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Original article

# The prognostic significance of computerised tomography findings in women with liver metastases from breast cancer

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ABSTRACT

*Aims:* While computerised tomography (CT) is used for diagnosis and assessing response to treatment little work has been performed on the prognostic significance of the CT findings in women with liver metastases. The aim of this study was to assess if the CT findings in women diagnosed with liver metastases at the time of first presentation with metastatic breast cancer have any prognostic significance.

*Materials and methods:* The staging CT scans of 78 consecutive women diagnosed with liver metastases at the time of first presentation of metastatic breast cancer were reviewed independently by two radiologists who were blinded to survival and the histological features of the tumour. The number and enhancement characteristics of liver metastases, whether metastases were solitary, multiple or diffuse, the diameter of the largest and the sum of the diameter of the five largest lesions, an estimate of % involvement (<10%, 10–50%, >50%), and the presence of metastases at other sites were assessed. HER-2 and ER status and histological grade of the patient's primary breast cancer were also recorded.

Survival was ascertained from hospital records. The prognostic significance of these factors was assessed in a univariate and multivariate fashion.

*Results:* At univariate analysis, number of liver metastases, sum of the diameter of the five largest lesions, percentage estimated involvement, presence of ascites, chest metastases and HER-2 status were significantly associated with reduced survival. Liver metastasis pattern (i.e. whether discrete or multiple), enhancement characteristics, ER status and histological grade were not associated with a significant outcome.

At multivariate analysis estimated percentage liver involvement and the presence of chest metastases retained prognostic significance. Estimated percentage involvement was reproducible with 90% concordance between the two observers.

*Conclusions:* The CT appearances of patients with liver metastases at first presentation with metastatic breast cancer provide prognostic information which may be clinically useful.



## Introduction

Liver metastases from breast cancer carry a poor prognosis, with a quoted median survival of a few months.[1]

Available data in the literature suggest that only in exceptional cases do these patients survive more than 2 years when given systemic therapy or supportive care alone.[2,3]

Computed tomography (CT) is more accurate than ultrasound at assessing the extent of disease in women with metastatic breast cancer and is recommended for assessing response to treatment according to Response Evaluation Criteria in Solid Tumours [RECIST] criteria.[4,5]

A previous study of liver metastases in women with newly diagnosed metastatic breast cancer has suggested that the ultrasound appearances may provide prognostic information. Solitary metastases and non-confluent multiple lesions were found to have an improved prognosis compared to multiple confluent or diffuse disease. The presence of ascites was also found to be a poor prognostic feature.[6]

As CT is more accurate and reproducible than ultrasound for the demonstration of metastatic disease it is our preferred method of assessing the liver. As far as we are aware, little has been written on the prognostic significance of the CT appearances in this group of patients.

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The aim of this study was to assess the prognostic significance of CT findings in women with liver metastases at the time of first presentation with metastatic breast cancer. The volume of disease was assessed in a quantitative fashion, and its relationship to long-term survival was evaluated. The prognostic significance of other features identified on the staging CT such as the phase of contrast-enhancement of liver metastases, the presence of intrahepatic duct dilatation, ascites or metastases at other sites was also investigated.

## Methods and materials

Details of patients presenting with newly diagnosed metastatic breast cancer following staging CT, performed between July 2007 and December 2008, were identified from the hospital's radiology computer system. The group consisted of patients who had symptoms or signs of metastatic disease who had a previous diagnosis of primary breast cancer or women who were being staged following the diagnosis of a local recurrence or locally advanced primary breast cancer.

CT studies of the chest, abdomen and pelvis were performed using a 16-slice GE Healthcare Light-Speed CT scanner with 2.5 mm collimation following 100 ml intravenous contrast medium (Niopam 300). The chest was imaged in the arterial phase, with images acquired from the diaphragm down during the portal venous phase. There was overlap of hepatic imaging with the cranial slices of the liver imaged during both arterial and portal venous phases.

A retrospective review of all the CT staging studies was performed from our radiology PACS system to ascertain the presence or absence of liver metastases. Those with liver metastases underwent independent review by two radiologists blinded to the histological findings of the primary tumour and survival.

The CT findings recorded were the number and enhancement characteristics of liver metastases, and whether metastases were solitary, multiple or diffuse (metastatic pattern). The maximum diameter of the largest lesion and the sum of the maximum diameters of the five largest lesions were measured on a work station. A visual estimate of percentage of the liver involvement was made and categorised as $<$10%, 10–50% or $>$50%. If there were five or less lesions, the sum of the longest diameters of all lesions present was recorded.

Associated features including ascites and intrahepatic biliary dilatation were also recorded. Also noted was the presence of metastases at other sites including lung, pleura, bone and brain.

We ascertained the histological features of the primary tumour from the pathology database. These included histological grade, HER-2 status, and estrogen receptor (ER) status.

Survival was ascertained from hospital records and the last date alive or date of death was established. All-cause mortality was recorded.

The prognostic significance of factors was assessed in a univariate and multivariate fashion using Kaplan–Meier survival curves and multivariate analysis. The significance of the presence of liver metastases was further tested by Wilcoxan-Gehan and Log rank tests.

Cox regression based survival analysis was conducted for the data. Initially, single component univariate analysis was conducted to determine the influence of factors on survival (time from surgery) based on proportional hazards.

Censoring was determined based on breast cancer specific (BCS) events. Factors in the Cox regression were considered significant with $p$ values of less than 0.05.

Those components identified as significant by univariate analysis were subsequently combined into a multivariate analysis again based on Cox regression to determine their independent prognostic significance from other factors in the set.

Concordance between the number of liver metastases and the percentage of liver involvement was determined by regression analyses. Discordance was measured by Kappa values.

## Results

Between July 2007 and December 2008, 170 patients underwent staging CT examinations at time of first presentation with metastatic disease.

78 (46%) patients, all female, had liver metastases at the time of presentation – 39 (50%) also had chest metastases, 40 (51%) had bone metastases and 2 (3%) had brain metastases. The mean age at metastatic presentation was 61 years (range 32–90 years).

13 (17%) had solitary metastases, 30 (38%) had multiple metastases while 35 (45%) had diffuse disease which was not measurable. Of women with multiple metastases 17 patients had 2–5 lesions, 4 patients had 6–10 lesions and 9 patients had $>$10 lesions. The mean diameter of the largest lesion was 29 mm and the mean sum of the five largest lesions was 82 mm. There was no significant difference in the number of liver metastases at presentation, the pattern of metastatic disease or the mean sum of the 5 largest diameters in women presenting aged 50 or less compared to women presenting aged over 50.

8 patients had lesions best seen on arterial phase imaging, 10 best seen on portal phase imaging, 49 equally seen on both and 11 not assessable. 10 patients had ascites and 3 had biliary duct dilatation.

There was concordance in 70/78 (90%) of cases between the two observers regarding the estimated percentage involvement. Correlation Coefficients were $>$0.90 for both the 'number of metastases' and the 'sum of the diameter of the largest 5 target lesions', indicating a good interobserver correlation.

The distribution of patients in the three metastatic involvement groups was: 27 patients with $<$10% involvement, 33 patients with 10–50% involvement, 18 patients with $>$50% involvement.

Data on histological grade, ER and HER-2 status were available in 75, 78 and 39 women respectively. Of women with liver metastases 4% had grade 1, 51% grade 2 and 45% had grade 3 primary tumours. 72% were ER positive and 21% were HER-2 positive. Table 1 shows the correlation between histological factors and liver metastases pattern.

During 12-month follow-up, 44 (56%) out of the 78 women with liver metastases died. At univariate analysis, the number of liver

**Table 1**
Liver metastases and relationship to histopathological grade, ER and HER-2 status.

| Variable | Number | Mean age at presentation (years) | ER positive | Grade 1 | Grade 2 | Grade3 | HER-2 pos | Ascites |
|---|---|---|---|---|---|---|---|---|
| Total liver metastases | 78 | 60.8 | 56 | 3 | 38 | 34 | 8 | 10 |
| Solitary | 13 (17%) | 63.4 | 9 (16%) | 0 (0%) | 4 (10%) | 8 (24%) | 0 (0%) | (0) 0% |
| Multiple | 30 (39%) | 61.8 | 24 (43%) | 2 (66%) | 14 (37%) | 12 (35%) | 2 (25%) | (1) 10% |
| Diffuse | 35 (45%) | 58.9 | 23 (41%) | 1 (33%) | 20 (53%) | 14 (41%) | 6 (75%) | (9) 90% |