

Staging for Breast Cancer: A Comparison Between Old and New Approaches

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Abstract. *Background/Aim:* Staging for breast cancer in advanced stages or prior to neoadjuvant chemotherapy is recommended to be performed with CT scan of the chest and abdomen and a bone scan. This recommendation is valid since 2012, when conventional staging with chest x-ray and ultrasound of the abdomen was replaced by the more sensitive CT scan. However, it remains unclear if this approach improves patient outcome and prognosis. *Patients and Methods:* We identified patients who were treated for breast cancer at the breast center of the St. Elisabeth Hospital, Cologne, in 2012 and 2014. Clinical information such as age at diagnosis, stage, tumor biology, grading, and the applied method for staging was abstracted from the patient chart. We also looked for local or distant recurrence and data of survival. *Results:* A total of 1,122 patients were identified. Of those, 104 patients developed local or distant recurrence and 54 died. Conventional staging with chest x-ray, abdominal ultrasound and a bone scan was more often in 2012 (482 cases) than in 2014 (135), but CT-staging was more often in 2014 (180 vs. 29 cases). In general, less patients were staged in 2014 than in

2012. There were no significant survival differences between the two groups. *Conclusion:* Staging habits changed in 2012 compared to 2014 according to the changes in guidelines. This change did not affect disease-free survival.

Among all cancers, breast cancer remains the most common cancer in the western civilization with 70.000 new cases each year in Germany alone (1, 2). Prognosis and survival rates have improved tremendously within the last decades, but still questions remain about the optimal care of patients with breast cancer (3).

National guidelines such as the S3-Leitlinie Mammakarzinom or the recommendations by the AGO (Arbeitsgemeinschaft Gynäkologische Onkologie, Working Group of Gynecological Oncology) Kommission Mamma are frequently updated to incorporate the most recent evidence-based medicine (4, 5). One recommendation that has changed over time is the use of radiation imaging for detecting distant metastases in asymptomatic patients. Up to the year 2012 it was recommended to perform a general pretherapeutic staging for all breast cancer patients using chest x-ray, ultrasound of the abdomen and a bone scan. However, the probability for primarily metastasized breast cancer is about 4% for all newly diagnosed breast cancer patients and decreases further in node-negative patients to below 1% (6, 7). One can imagine that a general staging for breast cancer caused a high number of unnecessary examinations. Those in turn caused unnecessary exposure to radiation, unnecessary psychological stress, false-positive results, and financial burden on the health care system (8, 9).

So, in 2012 the general staging recommendation changed to a more individual approach: only breast cancer patients that were diagnosed with a rather advanced stage of disease (node positive, large primary tumor) or those prior to neoadjuvant chemotherapy should undergo a staging and the recommended method changed to CT scan of the chest and the abdomen and

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Table I. Patient characteristics.

	Group 1 (2012)	Group 2 (2014)
Number of patients	566	556
Median age at diagnosis	61 years	60 years
Tumor stage UICC		
DCIS	9 (1.6%)	10 (1.8%)
I	279 (49.3%)	286 (51.4%)
II	205 (36.2%)	216 (38.8%)
III	66 (11.7%)	41 (7.4%)
IV	1 (0.2%)	2 (0.4%)
Missing	6 (1.1%)	1 (0.2%)
Tumor biology		
ER positive	495 (87.5%)	503 (90.5%)
PR positive	407 (71.9%)	423 (76.1%)
HER2 positive	103 (18.2%)	122 (21.9%)
TNBC	46 (8.1%)	35 (6.3%)
Grading		
1	94 (16.6%)	111 (20%)
2	327 (57.8%)	311 (55.9%)
3	144 (25.4%)	134 (24.1%)
Missing	1 (0.2%)	0
Applied staging		
Chest x-ray	482 (85.2%)	135 (24.3%)
Abdominal ultrasound	482 (85.2%)	135 (24.3%)
Bone scan	530 (93.6%)	335 (60.3%)
Chest CAT scan	29 (5.1%)	180 (32.4%)
Abdominal CAT scan	29 (5.1%)	180 (32.4%)
None of the above	24 (4.2%)	195 (35.1%)
Second imaging after initial conventional staging	64 (11.3%)	23 (4.1%)
Applied therapy		
Chemotherapy	229 (40.5%)	195 (35.1%)
Endocrine therapy	454 (80.2%)	479 (86.2%)
Radiation therapy	404 (71.4%)	405 (72.8%)
Recurrence		
Local	13 (2.3%)	17 (3.1%)
Distant	38 (6.7%)	36 (6.5%)
Outcome		
Survival	539 (95.2%)	529 (95.1%)
Death	27 (4.8%)	27 (4.9%)

a bone scan. The change of the latter recommendation was mainly based on the fact that a CT scan is the more sensitive examination. However, to our knowledge no data exist that compare conventional staging and staging with CT scan in terms of prognosis/survival (10, 11).

The aim of this study was to compare the outcome of breast cancer patients that were either staged conventionally with chest-x-ray, ultrasound of the abdomen and a bone scan with those patients who were staged with a CT and a bone scan.

Patients and Methods

We identified patients that were treated for breast cancer at the breast center of the St. Elisabeth Hospital of Cologne in 2012 and 2014. The following data were abstracted from the patient chart: age

at time of diagnosis, tumor stage, tumor biology (ER, PR, HER2), and grading. In terms of staging, we looked for chest x-ray, ultrasound of the abdomen, CT scan of the chest and abdomen, and bone scan. For all patients we noted application of adjuvant therapies such as chemotherapy, radiation therapy, and endocrine therapy. Information on local or distant recurrence and/or death was also abstracted from the patient chart.

Statistical analysis was performed by using SPSS 27.0 software (SPSS Inc., IBM, Chicago, IL, USA). Patient characteristics were described using count (percentage), mean±standard deviation (SD) or median [interquartile range (IQR)], as appropriate. Associations between two qualitative variables were tested using Fishers exact test. Kaplan–Meier curves were drawn for the comparison of survival times. Differences between survival curves were calculated using the Chi square statistic of the log-rank test to assess significance. All reported *p*-values are two-sided and considered statistically significant if ≤5%.

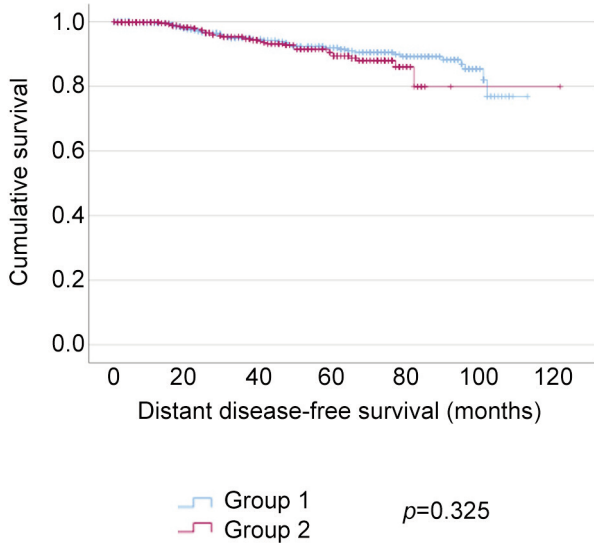


Figure 1. Distant disease-free survival was 103.6 months in group 1 (patients diagnosed in 2012) and 108.9 months in group 2 (patients diagnosed in 2014); $p=0.325$.

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Due to the retrospective character of the study, no new data was generated, and third party did not have access to the data. All data evaluation was performed anonymously. This retrospective review of patient data did not require ethical approval in accordance with local guidelines.

Results

A total of 1,122 patients were identified that were treated at the breast center of the St. Elisabeth Hospital in Cologne. Therefrom, 566 were diagnosed in 2012 (group 1) and 556 were diagnosed in 2014 (group 2). Please see Table I for the clinical details of the cohort such as age at diagnosis, tumor stage, tumor biology, and grading.

In group 1, almost all patients underwent routine staging with chest x-ray ($n=482$), abdominal ultrasound ($n=482$), and a bone scan ($n=530$). A small number underwent additional chest CT scan ($n=29$) or abdominal CT scan ($n=29$). In group 2, less patients underwent chest x-ray and abdominal ultrasound ($n=135$). A bone scan was performed in 335 cases. The number of CT scans increased to 180 (chest and abdominal scan).

Complete conventional staging using chest x-ray, abdominal ultrasound, and a bone scan was performed in 482 (group 1) and 135 (group 2) patients. A full CT-Staging using images of the thorax and abdomen was performed in 29 (group 1) and 180 (group 2) patients. There were also patients who received both, conventional staging and CT-staging for initial staging (28 and 17, respectively).

Of those patients who underwent conventional staging, some had to take additional imaging to rule out false positive results. These were 83 (13.8%) patients who underwent an additional CT scan and 38 (6.3%) patients that underwent an MRI. Of those patients who underwent primary staging via CT scan two patients (1%) underwent additional imaging. At the time of data collection in 2021, there were 13 (group 1) and 17 (group 2) local recurrences. Distant recurrences were 38 and 36, respectively. Distant disease-free survival was 103,6 months in group 1 and 108.9 months in group 2 ($p=0.325$, see Figure 1 for curves of survival).

Discussion

Our cohort of breast cancer patients consists of a total of 1122 patients. 566 were diagnosed in 2012 and 566 in 2014. With a median age at diagnosis of 60 and 61, respectively, our patients are a few years younger than the general breast cancer population in Germany (2). Stages are also distributed in favor for earlier stages which might be due to the fact that we were trying to exclude primarily metastasized patients (12). Most patients of our cohort were hormone receptor positive with over 80% of cases. HER2 positivity is in accordance with that of the general breast cancer population (less than 20%). Only triple negative breast cancer is less likely in our cohort with less than 10%.

We chose to compare patients diagnosed in 2012 and 2014 since this was the time when staging recommendations in guidelines were changed and we wanted to evaluate if this change in guidelines was reflected in clinical reality, if there are more false-positive findings with conventional staging followed by additional radiologic imaging, and if there is a prognostic difference (13, 14).

The latter was evaluated by comparing patients by year of diagnosis to evaluate if the change in guidelines had an influence on patients' outcome.

The changes in guidelines basically meant that less patients should be staged, but if there is an indication for staging, it should be performed with a more sensitive CT scan. When guidelines are changed usually there is a transition phase until changes are fully implemented. But already in 2014, a lower number of patients was fully staged. The number of patients that were staged decreased from 511 (90%) in 2012 to 315 (57%) in 2014. Also, the applied method changed in accordance with the guidelines: in 2012 there were 482 (94%) patients staged conventionally and only 29 (6%) using CT scan. However, in 2014, there were 135 (43%) patients staged conventionally and 180 (57%) using a CT scan. Since a bone scan was and is recommended, we did not put much effort in evaluating changes. However, it was also less often performed in 2014 (530 scans) than in 2012 (335 scans).

To our knowledge, this is the first study evaluating differences in staging methods, so we are not able to compare

our numbers with previous results from other studies or institutions. However, adherence to guidelines is a matter and it is evident that it improves patient outcome (15). In our previous study evaluating staging habits in German breast centers, we showed that even in more recent times, changes in staging recommendations are not fully implemented. This is very much dependent on each institution and certified breast cancer centers showed the highest adherence (7).

The reason for changing the staging recommendations at that time was often justified by the fact that conventional staging is less sensitive and that it might cause additional radiologic imaging due to false positive results (16).

In fact, of those patients who underwent conventional staging, 83 patients (14%) had additional CT scans. However, among those who were initially staged using CT scan, only 2 patients underwent additional imaging. Unfortunately, we did not look for biopsies or other interventions that rule out false positive results. It is very likely, that there were more false-positive results within the CT scan group, however, these might not have had additional imaging but invasive interventions. However, from previous studies evaluating this matter we know that there are false positive results with any radiologic imaging. Nam et al. found in their cohort of breast cancer patients an overall false-positive rate of 14.9% when abdominal CT was applied (17). This is in accordance with James et al. who reported a false-positive rate 15% for abdominal CT scans in breast cancer patients (16). FDG-PET/CT might be useful for nodal staging in breast cancer but is currently not applied for general staging (18).

Even considering the higher sensitivity of a CT scan, conventional staging has some advantages. Radiation exposure is definitely lower when staging is performed with chest x-ray and abdominal ultrasound. It is also less time consuming, more easily accessible and less expensive. The analysis of distant disease-free survival showed no significant differences, so that the change in staging habits did not influence patients' prognosis.

Ultimately, one can discuss the question if staging recommendations are already specific enough. Since the probability of detecting distant metastasis in all breast cancer patients is less than 4% and less than 1% in node negative patients, it definitely would be safe to omit staging in a lot more patients than we currently do independent from the applied method (19). This is supported by the fact that imaging for distant metastases frequently reveals indeterminate findings, most of which are not associated with disease recurrence (9).

Conclusion

Changes in staging recommendations were reflected by our study cohort. Although a CT scan might be the more sensitive imaging method, we did not find a prognostic difference for the groups staged in 2012 or in 2014.

However, there is no clear advantage for a CT-based staging, and it warrants further evaluation. A prospective study comparing conventional staging with CT staging vs. no staging would be the desired approach to clarify these issues.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

Verena Kirn, Sarah Bors and Fabinsy Thangarajah have made substantial contributions to the conception and the design of the study. Sarah Bors and Verena Kirn were responsible for data acquisition. Verena Kirn, Fabinsy Thangarajah, Claudius Fridrich, and Claudia Schumacher made substantial contributions to analysis and interpretation of data. All Authors were involved in drafting and revising the manuscript for intellectual content and final approval of the version to be published.

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