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Original research

The clinical features and management of women with ductal carcinoma in situ with microinvasion: A retrospective Cohort study

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HIGHLIGHTS

- DCISM was associated with comadonecrosis histologic subtype and presence of luminal B type.
- More positive lymph nodes involvement were detected in patients with DCISM.
- Patients with DCISM in the Chinese institution underwent less breast conserved surgery (BCS) and more axillary lymph node dissection (ALND).
- No significantly difference was found in the overall survival rate between patients with DCIS and DCISM after follow-up.

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ABSTRACT

Objective: The purpose of our study is to demonstrate the clinical features and management of patients with Ductal Carcinoma in situ with microinvasion (DCISM) in a single Chinese cancer center.
Methods: Retrospectively analysis of cases between 2003 and 2009 was performed in our institution. The type of treatments, pathological results, and axillary lymph nodes status, hormonal receptor statues (estrogen receptor (ER), progesterone receptor (PR) and Her2) were collected. The disease-free survival rate was calculated from the date of initial diagnosis using the Kaplan–Meier method.
Results: Five hundred and sixty-seven cases were enrolled in our study, 474 pure Ductal Carcinoma in situ (DCIS) and 93 DCISM were included. Among these, 168 (35.4%) was diagnosed with the grade I and 26(5.5%) with grade III in pure DCIS group, compared with 3 (3.2%) and 11(11.8%) with grade I and III in DCISM ($p < .0001$). We also found that DCISM was associated with comadonecrosis histologic subtype ($p < .0001$) and presence of luminal B type (ER/PR positive and Her-2 positive) ($p < .0032$). There were more positive axillary lymph nodes involvement in patients with DCISM than those with DCIS after performing ALND($p = .0284$). Patients with DCISM underwent more axillary lymph node dissection (ALND) in Chinese cancer center than those did in US centers (1.1% VS 47.8–68% and 86.1% VS 3.6–6.9%, respectively). No significantly difference was found in the overall survival rate between patients with DCIS and DCISM during median 100 months follow-up.
Conclusions: In a Chinese cancer hospital, the majority of cases underwent mastectomy and ALDN after the diagnosis of DCISM.The optimal treatments of patients with DCISM should be further investigated.

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1. Introduction

Breast cancer is the most frequent-occurring cancer in China and ranks the sixth leading cause of cancer-related death in Chinese women [1]. Ductal carcinoma in situ (DCIS) of the breast is a noninvasive breast cancer. So far, in China, DCIS has been increasing to 10%–15% of breast cancer and partially due to screening mammography in the women population in recent two decades. Ductal carcinoma in situ with microinvasion (DCISM) is defined as one or several areas of microscopic foci of tumor cells with the invasion of adjacent tissues on the background of Ductal Carcinoma In Situ (DCIS). DCISM is considered as the interim stage between DCIS and invasive ductal carcinoma (IDC) [2]. Although DCISM accounts for less than 1% of all breast cancer, it would progress to IDC if left untreated under the uncertain mechanism [3]. The clinical management of the early stage of breast cancer is critical, because of the potential progression of DCISM converting to more invasive breast cancer.

The definition of DCISM remains controversial, regarding the areas of stromal invasion (1–2 mm) or isolated cell foci less than 10 cells by different organizations [4]. DCIS and DCISM are rare and do not threaten life span, but axillary lymph nodes involvement, distant metastasis and upstaging to IDC should not be ignored during the clinical practice [5,6]. Thus, clinical features, the prognostic results and receptor status were assessed to make decisions for clinical managements of DCISM in the future.

We analyzed the clinical features and survival outcomes of women with DCISM compared with DCIS in China. The aim of our study is to elucidate the status of clinical management of patients with DCISM in a Chinese cancer hospital with during the past six years.

2. Methods

We retrospectively analyzed patients with DCIS who underwent the operation at Tianjin Cancer hospital and institution between February 2003 and April 2009. The data contained the type of surgery, pathological results, axillary lymph nodes procedure (axillary dissection and sentinel lymph node dissection), radiation therapy, chemotherapy and hormonal therapy (HT). The tumor size, histological type, histologic and nuclear grade, hormonal receptor statues (estrogen receptor, progesterone receptor and Her2) were collected. The final pathologic reports were analyzed to identify the invasive parts of DCIS and to categorize pathological types into pure DCIS and DCISM. The infiltration with budding or less than three invasive foci (<2 mm) or one focus was less than 10 cancer cells or invasive foci within the lobule were defined as DCISM. Hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) were performed on axillary and sentinel lymph nodes at our institution. In addition, the data of follow-up regarding recurrence and death in patients was collected. This protocol was approved by the Institutional Ethical Board of Tianjin Cancer Hospital and is compliant with STORBE criteria [28].

The comparison of patients with characteristics and different interventions of DCIS and DCISM were analyzed by SPSS Statistics Version 19.0.0 (IBM, Armonk, NY) using the Chi square test or Fisher exact test for categorical covariates. Time-to-death outcomes (overall survival) were estimated at the date of last follow-up using Kaplan–Meier methods. Overall survival was compared between two groups using the log-rank test. *P* values < .05 were considered significantly.

3. Results

Among total 567 patients, 474 pure DCIS and 93 DCISM were enrolled based on the variable pathological results. The average age of pure DCIS and DCISM were 48 years (median 48 years, range 28–83 years) and 50 years (median 50 years, range 30–75 years), respectively. The median follow-up period was 100 months and ranged from 68 to 132 months. The tumor sizes between these two types of DCIS had no significant difference (Table 1).

Of these, 168 (168/474, 35.4%) was diagnosed with the grade I in pure DCIS group, compared with 3 (3/93, 3.2%) was with grade I in DCISM. There were more patients diagnosed with grade III in DCIS (26/474, 5.5%) than those in DCISM (11/93, 11.8%) ($p < .0001$). We also found that DCISM was associated with comadonecrosis histologic subtype ($p < .0001$) and presence of luminal B type (ER/PR positive and Her-2 positive) ($p < .0032$). In our hospital, women patients with DCISM underwent more axillary dissection and had more positive lymph nodes involvement than DCIS did ($p = .0284$ and $p = .0188$) (Table 2). However, patients who underwent SLN dissection had no significant difference for lymph node involvement between the DCISM and DCIS group($p>.05$). When it comes to lymph nodes dissection therapies, we had more cases with axillary lymph node dissection (ALND) and less with sentinel lymph nodes dissection (SLN) compared to these two therapies in US cancer centers (86.1% VS 3.6–6.9% and 2.2% VS 94.4–100%, respectively) (Table 3).

Among the patients with DCIS or DCISM after modified radical mastectomy and breast conserving surgery (BCS), five (1%,5/503) and two (9.1%,2/22) patients were detected as ipsilateral breast cancer recurrence (IBCR) respectively, during the follow-up period. When comparing treatments of patients with DCISM in different national cancer centers, the data showed that there were less breast conserved surgery (BCS) performed in patients in Chinese cancer center than those in US patient large-volume centers (1.1% VS 47.8–68%) [20,26,27]. In addition, no significant difference of the overall survival rate between patients with DCIS and DCISM was observed after median 100 months follow-up (Fig. 1).

4. Discussion

DCIS and DCISM are not usually palpable during the clinic examination, but could be detected under the mammography by the features of calcification. Core needle biopsy or surgical open biopsy

Table 1
The basic characteristics of patients with DCIS and DCISM in Chinese cancer center.

Factors	No.	Pathological results		P value
		DCIS	DCISM	
No.	567	474(83.6%)	93(16.4%)	
Average age		48	50	
Rang		28-83	30-75	
Diameter				
<=2 cm		224(47.3%)	56(60.2%)	.0236
>2 cm		250(52.7%)	37(39.8%)	
Histological grade				
I		168(35.4%)	3(3.2%)	<.0001
II		280(59.1%)	79(84.9%)	
III		26(5.5%)	11(11.8%)	
Comedonecrosis		18(3.8%)	16(17.2%)	<.0001
Hormonal receptor		314	58	
ER/PR +		187(59.6%)	33(56.9%)	.7716
ER/PR -		182(57.9%)	25(43.1%)	.0438
Her2 ++~+++		152(48.4%)	36(62.1%)	.0635
Triple negative		25(7.9%)	6(10.3%)	.6035
Luminal A (ER/PR + Her2 -)		145(46.1%)	6(10.3%)	<.0001
Luminal B (ER/PR + Her2 +)		25(7.9%)	13(13.9%)	.0032

DCIS:Ductal Carcinoma in situ; DCISM: Ductal Carcinoma in situ with microinvasion; ER: estrogen receptor; PR: progesterone receptor; No.:Number.