification of earlier, less aggressive forms of DCIS. Previous studies reported that 85% of DCIS cases detected through screening were asymptomatic, although they could sometimes present as lumps or nipple discharge. DCIS often appears as distortions or microcalcifications on mammograms, with up to 80% showing clustered calcifications with linear branching or casting patterns [2].

The incidence of pure DCIS, which is not associated with invasive mammary carcinoma or metastasis, varies considerably across the globe, ranging from 9.5 to 26%, primarily reflecting the degree of screening mammography implementation [5]. In Saudi Arabia, the incidence rate of pure DCIS is not well defined; however, epidemiological studies from different regions indicate that it ranges from 3% to 8% [6-9].

From a biological and clinical perspective, DCIS that remains confined within the ductal system without an invasive component does not possess the potential to metastasize and, therefore, does not affect the survival rates of women. This finding is supported by studies that have shown that the presence of microinvasion or an invasive component significantly increases the risk of breast cancer-specific mortality and local recurrence, highlighting the non-metastatic nature of pure DCIS [10,11].

Research has shown that between 25 and 60% of untreated DCIS cases can progress to Invasive Ductal Carcinoma (IDC) over a follow-up period ranging from 9 to 24 years. After treatment, the overall recurrence rate of DCIS is approximately 20%. Of these recurrences, about half are *in situ* and the other half are invasive [12,13]. The progression from DCIS to IDC presents a considerable challenge for clinicians, as it remains uncertain which patients with DCIS will advance to invasive disease and how to optimize treatment without unnecessarily overtreating asymptomatic DCIS. Multiple advanced investigations have examined the complex process of progression from DCIS to IDC, proposing four models for this transition: three cell-intrinsic models (independent lineage, evolutionary bottleneck and multiclonal invasion) and one cell-extrinsic model (microenvironment-mediated invasion). The independent lineage model suggests that DCIS and IDC can arise from different initiating cells within the same breast, evolving independently [14,15]. The evolutionary bottleneck concept claims that one or a few dominant clones of DCIS cells possess invasive capabilities and particular genetic mutations, such as Phosphoinositide-3-kinase (PIK3CA) and that they penetrate the basement membrane and invade adjacent tissues [16-18]. The multiclonal invasion model suggests that multiple subclones within DCIS can escape the ducts and migrate into adjacent tissues, establishing invasive carcinomas [16,17,19]. The microenvironment-mediated invasion model, which is cell-extrinsic, involves interactions with the tumor microenvironment, including immune cells, fibroblasts and extracellular matrix components, which facilitate the transition from DCIS to IDC [20]. Each model is supported by varying evidence and it is possible that multiple models may occur simultaneously in different patients or even within the same tumor.

Pathological evaluation to predict the probability of local recurrence following surgery is essential in the management of DCIS. Key parameters include DCIS size, nuclear grade, central (comedo) necrosis and margin status. A high nuclear grade of DCIS and large tumor size correlate with an increased risk of local recurrence and invasive transformation, rendering them significant prognostic factors and emphasizing the need for precise measurement

and classification in the management of DCIS [21,22]. Morphological variations such as comedo, solid, papillary, apocrine and micropapillary DCIS typically have clinical insignificance; nonetheless, their identification and characterization may aid in treatment algorithms [22]. Moreover, numerous studies have classified DCIS into four intrinsic molecular subgroups analogous to those recognized in IDC: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-positive and basal-like. The distribution of these subtypes varies from that observed in IDC. Understanding these molecular subtypes can guide more precise treatment plans and help identify candidates for targeted therapy trials. Comprehensive pathological evaluation is crucial for accurate prognosis and personalized treatment planning in DCIS.

With breast cancer being highly prevalent in Saudi Arabia, understanding the specific characteristics and treatment approaches for pure DCIS is important, yet the incidence and outcomes of pure DCIS in Saudi Arabia are not well documented. We therefore explored the clinicopathological features and clinical outcomes of pure DCIS of the breast in a cohort from a Saudi tertiary center. Our aim was to offer insights into the prognosis and management of pure DCIS in a local population and contribute to its overall understanding in the wider literature.

METHODS

Data Collection

This retrospective observational study was conducted at King Abdulaziz University Hospital and included women diagnosed with pure DCIS between 2010 and 2020.

The study included women of all ages with confirmed diagnoses of pure DCIS based on surgical excision. Patients were enrolled in the study if their medical records encompassed all essential key features to guarantee comprehensive data. To maintain the focus on pure DCIS cases, strict exclusion criteria were applied. Patients were excluded if their records lacked essential information, if they had any invasive carcinoma components or lymph node metastasis, or if they had a history of invasive carcinoma or synchronous contralateral invasive mammary carcinoma. With this approach, we aimed to isolate pure DCIS for clearer insights into its unique characteristics and treatment outcomes.

Ethical approval for the study was granted by the institutional bioethical research committee (Reference number 109-25). Written informed consent from participants was not required in accordance with national guidelines due to the retrospective nature of the study. All participant data were kept confidential and accessible only to the research team to maintain privacy and comply with ethical standards.

The following information was meticulously extracted from medical records: age, sex, DCIS size and morphological pattern, nuclear grade, breast biomarker status, surgical margins, type of surgery performed and whether a Sentinel Lymph Node Biopsy (SLNB) was done or not. We also documented treatment options provided, such as hormonal therapy and radiotherapy. To evaluate

clinical outcomes, we tracked DCIS recurrence and progression to invasive carcinoma and recorded the follow-up period. This comprehensive approach enabled a thorough assessment of factors affecting pure DCIS outcomes.

Statistical Analysis

Data entry was performed by using Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA) and data coding and analysis were conducted with SPSS Statistics, version 27 (IBM Corp., Armonk, NY, USA). Categorical variables are reported as frequencies and percentages and continuous variables are expressed as means and standard deviations for normally distributed data or as medians and interquartile ranges for non-normally distributed data.

RESULTS

After reviewing the anatomical pathology database at King Abdulaziz University Hospital, we identified 1,909 breast cancer cases diagnosed between 2010 and 2020. Among these, 50 were classified as pure DCIS based on surgical excision findings, indicating a prevalence of approximately 3% within this population. All cases involved female patients, with a median age at diagnosis of 54 years (interquartile range: 44.75–58.25 years). Of the 50 patients, 46 (92%) had appropriate follow-up, with a median follow-

up time of 44 months. Most patients (98%) presented with unilateral DCIS, with one showing bilateral DCIS. In terms of surgical treatment, 40% (20 patients) underwent lumpectomy and 60% (30 patients) had a mastectomy. In addition, an SLNB was performed in more than half of the patients (62%).

The median size of DCIS was 16 mm, with a range of 9.5–34 mm. The most common morphological pattern observed was the solid pattern, present in 13 cases (26%), followed by the cribriform pattern in eight cases (16%) (Figure 1A and 1F). Other less frequent patterns observed included apocrine, flat (clinging), papillary and micropapillary (Figure 1B to 1E). In addition, Paget's disease was identified in two cases (4%), one of which coexisted with an underlying solid-pattern DCIS (Figure 1H). DCIS involvement in fibroadenoma was detected in one case (2%) and involvement in papilloma was observed in two cases (4%). In addition, 38% of the specimens exhibited more than one (mixed) morphological pattern. For nuclear grade, 13 cases (26%) were low grade (grade I), 20 cases (40%) were intermediate grade (grade II) and 17 cases (34%) were high grade (grade III) (Figure 2A-C). Moreover, central (comedo) necrosis was observed in more than half of the cases (52%) (Figure 1F). Regarding hormonal receptor status, 29 cases (58%) were ER positive and 22 (44%) were PR positive.

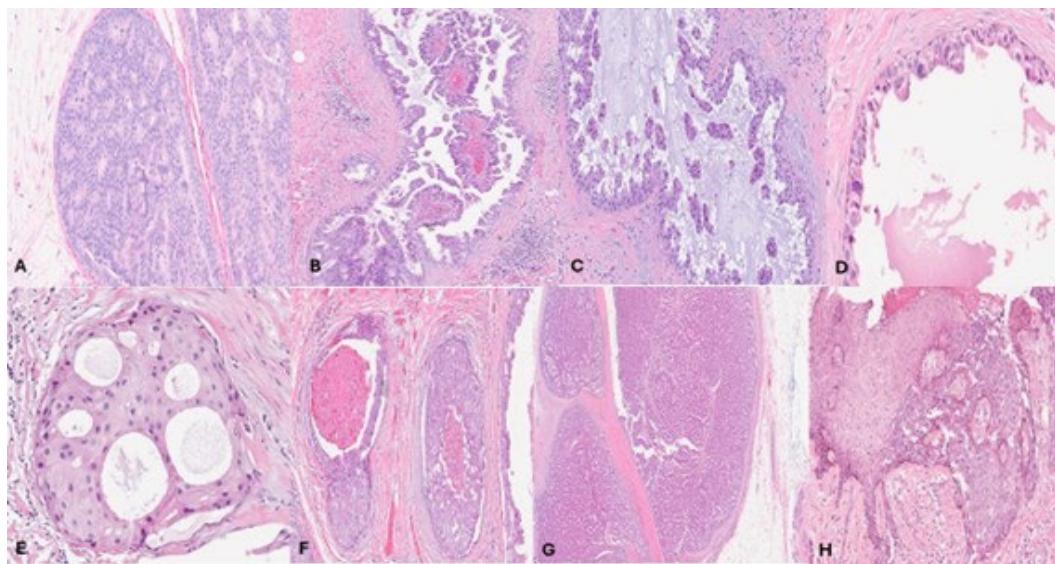


Figure 1: Morphological pattern of ductal carcinoma in situ. (A) Cribriform (H&E, x100). (B) Papillary (H&E, x100). (C) Micropapillary (H&E, x100). (D) Flat (clinging) (H&E, x200). (E) Apocrine (H&E, x200). (F) Solid with central (comedo) necrosis (H&E, x40). (G) Encapsulated papillary carcinoma (H&E, x40). (H) Paget's disease of the nipple (H&E, x100)

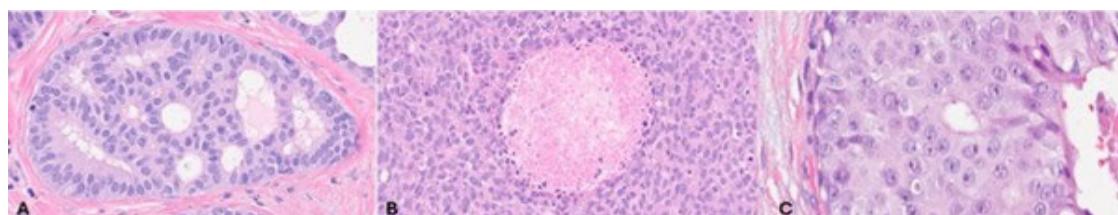


Figure 2: Nuclear Grade of Ductal Carcinoma in Situ (A) Low Grade (I) (H&E, x200) (B) Intermediate Grade (II) (H&E, x200) (C) High Grade (III) (H&E, x400)

Table 1: Patients' Clinicopathological Characteristics and Management Details

Characteristic	Value
Age at diagnosis (years)	54.0 (44.8-58.3)
Follow-up duration (months)	44.0 (23.8-76.0)
DCIS size (mm)	16.00 (9.50-34.00)
Site	
Unilateral	49 (98)
Bilateral	1 (2.0)
Type of surgery done	
Lumpectomy	20 (40)
Mastectomy	30 (60.0)
SLNB	
Yes	31 (62.0)
No	18 (36.0)
N/A	1 (2.0)
Morphological pattern	
Apocrine	1 (2.0)
Clinging	1 (2.0)
Papillary	1 (2.0)
Micropapillary	1 (2.0)
Pure Paget's disease	1 (2.0)
Paget's disease mixed with DCIS (solid)	1 (2.0)
DCIS involving fibroadenoma (cribriform)	1 (2.0)
DCIS involving papilloma (solid and cribriform)	2 (4.0)
EPC	2 (4.0)
Cribriform	8 (16.0)
Solid	13 (26.0)
Mixed morphological pattern*	18 (36.0)
Nuclear grade	
Low (I)	13 (26.0)
Intermediate (II)	20 (40.0)
High (III)	17 (34.0)
Central (comedo) necrosis	
Yes	26 (52.0)
No	24 (48.0)
ER	
Positive	29 (58.0)
Negative	11 (22.0)
N/A	10 (20.0)
PR	
Positive	22 (44.0)
Negative	13 (26.0)
N/A	15 (30.0)
HER 2	
Positive	10 (20.0)
Negative	13 (26.0)
Equivocal	4 (8.0)
N/A	23 (46.0)
Margins	
Positive	4 (8.0)
Negative	44 (88)
N/A	2 (4.0)
Radiotherapy	
Yes	12 (24.0)
No	35 (70.0)
N/A	4 (8.0)
Hormonal therapy	
Yes	17 (34.0)
No	29 (58.0)
N/A	4 (8.0)
Recurrence	
Yes	2 (4.0)
No	44 (88.0)
N/A	4 (8.0)
Death	
Yes	1 (2.0)
No	49 (90.0)
N/A	4 (8.0)

Values are presented as median (interquartile range) or number (%), DCIS:

Ductal Carcinoma *In Situ*; SLNB: Sentinel Lymph Node Biopsy, EPC: Encapsulated Papillary Carcinoma, ER: Estrogen Receptor, PR: Progesterone Receptor, HER2: Human Epidermal Growth Factor Receptor 2, N/A: Not Applicable (data are unavailable). Two or more patterns are involved in one case (solid and cribriform, etc.)

ER status was not available for 10 patients and PR status not available for 15 patients. HER2 status was documented for 23 specimens (46%), 10 (20%) with positive results and 13 (26%) with negative results. Negative surgical margins were achieved in the majority of cases (88%). Regarding adjuvant treatment, only 12 patients (24%) received radiotherapy and 17 patients (34%) received hormonal therapy. Because of the small sample size, no clinically significant differences were observed among the collected clinicopathological variables of DCIS in relation to clinical outcomes.

During the follow-up period of this study, recurrence was observed in two patients (4%). The first case was a 41-year-old woman who initially presented with Paget's disease of the nipple in the right breast, which was ER/PR negative and HER2 positive. Following diagnosis by biopsy, she underwent six cycles of neoadjuvant chemotherapy, consisting of doxorubicin, cyclophosphamide and docetaxel. She subsequently had a right total mastectomy with SLNB, which revealed only (pure) Paget's disease without underlying DCIS, invasive carcinoma, or changes indicating prior invasive carcinoma. However, the skin margin was positive for Paget's disease. She also received radiotherapy. Approximately 2 years later, she experienced a recurrence of Paget's disease in the contralateral breast, this time with underlying high-grade solid and cribriform DCIS featuring central (comedo) necrosis, again ER/PR negative and HER2 positive. She underwent a total mastectomy with SLNB; however, further follow-up data were not available. The second case involved a 40-year-old woman with a 2-cm mass of high-grade solid and cribriform DCIS with central (comedo) necrosis that was ER/PR positive and HER2 negative. She underwent a nipple-sparing mastectomy with SLNB and attained negative margins. She began hormonal therapy, but did not receive radiotherapy. Three years later, she developed grade 2 IDC on the same side, which was ER/PR positive and HER2 negative, accompanied by multiple bone metastases. She was treated with six cycles of chemotherapy and continued hormonal therapy. Unfortunately, follow-up data were unavailable after this point. In our cohort, one patient died from a non-oncological cause during the follow-up period. Histopathological characteristics of DCIS and the treatment outcomes are shown in Table 1.

DISCUSSION

Saudi Arabia currently lacks a comprehensive population-based screening program, which has led to a relatively low incidence rate of DCIS, ranging from 3-8% [6-9]. This trend is evident in our study, where the incidence rate was observed to be 3%, in contrast to the 9.5-26% reported in various international studies [5]. In addition, research indicates that the median age for a diagnosis of pure DCIS is 58 years [23,24], which aligns closely with the median age of 54 years found in our cohort.

The size of DCIS is a critical factor in determining the suitability and strategy for breast-conserving surgery. However, radiological methods such as mammography and ultrasound can often underestimate the true size of DCIS,

complicating surgical planning and the attainment of negative margins. When precise measurement is not feasible, an estimated extent of DCIS can still provide essential clinical insights. The literature reports the median size of DCIS to range between 14 and 27 mm [2,25], with cases varying from as small as 1 mm to extensively involving all four quadrants of the breast. In our study, the median DCIS size was 16 mm, consistent with previously reported figures. For DCIS lesions measuring up to 20 mm, achieving wide negative margins through breast-conserving surgery is generally feasible, facilitating effective treatment while preserving breast tissue [26]. When DCIS measures between 20 and 40 mm, obtaining adequate margins can be more challenging, frequently requiring additional surgical excision [13,27]. For lesions exceeding 40 mm, breast conservation may be impractical, raising the risk of undetected invasive areas if all DCIS regions are not thoroughly assessed. In such extensive disease, lymph node sampling may be recommended to ensure comprehensive treatment [25,28]. The management of DCIS is influenced by the use of SLNB. Routine SLNB is generally not recommended because DCIS is noninvasive and does not typically extend to lymph nodes. Instead, SLNB is frequently implemented to detect invasive carcinoma in the final pathological results in cases with elevated risk, such as those characterized by a larger DCIS size, high nuclear grade, or central (comedo) necrosis, or when a mastectomy is planned. Although the SLNB positivity rate in DCIS cases varies, it is generally low, often below 5% [29]. This low positivity rate has raised concerns that routine SLNB could lead to overdiagnosis and unnecessary treatment, particularly when preoperative evidence of invasive disease is lacking [29,30]. In our cohort analysis, the median size of DCIS for patients who underwent lumpectomy was 15 mm, whereas it was 18 mm for those who underwent mastectomy. The median size of DCIS in cases where SLNB was performed was 20 mm. These findings are consistent with contemporary research, which suggests that greater tumor size increases SLNB use in DCIS management due to the higher likelihood of invasive pathological findings.

There are several distinct morphological patterns of DCIS, such as solid, cribriform, papillary and micropapillary. Groen *et al.* [31] analyzed the prognostic values of pure DCIS in 332 cases from the Netherlands cancer registry and Dutch breast cancer screening program. The findings demonstrated that the dominant growth patterns are cribriform and solid, accounting for 89.8% of cases, compared with less frequent patterns such as clinging, papillary and micropapillary patterns. Notably, cribriform and solid growth patterns were associated with a higher risk of subsequent ipsilateral invasive breast cancer, with a hazard ratio of 3.70 (95% Confidence Interval [CI]: 1.34-10.23), suggesting their significant impact on prognosis. In a UK DCIS I randomized clinical trial of 1,224 cases, it was reported that a solid growth pattern was associated with the highest recurrence risk, with a recurrence rate of 15.2% [32]. Comparatively, micropapillary and cribriform patterns had recurrence rates of 14.3 and 7.3%, respectively. These findings emphasize that the morphological pattern plays a

crucial role in predicting the likelihood of recurrence in patients with DCIS. The UK Sloane Project examined 11,337 primary DCIS cases to determine pathological characteristics and outcomes [25]. The solid pattern was observed in 61% of cases, followed by the cribriform pattern in 51%. The investigators found that the morphological characteristics of DCIS do not predict ipsilateral or contralateral recurrence [25]. Our findings corroborate the results of the aforementioned studies, as the most common histological pattern was solid DCIS followed by cribriform. The nuclear grade of DCIS is a key predictor of disease behavior and prognosis. High-grade DCIS, comprising about 64% of cases in the UK Sloane Project, is linked to higher risks of recurrence and progression to IDC [25], with recurrence rates reportedly being as high as 25% within 12 years [33,34]. In addition, the solid morphological pattern is frequently associated with high-grade DCIS, indicating a more aggressive disease profile and reinforcing the need for careful management [12,35]. Central (comedo) necrosis in DCIS holds clinical significance, as it is often associated with high-grade lesions [25]. The presence of central (comedo) necrosis correlates with a higher likelihood of invasive recurrence, as noted in a study performed by Hanna *et al.* [12], where it was found in up to 30-50% of high-grade DCIS cases. However, assessing central (comedo) necrosis presents challenges due to interobserver variability, with reported discrepancies in its evaluation ranging from 20% to 30%, leading to concerns about the reliability and consistency of its assessment [35].

Our study revealed that an intermediate nuclear grade (grade II) was slightly more prevalent (40%) than a high nuclear grade (grade III; 34%). Notably, we observed that the solid morphological pattern was more commonly linked to a high nuclear grade (grade III; 26%) than to an intermediate nuclear grade (grade II; 20%). Central (comedo) necrosis was found exclusively in cases with intermediate and high nuclear grades, with 73.1% (19 of 26) of these cases exhibiting a solid morphological pattern. The case that recurred and progressed to IDC originally presented as high-grade solid DCIS with central (comedo) necrosis. Overall, these findings emphasize the critical role of nuclear grade, especially when combined with solid morphological patterns and central necrosis, as a significant factor in clinical assessments and treatment planning to effectively manage the risk of progression to IDC.

The clinical significance of ER, PR and HER2 in DCIS is multifaceted and crucial for understanding the prognosis and potential treatment strategies. ER and PR positivity in DCIS generally suggests a more favorable prognosis and indicates potential responsiveness to hormonal therapies, which can reduce recurrence risk [12,35]. On the other hand, HER2 overexpression in DCIS is associated with higher nuclear grade, presence of central (comedo) necrosis and lower ER and PR positivity, indicating a more aggressive phenotype and a higher risk of recurrence and progression to IDC, making it an important marker for identifying high-risk cases [25,33]. In this cohort, we found that 52% (15 of 29) of ER-positive DCIS cases were of intermediate nuclear

grade (grade II), 7% being low nuclear grade (grade I) and 7% high nuclear grade (grade III). Among HER2-positive DCIS cases, 50% (5 of 10) were high nuclear grade (grade III) and the remainder were grades I and II. These findings are broadly consistent with previous study findings. Despite the recognized value of these markers, their standardized application in routine DCIS management remains inconsistent, emphasizing the need for further research and agreement on their role in treatment planning [2,34,36,37].

In this study cohort, 88% of cases attained negative margins, with one case exhibiting recurrence and progression to invasive cancer. Eight percent of the cases revealed positive margins and one of these cases demonstrated recurrence in the contralateral breast. Clear surgical margins, typically defined as no cancer cells at the inked edge of the excised tissue, are associated with a reduced likelihood of local recurrence [25,33]. The standard for what constitutes an adequate margin can vary, with some guidelines recommending a minimum of 2 mm [12]. The presence of positive or close margins (less than 2 mm) is a strong predictor of residual disease and higher recurrence rates, necessitating re-excision or additional treatments [36,38]. Therefore, achieving clear margins during surgical excision is a key goal in the treatment of DCIS to optimize long-term outcomes and minimize the need for further interventions.

The treatment of DCIS remains a topic of debate, particularly regarding the balance between adequate treatment and overtreatment. The current management of DCIS typically involves surgery, with or without radiation therapy, based on the clinical and pathological features of the disease. Hormonal therapy may also be recommended for hormone receptor-positive cases in order to reduce recurrence risk. Chemotherapy is not usually indicated for pure DCIS, but understanding the molecular subtypes can help guide more precise treatment plans and identify potential candidates for targeted therapy trials. In our study cohort, we observed a very low recurrence rate, with only two of 46 (4.3%) followed-up patients experiencing recurrence of DCIS or progression to IDC and none of the cases resulting in disease-related mortality. This finding aligns with the growing evidence that many DCIS cases follow an indolent course and raises the question of whether current treatment strategies may lead to overtreatment in some patients.

Recent trials suggest that active monitoring may be a non-inferior alternative to the current standard surgical treatment for low-risk DCIS. The COMET trial reported that, at 2 years, the rate of ipsilateral invasive breast cancer was 5.9% (95% CI: 3.71%-8.04%) in the surgical group and 4.8% (95% CI: 2.31%-6.00%) in the active monitoring group. No significant differences were observed in mastectomy rates (5.5% vs. 3.7%) or breast cancer-related survival [1]. Long-term follow-up from ongoing trials (COMET, LORD, LORIS, LORETTA) is awaited to further evaluate the safety of active monitoring for low-risk DCIS [39,42].

To better tailor treatment, several predictive tools have been developed to estimate the risk of local recurrence and

progression of DCIS. These tools include the Memorial Sloan Kettering Cancer Center nomogram, the University of Southern California Van Nuys Prognostic Index, the Oncotype DX DCIS score and the NCCN prognostic index. Despite their usefulness, each tool has limitations and none has been established as the definitive standard [37]. Therefore, comprehensive pathological evaluation is crucial for accurate prognosis and individualized treatment planning.

CONCLUSION

This study provides an in-depth look at the clinicopathological characteristics of pure DCIS among Saudi Arabian women in a tertiary care setting. Our examination of factors such as DCIS size, morphological pattern, nuclear grade, ER/PR/HER2 status and treatment outcomes offers valuable insights into the prognosis and management of pure DCIS. This research fills an important gap in the literature by shedding light on the unique presentation and progression of DCIS in this population. By focusing on this group, the study enhances understanding and lays the foundation for future research and tailored clinical approaches in the region. This research may also contribute to the wider literature by adding data from an underrepresented population, enriching the overall understanding of pure DCIS and potentially guiding improved treatment strategies worldwide. Although these findings may enhance diagnostic and treatment strategies, the limited sample size and retrospective design of the study pose limitations that affect the generalizability of the results. Comprehensive, multi-institutional investigations are essential to corroborate these findings and enhance conclusions regarding the management and prognosis of DCIS.

Conflicts of Interest

The authors declare no conflict of interest.

Ethical Statement

Study Approval Statement

Ethical approval for the study was granted by the institutional bioethical research committee of our center (Reference number 109-25).

Consent to Participate Statement

Written informed consent from participants was not required in accordance with national guidelines due to the retrospective nature of the study. All participant data were kept confidential and accessible only to the research team to maintain privacy and comply with ethical standards.

Data Availability Statement

All data related to this research are presented within the manuscript, tables and figures.

REFERENCES

- [1] Sagara, Y. *et al.* "Survival benefit of breast surgery for low-grade ductal carcinoma in situ: A population-based cohort study." *JAMA Surgery*, vol. 150, 2015, pp. 739-745.
- [2] Grimm, L.J. *et al.* "Ductal carcinoma in situ: State-of-the-art review." *Radiology*, vol. 302, 2022, pp. 246-255.

[3] Ernster, V.L. *et al.* "Detection of ductal carcinoma in situ in women undergoing screening mammography." *Journal of the National Cancer Institute*, vol. 94, 2002, pp. 1546–1554.

[4] Kuerer, H.M. *et al.* "DCIS margins and breast conservation: MD Anderson cancer center multidisciplinary practice guidelines and outcomes." *Journal of Cancer*, vol. 8, 2017, pp. 2653–2662.

[5] Wadsten, C. *et al.* "A Validation of DCIS registration in a population-based breast cancer quality register and a study of treatment and prognosis for DCIS during 20 Years." *Acta Oncologica*, vol. 55, 2016, pp. 1338–1343.

[6] Bosaeed, K.M. *et al.* "Cross-sectional descriptive study on the epidemiology of operated female breast tumor cases in a tertiary Hospital of Saudi Arabia." *Saudi Surgical Journal*, vol. 6, 2018, pp. 71–74.

[7] Alamri, A.M. *et al.* "The Pathological pattern of breast cancer in the Najran Region of Saudi Arabia: A Retrospective Study." *Cureus*, vol. 16, 2024, e67621.

[8] Albasri, A. *et al.* "Histopathological features of breast cancer in Al-Madinah Region of Saudi Arabia." *Saudi Medical Journal*, vol. 35, 2014, pp. 1489–1493.

[9] Alnefaie, S.M. *et al.* "Incidence and characteristics of breast cancer in patients 40 years of age or younger." *International Surgery Journal*, vol. 11, 2024, pp. 335–338.

[10] Sopik, V. *et al.* "Impact of Microinvasion on breast cancer mortality in women with ductal carcinoma in Situ." *Breast Cancer Research and Treatment*, vol. 167, 2018, pp. 787–795.

[11] Giannakeas, V. *et al.* "A comparison of two models for breast cancer mortality for women with ductal Carcinoma in Situ." *Breast Cancer Research and Treatment*, vol. 169, 2018, pp. 587–594.

[12] Hanna, W.M. *et al.* "Ductal carcinoma in situ of the breast: an update for the pathologist." *Modern Pathology*, vol. 32, 2019, pp. 896–915.

[13] van Seijen, M. *et al.* "Ductal carcinoma in situ: To treat or not to treat, that is the question." *British Journal of Cancer*, vol. 121, 2019, pp. 285–292.

[14] Casasent, A.K. *et al.* "Multiclonal invasion in breast tumors identified by topographic single-cell sequencing." *Cell*, vol. 172, 2018, pp. 205–217.e12.

[15] Hagio, K. *et al.* "Genetic heterogeneity during breast cancer progression in young patients." *The Breast*, vol. 60, 2021, pp. 206–213.

[16] van der Borden, C.L. *et al.* "Avoiding overtreatment of ductal carcinoma in situ." *Trends in Cancer*, vol. 5, 2019, pp. 391–393.

[17] Casasent, A.K. *et al.* "Genome Evolution in ductal carcinoma in situ: invasion of the clones." *Journal of Pathology*, vol. 241, 2017, pp. 208–218.

[18] Sakr, R.A. *et al.* "PI3K Pathway activation in high-grade ductal carcinoma in situ." *Clinical Cancer Research*, vol. 20, 2014, pp. 2326–2337.

[19] Pareja, F. *et al.* "Whole-exome sequencing analysis of the progression from non-low-grade ductal carcinoma in situ to invasive ductal carcinoma." *Clinical Cancer Research*, vol. 26, 2020, pp. 3682–3693.

[20] Gibson, S.V. *et al.* "Everybody needs good neighbours: the progressive DCIS microenvironment." *Trends in Cancer*, vol. 9, 2023, pp. 326–338.

[21] Ponti, A. *et al.* "Low-grade screen-detected ductal carcinoma in situ progresses more slowly than high-grade lesions." *Breast Cancer Research and Treatment*, vol. 177, 2019, pp. 761–765.

[22] Zhao, M.R. *et al.* "Feasibility analysis of MRI-based radiomics for preoperative prediction of nuclear grading of DCIS." *Gland Surgery*, vol. 12, 2023, pp. 1209–1223.

[23] Cutuli, B. *et al.* "Ductal Carcinoma in situ: A French national survey." *Clinical Breast Cancer*, vol. 20, 2020, pp. e164–e172.

[24] Alaeikhanehshir, S. *et al.* "Effects of contemporary treatment of DCIS on the risk of ipsilateral invasive breast cancer." *Breast Cancer Research and Treatment*, vol. 204, 2024, pp. 61–68.

[25] Shaaban, A.M. *et al.* "Pathological features of 11,337 patients with primary DCIS." *British Journal of Cancer*, vol. 124, 2021, pp. 1009–1017.

[26] Goh, C.W. *et al.* "IDC/DCIS versus Pure IDC." *Journal of Cancer Research and Clinical Oncology*, vol. 145, 2019, pp. 1877–1886.

[27] Song, G. and Y. Zhang. "Breast DCIS with microinvasion." *Chronic Diseases and Translational Medicine*, vol. 9, 2023, pp. 5–13.

[28] Doebar, S.C. *et al.* "Extent of DCIS according to breast cancer subtypes." *Breast Cancer Research and Treatment*, vol. 158, 2016, pp. 179–187.

[29] Al-Ameer, A.Y. *et al.* "Sentinel lymph node biopsy in clinically detected DCIS." *World Journal of Clinical Oncology*, vol. 7, 2016, pp. 258–264.

[30] Davey, M.G. *et al.* "Sentinel lymph node biopsy in DCIS." *BJS Open*, vol. 6, 2022, zrac022.

[31] Groen, E.J. *et al.* "Prognostic value of histopathological DCIS Features." *Breast Cancer Research and Treatment*, vol. 183, 2020, pp. 759–770.

[32] Pinder, S.E. *et al.* "A New pathological system for grading DCIS." *British Journal of Cancer*, vol. 103, 2010, pp. 94–100.

[33] Badve, S.S. and Y. Gökmən-Polar. "Ductal carcinoma in situ of breast: Update 2019." *Pathology*, vol. 51, 2019, pp. 563–569.

[34] Wang, J. *et al.* "Progression from DCIS to invasive breast cancer." *Signal Transduction and Targeted Therapy*, vol. 9, 2024, p. 83.

[35] Schandiz, H. *et al.* "Subtypes of high-grade DCIS." *Breast Cancer Research and Treatment*, vol. 201, 2023, pp. 329–338.

[36] Howard-McNatt, M. *et al.* "Impact of cavity shave margins in DCIS." *Journal of the American College of Surgeons*, vol. 232, 2021, pp. 373–378.

[37] Kunkiel, M. and A. Niwińska. "Van Nuys prognostic index in DCIS." *Scientific Reports*, vol. 11, 2021, p. 22645.

[38] Sigal-Zafrani, B. *et al.* "Histological margin assessment for DCIS." *Modern Pathology*, vol. 17, 2004, pp. 81–88.

[39] Hwang, E.S. *et al.* "Active monitoring for low-risk DCIS: The COMET Trial." *JAMA*, vol. 333, 2024, pp. 972–980.

[40] Elshof, L.E. *et al.* "The LORD Study." *European Journal of Cancer*, vol. 51, 2015, pp. 1497–1510.

[41] Francis, A. *et al.* "The LORIS Trial." *European Journal of Cancer*, vol. 51, 2015, pp. 2296–2303.

[42] Kanbayashi, C. *et al.* "International collaboration of active surveillance trials for low-risk DCIS." *Journal of Clinical Oncology*, vol. 37, 2019, pp. 37, 2019, https://doi.org/10.1200/JCO.2019.37.15_suppl.TPS603