

BRUSTKREBSNACHSORGE

“Program Surveillance”

in women with early breast cancer

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Two prospective randomised trials published in 1994 (1, 2) continue to be the basis of international guidelines, e.g. ASCO (3, 4) rejects regular laboratory tests and radiological / ultrasound screening procedures in the follow-up of early breast cancer patients. According to these guidelines, follow-ups should be focused on the breast. Only patients with possible tumour related symptoms should be screened for metastatic disease. In this article, we will review the data of available surveillance studies which did not show an advantage for female patients with intensified follow-up, and discuss arguments for a systematic surveillance in breast cancer patients.

1. In the study published by Del Turco et al. (1994), X-ray of the chest and bone scan was used, in addition to standard procedures. However, neither ultrasound of the liver nor any laboratory tests were performed (1). In the trial published by the GIVO investigators, ultrasound of the liver was performed once a year (2). Both trials did not examine tumour markers (CEA, CA 15-3). Consequently, the experimental procedures of the two studies are not qualified as “intensive surveillance”

Furthermore, approximately 10% of the patients in the GIVO trial developed metastatic disease with a follow-up of 5 years (2). This is much lower than the known percentage from epidemiologic data (ca. 40%). The expected statistical death rate for the population in this study is 35% at 5 years (2). However, the study results show 18% and 20% death rates in the control group and in the intensive group respectively (2). The lower death rates can be explained by the fact that both studies enrolled mainly patients with ‘good-risk’ profile, as can be seen by the absence of axillary lymph nodes in approximately 50% of the patients, and by the very few number of patients (<10%) with pT3- or pT4-tumours at the time of diagnosis (1, 2). Therefore, it is not surprising that no differences in the survival rates had been observed in the two studies.

2. At the time when the surveillance studies discussed above were published, many substances, such as taxanes, vinorelbin, capecitabine, aromatase inhibitors and trastuzumab, were not yet available for treatments. We have seen evidence that with the introduction of new effective drugs, the overall survival rate of patients with recurrent breast cancer has improved significantly over the past years (5-6). The retrospective analysis conducted at the M.D. Anderson Institute in Texas (5) showed that 5-year overall survival rates in patients with recurrent breast cancer improved continuously, from 1974 (10%) to 2000 (40%). Similar results were reported from Canada (6). Even though these were retrospective investigations from individual clinics (which are, however, also world-wide leading institutes in this area), the results demonstrate significantly improved treatment possibilities, even in the case of metastatic illness. All of these suggest that cancer patients should be given adequate treatments with no fatalistic attitude to their diseases. There is no doubt that many of our patients really do take advantage from 3rd and 4th line treatments, and this experience is far from solely being “casuistic”. The positive development in stage IV breast cancer is expected to continue even in times of restricted financial resources (e.g. bevacizumab, lapatinib, etc.). The limited therapeutic spectrum, as available when the studies cited above (1, 2) had been performed, remains a real problem and current guidelines should definitely not be based on such biased comparative analyses.

3. Treatment options are considerably limited in advanced diseases if symptoms such as dyspnoea or jaundice are already present at the initial diagnosis of metastatic disease: The associated deteriorated general condition of the patient, as well as elevated levels of GOT/GPT and Bilirubin etc. are considered reliable indicators of an unfavorable prognosis. Patients with these symptoms are widely excluded from current study protocols. At the Tumor Center in Essen, there are numerous cases of patients with inoperable liver metastasis who survived for more than 5 years (7, manuscript in preparation). If their treatment had been started at the time when the first symptoms of visceral metastasis appeared, the patients would not have benefitted fully from an individually adjusted optimal therapeutic sequence, which makes use of all available options nowadays.

4. Patients who could obtain a complete remission (CR) with chemotherapy have the best chance of long-term survival (8, 9). A crucial prognosis factor to reaching CR is a small tumor load (8). In the case of diffuse liver or lung metastasis, CR is only rarely attainable. Patients with the best chance of CR are also those with still limited asymptomatic metastasis. They might only be detected with follow-ups which allow imaging diagnostic procedures, even in the case of asymptomatic diseases (10).

5. In the case of still localized metastasis, one option is surgical intervention, together with systemic therapies when necessary (11, 12). In terms of metastasis resection, by which a “no evidence of disease” status can be achieved, there are only non-randomized studies for metastatic breast cancer. Given that good results are reported after the resection of solitary visceral metastasis in colorectal cancer (15, 16), it is reasonable to draw an analogous conclusion. Even though there are no prospective randomized studies on the resection of metastasis of colorectal cancer, the results of non-randomized trials and retrospective analysis have been convincing enough that these measures are now included in the general treatment recommendations (17, 18). Therefore, regular screening of chest and abdomen by CT scans is strongly recommended in surveillance of colorectal cancer patients (17, 18), because these asymptomatic metastasis would otherwise not be detected. These localized therapies are in fact suitable for only a small number of patients. Since the treatments for metastatic breast cancer, according to general consensus, is an individual therapy, patients should not be deprived of these approaches that provide a chance of long term survival.

Overall, symptom guided follow-ups appear to be adequate for patients with small primary tumours and with no lymph node involvement, hence giving rise to a high curative probability. However, it is the authors' opinion that systematic surveillance should be recommended for high risk patients even in the absence of symptoms. Furthermore, in addition to the recommended procedures in the current guidelines, surveillance should also include ultrasound of the liver, X-ray of the chest and tumour markers CEA and CA 15-3 every 3 months. Bone scans appear to be dispensable, given that bone metastasis are usually noticeable at an early stage due to pain (19, 20). All patients, however, should be fully informed of the possibility of metastatic disease development and be given the option to select the quality of their postoperative follow-ups.

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