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A comparative study of risk factors and prognostic features between symptomatic and screen detected breast cancer

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Abstract

Aims: To compare prognostic factors in screen detected breast cancer (SDBC) and symptomatically presenting breast cancer (SBC).
Methods: Data were examined on 100 SDBC and 100 SBC. Multiple clinical patient factors were assessed including histopathological features. Using the Gail model each patient's risk of developing breast cancer was calculated and these data were examined for differences between groups.
Results: There was no difference in the mean age of patient presentation or in the risk of breast cancer development between groups (2.2% vs. 2.2%, SDBC vs. SBC, actuarial risk of cancer at 5 years). SDBC patients had a significantly lower grade (1.95 vs. 2.44, SDBC vs. SBC, $P < 0.05$), a smaller size of tumour (15.4 mm vs. 29.3 mm, SDBC vs. SBC, $P < 0.05$) and a higher rate of oestrogen (94% vs. 81%, $P < 0.05$) and progesterone (75% vs. 52%, $P < 0.05$) receptor positivity. When compared using the Nottingham Prognostic Index, SDBC was associated with a better prognosis ($r = -0.444$, $P < 0.001$).
Conclusions: Though both groups have similar demographics and risk, SDBC patients appear to have more favourable prognostic features. This has implications for the application of systemic therapy in breast cancer and supports the observation that SDBC is a more indolent form of disease.

Keywords: Breast; Neoplasm; Screening mammography; Prognosis; Risk factors; Comparative study

Introduction

Overall survival form breast cancer has improved in the last decade.[1] It is postulated that early detection, as a consequence of screening, and the wider use of adjuvant therapy is the main reason for this.[1–3] Screening mammography detects early stage breast cancer and reduces mortality.[2,4] However, controversies exist over the exact percentage reduction in mortality from breast cancer as a result of screening due to concerns over the quality of the randomized control trials used to assess its efficacy as an intervention.[5–7] A reduction in mortality of about one third by population mammographic screening for women aged 50–69 years appears to be the overall benefit of screening[8] but screening can also lead to over-diagnosis and over-treatment.[5,9–11] Joensuu et al. suggest that screen detected breast cancers (SDBC) have a better prognosis than symptomatic breast cancers (SBC), irrespective of tumour size.[12] These findings suggest that SDBC may be a biologically less aggressive form of disease.

Prior studies have not examined the existing risk factors at the time of presentation or the predicted outcome at the time of resection when comparing screened and symptomatically presenting cancers. Herein, we directly compare screen

Abbreviations: SDBC, screen detected breast cancer; SBC, symptomatic breast cancer; WLE, wide local excision; LN, lymph node; ER, oestrogen receptor; PR, progesterone receptor; LVI, lymphovascular invasion; NPI, Nottingham Prognostic Index; RR, relative risk; CI, confidence interval.

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detected and symptomatically presenting breast cancers using standard clinical and biological criteria combined with models for calculation of risk of development of disease and risk of recurrence following curative resection. Our aim is to determine if SDBC is a biologically more indolent form of disease and if screen detected tumours are associated with a more favourable prognostic profile independent of risk factors at the time of presentation.

Patients and methods

Study population

All data were collected and stored prospectively. The study population comprised of 200 patients who presented to the symptomatic ($n = 100$) and screening ($n = 100$) services of Mater Misericordiae University Hospital over a 2-year period (January 1, 2002–December 31, 2003), were diagnosed with a histologically confirmed invasive breast cancer and had undergone surgical resection. This interval was chosen to ensure that those SDBC examined were detected during the second round of screening and were thus incident, and truly asymptomatic. The symptomatic clinic was attended by patients who were referred with breast abnormalities, typically palpable lesions, by their primary care physicians. The screening population was derived from women attending the formalized Irish National Breast Screening Programme (BreastCheck), a population-based screening programme that offers mammographic screening to all women aged 50–64 years by postal invitation at two yearly intervals. The attendance rates for screening were in excess of 70%. The records of the Eccles Breast Cancer Screening and Symptomatic Breast Cancer databases were used to identify our study population. Women were treated for breast cancer in our institution by three consultant surgeons, each with a special interest in surgical oncology. One hundred incident, second round, SDBC were selected at random from the Eccles Breast Cancer Screening database and 100 SBC were selected from the Symptomatic Breast Cancer database from the same time period. Randomization was ensured by a database manager. Patients were not matched and there were no exclusion criteria.

Data extraction

All treating clinicians granted permission to access medical records following study approval. We examined the relevant patient databases, the hospital information system and patient records to determine multiple clinical patient factors. We utilized the modified Gail model to calculate each patient's individual, actuarial risk of developing invasive breast cancer over the coming 5 years from the time of presentation[13] to determine if existing risk factors at the time of presentation accounted for differences in predicted outcome.

The laboratory reports of resected breast cancer specimens were examined to determine the histopathological features of disease including size, grade, and presence of lymphovascular invasion, histological subtype, hormone receptor status and nodal status. The Nottingham Prognostic Index was calculated from these histopathological variables.[14]

Statistical analysis

Statistical analysis was performed using SPSS v.12. Both parametric and non-parametric methods were utilized to assess our data. Chi-squared test for categorical variables (e.g. histopathological characteristics, etc.) and ANOVA for continuous variables (e.g. age). We compared the differences in Nottingham Prognostic Index using a Spearman's rank correlation coefficient. For assessment of prognostic factor risk associated with detection method, we estimated the risk ratio (RR), with its variance and a 95% confidence interval (CI). Data were then combined across prognostic factors by the use of general variance methods with fixed and random effects models. The fixed effects analysis weighted the natural logarithm of each factor risk ratio by the inverse of its variance. The random effects analysis weighted the natural logarithm of each factor risk ratio by the inverse of its variance plus an estimate of the between-factor variance in the presence of between-factor heterogeneity.

Results

Patient demographics

When the patient demographics of the SBC and SDBC populations were examined no significant differences were found in their mean age of presentation (56.3 vs. 57.1, SBC vs. SDBC) or median age of presentation (53 vs. 57, SBC vs. SDBC).

Risk factors at presentation

When the Gail Model was applied we found no difference in the mean risk of developing breast cancer between our two patient groups at the time of presentation (2.2% vs. 2.2%, SDBC vs. SBC, actuarial risk of cancer at 5 years). However, there was an overall increased prevalence of positive family history (primary or secondary relative) in the symptomatically presenting group (18% vs. 30%, SDBC vs. SBC, $P > 0.05$). There was however an increased use of hormone replacement therapy in the screen detected population (34% vs. 10%, SDBC vs. SBC, $P > 0.05$).

Tumour histopathology

There was an equal distribution of the different pathological subtypes of breast cancer between the two groups (Table 1). SDBC patients had significantly lower grade tumours. SBC patients had a persistently larger tumour with a higher