CAUSES OF DEATH IN PATIENTS WITH STAGE 0-II BREAST CANCER

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CAUSES OF DEATH IN PATIENTS WITH STAGE 0-II BREAST CANCER (Abstract): Aim: To analyze the main causes of death in patients with stage 0-II breast cancer who undergo breast conserving surgery or radical mastectomy, and to establish the role of imaging surveillance protocols following breast cancer treatment. Material and methods: We conducted a retrospective medical record review between January 2005 and December 2012, when breast cancer was the primary cause of death for 113 inpatients. All patients were admitted to the Oncology Clinic of the Iasi Regional Cancer Institute (IRCI), Romania. Patients were stratified by clinical stage 0, I and II, of which 33 (29.2\%) patients were managed by breast conservation therapy and 80 (70.8\%) underwent radical mastectomy. From the patient medical records all diagnostic imaging studies performed (ultrasound, radiography and computed tomography) were identified and analyzed according to a standard protocol for imaging the postoperative breast. Results: Bone, liver, lung, lymph nodes and local-regional recurrence were the most common sites for metastasis, while the most frequent cause of death were metastases to the liver, pleura, lung and brain. The time interval between recurrence and death ranged from 0-24 years among patients with one type of metastasis, and decreased to 0-3 years since the last recurrence for patients with multiple metastases. Conclusions: The current imaging protocol for monitoring the postoperative breast could be optimized to improve the prognosis and quality of life in patients with stage 0-II breast cancer. Keywords: BREAST CANCER, METASTASES, IMAGING PROTOCOL.

The main cause of death for women in Europe is breast cancer (1, 2). Metastases to the liver, pleura, lung and brain, diagnosed by clinical and imaging protocols, are most often responsible for patient death (3). Diagnoses of local recurrence or distant metastases in infra clinic stages allow immediate therapeutic decision making in order to improve the quality of life. In this context, the current imaging surveillance protocols following breast cancer treatment are aimed to be improved based on internationally agreed guidelines proposed by the European Society for Medical Oncology (ESMO) (4), St. Gallen Consensus Conference, Advanced Breast Cancer Consensus Conference (ABC), the German Gynecological Oncology Working Group (AGO), and National Comprehensive Cancer Network (NCCN).

The objectives of this study were: to assess the risk of local recurrence and death after breast cancer surgery; to investigate the benefits and limitations of imaging
Causes of death in patients with stage 0-II breast cancer

studies in detecting local recurrence and distant metastases, and to improve the current imaging surveillance protocol following breast cancer treatment.

MATERIAL AND METHODS
We conducted a retrospective medical record review between January 2005 and December 2012, when breast cancer was the primary cause of death for 113 in patients admitted to the IRCI Oncology Clinic.

Breast cancer patients were stratified according to clinical staging at the time of diagnosis into stage 0, I and II. All patients had undergone breast surgery between January 1983 and December 2011, of which 33 (29.2%) patients were managed by breast conservation therapy and 80 (70.8%) underwent radical mastectomy.

Data drawn from patient medical records were compared using multiple regression analysis, regression coefficient, frequency distribution, chi-square test and Pearson’s product-moment r (-1 < r <1, the more closely the two variables are related, r = 0, there is no relationship between the variables). A P value of less than 0.05 was considered statistically significant. All statistical tests were performed with the Statistical Package for the Social Sciences (SPSS for Windows, Version 16.0. Chicago, IL, USA).

RESULTS
Of the 113 patients included in the study, 49 (43.4%) patients died of breast cancer-related causes and 64 (56.6%) patients had other causes of death (cardiac pathology, stroke, colon, stomach, pancreas and ovary neoplasms). Deaths resulting from breast cancer were due to local recurrence or distant metastases. The most common types of recurrence were bone metastases - 40 (35.4%) patients, liver metastases - 24 (21.2%) patients, lung metastases - 22 (19.5%) patients, local recurrence - 20 (17.7%) patients, and lymph node metastases - 18 (15.9%) patients. Most of the recurrences occurred within 3 years following the surgery. The mean survival time from recurrence to death ranged from 0.95 years (in patients with brain metastases) to 5.73 years (patients with local recurrence) (tab. I).

TABLE I
Case distribution by type of recurrence, minimum, maximum and mean survival time from recurrence to death

<table>
<thead>
<tr>
<th>Type</th>
<th>Patients (%)</th>
<th>Minimum survival time (years) from recurrence to death</th>
<th>Maximum survival time (years) from recurrence to death</th>
<th>Mean survival time (years) from recurrence to death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>20 (17.7)</td>
<td>&lt;1</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>40 (35.4)</td>
<td>&lt;1</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>24 (21.2)</td>
<td>&lt;1</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Lung metastases</td>
<td>22 (19.5)</td>
<td>&lt;1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Lymph node metastases</td>
<td>18 (15.9)</td>
<td>&lt;1</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Pleural metastases</td>
<td>12 (10.6)</td>
<td>&lt;1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Brain metastases</td>
<td>11 (9.7)</td>
<td>&lt;1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Skin metastases</td>
<td>9 (8)</td>
<td>&lt;1</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Peritoneal metastases</td>
<td>2 (1.7)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
Manuela Ursaru et al.

Of the 33 patients treated with breast conserving surgery, 11 (33.3%) patients had no recurrence and 22 (66.6%) patients had local recurrence or single/multiple organ metastases. Of the 22 patients with local recurrence or distant metastases in 17 (77.2%) the cause of death was breast cancer.

Of the 80 patients treated with radical mastectomy, 22 (27.5%) patients had no recurrence, and 58 (72.5%) patients had local recurrence or single/multiple organ metastases. Of the 58 patients with local recurrence or single/multiple organ metastases, 34 (58.6%) patients had breast cancer as the cause of death.

Comparative evaluation of local recurrence and distant metastases in breast cancer patients treated with breast conserving surgery or radical mastectomy showed that bone, liver, pleural and skin metastases were diagnosed in similar frequencies. Local recurrence, lymph node and brain metastases were more frequently observed in patients treated with breast conserving surgery. Metastatic spread to the lungs was significantly more frequent in patients treated with radical mastectomy.

Regardless of breast cancer surgery type, lung, pleural, liver and brain metastases were causes of death in breast cancer patients (p<0.0001). Pearson’s product-moment correlation coefficient showed a significant negative correlation between mean survival time from recurrence to death and the presence of lung (r= -0.562), pleural (r= -0.394), liver (r= -0.506) and brain (r= -0.375) metastases.

Imaging methods used to diagnose recurrence/distant metastases were:

- chest CT ± chest radiograph, for the assessment of lung and pleural metastases;
- abdominal ultrasound ± CT scan for the detection of liver metastases;
- CT brain ± MRI for the detection of brain metastases.

DISCUSSION

In this study group we found that the most common sites of secondary relapse include the bone, liver, lung, and local lymph nodes. Leading causes of breast cancer death were liver, pleural, lung and brain metastases (5-9). While breast cancer patients with bone metastases and local recurrence had the longest survival interval (10 years for bone metastases and 24 years for local recurrence), the most aggressive lesions were brain metastases that caused death within the first 2 years after diagnosis (fig. 1).

![Fig. 1. Time interval from the diagnosis of brain metastases diagnosis to death in breast cancer patients](image)

Patient survival was significantly influenced by relapses. We found that in patients with one metastatic lesion death occurred within 24 years from the time of their diagnosis, while in patients with two or more metastatic lesions death occurred within 3 years after the last recurrence.

All patients included in this study were monitored with different imaging tests at different times. For the diagnosis of lung and pleural metastases chest X-rays were
performed each year. When a clinical suspicion of lung or pleural metastasis was raised, thoracic CT was performed. It is noteworthy that metastatic lesions less than 5 mm in diameter are often not visible on standard chest X-rays (10). Hence, the necessity to include thoracic CT in the imaging surveillance protocols. For the diagnosis of liver metastases abdominal ultrasound at various time intervals (every 6 months or annually) was performed, and in doubtful cases an abdominal CT scan. The study showed that liver metastases occurred in the first 3 years after surgery, so it is appropriate to perform an abdominal ultrasound every 6 months during the first three years after surgery, then yearly. It was also noted that homogeneous ultrasound appearance of the liver does not exclude the presence of secondary lesions (11). The introduction of abdominal CT scans in imaging surveillance protocols for breast cancer patients could diagnose the liver metastases at infra clinic stage. For the diagnosis of brain metastases when clinical suspicion was raised, a cranial CT scan was indicated. In 3 of the 11 cases with brain metastases, brain MRI was indicated to establish the uniqueness of the lesion. Surgical treatment of brain metastases was indicated only if the lesion was unique and had an easily approachable location (12, 13). MRI imaging remains decisive in patients with brain metastases, which can be treated surgically.

**CONCLUSIONS**

In our study, the most common causes of death in breast cancer patients treated with breast conserving surgery or radical mastectomy were metastases to the liver, pleura, lung and brain. Optimizing current imaging surveillance protocols in patients surgically treated for breast cancer by using ultrasound, computed tomography and MRI can improve the quality of remaining life.

**REFERENCES**


EMULSIFYING AND ANTIOXIDANT PROPERTIES OF APPLE AND GRAPE TANNINS

Preparation of an emulsion requires amphiphilic compounds that can stabilize it. The emulsions are unstable due to the surface tension between water and oil which prevents the increase of the interfacial area. Moreover, the stabilizing agents are needed to control the two competing (attracting and repulsive) forces that occur in the preparation process. Another problem would be the oxidation of lipids which are added in an emulsified system. Therefore, compounds with both stabilizing and antioxidant properties are needed. Tannins are a class of polyphenols that are widely spread in nature. Figueroa-Espinoza et al. studied the properties of catechin, apple and grape seed tannins, as well as their stabilizing and antioxidant capacity. They used catechin and tannin fractions isolated from grape seeds (Vitis vinifera, var. Shiraz) and apples (Malus sylvestris, var. Kernerian). The degree of polymerization of tannin fractions was studied by HPLC after depolymerization. The antioxidant properties were evaluated using the conjugated autoxidizable triene method. The oil in water emulsions stabilized with tannins were compared with the emulsions obtained using polyvinylalcohol (PVA) and polyoxyethylene hydrogenated castor oil. The results showed that, in certain conditions, oxidized tannins provide an emulsion stability comparable to that of PVA. Furthermore, grape tannins showed higher antioxidant effects in comparison with the apple tannins. Therefore, oxidized tannins could be used as an alternative source of antioxidant emulsifiers (Figueroa-Espinoza MC, Zafimahova A, Maldonado Alvarado PG, Dubreucq E, Poncet-Legrand C. Grape seed and apple tannins: Emulsifying and antioxidant properties. Food Chem 2015; 178: 38-44).