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Diagnosis and Management of Benign Breast Disorders

Breast-related symptoms are among the most common reasons women present to obstetrician–gynecologists. Obstetrician–gynecologists are in a favorable position to diagnose benign breast disease in their patients. The purpose of a thorough understanding of benign breast disease is threefold: 1) to alleviate, when possible, symptoms attributable to benign breast disease, 2) to distinguish benign from malignant breast disease, and 3) to identify patients with an increased risk of breast cancer so that increased surveillance or preventive therapy can be initiated. Obstetrician–gynecologists may perform diagnostic procedures when indicated or may make referrals to physicians who specialize in the diagnosis and treatment of breast disease. The purpose of this Practice Bulletin is to outline common benign breast disease symptoms in women who are not pregnant or lactating and discuss appropriate evaluation and management. The obstetrician–gynecologist's role in the screening and management of breast cancer is beyond the scope of this document and is addressed in other publications of the American College of Obstetricians and Gynecologists (1–3).

Background

Benign breast disorders encompass a heterogeneous group of conditions. These conditions include masses, cysts, abnormalities detected by imaging, nipple discharge, breast pain (mastalgia), inflammatory breast disease, and skin disorders of the breast.

Benign Breast Lesions and Masses

Most benign breast lesions fall into one of three categories: 1) nonproliferative, 2) proliferative without atypia (sometimes referred to as “fibrocystic changes”), and 3) atypical hyperplasia. They may present as a palpable mass or lesion, a radiographic abnormality, pain, or nipple discharge (4). Epidemiologic studies have demon-

strated that these three categories are associated with different risks of development of breast cancer in the future (Table 1) (5). Other benign breast lesions include tubular adenomas and phyllodes tumors. Phyllodes tumors typically behave in a benign manner similarly to fibroadenomas but may invade locally and, uncommonly, may cause distant metastases. Lobular carcinoma in situ is another type of nonmalignant breast lesion that is noteworthy because it is associated with a significantly increased risk of future development of breast cancer (Table 1).

Nonproliferative Breast Lesions

Simple breast cysts are the most common type of nonproliferative breast lesion and can be found in up to

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The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Table 1. Breast Lesions and Breast Cancer Risk ↵

Lesion Type	Lesion Subtype*	Aggregate Relative Risk of Future Breast Cancer (95% CI)
Nonproliferative	Simple cysts	1.17 (0.94–1.47) [†]
	Mild hyperplasia (usual type)	
	Papillary apocrine change	
Proliferative without atypia	Fibroadenoma	1.76 (1.58–1.95) [†]
	Giant fibroadenoma	
	Intraductal papilloma	
	Moderate/florid hyperplasia (usual type)	
	Sclerosing adenosis	
	Radial scar	
Atypical hyperplasia	Atypical ductal hyperplasia	3.93 (3.24–4.76) [†]
	Atypical lobular hyperplasia	
Lobular carcinoma in situ		6.9–11 [‡]

*Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med* 1985;312:146–51.

[†]Dyrstad SW, Yan Y, Fowler AM, Colditz GA. Breast cancer risk associated with benign breast disease: systematic review and meta-analysis. *Breast Cancer Res Treat* 2015;149:569–75.

[‡]Confidence interval not reported. Data from Morrow M, Schnitt SJ, Norton L. Current management of lesions associated with an increased risk of breast cancer. *Nat Rev Clin Oncol* 2015;12:227–38.

one third of women aged 35–50 years (4). Breast cysts can vary in size from microscopic to clinically palpable (so-called gross cysts or macrocysts) cysts up to several centimeters in size. Cysts can be found on examination, imaging studies, or on breast biopsies done for other indications. Simple breast cysts (no internal septations or mural thickening) are nearly always benign and require aspiration only if they are bothersome to the woman.

Mild hyperplasia of the usual type has focal thickening of the duct epithelial cell layers (four or fewer) that does not fill the duct. Simple papillary apocrine change is focal thickening of the epithelial lining of an apocrine cyst. Both are considered nonproliferative disorders, which are not associated with an increased risk of future development of breast cancer (Table 1).

Proliferative Breast Lesions Without Atypia

Fibroadenomas are the most common cause of breast masses in adolescent girls and young women. The median age at which patients present with fibroadenomas is 25 years. Fibroadenomas also can be present in older women, accounting for 12% of all masses in menopausal women (6). The typical fibroadenoma is a small (1–2 cm), firm, well-circumscribed, mobile mass composed of a proliferation of epithelial and stromal elements (4). Fibroadenomas may be difficult to distinguish from breast cysts on physical examination, and they may appear similar on mammography. Ultrasonography is

useful in distinguishing a simple cyst from a fibroadenoma (solid mass). In most cases, a solid mass identified by ultrasonography requires further diagnostic testing.

Giant fibroadenomas (generally greater than 10 cm) are an unusual variant of juvenile and adult fibroadenomas, accounting for approximately 4% of all fibroadenomas (6). Giant fibroadenomas typically are seen in adolescents and young adults and present as enlarging masses that often distort the breast (7). Histologically, these benign lesions are composed of the same epithelial and stromal elements as adult fibroadenomas, although they tend to have more florid glandular elements with greater stromal cellularity.

Moderate (also called florid) hyperplasia of the usual type are multiple-duct epithelial cell layers (more than four) that fill the entire duct but do not have cytologic atypia. Sclerosing adenosis is characterized by increased numbers or size of glandular components within lobular units. These diagnoses are considered proliferative lesions without atypia and are associated with a small-to-moderate increased risk of future development of breast cancer (Table 1). Radial scars are an additional pseudoproliferative lesion and usually are incidental findings on biopsy. They may harbor or facilitate the development of atypical proliferations and usually are excised when found. Typically, no further treatment is needed, and risk reduction by chemoprophylaxis (eg, tamoxifen or raloxifene) is not indicated (4). However,

close adherence to routine breast cancer surveillance is recommended.

Intraductal papillomas are tumors in a lactiferous duct that may be solitary and centrally located near the duct opening or multiple and peripherally located in the breast. Solitary papillomas can present as nipple discharge (which can be bloody, serous, or clear) or, less often, as a palpable mass. They most commonly occur in women aged 30–50 years and typically are small (2–4 mm), though they can present as a palpable mass up to 5 cm in size (6). Unusual cases of atypical cells or ductal carcinoma in situ (DCIS) have been diagnosed within solitary papillomas, but they usually are not associated with cancer. If atypia is present on core biopsy of an intraductal papilloma, surgical excision is recommended because invasive or in situ carcinoma is diagnosed in 15–20% of women from whom excisional specimens are taken (8, 9). Multiple peripheral intraductal papillomas do not typically present with nipple discharge. Women with multiple papillomas tend to be younger and have bilateral breast involvement. Coexisting or subsequent breast cancer is diagnosed in approximately one third of these women (10).

Atypical Hyperplasia

Atypical hyperplasia, which includes atypical ductal hyperplasia and atypical lobular hyperplasia, typically is an incidental finding on histologic evaluation of abnormal mammography findings or breast masses (4). Histologic characteristics include ductal or lobular elements with uniform cells and loss of apical–basal cellular orientation (4). Women in whom atypical hyperplasia has been diagnosed have a substantially increased risk of subsequent invasive cancer in the affected breast and the contralateral breast (Table 1) (5, 11, 12).

Tubular Adenomas

Tubular adenomas, which consist of benign glandular cells with minimal stromal elements, can present as a breast mass or may be seen on routine breast imaging (13, 14). Lactating adenomas are seen during pregnancy or postpartum and consist of cuboidal cells that are identical to normal lactating tissue. These present as palpable masses and will appear solid on ultrasonography. Tissue biopsy is required for diagnosis of these benign lesions.

Phyllodes Tumors

Phyllodes tumors of the breast are uncommon fibroepithelial tumors that account for only 0.3–0.5% of all cases of breast tumors (15). These tumors have a wide range of biologic behavior, from a benign breast mass with a propensity for local recurrence to a sarcoma capable

of producing distant metastatic disease. Only 5% of all cases of phyllodes tumors exhibit this more aggressive sarcomatous behavior (16). Median age at presentation is 40 years, and the usual presentation is a single enlarging breast mass (16). Phyllodes tumors usually are larger than other fibroadenomas but have the same characteristics on palpation (firm, circumscribed, and mobile), and their rapid growth often causes visible stretching of the overlying skin. Breast imaging will demonstrate a solid mass but cannot distinguish between a fibroadenoma, a benign phyllodes tumor, or a malignant phyllodes tumor. Although fine-needle aspiration and core needle biopsy are useful tools for diagnosing fibroadenomas, excisional biopsy is appropriate for phyllodes tumors because they can be more difficult to diagnose accurately. Excising a wide margin (greater than 1 cm) of normal surrounding tissue is recommended to decrease the likelihood of local recurrence (17).

Lobular Carcinoma In Situ

Lobular carcinoma in situ (LCIS) is a histologic finding that typically does not present as a mass or with specific breast imaging abnormalities. It usually is diagnosed as an incidental finding at the time of breast biopsy for another lesion (18). Unlike DCIS, LCIS usually is not considered a precursor lesion for breast cancer. Rather, it is a risk marker for future development of breast cancer (Table 1) (19). Women in whom LCIS has been diagnosed have a substantially increased risk of subsequent invasive cancer in the affected breast and the contralateral breast (Table 1) (12, 19). Lobular carcinoma in situ often is multifocal in the ipsilateral breast and involves the contralateral breast in 30% of cases (19). Women in whom LCIS has been diagnosed have an estimated 10–20% risk of developing invasive ductal or invasive lobular cancer in the following 15 years (20). When an invasive cancer is diagnosed in women with LCIS, it occurs in the contralateral breast in 29–75% of cases (21, 22).

Nipple Discharge

Nipple discharge is a common breast symptom. In most cases, nipple discharge is benign. Benign discharge is more likely to be bilateral, only present when expressed, milky or green in color, and multiductal. Discharge that is unilateral, uniductal, and spontaneous indicates a higher risk of malignancy and requires more thorough evaluation (see *How is nonmilky discharge evaluated and managed?*). Bilateral milky nipple discharge is appropriate during pregnancy and lactation and may persist for up to 1 year postpartum or after cessation of breastfeeding. Galactorrhea, which is characterized by bilateral

milky discharge outside of pregnancy and the postpartum interval, is not caused by intrinsic breast disease. Elevated prolactin levels that lead to galactorrhea can be caused by multiple factors, including chronic breast stimulation, endocrinopathies (including hypothyroidism and prolactin-secreting adenomas), and medications that inhibit dopamine.

Mastalgia

Mastalgia (breast pain) is common in women and was the primary indication for 47% of breast-related visits in a 10-year study of women aged 40–69 years who were enrolled in a health maintenance organization (23). Women seek care for breast pain that interferes with sexual or physical activity, but many women report the symptom because of fear of cancer. Some mastalgia can be indicative of breast cancer and require evaluation. Mastalgia can be separated into three categories: 1) cyclical, 2) noncyclical, and 3) extramammary. Cyclic mastalgia is related to normal hormonal changes related to the menstrual cycle or to sex hormones cyclically administered for contraception, ovulation induction, or management of abnormal bleeding. Noncyclic mastalgia comes from a breast-related etiology but does not vary according to the menstrual cycle. These etiologies include mastitis, trauma, thrombophlebitis (Mondor disease), cysts, tumors, and cancer. Different types of extramammary problems can present with breast pain, including costochondritis, chest wall trauma, rib fractures, fibromyalgia, cervical radiculopathy, herpes zoster, angina, gastroesophageal reflux disease, and pregnancy. A variety of medications may cause breast pain, including certain types of hormonal medications, antidepressants, antihypertensive and cardiac medications, and antimicrobial agents (24).

Inflammatory Breast Disorders

Inflammatory breast disorders have infectious and non-infectious causes. Mastitis is the most common of these disorders, and most cases of mastitis are related to lactation (puerperal mastitis). Nonpuerperal breast infections generally are separated into periareolar and peripheral infections. Periareolar infection also is called periductal mastitis and is most common in younger women (median age 32 years). Smoking appears to be a major risk factor. It is characterized by inflammation around nondilated subareolar ducts. It presents as periareolar inflammation and can have an abscess at the time of presentation. Peripheral abscesses typically have no obvious cause, but they can be associated with trauma and conditions that impair immunity, such as diabetes and steroid use as well as rheumatoid arthritis and granulomatous lobular mastitis (25).

Mammary duct ectasia occurs in middle-aged and elderly women, although it can occur (rarely) in children and adolescents. Smoking and parity appear to be risk factors. Mammary duct ectasia is most frequently asymptomatic and diagnosed on the evaluation of mammographically detected microcalcifications. It presents clinically as nipple discharge, nipple inversion, a palpable subareolar mass, noncyclic mastalgia, or infection. It does not require surgery and should be managed conservatively (4).

Skin Changes of the Breast

Breast skin can be affected by common dermatologic problems, including psoriasis, eczema, and contact dermatitis. The skin folds under the breast are susceptible to *Candida* infection, especially when they are deep. The axilla are common sites for hidradenitis suppurativa. When common skin problems are identified, standard treatments should be used.

Breast skin abnormalities also can indicate inflammatory breast cancer, Paget disease, or other types of breast cancer. Inflammatory breast cancer should be suspected if peau d'orange (skin edema), warmth, and erythema are present and if patients with presumed mastitis are not responding appropriately to therapy. Inflammatory breast cancer does not necessarily involve palpable masses. Paget disease is a rare cancer of the nipple and areola that frequently is associated with DCIS and other types of invasive breast cancer. Paget disease can present as an ulcerated, crusted, or scaling lesion on the nipple that can extend to the areola. The nipple can be retracted or hyperpigmented, and the patient may have pain, burning, or itching (26). Skin ulceration of other parts of the breast are concerning for other breast malignancies.

Clinical Considerations and Recommendations

► What is the initial evaluation for a woman who presents with breast-related symptoms?

The initial evaluation of a woman with breast-related symptoms should include review of her history to characterize her symptoms and to identify risk factors for breast cancer. It also should involve performance of a clinical breast examination.

History

Breast-related symptoms should be characterized, including pain, mass, thickening, duration, location, change in

symptoms over time, and presence and color of spontaneous nipple discharge, if present. Risk factors for breast cancer should be identified. Factors that may alter breast cancer risk include patient age, family history, reproductive risk factors (length of reproductive life span, age at first birth, parity, history of breastfeeding, and menopausal hormone therapy), and individual lifestyle factors (1, 2, 6). Although breast cancer risk factors may not alter the evaluation of a woman with acute breast symptoms, women at the highest risk of breast cancer may be appropriate candidates for genetic counseling, enhanced breast cancer screening, and risk-reduction therapies (1, 2, 12, 27).

Clinical Breast Examination

A careful visual inspection of the breasts should be conducted. A commonly used method is to have the patient seated with her hands on her waist. Breast size and symmetry, erythema, skin edema or peau d'orange appearance, and bulging or retraction of the skin or the nipple-areolar complex should be noted if present, followed by palpation of the axillae and supraclavicular lymph node regions and, finally, palpation of the breasts. Most practitioners examine the breasts with the patient in the supine position, although some experts recommend palpation of the breasts with the patient in the seated position and the supine position. Any dominant masses or areas of palpable concern, such as thickening or asymmetry, should be noted and preliminarily characterized as either of low clinical suspicion or of concern for malignancy based on tissue characteristics. Clinical documentation of a breast mass should include size, tissue consistency, distance from areolar edge, and clock position (eg, a 2-cm, well-circumscribed, firm mass in the right breast, 3 cm from the areolar edge, at the 6:00 position).

► *What additional tests can be performed for evaluation of a woman with breast-related symptoms?*

Women with abnormal findings on initial clinical examination (ie, palpable breast mass, asymmetric thickening or nodularity, skin changes, or nipple discharge) require further evaluation. Additional testing can include diagnostic imaging and tissue sampling.

Diagnostic Imaging

Often, positive findings on the initial evaluation of a woman who has breast-related symptoms will require diagnostic breast imaging with ultrasonography, mammography, or digital tomosynthesis, with management dependent on the patient's age, clinical suspicion, the

Breast Imaging Reporting and Data System (BI-RADS) category (Table 2) (28), and other imaging characteristics (Fig. 1 and Fig. 2). Based on clinical or imaging findings, a tissue diagnosis may be indicated.

Histologic Evaluation

Three options are available for histologic evaluation of abnormal findings on diagnostic imaging: 1) fine-needle aspiration, 2) core needle biopsy, and 3) excisional biopsy. Fine-needle aspiration uses a small-bore (typically 21–25 gauge) needle to obtain a cytologic specimen. It is inexpensive and minimally invasive but requires pathologists with special expertise in the interpretation of the specimen. Another limitation of fine-needle aspiration is that findings of atypia or malignancy require a follow-up tissue biopsy. Core needle biopsy is a minimally invasive technique that provides a histologic specimen for diagnosis. The biopsy is performed using a large-bore (typically 12–16 gauge) cutting needle. Core needle biopsy and fine-needle aspiration can be guided by palpation or by imaging with mammography (stereotactic), ultrasonography, or magnetic resonance imaging. Core needle biopsy generally is the preferred biopsy method because it has few complications and minimizes surgical changes to the breast (20). Another advantage to core needle biopsy is the ability to place a clip to mark the lesion undergoing biopsy, which is helpful as a reference in future imaging studies or in cases in which additional surgical procedures of the area are required.

Excisional biopsy generally is reserved for specific scenarios. Some lesions are not amenable to stereotactic or ultrasound-guided biopsy because of location, imaging characteristics, or breast implants; therefore, excisional biopsy with or without wire localization may be the best option to remove these areas for histologic evaluation. Some histologic findings identified by core needle biopsy require that additional tissue be obtained to ensure that the benign diagnosis is correct. These findings include atypical hyperplasia, flat epithelia atypia, LCIS, mucinous tumors, possible phyllodes tumors, and radial scars (particularly if there is associated atypia). Excisional biopsy also is indicated if the core needle biopsy finding is nondiagnostic or is discordant with clinical examination or imaging findings (eg, a BI-RADS 4 or 5 mammography result with normal-appearing breast tissue on core needle biopsy).

► *How is a palpable breast mass evaluated?*

A palpable breast mass is the most common finding of symptomatic breast cancer. Evaluation of a breast mass begins with a detailed history, assessment of breast cancer risk, and physical examination and requires age-appropriate breast imaging. Imaging results based on the

Table 2. Breast Imaging Reporting and Data System Classification and Recommended Management ↵

BI-RADS Assessment Category	Likelihood of Cancer	Management		
		Mammography*	Ultrasonography*	MRI*
Category 0: Incomplete— Need additional imaging evaluation (and/or prior mammograms for comparison in the case of mammography screening)	N/A	Recall for additional imaging, comparison with prior examination(s), or both	Recall for additional imaging	Recommend additional imaging: mammography or targeted ultrasonography
Category 1: Negative	Essentially 0% likelihood of malignancy [†]	Routine mammography screening	Routine screening	Routine breast MRI screening if cumulative lifetime risk ≥20%
Category 2: Benign	Essentially 0% likelihood of malignancy [†]	Routine mammography screening	Routine screening	Routine breast MRI screening if cumulative lifetime risk ≥20%
Category 3: Probably benign	>0% but ≤2% likelihood of malignancy	Short-interval (6-month) follow-up or continued surveillance mammography	Short-interval (6-month) follow-up or continued surveillance	Short-interval (6-month) follow-up
Category 4: Suspicious	>2% but <95% likelihood of malignancy		Tissue diagnosis	
‡Category 4A: Low suspicion for malignancy	>2% to ≤10% likelihood of malignancy			
‡Category 4B: Moderate suspicion for malignancy	>10% to ≤50% likelihood of malignancy			
‡Category 4C: High suspicion for malignancy	>50% to <95% likelihood of malignancy			
Category 5: Highly suggestive of malignancy	≥95% likelihood of malignancy		Tissue diagnosis	
Category 6: Known biopsy-proven malignancy	N/A	Surgical excision when clinically appropriate		

Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; MRI, magnetic resonance imaging; N/A, not applicable.

*Identified imaging findings must correlate with clinical examination findings if using this system to determine management. If examination and imaging findings are discordant, then further work-up, including biopsy, should be considered. Examples of discordance include palpable mass with BI-RADS 1 imaging, BI-RADS 2 or BI-RADS 3 finding in different location from examination finding, and suspicious mass on examination with BI-RADS 2 result.

[†]BI-RADS 1 and BI-RADS 2 indicate that no malignancy was identified on imaging. However, it is important to note that the sensitivity of breast imaging for cancer detection is based on the imaging modality and breast density.

[‡]BI-RADS 4A–4C apply only to mammography and ultrasonographic findings.

Modified from Sickles EA, D’Orsi CJ, Bassett LW. ACR BI-RADS® atlas—mammography, breast ultrasound, and breast MRI. In: ACR BI-RADS® atlas, Breast Imaging Reporting and Data System. Reston (VA): American College of Radiology; 2013.

BI-RADS classification system (28) will guide management recommendations regarding the need for continued imaging observation or biopsy. Close clinical follow-up, biopsy, or both should be considered in the case of a discrete palpable mass with negative or discordant imaging results.

Unless previously evaluated and unchanged, all palpable masses require additional evaluation (Fig. 1 and Fig. 2). Evaluation of the mass should never be dismissed based on young age or the absence of risk factors, but consideration of these factors may be helpful in developing the diagnostic or treatment plan.

When a woman presents because of a mass, but the patient and physician are unable to identify the mass, a clinical follow-up examination is recommended. Women with dominant masses or concerning areas of thickening or asymmetry at the follow-up visit should undergo diagnostic breast imaging, with management dependent on the BI-RADS category (Table 2, Fig. 1, and Fig. 2) (28), age, imaging characteristics, and clinical suspicion (20).

Women with palpable masses require imaging. The appropriate diagnostic imaging study is determined based on the woman’s age. For women younger than 30 years with a palpable mass, ultrasonography is the

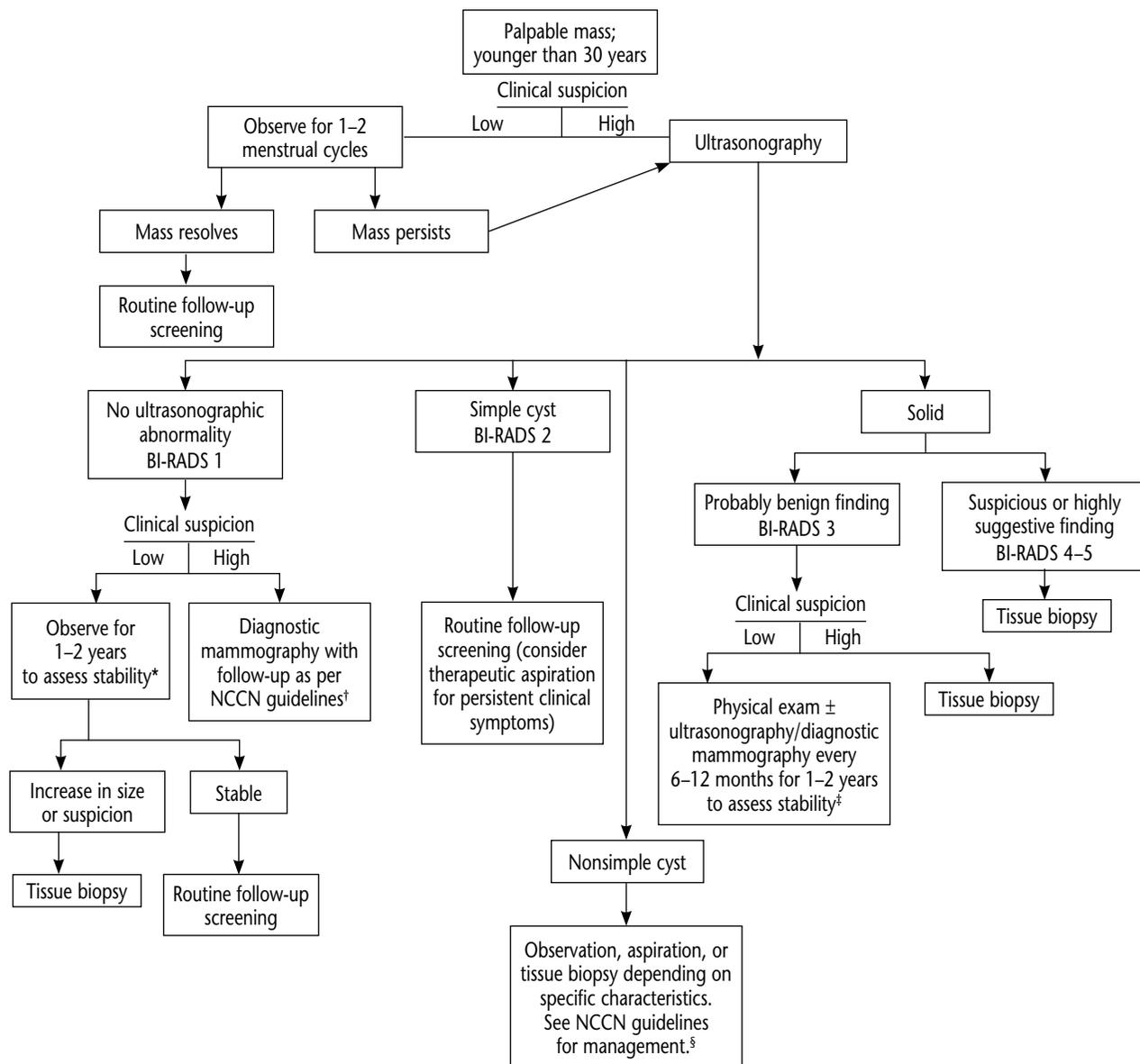


Fig. 1. Management of a palpable mass in women younger than 30 years. Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; NCCN, National Comprehensive Cancer Network. ↩

*Physical examination every 3–6 months with or without diagnostic imaging every 6–12 months for 1–2 years. Follow-up interval may be varied depending on level of suspicion.

†See BSCR-11 in National Comprehensive Cancer Network. Breast cancer screening and diagnosis. Version 1.2015. NCCN Clinical Practice Guidelines in Oncology [after login]. Fort Washington (PA): NCCN; 2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf. Retrieved February 23, 2016.

‡Follow-up interval may be varied depending on level of suspicion.

§See BSCR-5 in National Comprehensive Cancer Network. Breast cancer screening and diagnosis. Version 1.2015. NCCN Clinical Practice Guidelines in Oncology [after login]. Fort Washington (PA): NCCN; 2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf. Retrieved February 23, 2016.

Modified from Pearlman MD, Griffin JL. Benign breast disease. *Obstet Gynecol* 2010;116:747–58.

preferred initial modality (Fig. 1). If no abnormality is found on ultrasonography (BI-RADS 1), diagnostic mammography is recommended in cases in which there is clinical suspicion or significant risk factors for breast cancer (20). If there is no imaging correlate to the palpa-

ble mass, women younger than 30 years who are considered to be at low risk of cancer (ie, nonsuspicious mass) can be monitored for 1–2 years with physical examination and possibly diagnostic imaging for stability (Fig.1). For women 30 years or older with a palpable mass, diagnostic

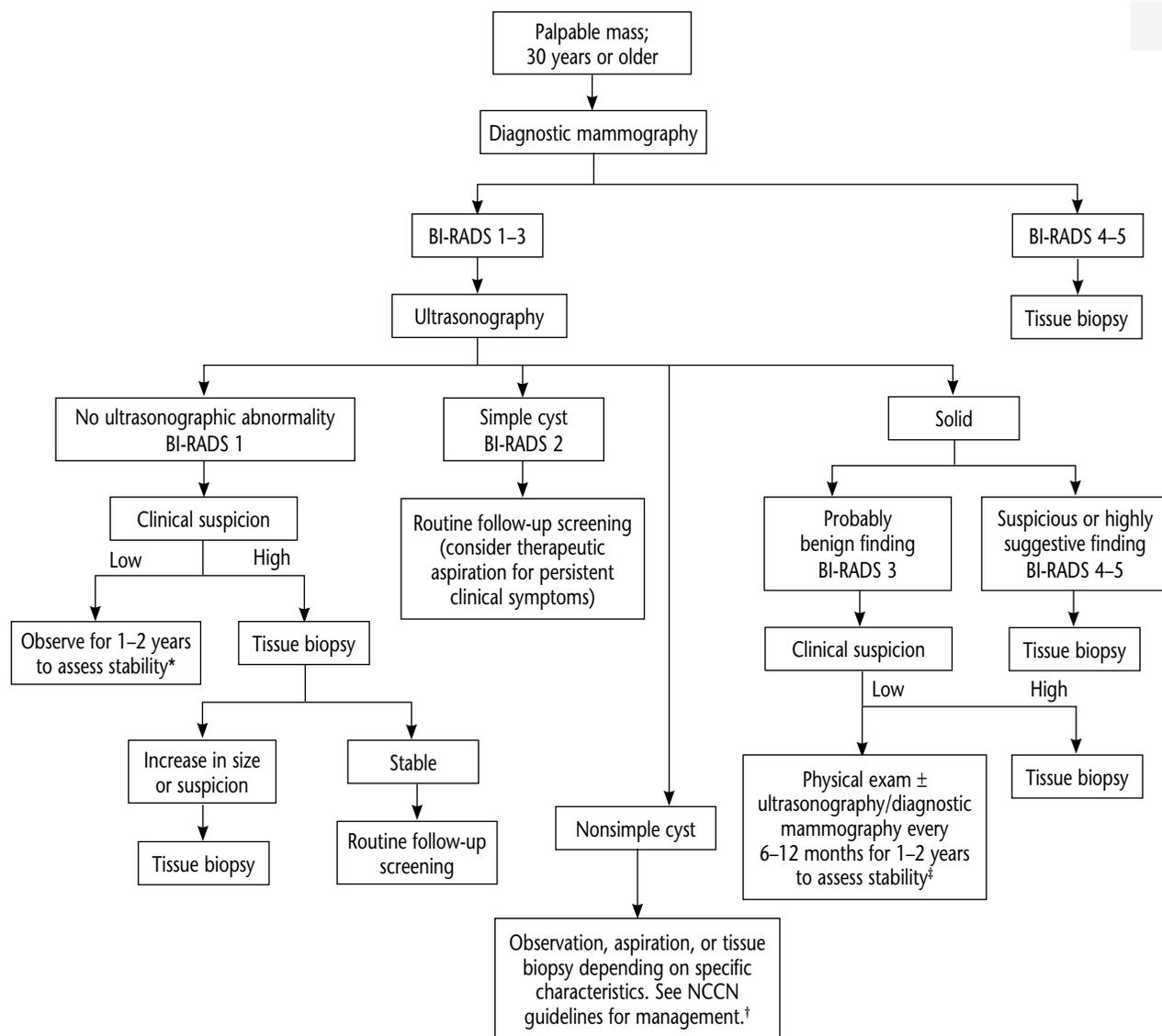


Fig. 2. Management of a palpable mass in women aged 30 years and older. Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; NCCN, National Comprehensive Cancer Network. ↩

*Physical examination every 3–6 months with or without diagnostic imaging every 6–12 months for 1–2 years. Follow-up interval may be varied depending on level of suspicion.

†See BSCR-5 in National Comprehensive Cancer Network. Breast cancer screening and diagnosis. Version 1.2015. NCCN Clinical Practice Guidelines in Oncology [after login]. Fort Washington (PA): NCCN; 2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf. Retrieved February 23, 2016.

‡Follow-up interval may be varied depending on level of suspicion.

Modified from Pearlman MD, Griffin JL. Benign breast disease. *Obstet Gynecol* 2010;116:747–58.

mammography should be obtained, and additional imaging with ultrasonography often is required (Fig. 2) (20). Because ultrasonography frequently is needed, many clinicians order an ultrasonographic examination at the same time as diagnostic mammography to reduce the need for repeat visits. Further management of masses depends on the results of imaging (Fig 2).

If there is an imaging correlate to the palpable finding, management is dependent on the BI-RADS

category (Table 2) (28), overall clinical suspicion, and whether imaging determines the mass to be solid or cystic (Fig. 1 and Fig. 2) (20). If there is no imaging correlate (BI-RADS 1), tissue biopsy is appropriate if the palpable finding is suspicious.

In women 30 years or older, nonsuspicious palpable findings with BI-RADS 1 imaging results can be monitored for 1–2 years with physical examination and possibly diagnostic imaging for stability (Fig. 2).

Suspicious changes in the mass on clinical examination (eg, enlargement) should result in tissue biopsy.

► ***What is the next step in the management of a solid breast mass?***

If imaging results are concerning (BI-RADS 4–5) in a woman with a solid breast mass, tissue biopsy should be obtained. If initial imaging results are indicative of low risk (BI-RADS 1–3) in a woman with a solid breast mass, then biopsy should be considered if there is an otherwise high clinical suspicion in women 30 years or older (Fig. 2) or additional imaging obtained in women younger than 30 years (Fig. 1). Close follow-up for 1–2 years (with physical examination every 3–6 months with or without diagnostic imaging every 6–12 months) may be an option to ensure stability of a mass that is of low clinical suspicion (20). A referral to a physician who specializes in the diagnosis and treatment of breast disease may be helpful in this circumstance. Skin changes that are suggestive of inflammatory breast disease or other malignancy typically are biopsied (see *How are inflammatory breast disorders evaluated and managed?*).

► ***What are the next steps in management of a cystic breast mass?***

If imaging suggests a simple cyst (no internal septations or mural thickening and BI-RADS 2) and if the history and examination also are consistent with benign disease, then routine clinical follow-up is recommended (Fig. 1 and Fig. 2) (20). Simple cysts usually are benign and do not require aspiration unless they are bothersome to the patient. If the patient desires aspiration of the cyst, then it can be performed using ultrasonographic guidance or by palpation.

If imaging suggests a complicated cyst (ie, non-simple cyst that is a round, circumscribed mass; contains low-level echoes without vascular flow; satisfies most but not all criteria for a simple cyst; and is BI-RADS 3), then decisions regarding aspiration or imaging observation for 1–2 years should be made after thorough discussion with the patient based on patient preference or overriding clinical concern (Fig. 1 and Fig. 2) (20). Lesions that are BI-RADS 3 correlate with a less than 2% chance of malignancy (Table 2) (28). If aspiration is performed and the fluid is not bloody and the mass resolves, then the fluid can be discarded. If the fluid is bloody or the mass does not resolve completely, then image-guided aspiration, core needle biopsy, or excision of the mass is indicated (20). If the clinical examination is concerning for malignancy and the imaging findings are otherwise not consistent with clinical findings,

biopsy is warranted. Complex cysts (nonsimple cysts with cystic and solid components and BI-RADS 4–5 imaging findings) require biopsy (Fig. 1, Fig. 2, and Table 2) (20, 28).

► ***How is mastalgia (breast pain) evaluated?***

The evaluation of mastalgia should include a history to elicit the timing, frequency, severity, and location of the pain, with attention to recent activities or trauma that may have caused or exacerbated the pain. The history will help to classify the type of mastalgia and also may assist the physician in identifying the rare cardiac, lung, or gastrointestinal problems the patient may be experiencing as breast pain. Mastalgia associated with breast cancer is more likely to be unilateral, intense, noncyclic, and progressive. A clinical breast examination should be performed to identify discrete or concerning abnormalities of the breast as well as to evaluate the chest wall separately from the breast to exclude the chest wall as a source of the pain. Causes of extramammary mastalgia include costochondritis (Tietze syndrome), which is characterized by point tenderness over the costochondral junction. Duct ectasia, periductal mastitis, and other inflammatory conditions may present with mastalgia as the primary symptom. If a palpable breast abnormality is identified, then imaging should be performed (Fig. 1 and Fig. 2) (20). In addition, breast imaging should be considered for focal mastalgia that is not explained by an obvious cause (eg, musculoskeletal), particularly if the pain is of new onset.

Superficial thrombophlebitis of the lateral thoracic vein (Mondor disease) is a rare condition that causes noncyclic breast pain and tenderness. Physical examination reveals a palpable cord, which initially is red and tender and subsequently is accompanied by linear skin dimpling. Because an association with breast cancer has been reported (29), age-appropriate breast imaging should be performed (Fig. 1 and Fig. 2) to rule out a non-palpable underlying cancer in patients with suspected Mondor disease of the breast.

► ***How is mastalgia managed?***

Mastalgia treatment depends on the assumed source of the pain. Management of extramammary sources depends on the specific cause and may require consultation from other specialists.

Reassurance

Breast cancer rarely is identified in the patient presenting with mastalgia and no other clinical findings. Reassurance is appropriate management for patients with cyclic mastalgia and normal physical examination

findings (30) and appeared to be effective in approximately 70% of patients in nonrandomized trials (31). Select use of diagnostic imaging may provide additional reassurance.

Nonpharmacologic Treatment

Well-fitted and supportive brassieres may be helpful in the treatment of mastalgia (30). Dietary changes such as restriction of methylxanthines, caffeine, fat, and salt intake and intermittent diuretic use are advocated frequently, although none of these changes have been conclusively demonstrated to reduce mastalgia (24). Evening primrose oil and its ingredient gamma-linolenic acid have been the subject of several studies. Although early trials demonstrated an improvement in pain compared with placebo, a meta-analysis that included more recent trials did not show overall benefit (32).

Pharmacologic Treatment

Although only limited data are available, analgesics such as nonsteroidal antiinflammatory drugs and acetaminophen are likely effective for the treatment of mastalgia (24). Nonsteroidal antiinflammatory drugs are the primary treatment for chest wall pain. Initiation of oral contraceptive pills is not a proven treatment for mastalgia. For women who use combined hormonal contraception and experience cyclic mastalgia, continuous dosage (skipping the hormone-free week) may improve symptoms. Postmenopausal women who developed mastalgia with initiation of hormone therapy may benefit from discontinuing hormone therapy or decreasing the estrogen dose.

Prescription medications are reserved for the most severe and refractory cases of mastalgia and generally are used for 3–6 months, then tapered off and discontinued. Danazol is the only medication with U.S. Food and Drug Administration approval for the treatment of mastalgia. Several studies have demonstrated that danazol (100 mg twice daily) reduces cyclic breast pain by a weighted mean difference in pain score of -20.23 (95% confidence interval, -28.12 to -12.34) on a 100-point visual acuity scale (32). However, androgenic adverse effects and its contraindication for use in women who are pregnant or who are attempting to become pregnant limit its utility. Tamoxifen, a selective estrogen receptor modulator, has demonstrated reduction of breast pain in more than 70% of patients with cyclic pain (32). Overall, there is a 1.92 relative risk (95% confidence interval, 1.42–2.58) for pain relief compared with placebo (32). A tamoxifen dosage of 10 mg/d appears to be as effective as 20 mg/d with fewer adverse effects (24). Thus, danazol and tamoxifen are effective for severe and refractory cases of mastalgia, but their use is limited by adverse effects.

The prolactin inhibitor bromocriptine (2.5 mg twice daily) has been shown to be more effective than placebo in reducing breast pain. However, nausea and dizziness result in high discontinuation rates (32).

► *How is atypical hyperplasia evaluated and managed?*

When atypical hyperplasia is diagnosed on core needle biopsy, National Comprehensive Cancer Network guidelines recommend surgical excision because either DCIS or invasive cancer is detected at the time of surgical excision in 10–20% of cases (20). Screening recommendations for women with atypical hyperplasia include annual mammography, clinical breast examination every 6–12 months, and breast self-awareness (20). Based on emerging evidence, annual magnetic resonance imaging can be considered for breast cancer surveillance for women with atypical hyperplasia who are 30 years and older (20). Risk-reduction therapy should be strongly recommended. Possible risk-reduction therapies include tamoxifen (for premenopausal or postmenopausal women), raloxifene (for postmenopausal women), and aromatase inhibitors (for postmenopausal women) (12). In addition, women with atypical hyperplasia should be counseled about maintaining a healthy lifestyle to help decrease the risk of breast cancer, including increasing physical activity, maintaining an ideal body weight, and reducing alcohol use (12).

► *How is lobular carcinoma in situ evaluated and managed?*

Women in whom LCIS is diagnosed on tissue biopsy typically have surgical excision to rule out adjacent more serious lesions such as DCIS or invasive carcinoma, although select patients may be suitable for monitoring in lieu of surgical excision. Multifocal or extensive LCIS involving more than four terminal ductal lobular units on core biopsy may be associated with an increased risk of invasive cancer on surgical excision (20). Patients with pleomorphic LCIS should be managed per the National Comprehensive Cancer Network guidelines for breast cancer (20).

Women with a history of LCIS should have more intensive screening. Screening should include annual screening mammography and clinical breast examination every 6–12 months beginning at diagnosis but not before age 30 years. Patients should be counseled about breast awareness and also should consider annual magnetic resonance imaging (20). Patient counseling should include discussion about healthy lifestyle modifications that may help to decrease the risk of breast cancer (12). National Comprehensive Cancer Network

guidelines advise that for women diagnosed with LCIS, risk-reduction therapy should be strongly recommended. Possible risk-reduction therapies include tamoxifen (for premenopausal and postmenopausal women), raloxifene (for postmenopausal women), and aromatase inhibitors (for postmenopausal women) (12). Prophylactic mastectomy is a possible option for women with LCIS (12).

► **How is milky nipple discharge evaluated and managed?**

Evaluation of patients with nipple discharge should begin with a patient history and a clinical breast examination (Fig. 3). Patients with bilateral milky nipple discharge should be tested for pregnancy. If the pregnancy test result is negative, then a galactorrhea workup should

be performed that includes a review of medications, measurement of thyroid-stimulating hormone levels, and measurement of prolactin levels. The following medications are associated with galactorrhea: phenothiazines and other antipsychotic drugs, metoclopramide, domperidone, methyl dopa, reserpine, verapamil, and combined oral contraceptives (33).

► **How is nonmilky discharge evaluated and managed?**

For women presenting with symptoms of nonmilky discharge, history taking should focus on characterizing the discharge, including whether the discharge is spontaneous or expressed; unilateral or bilateral; uniductal or multiductal; and clear, yellow, green, multicolor, or

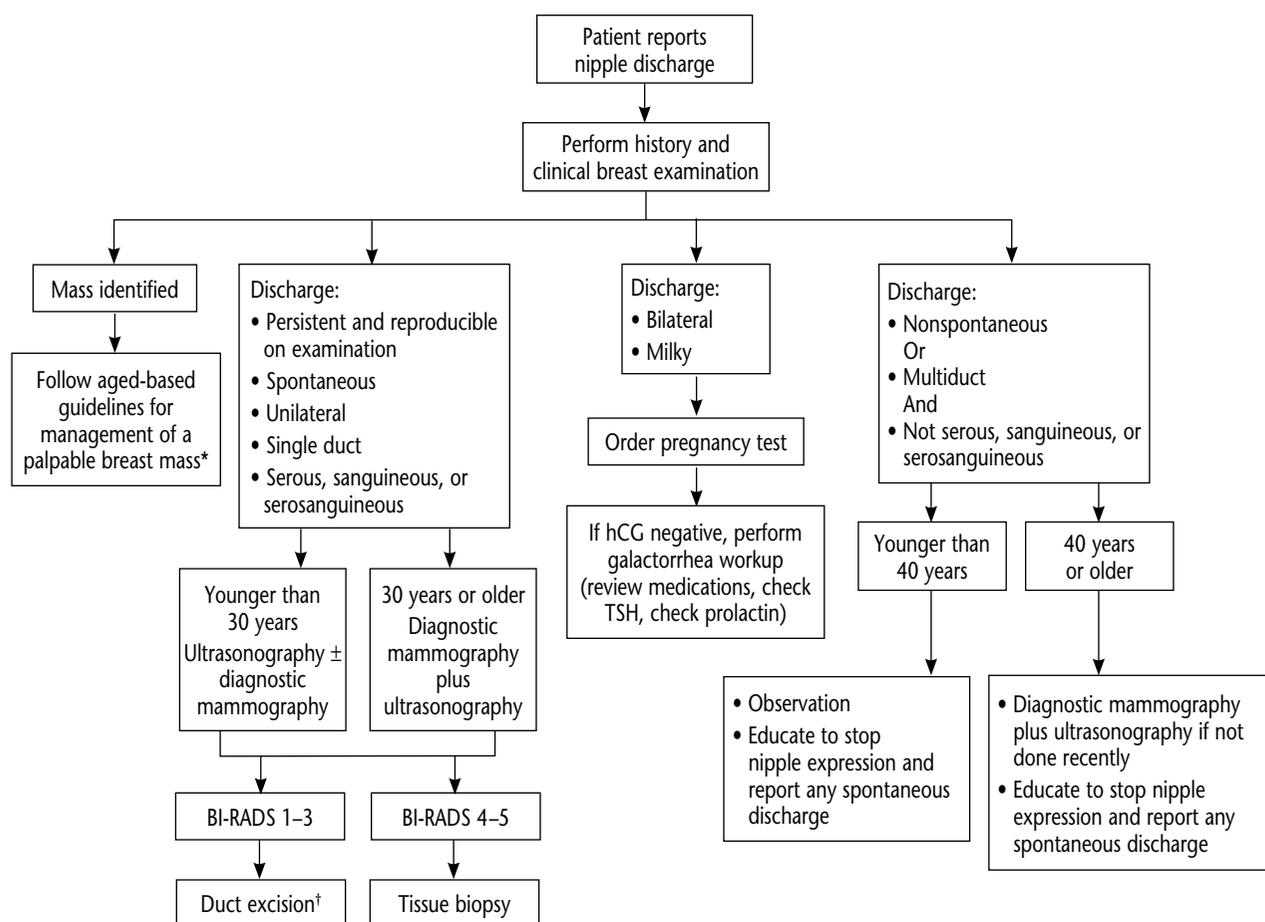


Fig. 3. Management of nipple discharge. Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; hCG, human chorionic gonadotropin; TSH, thyroid-stimulating hormone.

*See BSCR-4 and BSCR-10 in National Comprehensive Cancer Network. Breast cancer screening and diagnosis. Version 1.2015. NCCN Clinical Practice Guidelines in Oncology [after login]. Fort Washington (PA): NCCN; 2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf. Retrieved February 23, 2016.

†Either ductography or magnetic resonance imaging can be performed to guide the excision. Excision is indicated for abnormal discharge even if ductography is negative. The National Comprehensive Cancer Network algorithm also includes an option for surveillance with 6-month follow-up and imaging for 1–2 years.

Modified from Pearlman MD, Griffin JL. Benign breast disease. *Obstet Gynecol* 2010;116:747–58.

bloody (Fig. 3). A small amount of expressible clear discharge is physiologically normal. Concern for underlying pathology is raised if the discharge is persistent and reproducible on examination; spontaneous; unilateral; from a single duct; and clear, serous, or bloody (20). Information should be obtained about potential sources of nipple stimulation, timing, and circumstances when discharge was noted. A thorough breast examination should be performed. If a mass is palpated, it should be evaluated (see *How is a palpable breast mass evaluated?*). Particular attention should be given to the skin of the nipple–areolar complex. If the discharge is multiductal or nonspontaneous (ie, expressed only) and the examination findings are otherwise normal, then it likely represents a benign process. Evaluation includes counseling to stop nipple expression and diagnostic imaging for women 40 years and older (Fig. 3) (20).

Further age-based evaluation should be performed for spontaneous, unilateral, uniductal nipple discharge that is clear, serous, or bloody (Fig. 3) (20). Evaluation should begin with ultrasonography (all ages), with additional diagnostic mammography for women 30 years and older (optional in younger women). Women with imaging findings suspicious for malignancy (BI-RADS 4–5) require tissue biopsy. Women with BI-RADS 1–3 imaging results but abnormal discharge generally should undergo duct excision. Ductography or magnetic resonance imaging are optional and can help in planning the excision (Fig. 3) (20).

► ***How are inflammatory breast disorders evaluated and managed?***

Women presenting with signs and symptoms of breast inflammation, which may include breast erythema, warmth, pain, and fever, should be evaluated with a detailed history that notes the time, course, and duration of symptoms and breast history, including lactation, recent trauma, and any prior treatment for these symptoms. A complete breast examination should be performed with special attention to inflammatory changes and their location, skin changes (including rashes or breaks in the skin or nipple), axillary or supraclavicular adenopathy, and the presence or absence of a breast mass. In the context of a discrete mass on examination, age-appropriate breast imaging (starting with ultrasonography) is recommended.

Infectious mastitis is the most likely cause of this constellation of findings. Although mastitis is most common during lactation, nonpuerperal mastitis also may be encountered in routine practice. Early treatment of breast infections may decrease abscess formation, although an abscess may be present at the time of initial presentation.

Puerperal infectious mastitis most commonly is caused by infection with *Staphylococcus aureus*. Other organisms that can cause infectious mastitis include *Streptococcus* and *Staphylococcus epidermidis*, *Enterococcus*, and anaerobes. Skin-associated breast infections in nonlactating women can be treated empirically with amoxicillin and clavulanic acid or, for patients who are allergic to penicillin, erythromycin and metronidazole (34). If an abscess is suspected or symptoms do not resolve after empiric antibiotic therapy, breast imaging should be performed to exclude other pathology, and a biopsy should be performed based on the imaging results. Abscesses should be treated by aspiration or incision and drainage, with culture to guide antibiotic therapy.

The presentation of inflammatory breast cancer may overlap with that of infectious mastitis and may be accompanied by other skin findings, such as thickening, edema, or peau d'orange appearance, and nipple retraction. Patients with inflammatory breast cancer typically present with pain, progressive breast tenderness, and skin discoloration (erythema, “bruising”) and often have a firm and enlarged breast. When inflammatory breast cancer is considered in the differential diagnosis, diagnostic mammography and ultrasonography are appropriate first steps, and a punch biopsy of the breast skin should be performed when skin findings suggestive of malignancy are present and not responsive to antibiotic therapy (20).

Periductal mastitis presents as focal inflammation of the periareolar area and may be accompanied by abscess formation or even mammary duct fistula. It is most common in young women who smoke and may be recurrent. Periductal mastitis should be treated initially with empiric antibiotic therapy, including anaerobic coverage, and supported by culture results if available. Ultrasonography should be performed, and abscesses should be aspirated or incised and drained. In women with fistula formation or recurrent episodes, excision of the diseased ducts is indicated, which may require referral to an experienced breast surgeon. Smoking cessation should be encouraged (25).

► ***How are skin changes of the breast evaluated, and what are the treatment options?***

Most skin conditions found on the breast are similar to skin conditions found elsewhere on the body and should be treated similarly. Common skin conditions such as eczema and contact dermatitis affect the skin of the breasts and should respond to usual therapies. Other commonly encountered conditions include intertrigo in the folds beneath large, ptotic breasts and hidradenitis suppurativa, which may affect the axillae and lower

aspect of the breast. *Candida* infections of the skin are common and have the classic presentation of inflamed skin with satellite lesions. These infections typically occur in the skin folds in women with large breasts.

Skin changes can be of concern because some can be signs of underlying malignancy. Recurrent scabbing and eczema-like changes of the nipple may warrant full-thickness skin biopsy to exclude Paget disease, which is associated with an underlying invasive breast carcinoma or DCIS in 85% of cases (35). Skin findings of thickening, edema, peau d'orange appearance, unexplained and persistent erythema, nipple excoriations, and skin ulceration warrant further evaluation to rule out inflammatory breast cancer and other types of breast cancer. Inflammatory breast cancer can present without underlying masses. Suspicious skin changes should be evaluated with diagnostic mammography and ultrasonography. Imaging results of BI-RADS 4–5 require core needle biopsy and, possibly, punch biopsy or surgical excision of the skin lesion. Results of BI-RADS 1–3 should be followed by punch biopsy of the abnormal skin or nipple if clinical concern persists (20).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- ▶ Women in whom atypical hyperplasia has been diagnosed have a substantially increased risk of subsequent invasive cancer in the affected breast and the contralateral breast. Risk-reduction therapy should be strongly recommended. Possible risk-reduction therapies include tamoxifen (for premenopausal and postmenopausal women), raloxifene (for postmenopausal women), and aromatase inhibitors (for postmenopausal women).
- ▶ Danazol and tamoxifen are effective for severe and refractory cases of mastalgia, but their use is limited by adverse effects.
- ▶ Women in whom LCIS has been diagnosed have a substantially increased risk of subsequent invasive cancer in the affected breast and the contralateral breast. Risk-reduction therapy should be strongly recommended. Possible risk-reduction therapies include tamoxifen (for premenopausal and postmenopausal women), raloxifene (for postmenopausal women), and aromatase inhibitors (for postmenopausal women).

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

- ▶ Women with imaging findings suspicious for malignancy (BI-RADS 4–5) require tissue biopsy.
- ▶ If imaging suggests a simple cyst (no internal septations or mural thickening and BI-RADS 2) and if the history and examination also are consistent with benign disease, then routine clinical follow-up is recommended.
- ▶ If imaging suggests a complicated cyst (ie, nonsimple cyst that is a round, circumscribed mass; contains low-level echoes without vascular flow; satisfies most but not all criteria for a simple cyst; and is BI-RADS 3), then decisions regarding aspiration or imaging observation for 1–2 years should be made after thorough discussion with the patient based on patient preference or overriding clinical concern.
- ▶ Complex cysts (nonsimple cysts with cystic and solid components and BI-RADS 4–5 imaging findings) require biopsy.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- ▶ The initial evaluation of a woman with breast-related symptoms should include review of her history to characterize her symptoms and to identify risk factors for breast cancer. It also should involve performance of a clinical breast examination.
- ▶ Three options are available for histologic evaluation of abnormal findings on diagnostic imaging: 1) fine-needle aspiration, 2) core needle biopsy, and 3) excisional biopsy. Core needle biopsy generally is the preferred biopsy method because it has few complications and minimizes surgical changes to the breast.
- ▶ Evaluation of a breast mass begins with a detailed history, assessment of breast cancer risk, and physical examination and requires age-appropriate breast imaging. Imaging results based on the BI-RADS classification system will guide management recommendations regarding the need for continued imaging observation or biopsy.
- ▶ The appropriate diagnostic imaging study is determined based on the woman's age. For women younger than 30 years with a palpable mass, ultrasonography is the preferred initial modality. For

women 30 years or older with a palpable mass, diagnostic mammography should be obtained, and additional imaging with ultrasonography often is required.

- ▶ If initial imaging results are indicative of low risk (BI-RADS 1–3) in a woman with a solid breast mass, then biopsy should be considered if there is an otherwise high clinical suspicion in women 30 years or older or additional imaging obtained in women younger than 30 years. Close follow-up for 1–2 years (with physical examination every 3–6 months with or without diagnostic imaging every 6–12 months) may be an option to ensure stability of a mass that is of low clinical suspicion.
- ▶ Close clinical follow-up, biopsy, or both should be considered in the case of a discrete palpable mass with negative or discordant imaging results.
- ▶ Breast imaging should be considered for focal mastalgia that is not explained by an obvious cause (eg, musculoskeletal), particularly if the pain is of new onset.
- ▶ Reassurance is appropriate management for patients with cyclic mastalgia and normal physical examination findings.
- ▶ A small amount of expressible clear discharge is physiologically normal. Concern for underlying pathology is raised if the discharge is persistent and reproducible on examination; spontaneous; unilateral; from a single duct; and clear, serous, or bloody.
- ▶ Further age-based evaluation should be performed for spontaneous, unilateral, uniductal nipple discharge that is clear, serous, or bloody.
- ▶ When inflammatory breast cancer is considered in the differential diagnosis, diagnostic mammography and ultrasonography are appropriate first steps, and a punch biopsy of the breast skin should be performed when skin findings suggestive of malignancy are present and not responsive to antibiotic therapy.
- ▶ Skin findings of thickening, edema, peau d'orange appearance, unexplained and persistent erythema, nipple excoriations, and skin ulceration warrant further evaluation to rule out inflammatory breast cancer and other types of breast cancer.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000–November 2015. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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