

Current controversies in the treatment of ductal carcinoma in situ of the breast



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The incidence of ductal carcinoma in situ (DCIS), a noninvasive form of breast cancer, has increased markedly in recent decades, and DCIS now accounts for approximately 20% of breast cancers diagnosed by mammography. Laboratory and patient data suggest that DCIS is a precursor lesion for invasive cancer.

Controversy exists with regard to the optimal management of DCIS patients. In the past, mastectomy was the primary treatment for patients with DCIS, but as with invasive cancer, breast-conserving surgery has become the standard approach. A mini-review of the management of ductal carcinoma in situ is presented, and the roles and dilemmas of surgery, radiotherapy and endocrine therapy are discussed.

KEY WORDS: Breast, Ductal carcinoma in situ, Treatment.

Background

Ductal carcinoma in situ (DCIS) of the breast includes a heterogeneous group of malignant epithelial proliferations confined within the basement membrane of the mammary ducts¹⁻⁶.

Widespread use of screening mammography has resulted in a progressive increase of the incidence of DCIS over the last twenty years and today these lesions comprise 15–25% of all breast cancers detected at population screening programs. There is an estimate of more than 42,000 new cases diagnosed in the United States every year^{2,6}.

The lesions can be sub-classified according to the nuclear grade, presence of necrosis or architectural appearance. No single classification scheme has been universally accepted, and experts disagree as to which is the most reproducible. Moreover, many physicians favor classifica-

tion schemes that also have prognostic capabilities⁷⁻⁹. Although the natural history of DCIS remains unknown, it is estimated that approximately one third of low grade lesions develop into invasive carcinoma after 30 years if left untreated^{10,11}.

Management options

Currently available management options include mastectomy, local excision combined with radiation therapy, and local excision alone (Tab. I). However controversy exists with regard to the optimal management of DCIS patients^{12,15}.

Total mastectomy vs Breast-conservation surgery

Surgical treatment is aimed at complete removal of the entire lesion in order to minimize the risk of subsequent invasive or in situ recurrence.

The optimal cosmesis is a complementary goal of the different options for local control which include mastectomy and conservative surgery followed or not by radiotherapy.

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Fig. 1: Final result in a 39 year old woman which had right quadrantectomy with oncoplastic technique (the round block technique) for localized DCIS in periareolar zone .



Fig. 2: Final result in a 36 year old woman had right skin-sparing mastectomy with sentinel node biopsy and immediate reconstruction by prosthesis followed by reconstruction and tattooing of the nipple areola complex for extensive DCIS with microinvasive foci; contralateral additive mastoplasty

TABLE I - Therapeutic Options in DCIS.

-
- Breast-conservation surgery alone
 - Breast-conservation surgery + radiotherapy
 - Mastectomy±reconstruction
-

Total mastectomy allows more effective local control than breast-conservation surgery (BCS) and, in the past, has been considered the primary treatment for patients with DCIS. Silverstein et al. reported a disease-free survival (DFS) rate of 98% for mastectomy compared with 81% for BCS plus RT¹⁶.

Although a meta-analysis of studies published up to 1998 by Boyages confirms the reduction in recurrence rates with mastectomy versus breast-conserving surgery (1.4% for mastectomy versus 8.9% and 22.5% respectively for lumpectomy alone and lumpectomy with radiation), the lack of a difference in overall survival between these approaches has led to a decline in the use of mastectomy^{16,17}.

The use of breast-conservation therapy in the treatment of DCIS has thus progressively increased from 26% in 1983 to 60-75% in 2000, and today it is considered the standard surgical approach in the majority of patients¹⁵. However, in case of larger lesions or small-size breasts, the removal of adequate volumes of breast tissue to achieve tumor-free margins and reduce the risk of local relapse may compromise the cosmetic outcome, causing unpleasant results. In order to address this issue, also in the surgical treatment of DCIS, new surgical techniques, so-called oncoplastic techniques, have been introduced in recent years to optimize the efficacy of conservative surgery both in terms of local control and cosmetic results¹⁸. These new techniques may allow removal of larger amounts of breast tissue with safer margins without compromising the cosmetic outcome (Fig. 1).

Indications for mastectomy are limited to patients with

TABLE II - Breast-conservation surgery in DCIS.

-
- | Indications |
|--------------------------------------|
| - Absence of extensive multifocality |
| - Absence of multicentricity |
-

TABLE III - Mastectomy in DCIS.

-
- | Indications |
|---|
| - Large lesions or multiple tumors |
| - Diffuse malignant-appearing microcalcifications |
| - Extensive multifocality |
| - Multicentricity |
| - Persistent positive margins |
-

multicentric disease, large lesions, inadequate margins after BCS, other contraindications to breast conservation, or a personal preference for mastectomy (Tables II and III)¹⁵.

All patients requiring or requesting total mastectomy for DCIS should be offered the option of immediate breast reconstruction (IBR) which is associated with a psychological benefit, a similar oncological outcome and a superior cosmetic result. IBR is facilitated by skin-sparing mastectomy (SSM) approaches and the use of prosthesis (Fig. 2) and autologous tissue for volume replacement¹⁵.

Breast conservation surgery alone vs breast conservation surgery + RT

Controversies exist in the treatment of DCIS around the need for adjuvant radiotherapy after adequate local excision of localized lesions.

Three prospective randomized trials (the NSABP B-17, EORTC 10853, and the UK Coordinating Committee on Cancer Research trial) have all shown a consistent benefit in local control with the addition of radiation therapy^{19,27}. In the NSABP B-17 study, 818 women with DCIS were assigned to receive lumpectomy or lumpectomy combined with radiation therapy. After 12 years of follow-up, the cumulative incidence of invasive and noninvasive ipsilateral breast tumors combined was 31.7% in the lumpectomy-alone arm and 15.7% in the lumpectomy-plus-radiation arm. No significant differences emerged in the 12-year overall survival (86% for patients in the lumpectomy group and 87% for patients in the lumpectomy and radiation therapy group)²⁰.

The EORTC and the UKCCR trial also indicated a significant benefit in the reduction of ipsilateral breast tumour recurrence events (invasive or DCIS) with the use of adjuvant RT. Adjuvant RT reduced the risk of ipsilateral DCIS and ipsilateral invasive cancer respectively by 64% and 55%. Patients with high-grade DCIS lesions and positive margins benefited most from the addition of radiation therapy^{22,27}.

Nonetheless, several Authors have advocated for the use of the lumpectomy alone in low-risk patients. Schwartz et al. performed lumpectomy alone in 224 patients with low-risk DCIS (size of less than 2–3 cm, absence of invasion, margins greater than 10 mm, localized disease, low nuclear grade, probable good cosmetic result); after a median follow-up of 52 months, the recurrence rate was 19.7%¹⁵.

In the effort to help to decide the optimal treatment and to identify a subgroup of patients who could be safely spared adjuvant RT and its potential complications, Silverstein et al. designed a prognostic index (the University of Southern California/Van Nuys Prognostic Index) which combines tumour size, margin width, age, nuclear grade and the presence/absence of necrosis (Tables IV-V)^{28,29}.

Using a prospective database of 706 women who received BCS for pure DCIS, no statistical difference was shown in the 12-year local recurrence free survival rates in patients at low risk of VNPI score (4 to 6), regardless of whether or not RT was used. Patients with an inter-

TABLE IV - The Van Nuys Prognostic Index (VNPI).

Score	1	2	3
Size	≤15 mm	16-40 mm	≥41 mm
Margins	≥10 mm	1-9 mm	<1 mm
Pathology	Non HG without necrosis	Non HG with necrosis	HG with or without necrosis
Age	>60aa	40-60 aa	<40 aa

TABLE V - The Van Nuys Prognostic Index (VNPI).

Score	4,5,6	7,8,9	10,11,12
Recommended Treatment	Local excision alone	Local excision + RT	Mastectomy

TABLE VI - Sentinel lymph node in DCIS.

Indications
- Large tumors
- Presence of micro-invasion
- Mastectomy

mediate VNPI score (7 to 9) showed a statistically significant 12% to 15% local recurrence-free survival benefit when treated with RT^{28,29}.

Patients with high VNPI score (10 to 12) although showing the greatest absolute benefit from RT, experienced local recurrence rates of almost 50% at 5 years. According to these observations, RT could be omitted in patients with a low VPNI score while mastectomy should be considered as the optimal treatment in patients with a VPNI score of 10 to 12.

However, until further prospective studies provide a definitive answer to this question, radiation therapy should be recommended after lumpectomy for all patients without contraindications.

Management of axilla

As concerns the need for axillary dissection, it unanimously agreed that it should be avoided in patients with pure DCIS, owing to the very low incidence (1-2%) of axillary metastases. Sentinel-lymph-node mapping has been proposed in selected cases. In a recent study by Klauber-DeMore and colleagues, sentinel lymph node biopsies were positive in 5/38 patients with high-risk DCIS (13%) and in 5/36 patients who had DCIS with microinvasion (14%)³⁰. Even though clear recommendations do not exist at present time, sentinel node mapping can be considered for selected patients with a higher likelihood of occult microinvasive cancer, high-grade ductal carcinoma in situ, palpable masses or in patients undergoing mastectomy (Tab. VI)³⁰⁻³⁴.

Role of tamoxifen

The role of tamoxifen in the management of DCIS was addressed in the NSABP B-24 trial, in which 1804 women with DCIS were treated with excision and radiation and randomized to tamoxifen 20 mg daily or placebo.

bo for 5 years. Tamoxifen appears to significantly decrease the risk of local recurrence in estrogen receptor positive patients treated with local excision and radiotherapy. Therefore, tamoxifen is often offered to patients with hormone receptor positive DCIS, especially younger patients if the benefit is thought to outweigh the risk³⁵⁻³⁸.

Conclusions

DCIS is a heterogeneous disease which may be a precursor of invasive breast cancer. The incidence has increased markedly in recent decades. Currently available treatment options include mastectomy, local excision combined with radiation therapy, and local excision alone. The optimal management of DCIS is controversial, especially concerning the need for adjuvant radiotherapy after local excision and the role of endocrine therapy so that every treatment should be personalised and entail a systematic and rigorous multidisciplinary approach.

Riassunto

Il carcinoma duttale in situ della mammella è una malattia estremamente eterogenea e può essere un precursore del carcinoma invasivo; l'incidenza è progressivamente aumentata negli ultimi anni grazie alla diffusione dei programmi di screening rappresentando al momento circa il 20% dei tumori diagnosticati mammograficamente. Le opzioni di trattamento disponibili includono la mastectomia, l'escissione locale combinata con la radioterapia e la sola escissione chirurgica. Al momento il trattamento ottimale è ancora controverso soprattutto riguardo la necessità della radioterapia e dell'ormonoterapia. Gli Autori presentano una mini-review sul trattamento del DCIS analizzando il ruolo della chirurgia, della radioterapia e dell'ormonoterapia.

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