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REVIEW

Current management of DCIS: a review

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Abstract Ductal carcinoma in-situ (DCIS) is a heterogeneous disease, in terms of its radiological characteristics, histological morphology and molecular attributes. This diversity is reflected in its natural history and influences optimal treatment strategy. A significant proportion of DCIS lesions behave in a clinically benign fashion and do not progress to invasive disease. Reliable identification of these patients could allow treatment to be less radical or safely omitted. Management should be tailored to the individual within the context of a multidisciplinary team. Approaches such as biological profiling and molecular analysis represent an opportunity to improve our understanding of the tumour biology of this condition and rationalise its treatment. This article reviews the management strategies for DCIS in the context of recent randomized trials, including the role of sentinel lymph node biopsy, adjuvant radiotherapy and tamoxifen.

Keywords Ductal carcinoma in-situ · Local recurrence · Lumpectomy · Management · Margins · Mastectomy · Radiotherapy · Sentinel lymph node biopsy · Tamoxifen

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Introduction & background

Definition

Ductal carcinoma in-situ (DCIS) is a proliferation of abnormal epithelial cells, confined by the basement membrane of the mammary ductal system. By definition, stromal invasion is absent. DCIS is a non-obligate precursor of invasive carcinoma and does not fully express the phenotype of unlimited growth, invasiveness, angiogenesis and metastatic potential [1]. The progression to invasive breast cancer (IBC) is likely to result from the accumulation of genetic alterations, allowing clonal selection and the evolution of malignant capability.

Diagnosis

Historically, DCIS has been diagnosed in a small proportion of patients presenting with a palpable mass or pathological nipple discharge or occasionally as an incidental biopsy finding [2]. In modern practice, DCIS is most frequently identified in asymptomatic women with screen-detected micro-calcifications. Screening mammography has led to a significant increase in the incidence of DCIS over the last two decades [3]. Between 1980 and 1995, Western countries have experienced a four-fold increase in the incidence of DCIS, particularly in women of screening age [4]. Approximately one-fifth of all screen detected breast cancers are now DCIS [5].

Technological advances in breast imaging are likely to be associated with further increases in the incidence of DCIS. Full-field digital mammography (FFDM) combined with computer aided detection (CAD) has been demonstrated to be more effective than analogue film mammography in

screening pre- and peri-menopausal women and those with dense breasts [6]. Magnetic resonance imaging (MRI) has a higher sensitivity for breast cancer than mammography and is emerging as the best modality for screening young women at high risk [7, 8]. MRI may have particular utility in assessing the extent and distribution of disease in the breast [8]. However, the role of MRI in the management of DCIS has not been evaluated in the context of randomised trials. Recently, a prospective observational study has demonstrated MRI to be significantly more sensitive than mammography for the diagnosis of DCIS (92% vs. 56%). With regard to high grade DCIS, 48% of cases were missed by mammography, compared to only 2% for MRI. Interestingly, cases missed by one imaging modality were always detected by the other, suggesting that MRI would function best as an adjunct to screening mammography [9] (Fig. 1).

Direct visualisation of DCIS lesions has been achieved with mammary ductoscopy, however the potential role of this technology in the detection and management of DCIS requires further investigation [10]. Anatomical studies have identified several limitations to this approach, including the fact that not all ducts are accessible from the nipple [11]. Prior to surgery, the histological diagnosis of impalpable DCIS is currently established by stereotactic core biopsy of mammographic microcalcifications using automated technology. Vacuum assisted core biopsy (VACB) has been shown to increase the diagnostic yield and upgrade atypical ductal hyperplasia (ADH) to DCIS in approximately 25% of cases [12]. Impalpable lesions currently necessitate pre-operative wire localization and intra-operative specimen radiography to facilitate complete local excision [2].

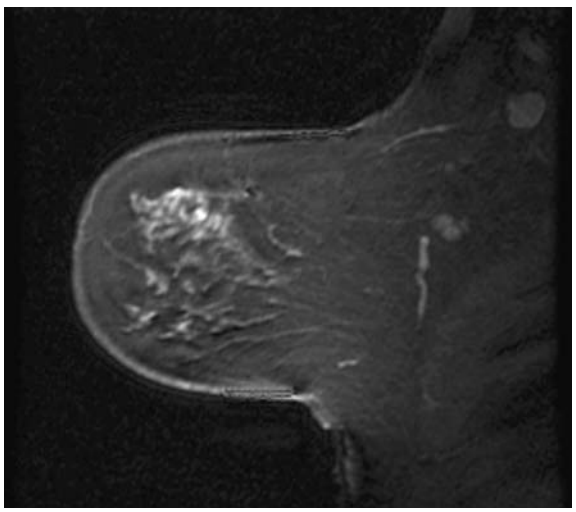

Fig. 1 This is a recurrence anterior to the lumpectomy site in the left breast of a 49-year-old female; her mammogram was normal and this was detected on a screening MRI. The MRI showed regional ductal enhancement in the upper outer quadrant of the left breast

Classification & natural history

DCIS has been traditionally classified according to its architecture and growth pattern, with histological groups including: comedo, solid, cribriform and micropapillary. These descriptive categories can be of limited clinical utility, particularly as individual DCIS lesions often demonstrate architectural and morphological heterogeneity. Classification systems based on nuclear grade and necrosis show greatest reproducibility and thus are more reliable for prognostication [13–16].

The biological diversity of DCIS lesions corresponds with variable malignant potential and consequently an elusive natural history. Though DCIS is defined as a pre-invasive condition, not all lesions will progress to invasive malignancy [17]. The natural history of small, non-comedo low grade DCIS treated by biopsy alone has been evaluated in studies with long-term follow-up. After a median of 31 years, 39% of patients developed IBC, all of which occurred in the same breast quadrant as the DCIS and 45% of these patients died of metastatic disease [18]. The overall progression of DCIS to invasive malignancy has been reported to range from 14 to 75% [19]. Hence, it would seem that patients who receive no treatment beyond a diagnostic biopsy remain at significant risk of ipsilateral IBC. Increased risk has been demonstrated in lesions of low, intermediate and high nuclear grade, however, the onset interval seems to be longest for low nuclear grade lesions. On the other hand, a significant proportion of DCIS lesions behave in a benign fashion and do not progress to invasive disease. Reliable identification of these patients could allow treatment to be less radical or safely omitted. As the incidence of DCIS continues to increase, particularly in asymptomatic women of screening age, accurately predicting the risk of progression and recurrence is of paramount importance for the formulation of rational management strategies.

Indicators of prognosis & recurrence

Clinical, histological and molecular attributes are associated with aggressive biological behaviour and poor prognosis in IBC. These include: patient age, large tumour size, involvement of margins, nodal positivity, hormone receptor negativity, high nuclear grade and a variety of molecular and genetic parameters. These characteristics have been evaluated in DCIS to further elucidate the natural history, particularly the likelihood of progression without treatment and recurrence following treatment.

Clinical features

Higher rates of recurrence have been identified in women with palpable DCIS and those who present symptomatically, compared to mammographically detected cases, 21.2% vs. 16.8% respectively [20]. This disparity persists even after the beneficial effects of adjuvant radiotherapy (RT) [21]. Hence, screen detected lesions may not necessarily follow the same natural history as their clinically detected counterparts [22]. One study has identified family history of breast cancer as a significant predictor of local recurrence (LR) risk in women treated with breast conserving surgery (BCS) and adjuvant radiotherapy (RT) [23]. Another study identified previous therapy with estrogens, either contraceptives or hormone replacement therapy, to be a significant predictor of LR [24]. Young age (<40 years) is an independent risk factor for LR after BCS with or without adjuvant RT [25]. The rate of LR has been reported to range from 18–30% in this group of patients, with the lowest rates in mammographically detected lesions [21, 25–29].

Histological features

Tumor size has been correlated with LR in patients treated by BCS±RT. In one study, DCIS treated by BCS alone was associated with 10-year LR rates of 11 and 48%, for lesions smaller and larger than 10 mm respectively [30]. On the contrary, the French study reported LR rates of 30 and 31% in the BCS group for lesions under or over 10 mm, respectively, and 11 and 13% for the same subgroups in the BCS + RT group [31]. It is noteworthy that accurate and reliable measurement of DCIS can be difficult and even landmark studies have been criticized for their performance in this regard [21, 26, 32].

In patients treated by BCS alone, studies have shown significant differences in LR according to margin width [33, 34]. Furthermore, in women treated with BCS and adjuvant RT, margin width remains an important risk factor for LR [35, 36]. Despite this, consensus regarding the definition of optimal margin width is lacking [32]. In a study of BCS patients with DCIS present at the surgical margin, histological examination of re-excision specimens identified residual DCIS in 40–82% [37]. Interestingly, the incidence of residual tumour was found to be related to margin width, with 41% at <1 mm, 31% at 1–2 mm and 0% with at least 2 mm of clearance. The French National Guidelines (November 2004) recommend that surgical margins should be at least 3 mm and that re-excision should be performed for margins <1 mm [38]. For intermediate margins, the need for re-excision should be discussed by a multidisciplinary team in the context of relevant patient and tumour related risk factors. Other centers recommend a 2 mm minimal margin width. In addition to clear surgical margins, total excision volume has also been associated with LR. The Joint Centre Experience reported LR rates at 5 years of 9 and 0% for volumes <60 and >60 cm^3 respectively [39]. Excision volumes <60 cm^3 have been shown to increase the relative risk of LR in women under 45 years [25].

High grade DCIS is associated with a greater risk of LR and IBC (Fig. 2). This has been illustrated in several studies of DCIS treated by BCS alone, with LR rates ranging from 6 to 31.5%, for low-grade and high-grade lesions respectively [20, 33, 40]. Nuclear grade has been consistently associated with poor prognosis and local recurrence in DCIS [20, 41–43]. The combination of nuclear grade and comedo necrosis was reported to correlate with the risk of LR after BCS [41, 42]. Similarly, the combination of nuclear grade and cellular polarization has been associated with the risk of LR [43]. However, cellular polarisation and mitotic frequency alone do not function significantly as prognostic factors [44].

Histological type, in particular comedo DCIS, has been identified as a risk factor for LR [45]. Favorable prognostic types include clinging and micropapillary [21]. The Van Nuys Prognostic Index (VNPI) is a combination of parameters (patients' age, tumour's size, surgical margin width, nuclear grade, and the presence/absence of comedonecrosis) which has predictive utility for LR after BCS (with or without adjuvant radiotherapy) and can facilitate clinical decision-making [24, 46, 47].

Occasionally, DCIS can be associated with lobular carcinoma in-situ (LCIS). In one study, the presence of LCIS did not appear to affect the overall 10-year LR rate, but the proportion of invasive LR was been reported to be higher, 67% in lesions with LCIS compared to 43% for

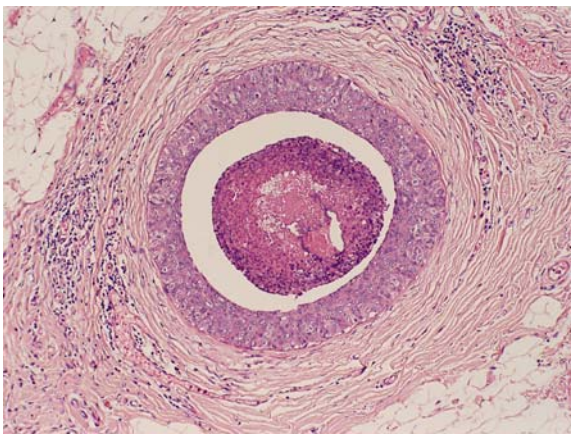

Fig. 2 This is high grade DCIS with necrosis: an important prognostic feature

pure DCIS [30]. In the French Cancer Centers series, the 7-year LR rate was similar in mixed lesions for patients treated with BCS alone, but greater in patients given adjuvant RT (23.8 and 11.7%, respectively) [48].

The hormone receptor profile of DCIS has prognostic and therapeutic implications. High grade DCIS lesions which are estrogen receptor (ER) and progesterone receptor (PR) negative are significantly associated with HER2 and p53 positivity. ER negative lesions tend to be PR negative and high grade lesions with micro-invasion tend to be HER2 positive and hormone receptor negative [49]. HER2 positivity and ER/PR negativity are individually associated with risk of recurrence [50]. HER2 over-expression represents an aggressive biological subtype of DCIS, correlating with high grade, p53 expression and hormone receptor negativity. On the other hand, hormone receptor positivity has been associated with low grade DCIS. Despite these findings, there is no evidence that ER, PR, and/or HER2 status provide prognostic information regarding local control, but they remain clinically useful in predicting response to endocrine therapy.

Molecular features

Advances in molecular biology have enabled DNA, RNA and protein analysis on a previously unprecedented scale. Conventional clinical and pathological features of DCIS are likely to be significantly enriched by a multitude of molecular characteristics. Though the individual relevance of each parameter may not be fully understood, combinations of features may enable the biological profiling of DCIS lesions into groups of similar natural history and prognosis. Chromosome-wide comparative genomic hybridization (CGH) has shown DCIS to be a genetically advanced lesion with alterations corresponding to adjacent invasive lesions and independent pathways of genetic evolution [51]. Gene expression profiling of DCIS, using complementary DNA micro-arrays, can provide a distinctive molecular portrait of each tumour, contributing to our understanding of clinical behaviour and progression to IBC [52]. Such a study has identified a gene expression classifier of 35 genes which differed between DCIS and IBC and a further 43 genes distinguishing between well- and poorly differentiated DCIS [53]. Similarly, molecular characterization can be achieved with protein expression profiling, using matrix-assisted laser desorption/ionization (MALDI) or surface-enhanced laser desorption/ionization (SELDI). Proteomics analysis of DCIS/normal breast tissue has identified differential expression patterns, distinct from previous nucleic acid-based studies and identified new facets of the earliest stage of breast cancer progression [54]. Expression of Syndecan-1, E-cadherin and c-met have recently been shown to be associated with angiogenic and lymphangiogenic factors in DCIS, including endothelin A and B receptors, vascular endothelial growth factor (VEGF)-A/C and fibroblast growth factor receptor (FGFR)-1 [55]. In addition to their potential utility in prognostication, studies such as this may yield putative molecular targets for directed therapy in the future.

Management of DCIS

The natural history and clinical relevance of DCIS is variable. The need for intervention is not absolute and the balance of benefit and risk will differ between patients who are symptomatic and those with screen detected pathology. It is paradoxical that in some cases DCIS will be treated more radically than confirmed IBC. At present it is not possible to reliably predict which lesions will progress, however, DCIS is curable and successfully treated patients do not develop IBC. In practice this means that all patients should be offered treatment, but in view of the disease heterogeneity, the optimal treatment of DCIS remains controversial [19, 35]. Management strategies for DCIS need to consider the breast and axilla, the need for local adjuvant treatment with radiotherapy and the role of systemic adjuvant therapy. Treatment of the breast can involve BCS, with or without adjuvant radiotherapy (RT), or total mastectomy (TM). Axillary interventions, including sentinel lymph node biopsy (SLNB) and/or axillary dissection (AD), deserve particular consideration in view of their low yield. Adjuvant systemic treatments for DCIS have mainly involved endocrine therapy, particularly with Tamoxifen.

Mastectomy

The primary intention of surgical treatment is to completely remove DCIS, reducing the risk of LR and IBC. Mastectomy is the procedure which provides greatest local control, approximately 98% at 7 years, with an overall recurrence rate of 1.5% [56]. Indications for mastectomy include: large tumours (>4 cm depending on breast size), multi-centric lesions, inadequate margins, recurrence after BCS and patient preference. In England and Wales between 1990 and 2001, the absolute number of mastectomies for in-situ disease increased by 400%, corresponding to the introduction of the national screening programme for breast cancer [57]. However, the rate of TM for DCIS has been decreasing over the last three decades and the procedure is now undertaken in approximately one-third of patients [58–61]. In women requiring or requesting TM for DCIS, skin-sparing mastectomy can facilitate immediate breast reconstruction with

an implant and/or autologous flap resulting in an excellent cosmetic outcome [62] (Fig. 3).

Breast conserving surgery

The increasing incidence of smaller, mammographically detected lesions has been associated with changes in management strategy. Complete local excision can often be achieved without TM. However, the oncological adequacy of BCS alone remains controversial. Despite the overall good prognosis, a significant number of patients undergoing BCS for DCIS develop LR, of which approximately half are invasive and up to one-fifth undergo long-term metastatic evolution. Studies have shown an overall LR rate of approximately 28% at 7 years, 45% of which were invasive [30, 33, 63–66]. Even in studies including only mammographically detected DCIS with complete excision, the 10-year LR rates were 27.8, 22 and 19% respectively, of which approximately 35% were invasive [40, 67, 68]. Furthermore, a single-arm prospective trial of BCS, including only small (mammographic extent of ≤2.5 cm), low/moderate grade DCIS with surgical margins of >1 cm, was terminated at 40-months median follow-up due to the unacceptably high rate of LR, corresponding to a 5-year rate of 12.5% [69]. On the other hand, acceptably low LR rates following BCS have been reported in the VNPI 4–6 group (3 LRs among 176 patients with 65-month median follow-up) or in the case of excision margins greater than 10 mm (4.6% LR rate among 197 patients) [33, 70]. Hence, small non-comedo DCIS can be potentially treated adequately by complete local excision, despite the lack of supporting evidence from prospective randomised trials.

Adjuvant radiotherapy

The combination of BCS with adjuvant RT has been advocated to address issues of oncological adequacy, particularly with regard to LR. Whilst risk reductions have been demonstrated in the three large randomized controlled trials discussed below, adjuvant RT should not be seen as a substitute for adequate surgery. The whole breast RT standard dose is 50 Gy in 25 fractions over 5 weeks [29, 31].

The National Surgical Breast and Bowel Project (NSABP B-17) trail randomized 818 patients after lumpectomy with complete excision of DCIS, to either whole breast RT or no further treatment [26]. After a median follow-up of 129-months, among 403 women treated by lumpectomy alone, 124 LRs occurred (31.7%), 67 of which were invasive (54%). Among the 410 women treated by lumpectomy and breast irradiation, 61 LRs were observed (15.7%) of which 29 were invasive (48%) ($P = 0.001$). The absolute reduction of LR increased with time. Despite the fact that RT was associated with a 57% reduction in LR (both invasive and in-situ), no differences were observed in metastasis and overall survival.

Another study of 1,010 patients, similarly randomized, was conducted by the European Organisation for Research and Treatment of Cancer (EORTC) [21]. With a 126-month median follow-up, local relapse-free rates were 85% in the RT group and 74% in the control group (hazard ratio: 0.53, $P < 0.0001$). In-situ LR rates were 7 and 13%, respectively, and invasive LR rates were 8 and 13% respectively [71]. Consistent with the NSABP B-17 trial findings, the absolute reduction of LR by RT increased with time from 7% at 4 years to 11% at 10.5 years. In univariate analysis, RT showed a statistically significant benefit in all subgroups of patients, but the size of this benefit varied. More specifically, as to the excision quality, the authors observed a 23.5 and 42.7% LR rate for complete and incomplete/doubtful excisions respectively in the lumpectomy alone group, vs. 14.7% and 24.7% for patients treated with RT in the same respective subgroups.

The UK/ANZ DCIS trial involved 1,701 patients treated by BCS, with subsequent randomisation to RT and/or tamoxifen [72]. Thus, there were four treatment groups:

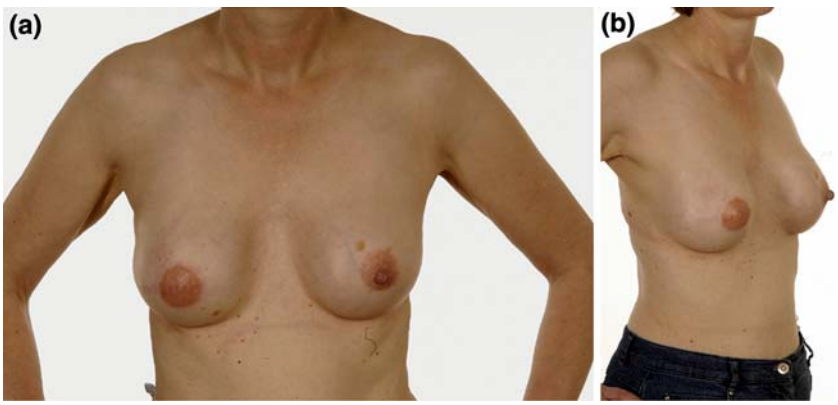

Fig. 3 The long-term aesthetic result of skin-sparing mastectomy and immediate reconstruction (right breast) in a 53-year-old woman who was diagnosed with extensive DCIS

BCS alone, BCS + RT, BCS + TAM and BCS + RT + TAM. About 90% of the participants were 50 years or older and their DCIS was detected through screening programs. After a median follow up of 53 months, the respective rates of LR were: 22, 8, 18 and 6%. The investigators observed that adjuvant RT was associated with a significant reduction (HR = 0.38, $P < 0.0001$) in all ipsilateral tumour recurrence (invasive or DCIS). RT reduced the risk of DCIS by 64% ($P = 0.0004$) and invasive cancer by 55% ($P = 0.01$).

A recent meta-analysis of randomized trials concluded that adjuvant RT significantly reduces the risk of LR after BCS by approximately 60%, with most benefit to patients with high-grade lesions and positive margins. However the rate of distant metastases and survival were not affected by RT [73]. Overall, LR rates have been reported to range from 2.7 to 18.9%, averaging 10% at 7 years, with invasive LR accounting for approximately 60% [74]. Significant criticisms have been made regarding the methodological quality of these trials, including a lack of: effective mammographic-pathologic correlations, routine specimen radiography, post-operative imaging, adequate definition and classification of lesions [26], measurement of tumour size [21] or margin clearance, consistent inclusion/exclusion criteria, conventional methodology for randomisation and data analysis, adequate statistical power to determine differences in overall survival. Whilst some of these issues can be resolved by a meta-analysis of the trials, others are being addressed by ongoing studies namely, the Eastern Cooperative Oncology Group registration trial (E5194) and the Radiation Therapy Oncology Group trial (98-04).

The trial findings have been confirmed by a recent population-based study of 798 patients, with 5-year recurrence free survival of 75% for DCIS treated by BCS compared to 91% for BCS + RT [34]. Further support comes from another population-based analysis with an average follow-up of 91-months, which demonstrated LR rates of 15 and 10.7% for women treated by BCS and BCS + RT respectively. The risk of invasive LR was 49% vs. 31% and the risk of breast cancer specific mortality was 2.7% vs. 0.8% ($P = 0.02$) respectively, despite the fact that the patients treated with BCS + RT tended to have worse tumor grade and larger tumor size [75].

Improved techniques of planning and delivering RT, such as lung density correction, allow increased dose homogeneity throughout the treated volume. This approach has been associated with high rates of local control in patients treated by BCS + RT, with 5- and 10-year recurrence rates of 5.9 and 9.8% respectively [23]. Whole breast RT, combined with a boost fraction to the vicinity of the primary tumour, has been to shown to be valuable in subgroups of women with IBC. Despite this, a study of 75 patients with DCIS treated by BCS + RT, with 20 women receiving an additional 10 Gy boost to the tumour bed, identified no reduction in LR after 81-months median follow-up [76]. Recent studies have also demonstrated the efficacy of partial breast RT in selected cases of IBC. However, the role of these approaches in the treatment of DCIS has yet to be defined [29, 77].

Tamoxifen use in DCIS

In the NSABP B-24 trial, women treated with BCS + RT, were subsequently randomized to placebo or tamoxifen (10 mg twice a day, for 5 years) [78]. After 7-years median follow-up, the LR rates were 11.1 and 8% in the placebo and tamoxifen groups, respectively ($P = 0.02$). The absolute reduction was significant for invasive LR. Despite this benefit, patients taking tamoxifen incurred a greater risk of endometrial cancer and thromboembolic events. No significant benefit was observed in the following groups: age >50 years, in-situ LR, complete local excision and absence of necrosis. The overall mortality was not affected [79]. A post-hoc analysis of ER status demonstrated that efficacy was limited to the 77% of cases which were ER positive [80].

The UK/ANZ DCIS trial showed that for patients not receiving RT, adjuvant tamoxifen did not significantly reduce the incidence of ipsilateral IBC or DCIS. However, the total number of DCIS events (ipsilateral and contralateral) was significantly reduced by tamoxifen (6% vs. 10%, $P = 0.03$). Tamoxifen had no significant effect for patients receiving adjuvant RT [72].

The use of adjuvant tamoxifen should be restricted to patients who are likely to benefit, such as young women who are receptor positive, in the absence of risk factors which may exacerbate the potential side effects. The role of other endocrine therapies, including aromatase inhibitors, are currently under evaluation in trials (IBIS II and NSABP B-35).

Management of the axilla in DCIS

Pure DCIS, by definition, is limited by the basement membrane, without risk of lymphatic or vascular invasion [19, 35]. However, extensive DCIS can harbour foci of micro-invasive disease. For this reason, lymph node involvement has been identified in 1–2% of patients [19]. In the last two decades, American studies have shown that the AD rate has decreased from 34 to 15% overall and from 51.5 to 10.4% in patients undergoing TM [81]. Whilst techniques such as SLNB provide an opportunity to rationalize axillary intervention in IBC, the low yield and risk of morbidity is likely to preclude routine use in patients

with DCIS [82]. Similar conclusions have been drawn from a recent retrospective analysis of patients from the NSABP B-17 and B-24 trials who were treated conservatively, with BCS+/–RT+/–Tamoxifen [83]. Indications for SLNB in DCIS include: histological confirmation of invasive disease, the presence of risk factors for invasion such as palpability and comedo morphology, and patients undergoing TM (due to difficulty with subsequent SLNB). The clinical significance of isolated tumour-cell metastases (micro-metastases) remains unclear and caution is required to avoid over-staging and over-treatment of the axilla. Interestingly, one group has recently hypothesised that the anatomical disruption following pre-operative biopsy procedures increases the likelihood of epithelial cell displacement and the frequency of SLN positivity [24].

Specific management dilemmas

Primary treatment for DCIS, including radical surgery, is associated with a significant failure rate. The natural history of recurrent disease differs considerably from native DCIS. LR may be in-situ or invasive, in which case there exists potential for axillary lymph node involvement (15–20%), systemic metastasis (13–18%) and attributable mortality [66, 84]. Interestingly, 75–80% of recurrences following BCS occur at the site of the original lesion or within the index quadrant. As the extent of primary treatment increases (BCS, BCS + RT, TM), the risk of LR decreases. Ironically, LR can be more aggressive in patients who were treated more aggressively. Whereas 40–50% of LR is invasive after BCS, LR is almost always invasive following TM. Similarly, invasive LR has been found to be relatively more frequent in women treated with adjuvant RT [85]. Compared to invasive LR, in-situ LR is more likely to be detected by mammography than clinical features such as a palpable mass, nipple discharge or Paget's disease [85]. The prognosis of invasive LR is significantly worse than in-situ recurrence. In particular, the risk of metastasis has been reported to be low for in-situ LR, ranging from 0–3.6%, however the overall rate of metastasis significantly increases after invasive LR to 13.2–18% [66, 84, 86]. Axillary recurrence may manifest with palpable lymphadenopathy or be identified histologically after AD. The rate of axillary lymph node involvement in women with invasive LR ranges from 11 to 30% [66, 86]. Therefore, management strategies for recurrent disease need to consider the breast and axilla. Following LR within the breast, particularly invasive LR, optimal disease control can be achieved with salvage mastectomy (SM). Overall, SM rates for LR range from 64 to 84% [66, 86]. It is noteworthy that SM rates are higher for LR in patients who underwent BCS and adjuvant RT than those treated by BCS alone. In the NSABP B-17 trial, the SM rate for LR was 48% in the BCS group and 62% in the BCS + RT group [26], consistent with similar studies reporting rates of 52.8 and 74.7% respectively [66]. Breast conservation strategies may be appropriate for some women, particularly in cases of in-situ LR, and adjuvant RT following complete local excision has been shown to reduce the risk of a second recurrence [85].

The management of DCIS in elderly patients is not founded on a large evidence base and this group has often been excluded from important trials and screening programs. There is a particular paucity of information regarding women over 70 years [26, 29, 47, 78, 79]. In keeping with this, there is evidence to suggest that choice of therapy remains independent of patient age [61]. In the French Cancer Center Study, 6.2% of women were 70 years or older and the diagnosis was made by screening mammography in over half of these cases. After 75-months follow-up, LR rates in the TM and BCS groups were 3.8 and 22.2% respectively, however no LR occurred in the BCS + RT group [48].

Women previously treated for hematological malignancies by irradiation, which has included the thorax, are at risk of developing secondary tumours. Breast cancer is the most common solid lesion, with DCIS accounting for 11–17.7% of cases. The risk is significantly increased at adolescence and young adulthood with a median onset interval of 16 years. In one study, the majority of these patients were treated with TM, however, 29% underwent BCS+/–RT [87].

Approximately 300 cases of pure DCIS have been reported in men, however the incidence of DCIS within IBC ranges from 0 to 17% with an average of 7% [88, 89]. Patients may presenting with a subareolar mass, Paget's disease or serosanguineous nipple discharge. Papillary and cribriform are the most common histological types. Optimum control is achieved with simple mastectomy, lumpectomy alone has been associated with a higher rate of LR.

Conclusions & recommendations for practice

DCIS should be managed in the context of a multidisciplinary team. In order to reduce the risk of LR, complete local excision should be undertaken with a surgical margin of at least 2 mm. Women who undergo BCS should be offered whole breast irradiation, providing there are no contraindications. RT may be safely omitted in some patients with small non-comedo lesions excised with adequate margin width; however this practice has not been validated by randomised controlled trials. Large, multicentric or recurrent lesions (particularly in cases of prior RT) should be treated by TM with the opportunity for

immediate reconstruction. Routine AD is not indicated and SLNB should be reserved for confirmed invasive disease, high risk lesions and patients undergoing TM. Adjuvant tamoxifen has some benefit in young women with hormone sensitive disease, but has not been shown to improve survival and is associated with thrombo-embolic events and endometrial cancer. Further research is required to determine the role of partial breast RT and contempory endocrine therapies.

Search strategy and selection criteria

Articles were identified by searches of MEDLINE and PubMed from December 1964 to August 2007 using the terms: "DCIS" or "ductal carcinoma in-situ" and "treatment" or "management" or "surgery" or "radiotherapy" or "radiation" or "mastectomy" or "sentinel node biopsy" or "natural history" or "tamoxifen" or "recurrence" or "invasive". Studies identified were screened for those that focused on DCIS treatment. All randomized controlled trials and large retrospective series were included. The reference articles in this review were selected to provide a balanced and representative overview of a complex subject with an extensive base of published work.

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