Prognostic Factors in Patients with Breast Cancer and Malignant Pleural Effusion

To the Editor:

Malignant pleural effusion (MPE) occurs frequently at some time during the course of metastatic breast cancer and has been associated with poor prognosis (1–3). However, a wide range in survival exists for individual patients (1–6). Various factors have been associated with an impaired prognosis in patients with any type of cancer and MPE, including low pleural fluid pH (<7.2 (4), <7.3 (7,8)), low pleural fluid glucose (<3.3 mmol/L (4,8)), unsuccessful pleurodesis (9,10) and a low performance score at time diagnosis (11). Factors associated with improved prognosis in breast cancer patients with MPE are unilateral effusion ipsilateral to the primary tumor, an objective response to therapy, a long interval from breast cancer diagnosis to the onset of MPE and MPE being the only site of breast cancer recurrence (3,5). Although survival of patients with metastatic breast cancer has recently improved considerably (12) most studies on MPE in breast cancer have been performed more than two decades ago.

To investigate current survival and predictors of prognosis in pleural metastatic breast cancer, we analyzed data of 49 patients with breast cancer and MPE registered between 2000 and 2006 at a Dutch teaching hospital. Patient records were reviewed for age, Karnofsky performance score at presentation of MPE, date of diagnosis and pathological classification (staging and histology) of primary breast cancer and MPE, the site of primary breast cancer in relation to the site of MPE, time to progression and sites of metastases, pH and glucose (mmol/L) of MPE, treatment modalities of breast cancer and MPE, recurrence of MPE and survival. Data were analyzed using SPSS version 14.0 and survival analysis was done with the Kaplan–Meier method. For calculation of significances Mann–Whitney test was used, p < 0.05 was considered significant.

The results are summarized in Table 1. The median follow up after the diagnosis of MPE was 49 months (range 13–83 months). Most patients (70%) had infiltrating ductal carcinoma, 50% had stage II breast cancer at presentation, 8% presented with stage IV. The majority of patients had lymph node positive breast cancer at presentation (63%). HER2neu was determined in 20 patients (41%), being overexpressed in four patients (20%). These patients had significant worse survival compared to HER2neu negative patients (p = 0.01). Age >60 years, low pH and glucose of MPE and repeated pleurodesis were not associated with worse survival. The mean survival of four patients with a low performance status at presentation of MPE (Karnofsky score <60), was lower than in patients with a score of 60 or higher but the difference was not significant. The median interval from diagnosis of breast cancer to detection of MPE was 5.3 years (range = 0–20.2). When MPE occurred within 5 years after the diagnosis of breast cancer, survival was significantly shorter. Most effusions were unilateral and ipsilateral to the affected breast (66%), but this was not associated with a significant survival benefit. Metastatic disease at other sites than pleural was common (89% of patients). MPE was the only symptom of breast cancer recurrence in five patients (11%), these patients had a significant survival benefit as compared to patients with metastases at other sites.

Systemic therapy was given to 48 patients (98%): 35 patients received hormone therapy (92%), 25 patients received chemotherapy (66%), 19 patients received both (56%). One patient was treated with trastuzumab and chemotherapy. Other HER2neu positive patients had insufficient condition for this treatment. Patients treated with hormone therapy survived significantly longer as compared to those who did not receive hormone therapy. The median survival from the onset of malignant pleural effusion was 9.3 months (mean = 19 months, range = 0.1–81, Fig. 1). In our series, 23 patients were alive (47%)
1 year after MPE diagnosis and 15 patients were alive after 2 years (31%). At the end of follow up 10 patients (26%) were still alive.

Table 2 depicts results on previous series of breast cancer patients with MPE. As compared to literature, patients in our study are older. In all studies including ours, survival is highly variable between individual patients, ranging from weeks to more than 5 years. One- and 2-year survival in our series (47 and 31%, respectively) compare favorably to results of most previous studies. In contrast, median survival is more comparable, which may be explained by shorter follow up.

In our study, low pleural fluid pH and glucose, unsuccessful pleurodesis and a low performance score at the time of the thoracoscopy did not significantly impair prognosis. However, our series may have been too small to detect differences.

The previously found favorable prognostic factors of a longer lag time from breast cancer diagnosis to the onset of MPE (3, 5, 6) and MPE as the only site of breast cancer recurrence (5) were confirmed in our series. These factors are probably the strongest prognostic predictors in breast cancer patients with MPE. MPE was the only site of recurrence in 11% of our patients. Of notice, these patients had a median survival of 55 months which is longer than reported before (5). The finding that a shorter interval between primary breast cancer and occurrence of MPE predicts poorer prognosis may reflect more aggressive disease or treatment failure.

New therapeutic agents have shown to improve survival in metastatic breast cancer (12). The role of trastuzumab in breast cancer patients with MPE has not specifically been investigated, although its efficacy
in HER2neu overexpressive disease has unanimously been established (13). Unfortunately, as only one patient was treated with trastuzumab in our series, no conclusion could be made regarding effect of this newer agent on prognosis in our patient group. Hormone receptor positive breast cancer has better prognosis than hormone receptor negative disease (14). We also found a trend for better survival in patients with hormone receptor positive breast cancer and a significant survival benefit for patients treated with hormone therapy.

In summary, prognosis of breast cancer patients with MPE is highly variable. Favorable prognostic factors are a long interval from initial diagnosis to MPE, MPE being the only site of recurrence, hormone therapy and lack of HER2neu overexpression. Compared to historic literature our results suggest that prognosis in breast cancer patients with MPE has improved over time.

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