

Work-up and management of breast pain

Pamela Li, Ashley Simpson, Jill Dietz

Department of Surgery, University Hospitals, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Contributions: (I) Conception and design: None; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Pamela Li. Department of Surgery, University Hospitals, Case Western Reserve University School of Medicine, Cleveland, OH, USA. Email: Pamela.Li@UHhospitals.org.

Abstract: Breast pain, or mastalgia, is a common symptom and a frequent reason for breast center referrals. It can be categorized as cyclical or non-cyclical pain. Cyclical breast pain is more common and varies with the menstrual cycle. Non-cyclical breast pain includes true breast pain and extramammary causes. Categorizing breast pain helps to guide the work-up and management. A thorough history and physical exam should be performed in all patients presenting with breast pain. Though breast pain alone is rarely a sign of breast cancer, breast imaging may be still be appropriate. If there are no concerning findings on the physical exam, the imaging work-up is determined by patient age and the type of breast pain. Management of breast pain without suspicious findings on physical exam or breast imaging is driven by the severity of the pain. Reassurance of the negative findings and that the patient does not have breast cancer is often all that is required. Breast pain frequently resolves spontaneously and no further treatments are necessary. If pain is persistent or impacting quality of life, initial management is centered on conservative therapies such as physical support. Medications can be considered for severe and persistent pain, but the side effects of these therapies need to be considered.

Keywords: Breast pain; mastalgia; cyclical; non-cyclical; extramammary

Received: 25 August 2020; Accepted: 21 January 2021; Published: 30 September 2021.

doi: 10.21037/abs-20-102

View this article at: <https://dx.doi.org/10.21037/abs-20-102>

Introduction

Breast pain is a common symptom experienced by women of all ages. Moderate to severe breast pain can impact quality of life. Breast pain is also frequently reported because of the fear of breast cancer. Though breast pain alone is rarely a sign of breast cancer, there is always a role for a thorough assessment of a patient's symptoms.

In this review, we will describe the ideal work-up and management of those women presenting to an outpatient office with a complaint of breast pain, as this is a common reason for outpatient referrals and can significantly impact quality of life of these patients. We will define the different categories of breast pain and describe an appropriate clinical and imaging work-up for a patient presenting with breast pain based on a thorough literature review of the

current evidence-based guidelines as outlined by National Comprehensive Cancer Network (NCCN) and the American College of Radiology (ACR). We will also review the available data regarding management and treatment.

Epidemiology

Though the true prevalence of breast pain is difficult to quantify, studies have shown that 50–80% of women will experience breast pain at some point in their lifetime (1,2). In a survey conducted in South Wales, 66% of survey respondents reported experiencing breast pain with 21% reporting severe breast pain. Breast pain is a frequent reason for breast center referrals and accounts for approximately 50% of breast-related office visits (3). Ader *et al.* surveyed patients who presented to a United States

obstetrics/gynecology clinic. Of the 1,171 patients who completed a questionnaire, 69% reported regular breast pain and 11% reported severe pain. Breast pain impacted quality of life related to sexual health in 48% of patients, physical activity in 37%, social activity in 12%, and work or school in 8% (4).

Although breast pain is a rare presentation of breast cancer, many patients who report breast pain have anxiety related to malignancy. Mastalgia associated with breast cancer is more likely to be unilateral and constant in nature (5). Breast cancer is especially rare in patients with breast pain as their only symptom. In multiple radiological studies, the incidence of breast cancer associated with breast pain ranged from 0–2.3% (6,7).

Classification

Breast pain can be more specifically categorized based on the pattern of pain. It is considered cyclical or noncyclical. Non-cyclical breast pain can be true breast pain or extramammary in origin (7). Classifying breast pain in this manner helps to guide work-up and management.

Cyclical breast pain

Cyclical breast pain is most common and accounts approximately 2/3 of the patients who present with breast pain (8). Cyclical breast pain varies with the menstrual cycle. It can also be referred to as physiological breast pain. Cyclical breast pain usually occurs within the luteal phase, two weeks before menses, and resolves or decreases with the onset of menses. It often recurs around the same time every month. It is usually bilateral and diffuse but can also be unilateral or asymmetric. It is often worst in the upper-outer breast and can radiate to the axillary region. Breast pain can be associated with breast swelling. It is often reported as breast heaviness or tenderness to touch (9).

Cyclical breast pain is thought to be secondary to the normal hormonal variations of the menstrual cycle. Estrogen stimulates ductal elements, progesterone stimulates the stroma, and prolactin drives ductal secretion. As progesterone levels rise to promote ovulation, it stimulates the proliferation of glandular breast tissue. Subsequent edema of the breast stroma can give the sensation of breast fullness and pain (10,11).

Cyclical breast pain also be caused by exogenous hormonal agents such as oral contraceptive pills or hormone

replacement therapy.

Noncyclical breast pain

Noncyclical breast pain does not follow the menstrual cycle. Noncyclical breast pain is more likely to be unilateral, focal, and can be anywhere throughout the breast. It can be constant or intermittent.

Because noncyclical breast pain is less commonly related to hormonal variations, there is more likely to be an anatomical cause. Large, pendulous breasts can contribute to non-cyclical breast pain. Without adequate support, Cooper's ligaments are under stretch and can result in breast pain. Breast cysts are frequently identified as a cause of focal breast pain. Breast infections, including mastitis and breast abscess, often present with a painful, red breast. Breast infection should be always ruled out as a cause of mastalgia. Mondor's disease, superficial thrombophlebitis of the anterolateral thoracoabdominal wall, can also present as breast pain. Patients with Mondor's disease present with a tender subcutaneous cord between the epigastric and axillary regions (12).

The role of diet and lifestyle choices as the etiology of breast pain is uncertain. A high-fat diet, smoking and caffeine intake have all been associated with breast pain, but there is no definitive evidence to support this (13).

Extramammary breast pain

Extramammary breast pain describes breast pain that originates from sources other than the breasts. This can include chest wall pain or pain from other medical conditions. Extramammary breast pain is not considered true mastalgia as it does not arise from the breast tissue. Extramammary pain has been found to be more common than true non-cyclical breast pain (8).

Extramammary pain can be musculoskeletal in origin. Chest wall pain secondary to costochondritis and pectoralis muscle injury can present as breast pain (14). Tietze's syndrome is a more specific form of costochondritis and typically presents as pain at the second and third costochondral junctions. Pain is often sharp or burning in quality (15).

Other medical conditions can also present as chest pain thought to be breast pain. This includes esophageal reflux, gallbladder disease, respiratory disorders and heart disease.

Clinical evaluation

The history and physical exam help to further classify breast pain as cyclical or noncyclical, while also evaluating for infection and cancer.

History

A thorough medical history, surgical history, and review of systems should be obtained. Medications should be confirmed. A breast cancer risk assessment should also be completed. Questions specific to breast pain should help to define if pain is cyclical, noncyclical, or extramammary in nature. Quality/nature/severity of pain, aggravating or alleviating factors, and associated symptoms should be explored.

Physical exam

The bilateral breasts, axilla, supraclavicular and infraclavicular regions should be examined. Start with visualization of the breasts. Note any skin changes, dimpling, scars, retraction, skin thickening, erythema, or lesions. Look for skin marks along the bra line that may indicate an ill-fitting bra. Palpate for enlarged or tender lymphadenopathy. Palpate for any breast masses. Check for nipple discharge.

The physical exam should also be used to delineate if there is extramammary pain. Extramammary pain is often more medial or laterally located. It is frequently reproducible by point pressure to a specific area of the chest wall. You can have the patient lay on her side to displace the breast tissue in order to more easily directly palpate the underlying chest wall.

Imaging

A thorough history and physical exam helps to determine whether imaging studies are indicated. Any findings on physical exam warrant further evaluation with diagnostic breast imaging.

If no concerning findings noted on exam, and routine breast cancer screening is up to date, breast imaging may still be appropriate. Mammogram and ultrasound can be used based on age and presentation. There is no data supporting the use of breast MRI in the setting of breast pain.

It has been reported that negative breast imaging helps

to reduce patient anxiety and provide reassurance (16,17). However, Kushwaha *et al.* suggests that imaging for breast pain contributes to an overutilization of health care resources. They looked at female patients who presented with breast pain to three community breast imaging centers over a 1-year period. Imaging in patients less than 40-year-old resulted in a cost of \$87,322 and for those over 40-year-old \$152,732. In the 454 imaging studies performed in patients less than 40-year-old, all findings were benign (7).

The ACR appropriateness criteria for breast pain (18) establishes evidence-based guidelines from an evaluation and analysis of current available literature. This group makes initial imaging recommendations based on 4 variants of clinical presentation:

- (I) In women with cyclical or diffuse, non-focal breast pain, regardless of age, with no suspicious findings, no imaging is indicated beyond routine age-appropriate screening as this type of pain is not associated with malignancy.
- (II) In women less than 30-year-old with focal or noncyclical breast pain, start with ultrasound. Because of denser breast tissue, mammography is less accurate than ultrasound in the evaluation of women less than 30 years old with breast symptoms.
- (III) In women aged 30–39, with focal and noncyclical breast pain, both mammogram and ultrasound are appropriate and equivalent alternatives.
- (IV) In women greater than 40-year-old with focal and noncyclical breast pain, both mammogram and ultrasound should be performed and are complementary.

NCCN guidelines similarly recommend imaging work-up based on type of breast pain and age, in the absence of concerning findings on physical exam (19).

Any imaging findings should be managed appropriately, for example, follow-up imaging or biopsy. Imaging work-up is summarized in *Figure 1*.

Management

If there is a clear etiology for the breast pain, for example, a simple cyst or an infection, treatment should be directed towards the finding. Otherwise, the treatment of breast pain depends on type of pain and severity. The treatment for cyclical and noncyclical breast pain overlap, although cyclical breast pain is often more responsive to treatment (20).

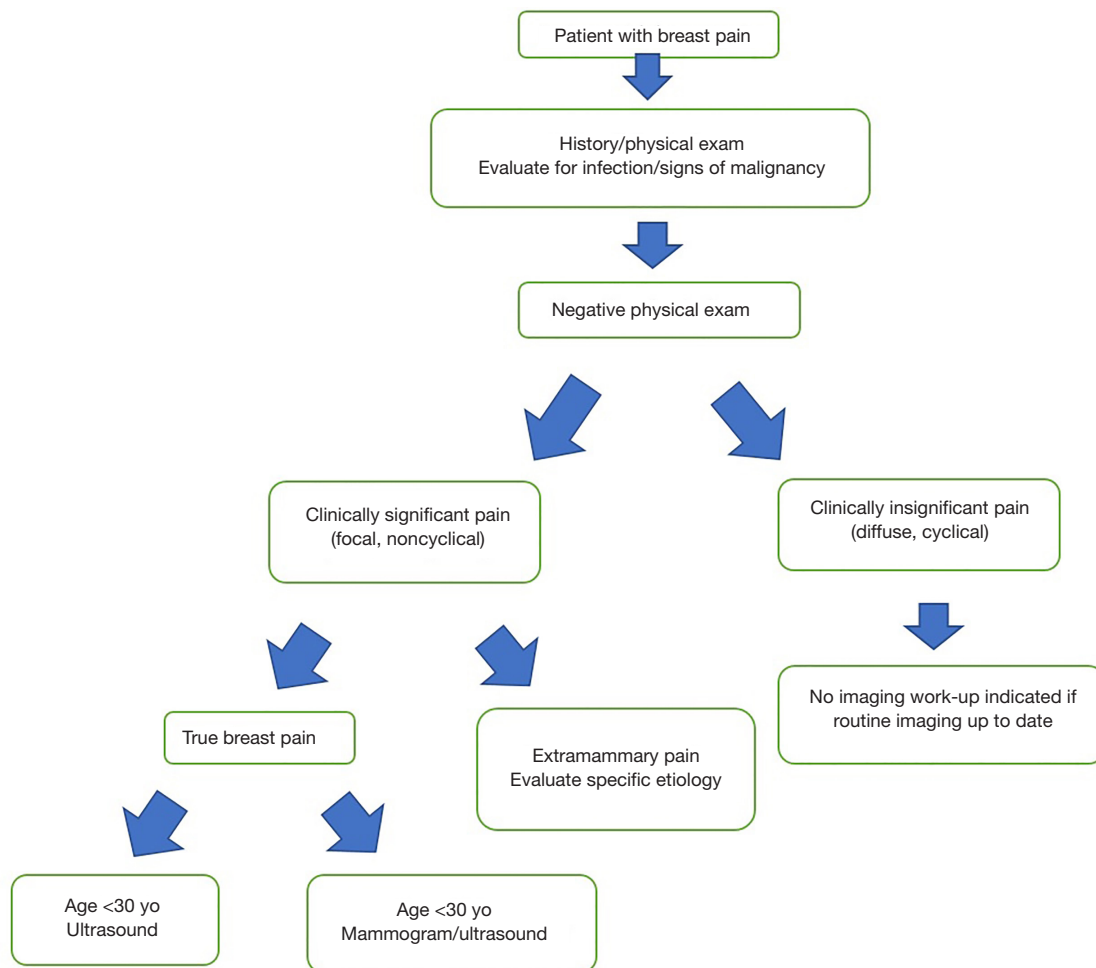


Figure 1 Evaluation of patient with breast pain.

Reassurance

With normal findings on physical exam and breast imaging, all patients with any type of breast pain should be reassured that their symptoms are not caused by breast cancer. For the majority of patients, reassurance results in significant relief and no additional interventions are required (21). Cyclical breast pain has been noted to resolve within 3 months of onset in 20–30% of women (22). Noncyclical breast pain resolves in about 50% of women (20). A follow-up appointment in 3–4 months can be offered to evaluate for persistent or recurrent pain.

If breast pain is persistent, or significantly impacts quality of life, additional therapies can be considered. It is important to note that breast pain alone is never an indication for breast surgery.

Conservative therapy

Conservative, non-pharmacological therapies should always be attempted first. Though there is little evidence for the success of conservative therapies, there is minimal risk involved. Good mechanical support for large, pendulous breasts can improve breast pain in many women. One study reported that all patients with breast pain treated with use of a sports bra during regular activities had some pain relief, while 85% of patients had complete relief of their pain (23).

Multiple studies suggest that patients with breast pain have increased levels of anxiety (24–26). Because stress can exacerbate pain, relaxation and stress management could be helpful for patients with breast pain. In one small study of 45 patients with breast pain, at 8-week follow-up, those assigned to relaxation therapy had significant improvement

Table 1 Relevant trials related to conservative management of breast pain

Reference	Trial type	Comparison	Cohort	Duration of treatment	Follow-up	Conclusion
Hadi (23)	RCT	Danazol vs. sports brassiere	200 women with mastalgia	12 weeks	12 weeks	Sports brassieres can relieve mastalgia
Boyd (31)	RCT	General dietary advice (control) vs. low fat, high carbohydrate diet (intervention)	21 patients with severe persistent mastalgia ×5 years	6 months	6 months	Significant reduction in severity of premenstrual breast tenderness and swelling in intervention group
Genç (32)	RCT	Exercise (3×/week ×6 weeks) vs. control	20 women with mastalgia	6 weeks	6 weeks post study	Exercise treatment beneficial for patients with mastalgia

RCT, randomized controlled trial.

in pain scores and number of pain-free days compared to patients in the control group (27).

As previously stated, the role of diet and lifestyle choices in breast pain is unclear. The elimination of caffeine has been shown to reduce breast pain in some studies but was not shown to be consistently effective in all studies (28,29). As there is little risk to avoiding caffeine, it is still frequently recommended. Observational studies and one small randomized controlled trial (RCT) have shown some benefit to a low-fat diet in reducing breast pain, but there is no significant data regarding this (30,31). Genç *et al.* looked at the effect of exercise on mastalgia in a small, randomized controlled study of 20 patients with breast pain. Those patients randomized to the exercise group completed an exercise program three times a week for 6 weeks. At 6-week follow-up, pain scores improved significantly in the exercise group (32). See *Table 1*.

Nutritional supplements

Multiple randomized controlled studies have evaluated the benefit of vitamin E and vitamin B6 in the treatment of breast pain. Studies varied in vitamin dosage and length of clinical follow-up. There is no clear data to support the routine use of these vitamins in the treating breast pain (33–35).

Evening primrose oil (EPO) is a nutritional supplement rich in gamma-linolenic acid, an essential fatty acid. Taking EPO is thought to restore the saturated/unsaturated fatty acid balance and decrease the sensitivity to steroidal hormones that may contribute to mastalgia (36). Dosing in various trials has ranged from 2,000–3,000 mg daily. There have been several studies published with conflicting results

regarding use of EPO on mastalgia (37,38). On meta-analysis, there was no clear benefit of EPO in breast pain reduction (38).

Medications

Medications can be considered for persistent or severe pain that does not respond to conservative therapy. Patient risk factors and medication side effects should be carefully considered before initiating these therapies. See *Table 2* for a summary of relevant trials.

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) can be given to treat breast pain with minimal risk. In a prospective, randomized, blinded, placebo-controlled trial, Colak *et al.* reported that the topical application of diclofenac was effective in reducing breast pain scores after 6 months of use in patients with both cyclical and noncyclical mastalgia (42). There is no clear evidence that oral NSAIDs are effective in treating breast pain (43) and there is no benefit to using oral NSAIDs over topical NSAIDs. Chest wall pain can also be managed with topical diclofenac. Because there is the potential for elevation of liver function tests with long-term use, patient transaminases should be monitored.

Danazol is an anti-gonadotropin agent with androgenic effects. It is the only medication approved by the US Food and Drug Administration for the treatment of breast pain. The standard dose is 100–400 mg/day. Danazol at various doses has been shown to reduce pain in patients with both cyclical and noncyclical breast pain (22,44). The androgenic side effects, however, need to be considered. Kontostolis reports that at a dose of 200 mg/daily, many patients reported weight gain (31%), menorrhagia (13%), deepening

Table 2 Relevant trials related to pharmacological treatment of breast pain

Reference	Trial type	Comparison	Cohort	Duration of treatment	Follow-up	Conclusion
Kontostolis (39)	RCT	Danazol 200 mg vs. tamoxifen 10 mg vs. placebo	93 women with severe cyclical mastalgia	6 months	12 months	(I) Danazol and tamoxifen both reduce cyclical breast pain compared to placebo; (II) no significant difference between tamoxifen vs danazol
Fentimen (40)	RCT	Tamoxifen 20 mg vs. placebo	60 premenopausal women with cyclical breast pain	3 months	3 months	Tamoxifen more effective than placebo in reducing breast pain
Mansel (41)	RCT	Bromocriptine 2.5 mg BID vs. placebo	272 patients	3–6 months	10 months	Bromocriptine more effective than placebo
Colak (42)	RCT	Topical NSAID (diclofenac) vs. placebo	108 women with cyclical (n=60) or non-cyclical (n=48) breast pain	6 months	6 months	Diclofenac effective in reducing both cyclical and non-cyclical breast pain

RCT, randomized controlled trial; NSAID, nonsteroidal anti-inflammatory drug.

of voice (13%) (39). Other side effects include male-pattern hair-loss, acne and muscle cramps. Danazol is teratogenic and should not be used in patients who are or are trying to get pregnant (44).

Bromocriptine is a dopamine agonist that inhibits the release of prolactin from the anterior pituitary gland. Side effects are frequently experienced and include headaches, dizziness and nausea. Bromocriptine has been shown to reduce breast pain in a randomized, placebo controlled, multicenter trial (41). However, when compared to danazol above, bromocriptine has not been shown to be as effective (45). Because of this, and the frequency of side effects, bromocriptine is not recommended for the treatment of breast pain.

Tamoxifen is a selective estrogen-receptor modulator used as adjuvant treatment for hormone receptor positive breast cancer. It has also been used as a treatment for breast pain. Multiple randomized studies have noted that tamoxifen is effective at treating breast pain at 10 and 20 mg/daily, with fewer side effects reported at the lower dose (39,40). Side effects of tamoxifen include thromboembolic events, endometrial cancer, vasomotor symptoms, menstrual irregularity, vaginal discharge, hair thinning and weight gain. Tamoxifen is also teratogenic.

Tamoxifen and danazol were both compared to placebo in a randomized trial of 93 women with cyclical breast pain (39). There was no statistically significant difference noted between danazol and tamoxifen; with 65% and

72% reporting pain relief respectively. Both danazol and tamoxifen were superior to placebo. After 1 year of follow-up, authors noted that those taking tamoxifen reported a continued resolution of symptoms compared to those taking danazol. Of the discussed medications, tamoxifen is noted to have the lowest frequency of side effects and is therefore the preferred recommendation (38).

Clinical scenarios

Scenario 1

A 28-year-old female presents to your office with breast pain. She reports that the pain bilateral, diffuse, and worse right before she gets her period. The pain improves after she gets her period. She otherwise has no medical problems and takes no medications. She has no family history of breast cancer.

On exam, bilateral breasts are symmetrical with no concerning findings. There is no lymphadenopathy.

Question: What imaging work-up would you order?

Answer: This patient is less than 30 years old with cyclical breast pain and no suspicious findings on exam. No imaging work-up is indicated.

Question: How do you counsel this patient regarding management?

Answer: The patient should be reassured that this is consistent cyclical breast pain and not suspicious for breast cancer.

Scenario 2

A 35-year-old female presents to your office with breast pain. She is able to point to the area in her left breast that is painful. It started about 1 week ago. She thinks she feels a mass in the area of pain. She has never had a mammogram. She denies fevers or any other associated symptoms. She has no family history of breast cancer.

You perform a physical exam. Breasts are symmetrical. There are no skin changes noted. There is no lymphadenopathy. The right breast is negative. In the left breast, at 1:00 about 4 cm from the nipple there is a 1.5 cm mass. This corresponds to the area of focal pain.

Question: What is imaging work-up would you order?

Answer: Given her age and findings on physical exam, diagnostic breast imaging is indicated. Bilateral mammogram with a targeted left breast ultrasound should be ordered.

Breast imaging is performed. In the area of focal pain in the left breast, a 1.5 cm simple cyst is noted. There are no additional imaging findings. The patient is reassured that this is a benign finding and no interventions are necessary.

Scenario 3

A 52-year-old female presents to your office with right breast pain. She reports no history of abnormal mammograms, breast biopsies or breast surgeries. She first noticed this pain about 3 months ago and reports that it is worst just lateral to her nipple. It is intermittent. Her last mammogram was 4 months ago and negative. She has no family history of breast cancer.

On exam, bilateral breasts are symmetrical. There are no skin changes, palpable breast masses, or nipple discharge. She is diffusely tender to palpation in the lateral breast, but there is no focal area of tenderness. There is no lymphadenopathy. There are no findings to suggest chest wall pain.

Question: What imaging work-up is indicated?

Answer: Given her age and history, diagnostic imaging should be ordered. The patient is up to date on screening. Right mammogram and targeted ultrasound to the lateral breast are appropriate.

Right breast imaging is performed and negative.

Question: What are your recommendations for this patient?

Answer: This patient is presenting with non-cyclical breast pain. There are no concerning findings on exam or

imaging. The patient can be reassured that breast cancer is not the cause of her breast pain. Short interval clinical follow-up can be recommended.

At a 3-month follow-up visit, the same patient reports worsening right breast pain. She is unable to sleep at night because of the pain.

Question: What are your recommendations for this patient?

Answer: You can start by recommending conservative measures for this patient, which include wearing a well-fitting bra. Though the data is controversial, there is little downside to recommending the elimination of caffeine, low fat diet, and regular exercise.

Conclusions

Breast pain is a very common symptom, but in the absence of concerning findings on physical exam or imaging, breast pain is rarely a symptom of breast cancer. All patients with breast pain should undergo a thorough history and physical exam to determine if further work-up with diagnostic imaging is indicated. Imaging work-up is determined by the age of the patient and type of breast pain. If there are no concerning findings on physical exam or breast imaging, management is based on the type of breast pain and severity. Frequently, reassurance is all that is required. Breast pain often spontaneously resolves, but if severe or persistent, conservative therapies should be attempted first. If pain is persistent or severe, there are several pharmacological therapies that can be considered, but patient should be appropriately counseled regarding the side effects of these medications. Given the lack of high quality data regarding the pharmacological management of breast pain, this could certainly be a topic of further investigation, with the understanding that the majority of patients will improve with reassurance and conservative therapies.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Katharine Yao) for the series “A Practical Guide to Management of Benign Breast Disease” published in *Annals of Breast Surgery*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at: <https://dx.doi.org/10.21037/abs-20-102>). The series “A Practical Guide to Management of Benign Breast Disease” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: All authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Olawaiye A, Withiam-Leitch M, Danakas G, et al. Mastalgia: a review of management J Reprod Med 2005;50:933-9.
2. Scurr J, Hedger W, Morris P, et al. The prevalence, severity, and impact of breast pain in the general population. Breast J 2014;20:508-13.
3. Barton MB, Elmore JG, Fletcher SW. Breast symptoms among women enrolled in a health maintenance organization: frequency, evaluation and outcome. Ann Intern Med 1999;130:651-7.
4. Ader DN, Browne MW. Prevalence and impact of cyclical mastalgia in a United States clinic-based sample. Am J Obstet Gynecol 1997;177:126-32.
5. Preece PE, Baum M, Mansel RE, et al. Importance of mastalgia in operable breast cancer Br Med J (Clin Res Ed) 1982;284:1299-300.
6. Owen WA, Brazeal HA, Shaw HL, et al. Focal breast pain: imaging evaluation and outcomes. Clin Imaging 2019;55:148-55.
7. Kushwaha AC, Shin K, Kalambo M, et al. Overutilization of health care resources for breast pain. AJR Am J Roentgenol 2018;211:217-23.
8. Iddon J, Dixon JM. Mastalgia. BMJ 2013;347:f3288.
9. Davies EL, Gately CA, Miers M, et al. The long-term course of mastalgia. J R Soc Med 1998;91:462.
10. Preece PE, Hughes LE, Mansel RE, et al. Clinical syndromes of mastalgia. Lancet 1976;2:670-3.
11. Vogel PM, Georgiade NG, Fetter BF, et al. The correlation of histologic changes in the human breast with the menstrual cycle. Am J Pathol 1981;104:23-34.
12. Salemis NS, Merkouris S, Kimpouri K. Mondor's disease of the breast. A retrospective review. Breast Dis 2011;33:103-7.
13. Santen RJ, Mansel R. Benign breast disorders. N Engl J Med 2005;353:275-85.
14. Maddox PR, Harrison BJ, Mansel RE, et al. Non-cyclical mastalgia: an improved classification and treatment. Br J Surg 1989;76:901-4.
15. Aeschlimann A, Kahn MF. Tietze's syndrome: a critical review. Clin Exp Rheumatol 1990;8:407.
16. Leung JW, Kornguth PJ, Gotway MB. Utility of targeted sonography in the evaluation of focal breast pain. J Ultrasound Med 2002;21:521-6.
17. Duijm LE, Guilt GL, Hendricks JH. Value of breast imaging in women with painful breasts: observation follow-up study. BMJ 1998;317:1492-5.
18. Holbrook AI, Moy L, Akin E, et al. American College of Radiology ACR appropriateness Criteria Breast pain. IRadiology ACo, ed., 2018;15:S276-S282.
19. NCCN Guidelines version 1. 2019. Breast Cancer Screening and diagnosis. Persistent or several breast pain.
20. Gateley CA, Miers M, Mansel RE, et al. Drug treatments for mastalgia: 17 years experience in the Cardiff Mastalgia Clinic. J R Soc Med 1992;85:12-5.
21. Barros AC, Mottola J, Ruiz CA, et al. Reassurance in the treatment of mastalgia. Breast J 1999;5:162-5.
22. Pye JK, Mansel RE, Hughes LE. Clinical experience of drug treatments for mastalgia. Lancet 1985;2:373-7.
23. Hadi MS. Sports brassier: is it a solution for mastalgia? Breast J 2000;6:407-9.
24. Colegrave S, Holcombe C, Salon P. Psychological characteristics of women presenting with breast pain. J Psychosom Res 2001;50:303-7.
25. Jenkins PL, Jamil N, Gateley C, et al. Psychiatric illness in patients with severe treatment-resistant mastalgia. Gen Hosp Psychiatry 1993;15:55-7.
26. Preece PE, Mansel RE, Hughes LE. Mastalgia: psychoneurosis or organic disease: Br Med J 1978;1:29-30.
27. Fox H, Walker LG, Heys SD, et al. Are patients with mastalgia anxious, and does relation therapy help? Breast 1997;6:138-42.
28. Millet AV, Dirbas FM. Clinical management of breast

- pain: a review. *Obstet Gynecol Surv* 2002;57:451-61.
29. Levinson W, Dunn PM. Nonassociation of caffeine and fibrocystic breast disease. *Arch Intern Med* 1986;146:1773.
 30. Goodwin PJ, Miller A, Del Giudice ME, et al. Elevated high-density lipoprotein cholesterol and dietary fat intake in women with cyclic mastopathy. *Am J Obstet Gynecol* 1998;179:430.
 31. Boyd NF, McGuire V, Shannon P, et al. Effect of a low-fat high-carbohydrate diet on symptoms of cyclical mastopathy. *Lancet* 1988;2:128-32.
 32. Genç A, Çelebi MM, Çelik SU, et al. The effects of exercise on mastalgia. *Phys Sportsmed* 2017;45:17-21.
 33. Shobeiri F. Clinical effectiveness of vitamin E and vitamin B6 for improving pain and severity in cyclic mastalgia. *Iran J Nurs Midwifery Res* 2015;20:723-7.
 34. Ernster VL, Goodson WH 3rd, Hunt TK, et al. Vitamin E and benign breast "disease": a double-blind, randomized clinical trial. *Surgery* 1985;97:490-4.
 35. Meyer EC, Sommers DK, Reitz CJ, et al. Vitamin E and benign breast disease. *Surgery*. 1990;107:549-51.
 36. Pruthi S, Wahner-Roedler DL, Torkelson CJ, et al. Vital E and evening primrose oil for management of cyclical mastalgia: a randomized pilot study. *Altern Med Rev* 2010;15:59-67.
 37. Blommers J, de Lange-De Klerk ES, Kuik DJ, et al. Evening primrose oil and fish oil for severe chronic mastalgia: a randomized, double-blind, controlled trial. *Am J Obstet Gynecol* 2002;187:1389.
 38. Srivastava A, Mansel RE, Arvind N, et al. Evidence-based management of mastalgia: a meta-analysis of randomized trials. *Breast* 2007;16:503-12.
 39. Kontostolis E, Stefanidis K, Navrozoglou I, et al. Comparison of tamoxifen with danazol for treatment of cyclical mastalgia. *Gynecol Endocrinol* 1997;11:393-7.
 40. Fentiman IS, Caleffi M, Hamed H, et al. Dosage and duration of tamoxifen treatment for mastalgia: a controlled trial. *Br J Surg* 1988;75:845-6.
 41. Mansel RE, Dogliotti L. European multicenter trial of bromocriptine in cyclical mastalgia. *Lancet* 1990;335:190-3.
 42. Colak T, Ipek T, Kanik A, et al. Efficacy of topical nonsteroidal anti-inflammatory drugs in mastalgia treatment. *J Am Coll Surg* 2003;196:525-30.
 43. Dionigi R, Interdonato PF, Scaricabarozzi I, et al. Evaluation of the efficacy and tolerability of nimesulide in the treatment of mastodynia. *Minerva Ginecol* 1992;44:511-4.
 44. O'Brien PM, Abukhalil IE. Randomized controlled trial of the management of premenstrual syndrome and premenstrual mastalgia using luteal phase only danazol. *Am J Obstet Gynecol* 1999;180:18.
 45. Cornell LF, Sandhu NP, Pruthi S, et al. Current management and treatment options for breast pain. *Mayo Clin Proc* 2020;95:574-80.

doi: 10.21037/abs-20-102

Cite this article as: Li P, Simpson A, Dietz J. Work-up and management of breast pain. *Ann Breast Surg* 2021;5:27.