



Original Article

Validation of a Nomogram in the Prediction of Local Recurrence Risks after Conserving Surgery for Asian Women with Ductal Carcinoma *in Situ* of the Breast



F. Wang^{*}, H. Li[†], P.H. Tan[‡], E.T. Chua^{*}, R.M.C. Yeo^{*}, F.L.W.T. Lim^{*}, S.W. Kim^{*}, D.Y.H. Tan^{*}, F.Y. Wong^{*}

^{*} Division of Radiation Oncology, National Cancer Centre Singapore, Singapore

[†] Unit of Health Services Research, Singapore General Hospital, Singapore

[‡] Department of Pathology, Singapore General Hospital, Singapore

Received 1 April 2014; received in revised form 9 June 2014; accepted 10 July 2014

Abstract

Aims: At our centre, ductal carcinoma *in situ* (DCIS) was commonly treated with breast-conservation therapy (BCT). Local recurrence after BCT is a major concern. The aims of our study were to review the outcomes of DCIS treatment in our patients and to evaluate a nomogram from Memorial Sloan Kettering Cancer Centre (MSKCC) for predicting ipsilateral breast tumour recurrence (IBTR) in our Asian population.

Materials and methods: Chart reviews of 716 patients with pure DCIS treated from 1992 to 2011 were carried out. Univariable Cox regression analyses were used to evaluate the effects of the 10 prognostic factors of the MSKCC nomogram on IBTR. We constructed a separate National Cancer Centre Singapore (NCCS) nomogram based on multivariable Cox regression via reduced model selection by applying the stopping rule of Akaike's information criterion to predict IBTR-free survival. The abilities of the NCCS nomogram and the MSKCC nomogram to predict IBTR of individual patients were evaluated with bootstrapping of 200 sets of resamples and the NCCS dataset, respectively. Harrell's c-index was calculated for each nomogram to evaluate the concordance between predicted and observed responses of individual subjects.

Results: Study patients were followed up for a median of 70 months. Over 95% of patients received adjuvant radiotherapy. The 5 and 10 year actuarial IBTR-free survival rates for the cohort were 95.5 and 92.6%, respectively. In the multivariate analysis, independent prognostic factors for IBTR included use of adjuvant endocrine therapy, presence of comedonecrosis and younger age at diagnosis. These factors formed the basis of the NCCS nomogram, which had a similar c-index (NCCS: 0.696; MSKCC: 0.673) compared with the MSKCC nomogram.

Conclusion: The MSKCC nomogram was validated in an Asian population. A simpler NCCS nomogram using a different combination of fewer prognostic factors may be sufficient for the prediction of IBTR in Asians, but requires external validation to compare for relative performance.

© 2014 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

Key words: Breast; DCIS; nomogram; prediction; recurrence

Introduction

Breast cancer has been the most common malignancy in Singaporean women in the past few decades. It accounted for 29.3% of all cancers in Singapore women between the years 2006 and 2010 [1]. The pilot Singapore Breast Screening

Project conducted between 1994 and 1997 led to the establishment of the national breast cancer screening programme in 2002 [2]. As a result, more women are diagnosed with early breast cancer with a resultant improvement in cancer-specific survival [3]. Among mammographically detected breast cancer cases, >30% were ductal carcinoma *in situ* (DCIS) [4]. In Singapore, patients with DCIS were historically treated with mastectomy. Many trials have since shown that breast-conservation surgery (BCS) followed by adjuvant radiotherapy, i.e. breast-conservation therapy (BCT), is similar to mastectomy in terms of disease control and survival [5–9].

Author for correspondence: F.Y. Wong, Division of Radiation Oncology, National Cancer Centre Singapore, 11 Hospital Drive, Singapore 169610, Singapore. Tel: +65-6436-8000; Fax: +65-6225-6283.

E-mail address: fuyong@yahoo.com (F.Y. Wong).

<http://dx.doi.org/10.1016/j.clon.2014.08.004>

0936-6555/© 2014 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

With the adoption of BCS for the management of early invasive breast cancer, it is also increasingly the preferred surgical option for DCIS. In a local retrospective review of 170 patients with DCIS, it was shown that patients who underwent BCS had equivalent cancer-specific survival compared with patients who underwent mastectomy. However, there were more cases of ipsilateral breast tumour recurrence (IBTR) in the BCS cohort. Close surgical margins and the lack of adjuvant radiotherapy were identified as factors that contributed to the increased risk of IBTR in breast-conserved patients [10].

IBTR is an inherent risk after BCS, which can be mitigated by the addition of adjuvant treatment. Studies have examined the role of various clinicopathological factors, alone or in combination, in predicting IBTR. From these factors, various prognostication tools have been formulated to aid the clinician in predicting the risk of breast events in these patients so as to guide further adjuvant treatment [11,12].

In 2010, Rudloff *et al.* [13] published a novel nomogram incorporating 10 clinicopathological variables for predicting IBTR after BCS for DCIS. This has been validated in other separate Western populations [14–16]. It remained unknown if the nomogram is generalisable to an Asian population with potentially different tumour-host biology [17–19].

Our study aimed to review the outcomes of patients with DCIS treated at our centre and to validate the Memorial Sloan Kettering Cancer Centre (MSKCC) nomogram in the Asian setting.

Materials and Methods

Ethics approval for the study was granted by the institutional review board. Retrospective chart reviews of patients who were diagnosed with pure DCIS were carried out. These patients were identified from databases kept at the Division of Radiation Oncology National Cancer Centre Singapore and at the Department of Pathology Singapore General Hospital. Only patients who were treated with BCS with or without adjuvant radiotherapy were included in the study. Patients with invasive breast cancer, contralateral breast cancer or any other previous malignancies were excluded.

Statistical Analysis

The primary end point was IBTR-free survival, which was defined as the interval between the definitive surgery and the histological diagnosis of recurrence. All survival estimates were based on the Kaplan–Meier method. Patients without events were censored on the date of the last follow-up.

Univariate Cox regression analyses were carried out to evaluate the effects of predictors included in the MSKCC nomogram on these survivals. Multivariate Cox regression was established by means of model selection, which has been used in previous studies [20,21]. This involved reduced model selection using a backward stepdown by applying

the stopping rule of Akaike's information criterion with systematic verification of proportional hazards assumptions for all proposed models [22].

Multivariate Cox regression coefficients were used to construct the National Cancer Centre Singapore (NCCS) nomogram to predict IBTR-free survival. The ability of the NCCS nomogram to predict IBTR-free survival of individual patients was calibrated by the bootstrapping of 200 bootstrap set of resamples. Calibration plots were generated to explore the performance characteristics of our nomogram at 5 and 10 years after surgery.

Harrell's *c*-indices were calculated to evaluate the concordance between predicted and observed responses of individual subjects in the NCCS nomogram and the MSKCC nomogram separately [23,24]. Decision curve analyses (DCA) were carried out to evaluate the performance measures of both nomograms [25]. All analyses were carried out using R 2.15.2 (<http://www.R-project.org>) and STATA version 11 (Stata Corporation, College Station, TX, USA).

Results

There were 716 patients included in the analysis. Patients' demographics, disease characteristics and treatment variables are listed in Table 1. The cut-off values for the variables of age and year of surgery were 45 and 1999, respectively, in order to maintain comparability with the MSKCC study.

The median follow-up was 70.2 (0.95–238.2) months. The 5 and 10 year actuarial overall survival rates were 99.1 and 97.2%, respectively.

Patients in this study were diagnosed at a median age of 49 (20–87) years old. Premenopausal women made up 54.5% of the study cohort. Three hundred and eighty-nine patients (54.3%) had screen-detected DCIS. Chinese patients made up the largest part of the study population (87.4%).

Most of the surgeries were carried out after 1999. Most patients required no more than two excisions (97.1%). Surgical margins were positive or close (≤ 2 mm) in 174 patients (24.3%). Low-grade DCIS was seen in 196 patients (27.4%) and the presence of necrosis was reported in 352 (49.2%).

With regards to adjuvant treatment, 681 patients (95.1%) received radiotherapy and 371 (51.8%) patients received adjuvant endocrine therapy.

At the time of analysis, 42 patients (5.9%) had developed IBTR. Of these 42 patients, 18 (42.9%) had recurrent invasive disease, whereas the other 24 patients (57.1%) recurred as DCIS.

Thirty-four patients (4.7%) developed contralateral breast cancer, 20 of whom (58.8%) developed invasive breast cancers, whereas the other 14 (41.2%) developed DCIS.

Ipsilateral Breast Tumour Recurrence-free Survival

The 5 and 10 year actuarial IBTR-free survival rates were 95.5 and 92.6%, respectively. Table 2 presents the univariate

Download English Version:

<https://daneshyari.com/en/article/5698510>

Download Persian Version:

<https://daneshyari.com/article/5698510>

[Daneshyari.com](https://daneshyari.com)