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Breast cancer survival in Soweto, Johannesburg, South Africa: A receptor-defined cohort of women diagnosed from 2009 to 11

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ABSTRACT

Background: South Africa's public healthcare system is better equipped to manage breast cancer than most other SSA countries, but survival rates are unknown.
Methods: A historical cohort of 602 women newly diagnosed with invasive breast carcinoma during 2009–2011 at Chris Hani Baragwanath Academic Hospital, Soweto, Johannesburg, was followed using health systems data to December 2014. 'Overall survival' time was defined from diagnosis to death or terminal illness. Cox regression was used to estimate hazard ratios (HR) associated with woman and tumour characteristics.
Results: During a median 2.1 years follow-up (IQR 0.5–3.8), 149 women died or were classified terminally ill; 287 were lost-to-follow-up. 3-year survival was 84% for early stage (I/II) and 56% for late stage (III/IV) tumours (late v early: HR 2.8 (95% confidence interval (CI): 1.9–4.1), however the 42% cumulative losses to follow-up over this period were greater for late stage, half of which occurred within 6 months of diagnosis. After mutual adjustment for stage, grade, age, receptor subtype and HIV status, lower survival was also associated with triple negative (HR 3.1 (95% CI: 1.9–5.0)) and HER2-enriched (2.5 (95% CI: 1.4–4.5)) compared to ER/PR+ HER2- tumours, but not with age or HIV-infection (1.4 (95% CI: 0.8, 2.3)).
Conclusion: In this South African cohort, breast cancer survival is suboptimal, but was better for early stage and hormone receptor-positive tumours. Efforts to reduce clinic losses in the immediate post-diagnosis period, in addition to early presentation and accelerated diagnosis and treatment, are needed to prevent breast cancer deaths, and survival improvements need to be monitored using prospective studies with active follow-up.

1. Introduction

Despite lower incidence rates of breast cancer in sub-Saharan Africa (SSA) compared to high income countries (HICs), mortality rates from breast cancer are similar in the two regions because of poorer outcomes in the former. Several studies have shown 5-year survival estimates in SSA to be approximately 50% [1–6] compared to 90% in the USA for women diagnosed with breast cancer during 2006–12 [7]. Although a

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limited number of breast cancer survival studies have been conducted in SSA, considerable variation is expected between the countries within this region.

The South African public healthcare system is considerably more advanced and equipped to manage breast cancer than most other SSA countries [8]. Availability of treatment is better and barriers to diagnosis and treatment are relatively fewer. Notably, South Africa has an extensive private and public hospital network; multiple tertiary hospitals equipped with specialized cancer treatment facilities; the highest number of radiotherapy machines per cancer patient in SSA [9]; and a standardized national public health laboratory system that supports histopathological diagnosis and routine receptor determination to aid therapeutic decisions [10].

In South Africa, as in other SSA countries, there is limited opportunistic and no population-wide breast cancer screening, thus tumour stage at first presentation is typically more advanced compared to HIC settings, but it may be more favourable than in other SSA settings [11,12]. Whilst the aforementioned factors would be expected to lead to improved survival in South Africa compared to other SSA countries, the complexities of cancer treatment are challenging [13] and it is unclear how the relatively high proportion of HIV-positive breast cancer patients in this setting (15–20%) affect survival [14,15]. Further, because resource-limited settings tend to have large losses to follow-up due to various factors including poor healthcare information systems [16], most breast cancer survival estimates from SSA have large uncertainty margins and might be biased.

The Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, Johannesburg, is South Africa's largest government hospital providing tertiary care to the 3–4 million population of Soweto and surrounding areas in Gauteng Province. CHBAH initiated a dedicated breast clinic around 2001 which provides surgical treatment as well as patient follow-up, and systematically uses an electronic clinic database to aid clinical management. This database records all patient contacts, including treatments and, ideally, 6-monthly check-ups, for at least 5 years post-diagnosis. Medical and radiation oncology treatment is provided at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary/quaternary hospital 18 km from CHBAH. Our previous articles describe key clinical characteristics, including an encouraging trend towards earlier presentation between 2006 and 12, a predominance of ER-positive disease and a considerable (17%) proportion of HIV-positive breast cancer patients [11,14,17]. In the present study, we aimed to estimate breast cancer survival using this unique resource, by assembling a historical cohort of women diagnosed during 2009–2011 at CHBAH. We also assessed the accrual of losses-to-follow-up because, using recent terminology [16], the use of 'ambient' data means such losses can be substantial and may cloud 'nominal' survival estimates.

2. Methods

2.1. Breast cancer patient cohort

In 2006, a patient management database was initiated at the CHBAH breast clinic, containing clinico-diagnostic and demographic factors. In early 2015, we assembled a historical cohort comprising women newly diagnosed with invasive, histologically-confirmed, primary breast carcinoma (ICD10 C50) at the CHBAH between 01 January 2009 and 31 December 2011. This diagnostic period was chosen because it allowed for a potential follow-up period of at least 3 years (to end of 2014) for all women. In our setting, diagnosis of breast cancer during this time period entailed referral or presentation to the CHBAH breast clinic; a triple assessment comprising (i) clinical examination and staging, (ii) imaging with mammography and ultrasonography and (iii) an image-guided core needle biopsy for histological diagnostic confirmation, tumour grade and receptor subtyping performed by the National Health Laboratory Service (NHLS) laboratory. Neither Ki-67 mitotic index testing nor FISH testing for equivocal HER2 results were routinely available during this period. Two to three weeks after presentation, when pathology reports were available, women were informed of their diagnosis and treatment plans were outlined. The initial treatment period typically involved surgery, surveillance and, when necessary, palliative care at CHBAH, and chemotherapy and radiotherapy at CMJAH. After completing treatment, follow-up visits were scheduled at 6-monthly intervals for the first 2–3 years, and at times were duplicated between departments involved in treatment at both CMJAH and CHBAH. A small number (n = 13, 2%) of women did not return for their diagnostic results and were not included in this analysis.

2.2. Follow-up and outcomes

We aimed to perform an analysis of overall survival amongst the breast cancer cohort. For this purpose, follow-up commenced on the date of breast cancer diagnosis, which for each woman was defined as the earliest of: histological confirmation of breast cancer, treatment decision meeting date, or, if the previous two were missing, date of first breast cancer treatment. Thereafter, follow-up of women and outcomes were based on 'ambient' data, that is, medical records routinely available in all treatment departments and hospital records of admissions or the hospital register of deaths. Prior to this study, these data were not routinely integrated thus the status of each cohort member during follow-up period was searched for in these records from both CHBAH and CMJAH. Survival time from diagnosis to death was the "ideal" outcome of interest, thus we initially ascertained whether there was any indication of death and the date thereof. For patients without such an indication, disease status at the time of last contact was determined from medical records as: (i) alive (specified as no evidence of disease; with stable disease; with disease progression; or alive but disease status unknown) or (ii) had terminal disease, was unlikely to survive more than 3 months and was receiving end-of-life care. The latter status was determined by a record review of all patients included in the study by senior clinicians and was included because, in this setting, many terminal patients do not die in the hospital, but rather in their own homes, supported by the CHBAH mobile palliative care team if they live in the nearby vicinity. Other urban South African cohorts have reported a similar end-of-life situation [18]. In the present study, there were as many patients who were considered terminal as there were patients known to have died. As we did not have permission to follow up beyond ambient data, we analysed the combined endpoint of time-to-terminal-illness or death as the best estimate of overall survival.

2.3. Prognostic indicators

Clinical staging information (AJCC and TNM), histology type, the Scarff-Bloom Richardson tumour grade (1 = well, 2 = moderate or 3 = poorly differentiated) and immunohistochemically-determined oestrogen (ER), progesterone (PR) and HER2 receptor status was collected on tumour specimens. For this study, cut-offs of > 1% (score 1, 2 or 3) were considered ER-positive and PR-positive while for HER2 status, immunohistochemical scores of 0, 1 and 2 were considered HER2-negative and score 3 as HER2-positive. During the period of this study, HIV testing following informed consent was encouraged, particularly in younger patients. Previous studies have shown the HIV-prevalence within this cohort to be similar to that of the catchment population [14]. Standard policy is to refer all HIV-positive patients for antiretroviral (ARV) therapy prior to starting chemotherapy.

2.4. Ethics approval

The study was approved by the International Agency for Research on Cancer (IARC) Ethics Committee (IEC14-14) and the University of the Witwatersrand Human Research Ethics Committee (M130369/M110562). Record retrieval was approved by the CEOs of CHBAH and