

Breast Ductal Carcinoma In Situ with Microinvasion: Clinicopathological Characteristics, Prognosis and Role of Surgery in Treatment

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Abstract

Background: Advances in screening have led to almost half of the reduction in breast cancer mortality. Precocious diagnosis increasingly needs clinicians to better treat early breast diseases, such as DCIS, or DCIS with microinvasion (DCIS-Mi). Due to the increasing prevalence of DCIS-Mi. In this review, we will focus on study this entity and define current treatment options, especially the role of surgical approach in the overall treatment of DCIS-Mi to explore the current and future optimal management of DCIS-Mi.

Methods: A PubMed search for relevant articles was performed using the following keywords by MeSH and free-word: breast cancer, DCIS, DCIS-Mi, microinvasion, invasive ductal carcinoma (IDC), clinicopathological characteristics, prognosis and treatment.

Results: Until 1997, the American Joint Committee on Cancer (AJCC) defined DCIS-Mi as a tumor with an area of invasion less than or equal to 1 mm as T1mic in the TNM staging system. Histologically, two distinct types of DCIS-MI was classified. Comedocarcinoma subtype of DCIS, the larger the size of a tumor's DCIS component and multicentric foci of DCIS are more commonly associated with microinvasion. The roles of surgery in treatment of DCIS-Mi includes breast-conserving surgery, mastectomy, and surgical evaluation of the axilla. Current guidelines from the National Comprehensive Cancer Network (NCCN) recommend treating DCIS-Mi following surgery guidelines for DCIS. The overall prognosis of DCIS-Mi is excellent with survival at 5 years.

Conclusions: An supposition of current available data indicates no survival benefit to an individual undergoing mastectomy versus lumpectomy and radiation (breast-conserving surgery). Whenever possible, breast-conserving therapy is the treatment of the first choice of DCIS-Mi. Among those unfavorable factors, the key factor is the ability to achieve negative final pathologic margins. Surgical assessment of the axilla, such as sentinel lymph node biopsy on all DCIS-Mi is recommended.

Introduction

In order to favour precocious cancer detection and early diagnosis-the recognition of symptomatic cancer at an early stage, and screening in a target population of apparently healthy individuals will improve outcomes for all breast cancer (BC) patients [1]. Screening have resulted in a dramatic shift that ductal carcinoma in situ (DCIS) accounted for a only 1% of all breast cancer diagnoses more than 20 years ago represented nearly 20% of new cases today [2]. Efforts in precocious cancer detection and early diagnosis have also resulted in almost half of the reduction in breast cancer mortality. Precocious diagnosis increasingly needs clinicians to better treat early breast diseases, such as DCIS, or DCIS with microinvasion (DCIS-Mi). DCIS-Mi is a subtype of DCIS and display a small number of tumor cells invade the ductal basement membrane. Clinically, DCIS-Mi presents as microcalcifications, a palpable lump, Paget's disease, or as serous or bloody nipple discharge [3,4]. Due to the increasing prevalence of DCIS-Mi, in this review, we will focus on study this entity and define current treatment options, especially the role of surgical approach in the overall treatment of DCIS-Mi to explore the current and future optimal management of DCIS-Mi.

Definition & clinicopathological characteristics of DCIS-Mi

The definition of DCIS-Mi changes in the different literature published in different time. DCIS-Mi ever was defined as DCIS with an invasive component of less than or equal to 2 mm [5,6]. Until 1997, the American Joint Committee on Cancer (AJCC) defined DCIS-Mi as a tumor with an area of invasion less than or equal to 1 mm as T1mic in the TNM staging system [7,8]. Nowadays, it is most widely accepted as DCIS with an area of focal invasion 1 mm or less in diameter by the majority of pathologists and clinicians [9,10]. According to the definition of DCIS-Mi, It is important to distinguish DCIS-Mi from another premalignant and malignant breast lesions, such as DCIS and invasive breast cancer.

Histologically, DCIS-Mi shows as clusters of neoplastic cells infiltrating the periductal stroma or occasionally as a projection of neoplastic cells through a disrupted basement membrane in continuity with the DCIS. Microinvasive component tend to be accompanied by a stromal response consisting of scattered chronic inflammatory cells arranged with pale staining loose arrays of new collagen [5,11,12]. The stromal inflammatory response often can result in a definitive diagnosis of microinvasive component difficult. Serial sectioning and the labeling of basement membrane or myoepithelial cells with immunohistochemical markers may contribute to identify the microinvasion. Occasionally, the microinvasive component cannot be definitively identified and usually be categorized as "possible microinvasion" [5,13]. Two distinct types of DCIS-MI was classified by Mascarel et al. Type 1 with a single site of infiltration beyond the basement membrane behaves similar to DCIS and treats as DCIS. Type 2 with numerous clusters of microinvasion shows a worse prognosis and needs to be treated more aggressively [14]. Schwartz et al. demonstrated that comedocarcinoma subtype of DCIS are more commonly associated with microinvasion [15]. Silverstein et al. revealed that the larger the size of a tumor's DCIS component, the more likely it is to harbor a focus of microinvasion [16]. In a palpable DCIS mass, microinvasion was more likely found and positive axillary lymph nodes were more likely manifested [17]. Schwartz et al. noted microinvasion is more common in multicentric foci of DCIS [15]. In the AJCC classification system, only the largest focus of microinvasion was

considered in cases with multiple sites of DCIS-Mi and the total tumor burden does not be accounted. The increasing evidences published showed that the number of foci of microinvasion and the entire tumor burden of microinvasion may affect the metastatic nature of the lesion and need be brought into treatment strategies [11,12].

Role of surgery in management

Similar to pure DCIS and small invasive tumors, the roles of surgery in treatment of DCIS-Mi includes breast-conserving surgery, mastectomy, and surgical evaluation of the axilla. Current guidelines from the National Comprehensive Cancer Network (NCCN) recommend treating DCIS-Mi following surgery guidelines for DCIS.

Breast-conserving surgery

Breast-conserving surgery is the most common surgical treatment for DCIS-Mi. After wide local tumor excision, radiation therapy is used to treat the remainder of surrounding breast tissue [18,19]. For stage I and II breast carcinomas, lumpectomy and radiation had the same rate of survival as that of mastectomies [18,20,21]. But the data looking specifically at whether mastectomy is superior to lumpectomy and radiation for DCIS-Mi are limited. Solin et al revealed that the median time of local recurrences for DCIS-Mi was 42 months (mean 53, range 20 to 116), after breast-conserving surgery. The majority of the local recurrences for DCIS-Mi was invasive carcinoma. For local recurrence alone, 80% was invasive ductal carcinoma recurrence, and 20% was intraductal recurrence [22].

Several factors contribute to predict the incidence of local recurrence and unfavorable conditions to perform breast conservation. One of the important factor of local recurrence was the final pathologic margins were unknown, positive, or close and lower to negative final pathologic margins [23]. The significance of obtaining pathologic negative margins was emphasized at the time of resection or reexcision to optimize local control. If pathologic negative margins cannot be definitively obtained, a mastectomy may be better choice. Pathologic characteristics were also another important factor to affect the incidence of local recurrence. Among the pathologic characteristics, comedo subtype and high nuclear grade of the non-invasive and the invasive component have increased incidence of local recurrence [4].

Mastectomy

When the contraindications of breast-conserving surgery exist, a mastectomy of DCIS-Mi would be recommended. these contraindications include the breast or chest wall undergone radiation therapy, scleroderma, a noncompliant patient, pregnancy, diffuse microcalcifications, multicentric foci, male sex, the inability to obtain pathologic negative margins. A sizable cosmetic deformity is also significant consideration. Another clear factor favoring mastectomy is patient preference. Recurrence after a mastectomy of DCIS-Mi with negative lymph nodes is less than 1% [24].

Surgical evaluation of the axilla

Surgical evaluation of the axilla is another controversial issue in the treatment of DCIS-Mi. Once tumor cells violated the basement membrane, there exited the possibility of lymph node metastases. The question is whether the risk of axillary involvement is high enough to warrant the morbidity of axil-

lary examination. Nowadays, hematoxylin and eosin staining is the standard examination of lymph nodes. In DCIS-Mi patients, systemic treatment is typically dictated by nodal status. Inability to perform surgical evaluation of the axilla could result in significant understaging, altered treatment strategies, and increased probability of local and systemic recurrence [25].

Prognosis

The overall prognosis of DCIS-Mi is excellent with survival at 5 years to be between 97% and 100%. The survival of the DCIS-Mi was intermediate between the DCIS without microinvasion and invasive ductal carcinoma with node negative [22,26]. Triple-negative DCIS-Mi more associated with high rates of tumour recurrence, especially invasive recurrence [27,28].

Conclusions and future directions

There are several suggestions for DCIS-Mi based on this review. The current DCIS-Mi comprehensive treatment strategy scenario appears dynamic and heterogeneous. An supposition of current available data indicates no survival benefit to an individual undergoing mastectomy versus lumpectomy and radiation (breast-conserving surgery). Whenever possible, breast-conserving therapy is the treatment of the first choice of DCIS-Mi. Unfavorable pathologic characteristics should be paid close attention, and among those unfavorable factors, the key factor is the ability to achieve negative final pathologic margins. Since adjuvant therapy for DCIS-Mi is based on the absence or presence of metastasis in the axilla, surgical assessment of the axilla is recommended. Thus, firstly, performing sentinel lymph node biopsy on all DCIS-Mi is also recommended.

In the current era of precision medicine, considering the growing value of pathological, molecular, and genomic peculiarities in defining the prognosis of DCIS-Mi, the research view should always focus on predicting the selected class of risk, for guiding breast surgeons in clinical practice, recognizing the future perspective of soft computing technologies and machine learning algorithms' role in clinical decision-making. The challenge in DCIS-Mi is to reach a balance between the risks of overtreatment versus undertreatment, and future research has the task of providing solid results that allow outlining rigorous recommendations in DCIS-Mi management, especially in axillary surgery strategy. The goal is to choose a better care strategy and minimise unnecessary overtreatments, preventing the related unfavourable effects and promoting an improvement in patients' well-being and quality of life.

Declarations

Conflicts of interest: The authors declare no conflict of interest.

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