

BREAST PROBLEMS

Epidemiology/Pathophysiology

Current statistics, reported in the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI), confirm that breast cancer is the most common cancer among women in the U.S., with an estimated >252,000 new cases in 2017. In the same year, an estimated 40,000 women in the U.S. will die resulting from breast cancer. Based on data from 2012-2014, the risk that a woman will develop breast cancer in her lifetime is 12.4 percent. With this incidence, breast cancer is a topic of concern for the public. Therefore, understanding the evaluation and management of breast concerns is very important for physicians, particularly those in primary care, women's health, and surgical fields. The goal of this section is to equip third year medical students with the knowledge to diagnose and manage benign and malignant breast conditions.

Signs and Symptoms

There are several well established factors that, when present, particularly in combination, present an increased risk for developing breast cancer. While taking a complete breast history, it is important to inquire about these risk factors. This information is *most* helpful in general patient education, and in identification of individuals at "high risk" for developing breast cancer, as once cancer is diagnosed, there is little (aside from genetic evaluation) these risk factors contribute to treatment. Breast complaints should not be ignored with a lack of risk factors. Evaluation of risk in a healthy, unaffected patient provides the knowledge and opportunity to participate in a "high risk screening program" at a minimum, increasing early detection.

Being a woman and getting older are the two most common risk factors in developing breast cancer. Other major risk factors center around estrogen exposure: early menarche (<12 years old), late menopause (>55 years old), nulliparity, first completed pregnancy over 30 years of age, not breast feeding, hormonal contraception medications/devices, and postmenopausal hormone replacement therapy. Other risk factors include: having family members with breast cancer, having a genetic mutation associated with developing breast cancer (BRCA1, BRCA2, Li-Fraumeni, ATM, among others) having a personal history of breast cancer, having a personal history of proliferative breast lesions – particularly with atypia (atypical ductal or lobular hyperplasia), having a personal history of lobular carcinoma in situ (LCIS), exposure to chest radiation (particularly as a teen or young adult), and exposure to diethylstilbestrol (DES). Several "modifiable" risk factors have been identified with an increased risk of breast cancer development: alcohol consumption, being overweight or obese, and having a sedentary lifestyle. Many patients have concerns around environmental exposures and breast cancer risks. Currently there is no scientific data supporting links between specific items in diet, bras, antiperspirants, and breast cancer development.

Patients present with various concerns related to their breasts, but commonly encountered situations include: palpable lump (in either the breast or the axilla), nipple discharge, skin

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changes, breast pain, breast infection, and radiographic abnormalities. In evaluating a patient with a breast problem, a complete history with a focused physical examination is required. With respect to any patient reported findings, it is important to note the duration of the concern and any changes in the area – both since onset and cyclical. It is also of importance to question the patient about changes in the breasts with respect to size, shape, and symmetry. Any previous breast biopsies, breast surgeries, treatments, etc., are important to recognize. Associated findings of breast trauma and of nipple discharge should also be documented.

It is always good practice to ask a patient for permission to perform a physical examination. To examine the breasts, a patient will need to remove all clothing from the waist up. She should be provided with an examination gown for this purpose. While examination of a “sensitive area” deserves attention to patient comfort and modesty, a complete and comprehensive breast examination includes examining a patient in both the sitting and supine positions while disrobed. To start the examination, it is recommended that the “non-breast” portions be completed with the patient’s breasts covered with the robe – including the cardiac and pulmonary examinations. This allows the examiner to gradually build rapport with the patient prior to exposing the breasts for examination. It is advised that a patient be alerted that their robe will need to be opened to allow inspection and examination of the breast tissue, when that portion of the examination is reached.

Breast examination involves both inspection and palpation. With the patient in a sitting position, and the arms at her sides, the breasts are inspected visually – noting any obvious abnormalities or asymmetries in either the breasts and/or the nipples. Additionally, it is prudent to note the size of the breasts and general shape/contour – including the degree of ptosis, the breast symmetry, and the presence or absence of any retractions, skin/nipple changes, such as erythema, edema, or peau d’orange. Next, the patient should be instructed to slowly raise her arms above her head, and while she is doing so, the breasts should be observed for any changes this may cause, such as retraction of the skin or nipple. With the patient in the sitting position, the lymphatics should be examined, both the cervical and supraclavicular, but more specifically, the axilla. Asking the patient to place her hands on her hips provides good access and positioning for examination of the axilla. The presence of abnormally large, firm, and/or fixed lymph nodes is important to note.

After this is completed, the patient should be helped into the supine position to complete the examination. The use of a pillow behind the head improves the patient’s comfort, as does helping them bend their knees, putting their feet flat on the end of the examination table. With the patient in the supine position, the patient’s arms are raised above her head. This helps to spread the breast tissue across the anterior chest wall, allowing for palpation of the breast tissue against the chest wall. To help provide some added comfort, the contralateral breast should be covered with the examination robe. The breast tissue is then palpated using both of the examiner’s hands – particularly the pads of fingers 2-4. All 4 quadrants of the breasts, including the nipple and areolar regions, must be carefully palpated, noting any masses. The area palpated should include the clavicle superiorly, sternum medially, axilla laterally, and inframammary fold inferiorly. The parenchyma of the breast is examined using small circular

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motions with the fingers, while maintaining constant contact with the skin. In the nipple-areolar region, the tissue is palpated for masses and attempts to elicit nipple discharge are made. If nipple discharge is observed, it is important to note if it comes from a single duct (versus multiple ducts), and the color and consistency of the discharge. Further evaluation with radial compression may give some clues as to the location of the affected duct (quadrant location).

With palpation of the breast parenchyma, the presence of any masses or asymmetries is important, noting the location for documentation. A frequently used descriptor regarding the position in the breast is the “clock-face location”. In addition, a mass should be described by the size, consistency/texture, and pain. It should be noted if the mass is mobile or fixed to either the skin or the underlying chest wall.

Relevant Diagnostic Studies

Mammography is an X-ray evaluation of breast tissue. “Screening mammograms” are performed when a patient is asymptomatic – without specific breast concerns. It is aimed at “screening” to identifying breast conditions before there are palpable abnormalities. There have recently been some discrepancies in several of the societies’ guidelines regarding screening recommendations. The American Cancer Society (2015) recommends offering the option of yearly screening mammography at age 40-44, with a risk/benefit/cost discussion with the patient. Starting at age 45, and continuing until life expectancy is less than 10 years, annual mammography is recommended. This is in contrast to the most recent (2016) U.S. Preventative Services Task Force guidelines recommending annual mammography commence at age 50 and continue biannually until age 75. This controversy highlights the need for an informed discussion with eligible patients, with attention to the “pros and cons” and the cost of these studies.

Mammography evaluates differences in density, breast architectural distortions, masses, and calcifications. With a bilateral examination, asymmetries may be observed. Standard views in this study are craniocaudal (CC) and medial-lateral oblique (MLO). MLO view includes the axillary tail and often portions of the axilla (images to show the different views). Abnormalities identified on this study may warrant additional evaluation, with either magnification mammogram views and/or ultrasound to characterize further. Attempts are made by the breast radiology departments to obtain and review recent prior mammograms for comparison. The level of suspicion is reported with the Breast Imaging Reporting Data System (BIRADS). Mammography alone fails to detect 10-20% of breast cancers (false negative rate). Therefore, any clinically suspicious lesions warrant further investigation and evaluation.

Diagnostic mammography is utilized when there is a palpable abnormality or other concern on physical examination, or when screening mammography identifies an area that requires additional characterization. This involves additional tissue compression with magnification to help further delineate identified abnormalities, resolving “summation artifact,” or improving the assessment of concerning findings, such as spiculation and microcalcifications.

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Utilizing ultrasound in evaluation of the breast allows the tissue to be evaluated using a different modality, without additional ionizing radiation. It aids in the ability to further characterize a palpable mass noted on physical examination and/or a lesion noted on mammography. It is very helpful in identifying solid versus cystic masses noted on mammogram and/or physical examination. Ultrasound is also a technically convenient way to radiographically guide biopsy (or therapeutic cyst aspiration), so verifying this as a potential modality for tissue biopsy is helpful. Benign ultrasound features include: well-defined borders, anechoic (in the case of a simple cyst), uniformly hyperechoic (in the case of a solid mass), posterior enhancement, oval shape/parallel to the skin (wider than tall). Ultrasound features that are concerning for malignancy are: irregular margins with angulation and spiculation, hypoechogenicity, posterior shadowing, increased anterior/posterior size ratio (taller than wide).

Currently the appropriateness and applicability of the use of Magnetic Resonance Imaging (MRI) of the breast is a debated topic among the experts in the field. One strength of this type of study is that it is a very sensitive test to evaluate breast tissue, helping to better delineate abnormalities. It has a high “false positive” rate, however, limiting its usefulness and bringing into question the risk versus benefit and the overall cost. It is currently recommended as an adjunct to screening “high risk” patients – i.e., those with a greater than 20% lifetime risk of developing breast cancer. It also may be useful working up a breast malignancy in a woman with dense breast tissue.

To reach a definitive diagnosis for the etiology of a breast mass on radiographic findings, sampling of the tissue is required. The most direct and least invasive way to accomplish this is needle biopsy. Using radiographic means to guide the biopsy (mammography for stereotactic biopsy or ultrasound) facilitates rapid and accurate diagnosis. Depending on the radiographic appearance and the location, as well as different patient considerations, one biopsy modality may be preferred over another – on an individualized patient basis. Ultrasound is often used to guide needle placement and tissue acquisition for palpable lesions, as well as non-palpable lesions that are visible with ultrasound. Microcalcifications and lesions not visible on ultrasound require stereotactic localization (mammography) and needle placement for accuracy. Core needle biopsies samples are most commonly performed. This gives the pathologist the ability to review tissue architecture so that histology can be reported. This also provides additional tissue for ancillary testing on malignant histology. Fine needle aspiration provides cells only (cytology), but in some situations, may be sufficient to identify malignant cells. The report from pathologic evaluation must be reviewed, in the scope of the biopsy and the physical examination, to ensure that appropriate tissue was submitted and the results are “concordant”. The “triple test” ensures that there is concordance between: 1.) the findings on physical examination, 2.) radiographic features, and 3.) pathology. Any discrepancy in this triple test requires further evaluation to exclude malignant disease and may require surgical excisional biopsy.

When a patient presents with complaints of a breast mass, the patient’s gender, age, personal and family histories, and physical findings must be taken into consideration when pursuing a

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diagnostic work-up. When a palpable mass is clinically identified in a patient younger than 30 years old, a targeted ultrasound is the test of choice. In a woman older than 30 years, this is also recommended, in addition to a diagnostic mammography. These radiographic tests, in conjunction with the patient's history and physical examination findings, will direct additional steps for diagnosis.

Breast cysts are a common reason for breast masses. These lesions may present as a clinically palpable mass, usually tender with some hormonal fluctuations on menstrual cycle, or they may be noted on screening mammography. They may be single or multiple in number. Ultrasound is particularly helpful in the diagnosis – noting an anechoic or hypoechoic, well demarcated mass, with increased through transmission (posterior enhancement). If the ultrasound identifies a simple cyst, and the patient is asymptomatic, reassurance is provided and no further imaging is required. If a symptomatic cyst is identified, aspiration should be recommended with plans to repeat imaging in 3-6 months to ensure resolution and the absence of an associated mass.

The most common benign tumor of the breast is a fibroadenoma. Clinically, this usually is palpated as a smoothly marginated, discrete, firm, and freely mobile mass. Ultrasound of this type of lesion shows a hyperechoic, solid mass with well-demarcated borders and oval shape (wider than tall). Fibroadenomas typically are identified in patients in their late teenage years through thirties. These lesions, if less than 3 cm in size, with histology confirming a fibroadenoma, can be monitored with ultrasound to document stability, avoiding surgery unless there is a change. These lesions are estrogen sensitive and may enlarge during pregnancy.

Nipple discharge is further evaluated and classified as either unilateral or bilateral, and spontaneous or non-spontaneous. Nipple discharge can be physiologic (normal), if it is determined to be non-spontaneous (occurring only with nipple/breast manipulation), bilateral, and from multiple ducts. This can be the result of pregnancy, lactation, physical stimulation, thyroid disease, or medication side effects. Therefore, a thorough history and physical examination with a critical evaluation of all medications is needed to properly assess this concern. Spontaneous nipple discharge (occurring without nipple/breast manipulation) is usually the result of an abnormality in the breast, with a differential that includes both benign and malignant etiologies. The most common cause of spontaneous, unilateral, bloody nipple discharge from a single duct is an intraductal papilloma. Most commonly these are benign, however, there is a 10% chance of malignancy and further workup to exclude malignancy is required, often resulting in surgical biopsy with duct excision.

Breast pain, mastodynia, is a frequent complaint of women. With the hormonal fluctuations with menstruation, it is common for a woman to have cyclic breast tenderness, bilaterally, in the days preceding menstruation. Although pain is rarely associated with breast cancer, it can be an alarming finding for women, and requires a complete clinical workup, and possibly diagnostic imaging to ensure there is not a underlying malignant etiology. Reassurance may be sufficient to allay the concerns of the patient, and, in addition, a properly fitting supportive bra and the use

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of a heating pad and/or NSAIDs may help improve symptoms. Anecdotal reports exist with noted improvement with caffeine avoidance, and addition of the herbal supplement evening primrose oil.

Ductal carcinoma in situ (DCIS) is a condition of preinvasive ductal cancer. Pathologically, it represents ductal carcinoma cells completely surrounding with an intact duct. This has a 50% chance of developing into invasive disease, if left untreated.

Invasive ductal carcinoma (IDC) is the most common type of breast cancer (80%) followed by invasive lobular carcinoma (ILC) (10%). While these are clinically treated the same, they often present much differently. IDC, when palpable, is usually associated with a firm mass with irregular margins on physical examination. These lesions are usually visible with mammography and ultrasound. In contrast, ILC has indistinct borders and can blend in with adjacent breast tissue on physical examination and on imaging. The remaining breast cancers are the result of less commonly seen entities.

Breast cancer treatment is based on staging with TNM criteria as well as other ancillary tumor specific studies. The TNM evaluation – tumor size, lymph node status, and distant metastasis allows for the staging to be defined. As breast cancer metastasizes, it commonly involves the lymphatic drainage in the contralateral axilla. Beyond this, the most common sites of metastasis are the bones, lungs, liver, and brain. Additionally, the ancillary studies: estrogen receptor status (ER), progesterone receptor status (PR), HER-2/neu, and nuclear grade are considered when breast cancer therapies are being recommended. Having a reliable resource available for reference is very useful in caring for oncology patients, and the National Comprehensive Cancer Network has readily available online access that provides a trusted set of guidelines.

Management

Like the management of many types of malignancies, the treatment of a patient with breast cancer requires a multidisciplinary approach. To provide comprehensive care for a patient with breast cancer, surgeons team with medical oncologists, radiation oncologists, breast radiologists, pathologists, plastic surgeons, as well as support staff including nurse navigators and social workers.

Most patients with breast cancer will require the care of a breast surgeon, who often participates in the diagnosis, but also functions to remove the cancer (via partial mastectomy or mastectomy) in combination with surgical staging of the contralateral axilla. Partial mastectomy involves removal of the affected tissue, while preserving the remaining breast tissue. In general, partial mastectomy is a reasonable option for most patients with T1 disease and some with smaller T2 disease, provided that the patient is a good candidate to complete adjuvant whole breast radiation therapy. Mastectomy involves removal of the entire breast tissue volume, with the underlying pectoralis major muscle fascia. While some patients prefer this option, this is the recommended surgical procedure for patients who are not candidates for or refuse adjuvant radiation therapy, those with large tumors (T3 and some T4) or smaller tumors

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that when resected will leave an unacceptable cosmetic result, and patients with disease in two quadrants of the affected breast (multicentric disease). In most situations, both management of the breast cancer (with lumpectomy or mastectomy) and staging of the axilla (with SLNB or axillary dissection), are done in one operation.

In general, radiation therapy as used for breast cancer is aimed to reduce recurrence rates when a patient has undergone breast conserving therapy (partial mastectomy). Like surgery, it is a local therapy – involving the breast and adjacent tissues. Whole beam external beam radiation therapy plans are made in consultation with a radiation oncologist. This is typically administered once daily, 5 days per week, for 6 weeks.

The current standard of care in identification of local metastasis in staging of breast cancer is sentinel lymph node biopsy (SLNB). Using this method, the “first order lymph nodes” responsible for draining the tissue from the affected breast are removed from the axillary lymph node basin. To identify these lymph nodes, radiotracer, blue dye, or a combination of the two, is injected into the breast. This is traced to the ipsilateral axilla, where the draining lymph nodes are removed, with less dissection and disruption of the remaining lymphatics. Pathologic evaluation of these sentinel lymph nodes (SLNs) is accepted in staging, and may spare the patient complete axillary lymph node dissection – a procedure which has the potential for the complication of lymphedema. If the SLNs contain metastatic disease, additional surgery with axillary lymph node dissection may be recommended (>2 involved SLN), but several patient factors and tumor factors are involved in this decision. Methylene blue is contraindicated in pregnant patients and patients may have an allergic response to it.

In general, a patient is not a candidate for SLNB if there are clinically involved lymph nodes. Axillary lymph node dissection involves removal of the tissue from the axillary vein superiorly to the chest wall medially (pectoralis minor muscle), the latissimus dorsi muscle laterally, and the subscapularis muscle posteriorly. Classically, this is level I and II dissection. Level III is posterior to the pectoralis minor, and only removed if pathology is suspected clinically. Within the axillary contents are two motor branches of the brachial plexus, the long thoracic nerve which innervates the serratus anterior muscle (damage results in winged scapula) and the thoracodorsal nerve which innervates the latissimus dorsi muscle (damage results in some compromise to upper extremity motion). There are sensory nerves, (intercostobrachial nerves) which provide innervation to the upper, inner aspect of the upper extremity.

Chemotherapy is one of the systemic lines of treatment, aimed at treating metastasized cells. This treatment, administered by a medical oncologist, typically is utilized when there is evidence of metastatic disease, such as node-positive disease; however some tumors will require chemotherapy based on their biology, regardless of nodal status (i.e., ER/PR negative).

Endocrine therapy involves using selective estrogen receptor modulators (SERMs such as tamoxifen) and aromatase inhibitors (AIs such as anastrozole) to decrease estrogen and the effects on tissues, thereby decreasing recurrence rates. These are only applied when a

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malignancy has estrogen and progesterone receptors. Typically they are used for 5 years, and are started after all other adjuvant therapies are completed.

Breast reconstruction, with the goal of restoring the shape of a breast after breast cancer treatments, is usually performed by plastic surgeons, often in combination surgery with breast surgeons. In general, the use of autologous tissue or prosthetic material (breast implants) is used to recreate the shape of a breast after mastectomy. There are also options for post-lumpectomy reconstruction in patients who are unhappy with their cosmetic result after lumpectomy and radiation therapy treatments.

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