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Original article

Time trends and inter-hospital variation in treatment and axillary staging of patients with ductal carcinoma in situ of the breast in the era of screening in Southern Netherlands

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ABSTRACT

Background: To examine variation in time and place in axillary staging and treatment of patients with ductal carcinoma in situ (DCIS) of the breast.
Methods: Trends in patients with DCIS recorded in the Eindhoven Cancer Registry diagnosed in 1991–2010 ($n = 2449$) were examined.
Results: The use of breast conserving surgery (BCS) went from 17% to 67% in 1991–2010 and administration of radiotherapy after BCS increased to 89%. Axillary lymph node dissection decreased to almost 0%, while sentinel node biopsy was performed in 65% of patients in 2010. The proportion who underwent BCS varied between hospitals from 49% to 80%; the proportion without axillary staging ranged from 21% to 60%. Patients with screen-detected DCIS were more likely to receive BCS.
Conclusion: There was considerable variation in the use of BCS, radiotherapy, and axillary staging of DCIS over time and between hospitals. Patients with DCIS were more likely to be treated with BCS if their disease was detected by screening.

Introduction

Ductal carcinoma in situ (DCIS) of the breast is a precursor of breast cancer. DCIS is usually detected during mammography screening and remains often asymptomatic [1]. The detection rate of DCIS increased from 3/100 000 in 1984 to 34/100 000 person years in 2006 in Southern Netherlands, mainly as a result of mass screening for breast cancer [2]. Few patients with DCIS ultimately die from breast cancer; in a population-based study, only 2% of patients with DCIS had died of breast cancer in the first 10 years after diagnosis [3]. Therefore, a major objective of the treatment of patients with DCIS is to prevent the development of invasive cancer with a minimal risk of adverse effects.

The clinical practice guidelines for DCIS recommend a microscopically complete excision by either mastectomy or breast conserving surgery (BCS). A randomized controlled trial to compare mastectomy and BCS in treatment of DCIS has never been carried out, although retrospective studies have not revealed any differences in breast cancer-related survival for both treatment modalities [4,5]. Mastectomy is generally indicated for patients with larger or multifocal lesions and residual disease, although treatment guidelines are not very explicit about the indications for both types of surgery [6] due to lack of evidence from randomized studies. Since 2000, several randomized controlled trials have clearly demonstrated the potential of radiotherapy to reduce the risk of local recurrence in patients with DCIS who undergo BCS, irrespective of their age [7–10]. According to population-based studies from the US and Europe, these findings have resulted in a significant increase in the proportion of patients receiving radiotherapy after BCS [11–13].

Although there is no clear evidence about axillary staging, the general opinion is that axillary staging should be considered for

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DCIS patients with relatively large lesions, comedo-necrosis, or with one or more risk factors of having an invasive component. Risk factors include age <55 years, a solid component seen on mammography, suspicion based on histological biopsies, or moderately/poorly differentiated DCIS in biopsies [6].

The aim of this study was to examine time trends and inter-hospital variation in use of BCS and mastectomy, radiotherapy following BCS, and axillary staging of DCIS in the period 1991–2010, using population-based data from southern Netherlands. It was hypothesized that differences between hospitals would be largest for the use of BCS, mastectomy, and axillary staging, for which no evidence-based guidelines exist. Explanatory factors for treatment and staging were analysed with a special focus on the differences between screen-detected and clinically detected DCIS.

Materials and methods

Eindhoven Cancer Registry

Population-based data from the Eindhoven Cancer Registry (ECR), which is maintained by the Comprehensive Cancer Centre South, were used. The ECR records data on all patients newly diagnosed with cancer in the southern part of The Netherlands, an area with ten community hospitals, six pathology departments, and two radiotherapy institutes. Information on patient characteristics such as gender, date of birth, and tumour characteristics such as date of diagnosis, tumour type, subsite (International Classification of Diseases for Oncology (ICD-O-3)) [14], histology, stage (Tumour Lymph Node-Metastasis (TNM), clinical classification) [15], grade, and treatment, are obtained routinely from the medical records [16]. The ECR does not contain information about grading or size of DCIS [16]. Thorough training of the registrars and computerized consistency checks at regional and national levels resulted in high quality data. Completeness is estimated to be at least 95% [17]. In case of the presence of positive axillary lymph nodes in patients with DCIS these patients were no longer considered to have DCIS, but were documented as invasive cancers in the ECR. Therefore, this coding rule does not allow us to present the positivity rate of the axillary staging of patients with DCIS. Treatment was categorized into breast conserving surgery (BCS) and mastectomy with or without radiotherapy. Patients who underwent irradical BCS followed by mastectomy were considered as patients who underwent mastectomy.

For the present study, all patients diagnosed with primary DCIS of the breast registered between 1991 and 2010 in the ECR area were included ($n = 2449$). These patients were divided into age groups according to the age limits used by the screening programme (<50, 50–69, 70–75, and 76+ years).

Treatment guidelines

The Dutch clinical practice guidelines for DCIS recommend a microscopically complete excision by either mastectomy or BCS. BCS should be followed by adjuvant radiotherapy. Mastectomy is generally indicated for patients with larger or multifocal lesions and residual disease. Axillary staging, nowadays preferably by a sentinel node procedure is indicated for patients with an indication for mastectomy due to size of the lesion and patients indicated for BCS with one or more of the following risk factors for an invasive component: age <55 years, solid component on mammography, suspicion of invasive cancer based on histological biopsies, or poor/medium differentiated DCIS in biopsies [6].

Breast cancer screening

In southern Netherlands, the first round of a population-based screening program for breast cancer was implemented during the period 1991–1996, offering free biennial mammography to women aged 50–69 years with a response rate of almost 85% [18]. Since 1998, women aged 70–75 years are also invited. Analogue two-view mammography (medio-lateral-oblique and cranio-caudal view) of each breast was performed in initial screens. In subsequent screens, generally one-view mammography (medio-lateral-oblique) was carried out. Additional cranio-caudal views of each breast were obtained in almost half of subsequent screens and indications for this two-view mammography included any changes in mammographic findings at screening, complicated judgement due to dense breast tissue, a more than two-year interval since the previous screen and previous breast surgery.

The ECR was linked to the database of the population-based screening program for breast cancer in southern Netherlands (BoBZ), which include data about screen detection for the period 1991–2005. This resulted in a study population of 1600 newly diagnosed DCIS cases with treatment information available. Screening information linked to the ECR is not yet available after 2005. A tumour was considered to be screen-detected if the patients was referred and diagnosed within one year after the screening [19].

Statistical analysis

Trends over time and variation between hospitals in treatment and axillary staging of DCIS were expressed using proportions. Multivariable logistic regression analysis was conducted to determine factors independently associated with BCS in patients with DCIS and for radiotherapy following BCS. Similarly, factors associated with BCS and radiotherapy following BCS in the subset of patients for whom screening information was available was conducted. Variables added in the multivariable models were determined a priori and included age, period of diagnosis, and hospital of treatment. In the models including screening information, adjustments for age and period of diagnosis were made. No adjustment for hospital of treatment was made, since subgroups became too small. SAS system 9.2 (SAS Institute, Cary, NC) was used for the statistical analyses.

Results

During 1991–2010 2449 patients were diagnosed with DCIS, with an increasing number of patients per year. The large majority of patients were diagnosed between 50 and 69 years of age (Table 1).

Treatment

Treatment of DCIS changed over time. The proportion of patients who underwent mastectomy (simple or modified and with or without radiotherapy) decreased from 83% in 1991 to 32% in 2010 (p for trend <0.0001). In the same period, the use of adjuvant radiotherapy in patients who underwent mastectomy also diminished from 7% to almost none (p for trend 0.5). The proportion of patients who underwent BCS increased over time from 17% in 1991 to 67% in 2010 (p for trend <0.0001). Of the patients undergoing BCS the proportion receiving adjuvant radiotherapy increased from 23% in 1995 to 89% in 2010 (p for trend <0.0001) (Fig. 1). Tamoxifen was offered to 2% of the patients with DCIS. The percentage of patients undergoing BCS (with or without radiotherapy) ranged from 49% to 80% between hospitals in the period 2005–2010. The