Prognostic factors in breast carcinoma patients with metastatic disease in the peripheral skeleton

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Abstract

Background: Bone is the most common site of metastatic breast cancer;[1] approximately 60% to 70% of breast cancer patients develop bone metastases during their disease course.[2–4] The decision to operate, as well as the choice of surgical procedure, is predicated on a patient's estimated survival.[5] Implant failure and reoperation rates up to 14% and significant post-surgical complication rates of 20% have been reported in several European breast cancer studies;[6–8] causative factors include patient selection.[9] Surgical intervention must reflect the comparatively long survival of this group of patients.[6,7,10] Few studies have investigated the variables predictive of survival with skeletal breast metastases. Weiss et al. reported that age greater than 60 years, haemoglobin <110g/L and complete pathological fractures predicted worse survival in patients with osseous metastases.[8] The authors did not evaluate the prognostic factors for primary breast cancer (hormone status chemotherapy, primary surgery, nodal involvement, hypercalcaemia, stage) in that study.

Purpose: We aimed to identify the prognostic factors for skeletal breast metastases, such that patient specific decisions regarding surgical (or non-surgical) management can be made. The analysis was aimed to be relevant in guiding prognosis and subsequent orthopaedic treatment for general orthopaedic trauma surgeons.

Patients and Methods: A retrospective review was undertaken of all patients with metastatic disease presenting to a supra-regional orthopaedic oncology centre in the United Kingdom. Data had been collected on a secure institution database. Inclusion criteria were histologically proven breast metastases of the extremities. Patients were excluded if no histological confirmation of breast metastases had been obtained or if the patient presented with spinal metastases.

Between 2001 and 2011, 432 patients with suspected metastatic bone disease were referred to our unit. Of these, 132 had carcinoma of the breast. Demographics and disease specific markers were collated. Recorded variables included age, gender, hormone receptor status, stage of breast carcinoma, axillary nodal involvement, primary breast surgery intervention, chemotherapy, bisphosphonates, number and type of metastases, previous episode of hypercalcaemia, and orthopaedic surgery. Multivariate and linear discriminant analysis was performed on the continuous variables with a binary outcome of survival greater or less than 1 year.

Results: One hundred and thirteen successive metastatic breast cancer patients' records were analysed for clinical, radiological, serological and surgical outcomes. Median age was 61 (29 to 90) years and median orthopaedic follow-up was 1.6 years (SD 1.9 years, 95% CI: 0 to 5.9 years). The cumulative one and five-year survival rate was 68% and 16% (95% Cl: 60 to 77% and 10 to 26% respectively).

Multivariate and linear discriminant analysis identified a 'quadruple A' predictor of survival by reclassifying the sum of the albumin, adjusted calcium, alkaline phosphatase and age covariates each multiplied by a determined factor. The accuracy of this 'quadruple A' predictor was 90% with a sensitivity of 100% and a specificity of 88%. A receiver operating characteristic curve revealed an area under the curve of 79%. Survival analysis for this 'quadruple A' predictor (<=1 or >1 year survival) using the log rank test (p=0.0004) and Cox proportional hazard (p=0.0012) was statistically significant (Figure 1).

Survival analysis revealed that the following were positive predictors of survival: fewer than three metastatic sites, absence of metastases at diagnosis of breast cancer, absence of visceral metastases, no history of hypercalcaemia, primary breast tumour excision and a disease-free interval greater than two years. Combining four or more of these factors was highly significant for survival greater than two years (log-rank p= 0.00003, Cox proportional hazard p= 0.000124).

Conclusions: We evaluated a cohort of successive metastatic breast cancer patients who underwent consideration of surgical intervention. The six independent parameters for survival were number of metastatic sites, metastases at diagnosis, previous breast surgery, visceral metastases, disease free interval and previous hypercalcaemia. Combining four or more of these positive predictors of survival was found to be highly predictive of prognosis.

Age was found to be a covariate with albumin, alkaline phosphatase and adjusted calcium which were reclassified as a categorical variable named the 'quadruple A' predictor which had a statistical accuracy of 90% for determining survival at one year.

Awareness of the survival implications of these factors will aid the selection of the most appropriate surgical and non-surgical options. An improved characterisation of a patient's prognosis may enable more appropriate and cost-effective care for metastatic breast cancer patients.

Figure 1. Kaplan Meier survival for the 'Quadruple A' predictor with a score greater or less than 1.
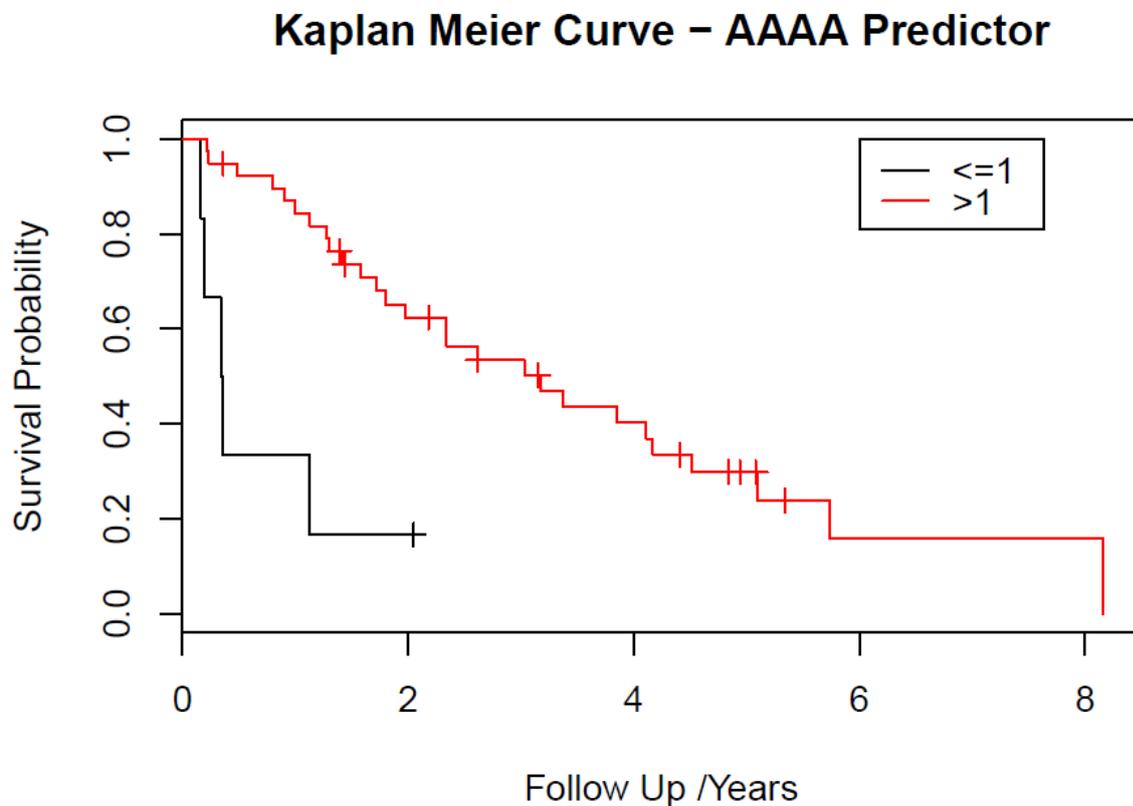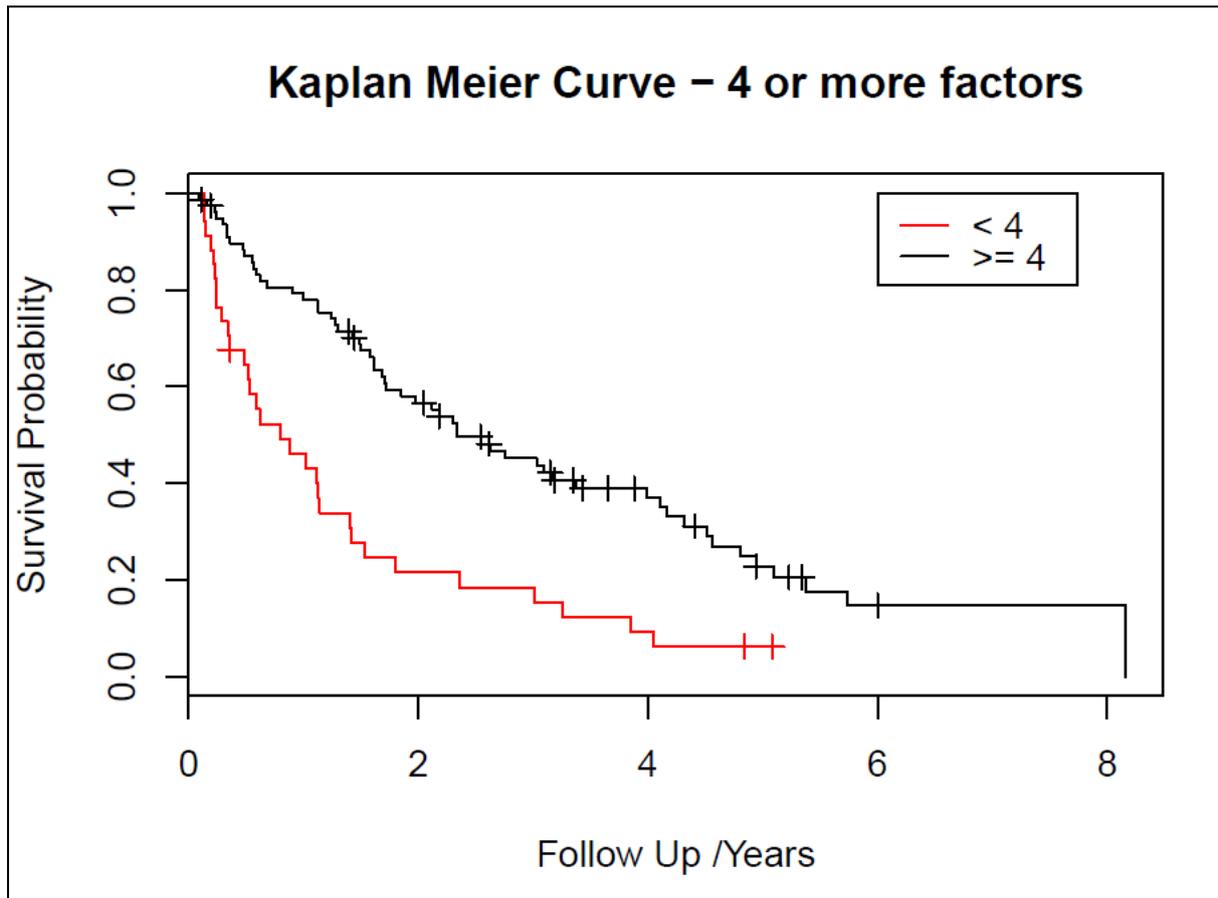

Figure 2. Kaplan Meier survival for greater and less than four positive predictors or survival.

Kaplan Meier Curve − 4 or more factors

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