As mammary carcinoma is the most frequent malignant disease in women, early detection is important. There are numerous diagnostic tools available, the mammogram being the gold standard. The next step would be developing a treatment plan that is individualized for the patient and the type of carcinoma. The following article will teach you to accurately diagnose mammary carcinoma and to initiate the appropriate therapy.

You may read everything concerning causes, risk factors, symptoms and special types of mammary carcinoma in the following article: Breast Cancer (Mammary Carcinoma) — Causes, Classification, and Symptoms
Diagnosis of Breast Cancer (Mammary Carcinoma)

Patient history and clinical examinations in cases of breast cancer

History and physical examination are the cornerstone in every disease, including breast cancer. Though patients with breast cancer are often asymptomatic, it is important to ask targeted questions regarding the aforementioned symptoms (changes in the size of the breast, differences between both sides, skin retraction, etc.), as well as individual risk factors.

The physical examination should be done with the patient’s upper body unclothed and her arms down, as well as with her arms raised up. Palpation should be done after the end of menstruation. It is important to palpate the supraclavicular and axillary lymph nodes.

![Image: 'Self-Exam' by Stevenfruitsmaak. License: public domain]

Diagnostic tools for mammary carcinoma

**Breast Exam**

Traditionally, women were encouraged to regularly perform breast self-exams and palpation but the current United States Preventive Services Task Force (USPSTF) recommends against breast self-examination as it does not reduce breast cancer-related mortality and leads to excessive anxiety.

Therefore a regular breast exam, self-exam or by the medical expert, is not recommended. Still, all women should be familiar with the look and feel of their breasts and must consult a medical expert if any changes are noticed.

**Mammography**

Mammography is the gold standard of the instrument-based examination of the breast for the early detection of mammary carcinoma.

The USPSTF recommends biennial (every 2 years) screening mammography for women between the ages of 50-74 years.
In women younger than 50 years, the decision to start screening mammography should be an individualized 1 depending upon the patient’s risk factors.

Mammography is a specific type of low-dose X-ray imaging in which radiopaque structures such as carcinoma, calcifications or fibroadenomas create shadows but appear light on the scan, whereas fatty tissue appears dark.

While benign tumors mostly appear homogenous, smoothly outlined, and dense, the following criteria are signs of malignant findings:

- Asymmetric focal findings with unsharp delineation
- Inhomogeneous band- and mesh-like shadows
- Star-shaped thickening with spicules
- Polymorphic clustered microcalcifications (pointing toward ductal carcinoma in situ (DCIS)!)
- Surrounding tissue: retraction phenomenon
- Outlined thickening/retraction (skin and mamillary gland)
Note: Polymorphic, clustered microcalcifications are suspicious and are to 80 or 90% a sign of in situ or early-stage carcinoma, respectively! Mammography has a sensitivity of between 85-90%, depending on the tissue density: the fattier the tissue, the better the sensitivity. The specificity, however, is very limited.

Mammography findings are classified according to BI-RADS (Breast Imaging-Reporting and Data System):

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>Diagnosis/Findings</th>
<th>Procedure</th>
<th>Risk of carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Imaging has not been concluded</td>
<td>Further clarification is necessary</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>Unremarkable findings</td>
<td>Normal care</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>Benign findings</td>
<td>Normal care</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>Unclear, probably benign findings</td>
<td>Requiring follow-up (after six months)</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>4</td>
<td>Suspect findings</td>
<td>Histological clarification</td>
<td>2 - 90%</td>
</tr>
<tr>
<td>5</td>
<td>Suspecting carcinoma</td>
<td>Histological clarification</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>6</td>
<td>Histologically confirmed carcinoma</td>
<td>-</td>
<td>100%</td>
</tr>
</tbody>
</table>
Other imaging diagnostic tools

In addition to the aforementioned methods, the following tests may be done:

1. Sonography
   - Most important complementary test in addition to mammography.
   - Benefit: no radiation exposure, differentiates solid (such as a benign fibroadenoma or cancer) from fluid-filled cystic (such as a benign cyst) lesions
   - Disadvantage: highly operator-dependent, not suited for screening

2. Galactography
   - Imaging of the milk-producing ducts using contrast agent injections, followed by X-rays with mammillary gland secretion.
   - Pathological findings: caliber fluctuations in the milk ducts, discontinue contrast agent

3. Magnetic resonance tomography (MRT)
   - Conclusive findings are only possible with contrast agents.
   - Benefit: high soft-tissue contrast, very high sensitivity
   - Disadvantage: low specificity, no detection of microcalcifications
If metastases are suspected, pre-therapeutic staging to include chest X-rays, liver sonography, as well as skeletal scintigraphy, should be pursued.

**Biopsy and histology**

The histological examination of the suspected breast cancer is important to confirm the diagnosis of breast cancer, its type, grade, the presence of certain receptors and genes, and to further plan therapy. For this purpose, breast tissue samples are collected from the suspicious area via minimally invasive procedures and subsequently examined microscopically.

Immunohistochemical staining of tumor cells is used in the diagnosis of tumors and may determine therapy. Hereby, the **hormone receptors** (estrogen, progesterone, and steroid hormones), as well as the growth factor receptors (human epidermal growth factor receptor 2 (HER2)/neu), play a role.

If more than 10% of the tumor cells stain positive for estrogen and/or progesterone receptors (ER/PR), the mammary carcinoma is hormone-receptor-positive. This means that it is suitable for endocrine therapy and has, in addition, a **better prognosis**.

In cases of invasive mammary carcinoma, HER2/neu is overexpressed, which is referred to as HER2-positive. This status of over-expression indicates the direction of therapy: In cases of HER2/neu positive, patients are treated with **trastuzumab, a HER2 antibody**.
Differential Diagnosis

The breast cancer has to be differentiated from benign breast lesions, such as:

- Fibroadenomas
- Lipomas
- Cystic changes
- Papillomas
- Mastitis

Therapy of Breast Cancer

Neoadjuvant therapy

Neoadjuvant therapy is the therapy that is given before surgery in order to shrink large tumors.

Surgery

Surgery is the main treatment for breast cancer. It includes either radical mastectomy or breast-conserving surgery with the same goal of removing the tumor, as well as affected regional lymph nodes.

Breast-conserving surgery

The breast-conserving treatment (BCT) followed by radiation therapy is the standard surgical treatment of care. The prerequisite is that the tumor has not yet infiltrated the surrounding tissue and that there is a favorable ratio between the size of the tumor and the volume of the breast.

- **Lumpectomy:** The lump (tumor) is removed along with the removal of 1 cm of healthy tissue on all sides. In some cases, the removal of the nipple may be necessary as well. The removal of the axillary lymph nodes is done with a 2nd incision.
- **Quadrantectomy:** Removal of the quadrant of the breast where the tumor is located, as well as the axillary lymph nodes.
Mastectomy

If the tumor is large, multicentric, or if the patient is contraindicated for post-surgery radiation, BCT will not be an option. In these situations, a modified radical mastectomy is performed.

During this procedure, the breast, the axillary lymph nodes, as well as the pectoral fascia, are removed, while the pectoral musculature (as opposed to a Halsted radical mastectomy) is preserved. In cases of inflammatory mammary carcinomas, there is an indication for a mastectomy as well.

Breast Reconstruction

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Breast reconstruction

Women must be educated on the option of breast reconstruction, which may take place simultaneously or after a latent period of at least 6 months. Suitable materials include heterologous implants or autologous tissue. Autologous tissue allows for the following flap technique reconstructions:

- Thoraco-epigastric flap reconstruction
- Latissimus dorsi flap reconstruction
- (Transverse) rectus abdominis (myocutaneous) flap reconstruction (TRAM)

**Note:** Both, mastectomy and BCT are to be regarded as equal with regard to survival rates, whereby the risk for a local recurrence is elevated for patients who have undergone BCT.

Lymphonodectomy

In order to determine a patient's nodal status, it is necessary to perform a lymphonodectomy. When the lymph nodes are removed, there is an increased risk of lymphedema.

If the tumor is < 3 cm in size, the axillary lymph nodes have not been affected and, if there are no contraindications (i.e. a multifocal, multicentric, metastasizing or inflammatory mammary carcinoma, Paget disease), the **sentinel lymph node** should be removed.

During this procedure, the lymph node that is attacked by the tumor cells 1st because of the lymph flow (**sentinel/guardian lymph node**) is marked via injection of peritumoral subdermal dye or radionuclide.

If this lymph node is free of tumor (sentinel negative), the removal of the axillary lymph node is not necessary resulting in reduced shoulder-arm morbidity.

If the sentinel lymph node is positive, axillary dissection with removal of a minimum of 10 lymph nodes is indicated.
Adjuvant therapy of mammary carcinoma

Adjuvant therapy takes place after the resection of the tumor with the goal to reduce the risk of a local recurrence and to eliminate potential tumor cells in the body. This can be systemically achieved via local radiation, chemotherapy, or via endocrine or monoclonal antibody therapy, respectively.

Radiation

Adjuvant postoperative radiation following BCT is an obligatory measure in order to reduce the risk of local recurrence. Following a mastectomy involving large tumors (postsurgical T3 (pT3), primary tumor stage 4 (pT4)), in cases of skin infiltration or extensive lymphangiosis and if > 3 axillary lymph nodes are affected, adjuvant radiation therapy is indicated.

Chemotherapy

Chemotherapy is indicated if there is an increased risk of recurrence and it should begin 1–2 weeks following surgery. The most frequent medications used are a combination of cytostatic drugs for which regular recommendations are established in the guidelines.

Monoclonal antibodies

In cases of HER2/neu-positive cancers, it is imperative to administer the monoclonal antibody **trastuzumab** for 1 year in addition to chemotherapy (see above).

Endocrine therapy

For ER-/PR-positive women (see above), endocrine therapy is indicated. The goal is estrogen deprivation in order to decrease the growth of carcinoma cells. The standard medication being used is tamoxifen. Another option for premenopausal patients is the administration of gonadotropin-releasing hormone (GnRH) analogs in order to suppress ovarian function. Aromatase inhibitors are indicated for postmenopausal patients.

Follow-up, Prognosis, and Prevention of Mammary Carcinoma

Follow-up care in cases of mammary carcinoma

After locoregional primary therapy, regular follow-ups are recommended, usually every 3 months during the 1st 3 years, every 6 months during the 4th and 5th year, and annually after the 6th year. After a mammary carcinoma, the risk of contralateral breast cancer is 2–5 times higher which is why there should be an annual instrument-based check-up in that area as well.

Prognosis

The prognosis of breast cancer depends on multiple factors, including tumor stage, grade, HER2/neu and hormone receptor status. The earlier it is detected and treated, the better the prognosis. In early breast cancers, the therapy is curative. This underlines the importance of breast cancer screening in women.

**Note:** The most important prognosis factor with regard to remote metastases is if the axillary lymph nodes are affected!
In cases of remote metastases (in 5% of female patients when they are 1st diagnosed and in 30% of patients during the progression of the disease), therapy will take a palliative course as healing is no longer possible. The median survival time is approx. 2 years and the 5-year survival rate is approx. between 5-10%.

Prevention

In order to prevent mammary carcinoma (primary prevention), the following options are available:

- In cases of hereditary mammary carcinoma, a bilateral mastectomy with a risk reduction of 90% and/or a bilateral adnexectomy with a risk reduction of 50% should be considered.
- In cases where the patient is at increased risk, drug therapy with tamoxifen, strictly according to the indication, may be an option.

Early detection screenings serve as secondary prevention (see above).

References


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