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Research Article

Are we Over Treating Ductal Carcinoma in Situ? – Single Center Experience

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Abstract

Background and Aim: Breast cancer is the most common cancer among females worldwide. Ductal carcinoma in situ (DCIS) is a heterogeneous group of neoplastic lesions confined to the breast ducts with the absence of the basement membrane infiltrations. It is usually diagnosed accidently as micro calcifications on mammograms.

Materials and Methods: This is a retrospective cohort study which includes all patients who were managed surgically as cases of DCIS at Royal hospital between 2006 and 2019. Clinicopathological data were collected for all patient. The samples were divided into three groups according to their pathological analysis: Positive margin, close margin (0.1 mm to 1.9 mm), and negative margin group ($\geq$ 2 mm). The recurrence rate for each group was assessed. A p-value <0.05 was considered statistical significant.

Results: 72 patients with pure DCIS were included in the present analysis, the mean age was 47.9 years. Ten (13.0%) patients had a positive margin, 29 (37.7%) patients had a close margin, and 33 (42.9%) patients had a negative margin. There was recurrence in 3 patients) 30%) in positive margin group and 7 patients (70%) had no recurrence. On the other hand, 5 patients (17.2%) in close margin group and 1 patient (3%) in clear margin group had recurrence. The recurrence rate was higher in the non-re-excision group compare to the re-excision group. In univariate analysis, there was a significant difference in IBTR by comparing positive versus close and negative margins of excision (p = 0.040).

Conclusion: The optimal margin for DCIS tumors remain controversial, nonetheless, our study highlighted the importance and the effect of following the current recommendations of a minimal 2 mm margin width in the breast conserving surgery of DCIS. Also, we have concluded that radiotherapy and hormonal therapy cannot replace obtaining a clear margin of $\geq$ 2 mm after breast conserving surgery in DCIS.

Keywords: ductal carcinoma in situ; breast cancer; breast conservative surgery; margin width

Introduction

Breast cancer is the most common cancer among females worldwide. According to a report released by the ministry of health in Oman, which is represented by the National Cancer Registry, in 2017, breast cancer was reported to be the most common cancer in females and the most common lethal cancer among the same category [1].

DCIS is a heterogeneous group of neoplastic lesions confined to the breast ducts that differ in histologic appearance and biological potential. It is defined to be in situ because of absence of the basement membrane infiltrations. The abnormal cells have not spread outside the duct to other tissues of the breast. However, in some cases, DCIS may turn to become invasive cancer and spread to other tissues [2]. There are up to 20-25% increase of new DCIS cases because of the increased awareness and the screening mammography [1]. There are no specific clinical manifestations for patients with DCIS but suspicious microcalcifications on mammography may indicate DCIS.

DCIS is most likely diagnosed accidently on Mammogram as microcalcifications. Although there are some reports which indicate that 70% of pure DCIS will never become invasive cancer, it remains concerning for clinicians as they cannot determine which tumour will remain in its non-invasive status and which will behave otherwise [3, 4]. Another concern is that when DCIS diagnosed in a patient, there is a 20% chance that there is a concomitant invasive focus, and a 30 % possibility

of multifocal disease, making the controversy in treatment more justified [3]. Due to the mentioned uncertainty, the treatment of DCIS widely varies and may include a combination of breast conserving surgery (BCS) with or without radiation, unilateral or bilateral total mastectomy, contralateral prophylactic mastectomy, breast reconstruction, and anti-estragon hormone therapy [5-10]. Given the fact that the number of breast cancer cases diagnosed among the Omani population is increasing, the best treatment option for each cancer stage must be determined in order to adopt the best management and most effective plans, and this includes the management of pure DCIS. So the aim of this study is to determine.

Materials and Methods:

This is a single-institution retrospective cohort study. All patients included are diagnosed with DCIS and were surgically managed and followed up. Our exclusion criteria included patients who had an Invasive component within the DCIS and those who decided to follow up elsewhere.

Data was collected retrospectively from the available electronic medical records (AL Shifa 3 +). All patient who underwent surgical management for DCIS were checked for eligibility before recruiting them in our study. All included participants had standardized data collection as following; Demographic information including age, menopausal status, weight, pregnancy, family history were collected. The clinicopathological data including; presenting complaint, tumour status (single, multifocal, multicentric), margin status (positive, close and negative), factor associated with primary operation selection, re-excision, presence of residual tumour in the re-excision specimens were collected as well. Also, the postoperative chemotherapy and hormonal therapy usage and recurrence rate were gathered.

Initially, our sample included 364, however, after filling in our inclusion and exclusions criteria, 292 patients were excluded. A total of 72 patients were included in this study. The data was analysed using IBM Statistical Package for the Social Sciences (SPSS) 23 computer program. The Sample was divided into three groups according to their pathological analysis either positive margin, close margin (0.1 mm to 1.9 mm), and negative margin group (> 2 mm). The data were expressed as frequencies and percentages. The Chi-square test was used to study the relationship between categorical variables. The recurrence rate for each group was assessed. A p-value < 0.05 was considered statistically significant.

Results:

Table 1, represents clinicopathological data of participants Out of the 364 patients that were diagnosed with DCIS in the given period, 72 patients were included in this study based on the eligibility and the inclusion criteria. The mean age was 47.9 years. The included 72 patients were subdivided into three groups depending on the margin associated with the excision of their tumour. Those were positive margin, close margin of 0.1mm -1.9mm and the negative margin group >2mm. Most of the patient either had a negative margin (45.8%) or a close margin (40.3%) and only 13.9% had positive margin.

Variables		Number	Percentage (%)
Gender	Female	72	100
	Male	0	0
Menopausal status	Pre-menopausal	40	55.5
	Post-menopausal	26	36.1
	Unknown	6	8.4
Family history of breast cancer	Yes	12	16.7
	No	60	83.3
Type of surgery	Mastectomy	25	34.7
	BCS	47	65.2
Margin	Positive	10	14.0
	Close	29	40.2
	Negative	33	45.8
Re-excision	Yes	19	26.4
	No	53	73.6

Table 1: *Clinicopathological data of participants*

As it is shown in table 2, There was recurrence in 3 patients) 30%) in positive margin group and 7 patients (70%) had no recurrence. On the other hand, 5 patients (17.2%) in close margin group and 1 patient (3%) in clear margin group had recurrence. However, the majority in close and negative margin had no recurrence. In univariate analysis there was a significant difference in IBTR by comparing positive versus close and negative margins of excision (p=0.04).

Variables		No Recurrence	Recurrence	P Value
Margin	Positive	7 (70.0%)	3 (30%)	0.04
	Close (0.1 mm to 1.9 mm)	24 (82.8%)	5 (17.20%)	
	Negative (>2mm)	32 (97.0%)	1 (3%)	

Table 2: *Recurrence rate among different group based on the margin status*

Table 3 subdivide patients who have positive or close margin into 2 groups and look for the recurrence rate. Group 1, those who underwent re-excision and group 2 did not go for re-excision. A total of 39 patients had either positive or close margin. Out of those patients, 19 patients had re-excision & 20 patients did not have re-excision. The recurrence rate was higher in the non-re-excision group compare to the re-excision group. Out of 19 patients who had re-excision, only one patients had recurrence. Sven out of twenty patients in Non-re-excision group had recurrence. P value was statically significant (0.002) when comparing patient who had either positive or close margin in non-re-excision group.

Variables			No Recurrence	Recurrence	*P* Value
Group1(Re-excision)	Margin	Positive	**6 (100%)**	**0 (0%)**	0.061
		Close	**12 (92.3%)**	**1 (7.7%)**	
Group2(Non re-excision)	Margin	Positive	**1 (25%)**	**3 (75%)**	0.002
		Close	**12 (75%)**	**4(25%)**	

Table 3: *Recurrence rate in patients who had Re excision and those who did not underwent Excision*

As showed in table 4, radiotherapy is decreasing the local recurrence rate in close margin group. However, there is no significant difference in the recurrence rate whether radiotherapy or hormonal therapy were given or not

Variables		No Recurrence	Recurrence	*P* Value
Radiotherapy	yes	17 (85%)	3 (15%)	0.6
	No	7 (77.8%)	2 (22.2%)	
Hormonal Therapy	Yes	8 (80%)	2 (20%)	0.002
	No	16 (84.2%)	3 (15.8%)	

Table 4: *Recurrence rate in patients with close margin and underwent Adjuvant therapy.*

Discussion:

The overall findings of long term treatment and outcome of DCIS showed that the more aggressive and combined the treatment, the lesser chances there are for local recurrence of DCIS. Globally, studies have shown that patients who underwent mastectomy or had a re excision due to positive or close margins, followed by adjuvant chemotherapy, ended up with lower recurrence rates [3]. In this study, the observation long term outcome was in agreement with international data. The overall recurrence was noted in 9 patients (12.5%), around 44.5 % of the recurrence were invasive cancer and 55.5 % recurred as DCIS. A meta-analysis from the United States which included 2996 patients with pure DCIS showed that the recurrence rate was 12.1 % which is equal to the recurrence rate in our study [3].There are several demographic, clinical and pathological variables which are related to local control of DCIS. The margin width is the only factor that can be controlled by the surgeon to prevent the local recurrence of DCIS. Several studies report that larger margin width is associated with lower recurrence rate [7, 11-15]. As it is observed in this study, r-excision of closed margin decreases the recurrence rate comparing to non-re-excision with statistically significant P value of 0.002. Other factors that contribute to reduction in the rate of recurrence includes further treatment with a combination or radio and chemotherapy, or radiotherapy alone. The same previous study showed that the width of margin is strongly associated with recurrence in women who did not receive radiotherapy, however, with women who received RT, there was no significant association [12]. There is a significant reduction of 28 to 13% in ipsilateral event with the use of radiotherapy [3]. The main area of controversy is the close margin. Dunne C et al reported that re excision of close margin reduces the risk of further requirement of surgical intervention [2]. In our study, the recurrence rate in close margin group was 17.2%, however, patients who underwent re-excision had lower recurrence rate. This supports the fact that the wider the width margin is along with radiotherapy are considered as important factors in determining the risk factors of recurrence.

Potential limitation of this study is includes it being a retrospective analysis which is carried out at a single centre study with a small sample size. The study was carried on a prolonged duration of 14 years, and so the operating surgeons and their techniques differed. Also, the sample size is low. Surgical management of DCIS and its involved margins remains controversial and is still undergoing extensive research. Further evidence and data is required in order to obtain convincing results.

Conclusion:

In our study we highlight the importance of obtaining a negative 2mm margin in the management of DCIS tumours. Since our data supported the statement mentioned above, this concludes that we are not over treating DCIS surgically. We also conclude, that patients with a close margin have reduced chances of developing local recurrence if they received? Neoadjuvant radiotherapy. However, radiotherapy and hormonal therapy cannot replace obtaining clear margin of > 2mm after breast conserving surgery in DCIS.

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