Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Ader DN, Browne MW. Prevalence and impact of cyclic mastalgia in a United States clinic-based sample. Am J Obstet Gynecol. 1997;177(1):126-132.	Review/Other-Dx	1171 patients	To examine the prevalence of premenstrual breast symptoms, the impact of cyclic mastalgia on various activities, and associated patterns of health care utilization.	Sixty-nine percent of women reported regular premenstrual discomfort; 36% had consulted a health care provider about the symptoms. Current moderate-to-severe cyclic mastalgia was found in 11%. Women <36 years old with cyclic mastalgia were 4.7 times as likely as asymptomatic young women to have had a mammogram. Mastalgia interferes with usual sexual activity in 48% of women and with physical (37%), social (12%), and work or school (8%) activity.	4
2. Ader DN, Shriver CD. Cyclical mastalgia: prevalence and impact in an outpatient breast clinic sample. J Am Coll Surg. 1997;185(5):466-470.	Review/Other-Dx	231 patients	To examine prevalence of premenstrual breast symptoms, impact of cyclical mastalgia on various activities, and associated patterns of health care utilization among breast clinic outpatients.	Seventy-nine percent reported having regularly experienced cyclical breast symptoms; 48% have asked a health care provider about their mastalgia. Young women (< or = 35 years) were more than three times as likely to have had a mammogram (75%) if they regularly experienced cyclical mastalgia than if they did not (24%; $p < 0.05$). Current moderate to severe mastalgia lasting 5 days or more monthly was reported by 30% of women. This "clinical" level of mastalgia interferes with usual sexual activity for 33%, with physical activity for 29%, with social activity for 15%, and with work for 15% of these women.	4
3. Kataria K, Dhar A, Srivastava A, Kumar S, Goyal A. A systematic review of current understanding and management of mastalgia. Indian J Surg. 76(3):217-22, 2014 Jun.	Review/Other-Dx	N/A	To review the current understanding and management of mastalgia.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
4. Leinster SJ, Whitehouse GH, Walsh PV. Cyclical mastalgia: clinical and mammographic observations in a screened population. Br J Surg. 1987;74(3):220-222.	Review/Other-Dx	5087 women	To investigate the epidemiological features of cyclical mastalgia in a population of "well women" from a breast screening program, and to determine if there was any relationship between cyclical mastalgia and breast pattern.	The incidence of cyclical mastalgia in well women presenting for breast screening was 69 per cent. The incidence of cyclical mastalgia increases with age up to the menopause. There was a higher incidence of 'high risk' mammographic patterns and a lower incidence of 'low risk' patterns, according to the Wolfe classification, in women with cyclical mastalgia compared with the rest of the screened population. This finding correlated with the severity, duration and need for treatment. The differences in breast pattern did not persist after the menopause.	4
5. Scurr J, Hedger W, Morris P, Brown N. The prevalence, severity, and impact of breast pain in the general population. Breast J. 20(5):508-13, 2014 Sep-Oct.	Review/Other-Dx	1,659 females	To review the prevalence, severity, and impact of breast pain in the general population.	Over half the sample (51.5%) experienced breast pain, with a severity similar to that reported in clinical populations. There was a higher prevalence of breast pain in older participants, larger breasted participants and those who were less fit and active. Of symptomatic participants, 41% and 35% reported breast pain affecting quality of life measures of sex and sleep and 10% of symptomatic participants had sufferer for over half their lives.	4
6. Arslan M, Kucukerdem HS, Can H, Tarcan E. Retrospective Analysis of Women with Only Mastalgia. J Breast Health (2013). 12(4):151-154, 2016 Oct.	Observational-Dx	789 cases	To investigate the examinations and the results of the females referred to our outpatient clinics with mastalgia and to determine the frequency of malignancy.	Mean age was 42.97+/-12.36 (16-74) years. 59.7% (n=471) of the women had bilateral mastalgia and 91.1% (n=719) of the breast examinations were found to be normal. Ultrasonography (USG)was required from 664 (84.2%) women and mammography was required from 448 (56.8%) women. Considering diagnoses; fibrocystic changes in 32.3% (n=201), ductal ectasia in 8.8% (n=55), fibroadenomas in 6.1% (n=38), reactive lymphoid hyperplasia in 1.1% (n=7) was observed. Only 1 (0.2%) woman was diagnosed with invasive ductal carcinoma.	3

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. 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(8):651-657.	Review/Other-Dx	2400 women	To determine how often women present with breast symptoms, how these symptoms are evaluated, and how often cancer is diagnosed.	Sixteen percent of the HMO population presented with a breast symptom during the 10-year period, for a rate of 22.8 presentations per 1000 person-years. Women younger than 50 years of age presented nearly twice as often as older women (P = 0.001). Women with breast symptoms had lower rates of screening than other women before presenting but higher rates of screening afterward (P < 0.001). Symptoms were evaluated beyond the initial visit in 66% of patients, and invasive procedures were performed in 27% of patients. Cancer was found in 6.2% of patients and 4.5% of episodes; rates of cancer detection varied significantly by type of symptom but not by patient age.	4
8. Chetlen AL, Kapoor MM, Watts MR. Mastalgia: Imaging Work-up Appropriateness. Acad Radiol. 24(3):345-349, 2017 Mar.	Review/Other-Dx	236 patients	To evaluate the diagnostic work-up of women presenting with solitary complaint of breast pain, identify the outcomes of the diagnostic work-up, and review the use of these criteria within our own practice.	Of the 236 patients, 10 women had cyclical breast pain, 116 had noncyclical, nonfocal breast pain, and 110 had noncyclical, focal breast pain. No imaging correlates were discovered to explain the etiology of cyclical pain, supporting the American College of Radiology Appropriateness Criteria rating values. A definitive imaging correlate for breast pain was identified in seven women (3%) with noncyclical, focal pain, one of which was a cancer diagnosis (0.4%), which correlates with the American College of Radiology Appropriateness Criteria ratings. No imaging correlates were found in women with noncyclical, nonfocal pain, supporting the American College of Radiology Appropriateness Criteria ratings.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Cho MW, Grimm LJ, Johnson KS. Focal Breast Pain: Does Breast Density Affect the Need for Ultrasound?. Acad Radiol. 24(1):53-59, 2017 Jan.	Observational-Dx	413 cases	To determine the utility of directed ultrasound and digital mammogram for evaluating focal breast pain in women with different mammographic breast densities.	Eighteen percent (76 of 413) of cases demonstrated an imaging correlate. Of these, 74% (56 of 76) occurred in dense breasts and 26% (20 of 76) in nondense breasts. Seventy percent (14 of 20) of lesions in nondense breasts were seen with mammography and ultrasound, whereas 30% (6 of 20) were detected only with ultrasound. Of lesions detected in dense breasts, 29% (16 of 56) were seen with mammography and ultrasound, whereas 71% (40 of 56) were detected only with ultrasound. Thirty-one percent (24 of 76) of cases were biopsied, 42% (10 of 24) of which were detected by ultrasound only. No cancer was detected in initial workup. At 2-year follow-up, three women, all with dense breasts, developed cancer in the same quadrant as the initial pain.	3
10. Fariselli G, Lepera P, Viganotti G, Martelli G, Bandieramonte G, Di Pietro S. Localized mastalgia as presenting symptom in breast cancer. Eur J Surg Oncol. 1988;14(3):213-215.	Review/Other-Dx	200 women with localized mastalgia; 478 women with operable breast cancer.	To investigate the incidence of subclinical breast cancer in patients with localized mastalgia and to determine by accurate anamnesis, the onset of pain as first symptom in patients with operable breast cancer.	In the first group, mammography detected five cases of subclinical breast cancer at the site of pain. In the second group, 86 patients (18%) reported localized pain as presenting symptom, followed, at different intervals, by the detection of a breast lump. Localized pain can be considered a presenting symptom of breast cancer thus requiring a careful physical and mammographic examination, especially when risk factors are associated.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Leddy R, Irshad A, Zerwas E, et al. Role of breast ultrasound and mammography in evaluating patients presenting with focal breast pain in the absence of a palpable lump. Breast J. 19(6):582-9, 2013 Nov-Dec.	Observational-Dx	257 patients	To determine if ultrasound and/or mammography is helpful in detecting breast cancers in patients presenting with focal breast pain.	The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of mammogram-alone and ultrasound (US)-alone for detection of breast cancer in these patients were 100%, 87.6%, 10.7%, 100% and 100%, 92.5%, 13.6%, and 100%, respectively, while for combined mammogram and US was 100%, 83.7%, 8.3%, and 100%. The sensitivity, specificity, PPV, and NPV of mammogram for identifying an underlying suspicious mass lesion that was subsequently detected by US was 58%, 91%, 39%, and 95%. The NPV of a Breast Imaging Reporting And Data System (BIRADS)1 mammogram for any underlying mass lesion was 75%. Addition of an ultrasound to a mammogram did not detect additional cancers; likely due to low cancer incidence in these patients. However, US detected underlying mass lesions in 25% cases with a BIRADS 1 mammogram result.	3
12. Leung JW, Kornguth PJ, Gotway MB. Utility of targeted sonography in the evaluation of focal breast pain. J Ultrasound Med. 2002;21(5):521-526; quiz 528-529.	Observational-Dx	110 targeted sonographic examinations were performed in 99 patients	To determine the utility of targeted sonography in the evaluation of patients with focal breast pain.	No cancer was identified in any of the 110 examinations. Eighty-five (77.3%) of the examinations had negative findings. Cysts were identified in 15 cases (13.6%), and 3 solid masses (2.7%) were identified. Two of these 3 solid masses had biopsies and were shown to be benign, whereas the third mass was followed for 29 months without change. Most patients were premenopausal, had no family or personal history of breast cancer, and were not taking exogenous hormones. Eighty-five patients (77%) were referred by primary care physicians.	3

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
13. Locker AP, Manhire AR, Stickland V, Caseldine J, Blamey RW. Mammography in symptomatic breast disease. Lancet. 1989;1(8643):887-889.	Observational-Dx	5080 patients	To evaluate the contribution of mammography in women presenting with various symptoms of breast disease, and to better define the most effective use of mammographic facilities.	The sensitivity of mammography was 88%. Only 18 cancers were detected by mammography alone, and of these 3 were in the other breast. 7 of the remaining 15 cancers had clinical signs which would have been pursued to open biopsy in the absence of mammography.	3
14. Duijm LE, Guit GL, Hendriks JH, Zaat JO, Mali WP. Value of breast imaging in women with painful breasts: observational follow up study. BMJ. 1998;317(7171):1492-1495.	Review/Other-Dx	987 patients	To determine the value of breast imaging in patients with localised or diffuse pain in the breast in whom physical examination shows no abnormalities.	Radiological examination of the painful breast(s) showed the following: normal findings in 854 (86.5%) women, benign abnormalities in 85 (8.6%; mainly small cysts or mastopathy), abnormalities that were probably benign in 36 (3.6%), suspicious findings in 8 (0.8%), and malignancy in 4 (0.4%). Biopsy of the painful area was performed in 10 of the 939 women with normal findings or benign abnormalities, in two of 36 women with radiological abnormalities that were probably benign, and in all women with suspicious or malignant findings. Only the four lesions that had been classified radiologically as malignant were found to be malignant at surgery. The prevalence of breast cancer was similar in symptomatic and control women.	4

Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Khan SA, Apkarian AV. Mastalgia and breast cancer: a protective association? Cancer Detect Prev. 2002;26(3):192-196.	Observational-Dx	5463 women	To examine the association between mastalgia and breast cancer in the patient population of the Breast Care Center of University Hospital, Syracuse, New York.	Of 5463 women with complete breast cancer risk factor information, 1532 (28%) reported breast pain as an incidental complaint at their initial visit, and 861 were diagnosed with breast cancer. Forward stepwise logistic regression was used to analyze the association between breast pain and a diagnosis of breast cancer. The age-adjusted OR for breast cancer was 0.60 (95% CI 0.50-0.74). Adjustment for additional risk factors (early menarche, late first birth, late menopause, exogenous hormone use, positive family history) yielded an OR of 0.63, 95% CI 0.49-0.79.	4
16. Brown N, Burnett E, Scurr J. Is Breast Pain Greater in Active Females Compared to the General Population in the UK?. Breast J. 22(2):194-201, 2016 Mar-Apr.	Review/Other-Dx	234 patients (first cohort); 1285 patients (second cohort)	To investigate the prevalence and severity of breast pain in an active cohort, compared to a random cohort.	Breast pain prevalence was significantly lower in the active cohort (32.1%) compared to the random cohort (43.6%), however, the severity and frequency of breast pain was similar in both cohorts. Females in the active cohort undertook significantly more physical activity, were lighter, had greater nulliparous rates, greater adherence to sports bra use, but less adherence to professional bra fitting. With lower breast pain rates in the active cohort the hypothesis of a compound effect of multiple forms of breast pain causing an increase in prevalence and severity is rejected.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Brown N, White J, Brasher A, Scurr J. The experience of breast pain (mastalgia) in female runners of the 2012 London Marathon and its effect on exercise behaviour. BJSM online. 48(4):320-5, 2014 Feb.	Review/Other-Dx	1285 patients	To determine the prevalence and severity of mastalgia in female marathon runners, identify factors that increase mastalgia and methods used to overcome mastalgia, and explore the impact that mastalgia may have on marathon training.	32% of participants experienced mastalgia. This was significantly related to cup size and was greater during vigorous compared with moderate physical activity. Exercise-related factors were the primary factors reported to increase mastalgia participation. Seventeen per cent of symptomatic participants reported that mastalgia affected their exercise behaviour. Methods reportedly used to overcome mastalgia included pain medication and firm breast support; however, 44% of participants took no measures to relieve symptoms despite over half describing their mastalgia as discomforting.	4
18. Burbage J, Cameron L. An investigation into the prevalence and impact of breast pain, bra issues and breast size on female horse riders. J Sports Sci. 35(11):1091-1097, 2017 Jun.	Review/Other-Dx	1265 surveys	To establish the prevalence of breast pain and bra issues in female horse riders and explores the impact of breast size on breast pain and bra issues.	Breast pain was experienced by 40% of all participants and this was significantly related to self-reported cup size (chi2 = 54.825, $P < 0.001$), increasing linearly. Breast pain was experienced most frequently during sitting trot and 21% of symptomatic participants reported that breast pain affected their horse riding performance. At least one bra issue was reported by 59% of participants; larger-breasted participants reported experiencing all bra issues more frequently than smaller-breasted participants ($P < 0.001$).	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
19. Genc A, Celebi MM, Celik SU, et al. The effects of exercise on mastalgia. Phys Sportsmed. 45(1):17-21, 2017 Feb.	Observational-Dx	20 women	To investigate the effects of exercise on mastalgia.	No significant differences were detected with respect to age, body mass index, menopausal status, psychiatric condition, and existence of unexplained pain syndromes between the groups. Total breast pain scores were similar in both groups. The sensory component of breast pain questionnaire and visual analogue scale values significantly improved via exercise in only exercise group ($p = 0.012$ and $p = 0.016$). There was no significant difference between groups in serum levels of cytokines. SF-36 subscale scores for general health and social functioning significantly improved in the control group and scores for role physical, bodily pain, and social functioning improved in exercise group.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Langford DJ, Schmidt B, Levine JD, et al. Preoperative Breast Pain Predicts Persistent Breast Pain and Disability After Breast Cancer Surgery. J Pain Symptom Manage. 49(6):981-94, 2015 Jun.	Observational-Dx	398 patients	To determine how women who experienced both preoperative and persistent postsurgical breast pain (n=107) differed from women who did not report preoperative breast pain and did (n=158) or did not (n=122) experience persistent postsurgical breast pain.	Between-group differences in demographic and clinical characteristics as well as trajectories of shoulder function and quality of life [QOL] were identified. Women with both preoperative and persistent postsurgical breast pain were younger; were more likely to report swelling, strange sensations, hardness, and numbness in the affected breast before surgery; and were more likely to have reconstruction at the time of surgery. Women with both preoperative and persistent postsurgical breast pain had more biopsies in the prior year, more lymph nodes removed, and reported more severe acute postsurgical pain than women without preoperative breast pain. The Linear mixed effects (LME) modeling revealed significant group effects for most outcomes evaluated. Over the six months of the study, women with both preoperative and persistent postsurgical pain had persistently poorer shoulder flexion and physical well-being than women without preoperative breast pain.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
21. Maddox PR, Harrison BJ, Mansel RE, Hughes LE. Non-cyclical mastalgia: an improved classification and treatment. Br J Surg. 1989;76(9):901-904.	Observational-Dx	72 patients	To see if improved differentiation of subgroups of noncyclical breast pain leads to an improvement in management.	True non-cyclical mastalgia was commonly bilateral and located within the upper outer quadrant of the breast, whereas musculoskeletal pain was almost always along the lateral chest wall or costochondral junctions and unilateral in 92 per cent of cases. Breast nodularity was present in 54 per cent of patients with non-cyclical mastalgia, but in only four cases (11 per cent) in the musculoskeletal group. Nine of 14 patients (64 per cent) with non-cyclical mastalgia obtained a good clinical response to drug therapy (over half responding to danazol alone); 19 underwent spontaneous remission, but there was a prolonged mean time to pain resolution of 27 months. In the musculoskeletal group 33 of 34 patients (97 per cent) had a good response to steroid and local anaesthetic injection; three resolved spontaneously without treatment, with a mean time to pain resolution of 17 months.	3
22. Ozkan Z, Kanat BH, Gonen AN, Kanat Z, Bugra BM. A Rare Clinical Entity in the Differential Diagnosis of Mastalgia: Thoracic Zona. J Breast Health (2013). 11(4):168-171, 2015 Oct.	Review/Other-Dx	12 patients	To investigate and represent the characteristics of patients with Mastalgia.	The study included 12 patients. All of them were female, and the mean age of patients was 51.66 (36-72) years. Eight of the zona cases were seen in the right breast (66.6%), and four of them were seen in the left breast (33.4%). Complaints of patients were pain (100%), eruption (70%), and burning sensation (60%). Underlying pathology was seen in one of the cases. Physical examination at admission revealed that four of the patients did not have any physical abnormality (33.3%). On the contrary of vesicular lesions, typical physical findings of zona, were seen in eight patients (66.7%).	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
23. Pereira S, Fontes F, Sonin T, et al. Neurological complications of breast cancer: A prospective cohort study. BREAST. 24(5):582-7, 2015 Oct.	Review/Other-Dx	503 patients	To quantify the incidence of neurological complications of breast cancer treatment during the first year after diagnosis.	Just over half of women had breast cancer stage 0 or I. A total of 6.9% were submitted to neoadjuvant chemotherapy but most of them completed adjuvant treatment - endocrine therapy, radiotherapy or chemotherapy (83.9%, 73.0% and 52.5%, respectively). The cumulative incidence of at least one oncological-related neurological complication during the first year after diagnosis was 48.4% (95%CI: 44.1-52.8); the most frequent were neuropathic pain (30.8%, 95%CI: 27.0-35.0), chemotherapy-induced peripheral neuropathy (16.8%, 95%CI: 13.8-20.3), phantom breast pain/syndrome (16.6%, 95%CI: 13.6-20.1) and cognitive decline (8.1%, 95%CI: 5.8-11.1).	4
24. Pirti O, Barlas AM, Kuru S, et al. Mastalgia Due to Degenerative Changes of the Spine. Adv. Clin. Exp. Med.. 25(5):895-900, 2016 Sep-Oct.	Review/Other-Dx	139 patients	To evaluate the incidence of vertebral pathologies in patients with non-cyclic mastalgia and the efficacy of conservative treatment of these pathologies on relieving breast pain.	Among 96 patients that had pathological findings on magnetic resonance imaging (96%), 49 women had diffuse annular bulging of the cervical spine, and 47 had cervical disc protrusion. Additionally, 12 patients had thoracic disc protrusion. At the end of the three-month period, the patients who were given only conservative treatment returned for follow-up evaluations. According to the VAS scores, five patients had mild to moderate improvement, 55 showed significant improvement, and 29 achieved complete remission.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
25. Preece PE, Mansel RE, Bolton PM, Hughes LM, Baum M, Gravelle IH. Clinical syndromes of mastalgia. Lancet. 1976;2(7987):670-673.	Review/Other-Dx	232 patients	To define clinical patterns of patients with mastalgia, correlate symptoms with underlying pathological processes and record the natural history of any syndromes.	232 patients attending a breast clinic with breast pain as the primary presenting symptom were studied prospectively to define clinical syndromes and to attempt to elucidate aetiological factors. Those women in whom mastalgia was a minor aspect of their complaint, or who were primarily seeking reassurance that they did not have cancer, were excluded. Most mastalgia patients could be placed into well-defined subgroups on the basis of clinical, radiological, and pathological features. After excluding causes of pain arising outside the breast, six specific groups with widely differing aetiological bases were defined, leaving only 7% unclassified lithout known aetiology. The six defined groups were cyclical pronounced mastalgia, (believed to be hormonally based), duct ectasia. Tietze syndrome, trauma, sclerosing adenosis, and cancer. Psychological factors were found to be less important than has been previously suggested. Classification of patients with mastalgia into homogeneous subgroups is a prerequisite of any therapeutic study.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
26. Sen M, Kilic MO, Cemeroglu O, Icen D. Can mastalgia be another somatic symptom in fibromyalgia syndrome?. Clinics. 70(11):733-7, 2015 Nov.	Observational-Dx	61 Mastalgia patients; 53 FMS patients	To determine the coexistence of mastalgia and fibromyalgia, to investigate the effects of this combination on pain patterns, and to discuss the status of breast pain in the diagnostic algorithm of fibromyalgia syndrome.	Approximately half of the patients with fibromyalgia syndrome (47.2%) reported having mastalgia at the time of admission and 37.7% of the patients with mastalgia met the diagnostic criteria for fibromyalgia syndrome. The patients with mastalgia in the fibromyalgia syndrome group had significantly higher total breast pain scores compared with the women in the mastalgia group. In addition, the patients with fibromyalgia syndrome in the mastalgia group had significantly higher Widespread Pain Index and Symptom Severity Scale scores than the patients with fibromyalgia syndrome.	3
27. Preece PE, Baum M, Mansel RE, et al. Importance of mastalgia in operable breast cancer. Br Med J (Clin Res Ed). 1982;284(6325):1299-1300.	Review/Other-Dx	36 patients	To assess the importance of pain as a presenting symptom of breast cancer in a series of patients with operable breast cancer over four years.	From an analysis of the case histories of 36 patients the diagnosis proved difficult in one-quarter of the cancers. This is explained by the high incidence of subclinical and lobular carcinoma in the group. Cancer must be seriously considered as a diagnosis in patients presenting with well-localised breast pain of recent onset.	4
28. Brandt KR, Craig DA, Hoskins TL, et al. Can digital breast tomosynthesis replace conventional diagnostic mammography views for screening recalls without calcifications? A comparison study in a simulated clinical setting. AJR Am J Roentgenol. 2013;200(2):291-298.	Observational-Dx	146 women	To evaluate digital breast tomosynthesis (DBT) as an alternative to conventional diagnostic mammography in the workup of noncalcified findings recalled from screening mammography in a simulated clinical setting that incorporated comparison mammograms and breast ultrasound results.	Agreement between DBT and diagnostic mammography BI-RADS categories was excellent for readers 1 and 2 (kappa = 0.91 and kappa = 0.84) and good for reader 3 (kappa = 0.68). For readers 1, 2, and 3, sensitivity and specificity of DBT for breast abnormalities were 100%, 100%, and 88% and 94%, 93%, and 89%, respectively. The clinical workup averaged three diagnostic views per abnormality and ultrasound was requested in 49% of the cases. DBT was adequate mammographic evaluation for 93-99% of the findings and ultrasound was requested in 33-55% of the cases.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Gennaro G, Hendrick RE, Toledano A, et al. Combination of one-view digital breast tomosynthesis with one-view digital mammography versus standard two-view digital mammography: per lesion analysis. Eur Radiol. 2013;23(8):2087-2094.	Observational-Dx	463 breasts of 250 patients	To evaluate the clinical value of combining one-view mammography (cranio-caudal, CC) with the complementary view tomosynthesis (mediolateral-oblique, MLO) in comparison to standard two-view mammography (MX) in terms of both lesion detection and characterization.	The 463 cases (breasts) reviewed included 258 with one to three lesions each, and 205 with no lesions. The 258 cases with lesions included 77 cancers in 68 breasts and 271 benign lesions to give a total of 348 proven lesions. The combination, DBT(MLO)+MX(CC), was superior to MX (CC+MLO) in both lesion detection (LDF) and lesion characterization (LCF) overall and for benign lesions. DBT(MLO)+MX(CC) was non-inferior to two-view MX for malignant lesions.	2
30. Waldherr C, Cerny P, Altermatt HJ, et al. Value of one-view breast tomosynthesis versus two-view mammography in diagnostic workup of women with clinical signs and symptoms and in women recalled from screening. AJR Am J Roentgenol. 2013;200(1):226-231.	Observational-Dx	144 women	To compare the diagnostic value of one-view digital breast tomosynthesis versus two-view full-field digital mammography (FFDM) alone, and versus a combined reading of both modalities.	Eighty-six of the 144 patients were found to have breast cancer. The BI-RADS categories for one-view digital breast tomosynthesis were significantly better than those for two-view FFDM ($p < 0.001$) and were equal to those of the combined reading in both women admitted for diagnostic workup and women recalled from screening. The sensitivity and negative predictive values of digital breast tomosynthesis were superior to those of FFDM in fatty and dense breasts overall and in women admitted for diagnostic workup and in women recalled from screening. Only 11% of digital breast tomosynthesis examinations required additional imaging, compared with 23% of FFDMs.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Yang TL, Liang HL, Chou CP, Huang JS, Pan HB. The adjunctive digital breast tomosynthesis in diagnosis of breast cancer. Biomed Res Int. 2013;2013:597253.	Observational-Dx	59 breasts of 57 patients.	To compare the diagnostic performance of digital breast tomosynthesis (DBT) and digital mammography (DM) for breast cancers.	A total of 59 breast cancers were reviewed, including 17 (28.8%) mass lesions, 12 (20.3%) focal asymmetry/density, 6 (10.2%) architecture distortion, 23 (39.0%) calcifications, and 1 (1.7%) intracystic tumor. Combo DBT was perceived to be more informative in 58.8% mass lesions, 83.3% density, 94.4% architecture distortion, and only 11.6% calcifications. As to the forced BIRADS score, 84.4% BIRADS 0 on DM was upgraded to BIRADS 4 or 5 on DBT, whereas only 27.3% BIRADS 4A on DM was upgraded on DBT, as BIRADS 4A lesions were mostly calcifications. A significant P value (<0.001) between the BIRADS category and index lesions was noted	3
32. Saenz RB. Evaluation of common breast problems in family practice. Am Fam Physician. 2000;61(8):2327-2328.	Review/Other-Dx	N/A	Editorial on the evaluation of common breast problems in family practice.	No results stated in abstract.	4
33. Zarei F, Pishdad P, Hatami M, Zeinali-Rafsanjani B. Can breast ultrasound reduce patient's level of anxiety and pain?. Ultrasound. 25(2):92-97, 2017 May.	Observational-Dx	51 patients	To assess the severity of pain and anxiety in patients with breast pain and normal examination, before and after breast sonography.	Sonography findings indicated that 88% of patients have normal sonography without any finding. The average amounts of pain severity before and after sonography were 3.3 and 2.4, respectively ($p < 0.005$). The average amounts of anxiety severity in patients before and after sonography were 51.9 and 37.9, respectively ($p < 0.005$).	3

Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Howard MB, Battaglia T, Prout M, Freund K. The effect of imaging on the clinical management of breast pain. J Gen Intern Med. 2012;27(7):817-824.	Observational-Dx	916 patients	To determine if initial imaging for breast pain reduces subsequent utilization.	60% of women were age 40 or younger, 87% were from racial/ethnic minority groups. 25% had imaging ordered at initial visit. Of those who received initial imaging, 75% had normal radiographic findings, yet 98% returned for additional evaluation. In adjusted analyses, women with initial imaging had increased clinical services utilization (OR 25.4, 95% CI: 16.7, 38.6). Women with normal clinical breast exams who received initial imaging exhibited increased odds for subsequent clinical services utilization (OR 23.8, 95% CI: 12.9, 44.0). Six cancers were diagnosed; imaging in the absence of clinical breast exam abnormalities did not result in any cancer identification.	3
35. Olcucuoglu E, Yilmaz G. Mastodynia: is imaging necessary in young patients?. TURK. J. SURG.. 29(1):17-9, 2013.	Observational-Dx	98 patients	To evaluate the necessity of imaging in patients who have applied for cyclic or non-cyclic breast pain, with normal physical examination, and without a family history.	The breast examination was normal in all patients. Ultrasound imaging results were completely normal in 98 (48%) patients. 47 (23.5%) patients were found to have fibroadenoma, with a mean diameter of 9.6 mm (5 mm-14 mm). 45 (22.5%) patients had simple cysts with a mean diameter of 7.8 mm (3 mm-11 mm). 6 (3%) patients were found to have intraductal papillomas and 4 (2%) to have lipomas. All patients were classified as either breast imaging reporting and database systems (BI-RADS) 1 or BI-RADS 2.	3
36. Harper AP, Kelly-Fry E, Noe JS. Ultrasound breast imaging-the method of choice for examining the young patient. Ultrasound Med Biol. 1981;7(3):231-237.	Observational-Dx	116 patients	To determine if masses in the breasts of "symptomatic" patients under 30 years could be definitely imaged and diagnosed by means of ultrasound visualization.	Approximately 50% of the patients were diagnosed by ultrasound as fibroadenoma cases; biopsy of 22% of these cases indicated 101~o diagnostic accuracy for the ultrasound technique. Thirty-one percent of the cases diagnosed as fibroadenoma by ultrasound were also examined by X-ray mammography; in 80% of these cases, X-ray mammography did not adequately image the mass.	3

Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Loving VA, DeMartini WB, Eby PR, Gutierrez RL, Peacock S, Lehman CD. Targeted ultrasound in women younger than 30 years with focal breast signs or symptoms: outcomes analyses and management implications. AJR Am J Roentgenol. 195(6):1472-7, 2010 Dec.	Observational-Dx	830 patients	To assess the accuracy of targeted breast ultrasound in women younger than 30 years presenting with focal breast signs or symptoms.	Among 830 study patients, lesions were assessed as BI-RADS category 1 or 2 in 526 (63.4%), BI-RADS category 3 in 140 (16.9%), BI-RADS category 4 in 163 (19.6%), and BI-RADS category 5 in one (0.1%) patient. Three malignancies were detected, for a cancer yield of 0.4%. No BI-RADS category 3 lesions, two BI-RADS category 4 lesions, and the single BI-RADS category 5 lesion were malignant. Ultrasound sensitivity was 100%, specificity was 80.5%, NPV was 100%, PPV2 was 1.8%, and PPV3 was 1.9%.	3
38. Tumyan L, Hoyt AC, Bassett LW. Negative predictive value of sonography and mammography in patients with focal breast pain. Breast J. 2005;11(5):333-337.	Observational-Dx	86 patients	To determine the negative predictive value of mammography and sonography in a population of patients with focal breast pain referred for imaging evaluation.	Of the 86 patients, 26 patients were lost to follow-up and did not appear in the institution's cancer registry. Four patients were diagnosed with breast carcinoma, two of whom had incidental cancers that were detected mammographically by microcalcifications and were separate from and unrelated to the area of pain. Seven patients underwent biopsy at the site of breast pain with benign diagnosis. Imaging and clinical follow-up for the 51 patients with benign or negative imaging at the site of pain showed no abnormality with a mean follow-up of 26.5 months. The negative predictive value of mammography and sonography in patients with breast pain was 100%. The negative predictive value of mammography and sonography for focal breast pain is high. Negative mammography and sonography can be reassuring to the treating clinician if follow-up is planned when physical examination is not suspicious. However, if physical examination is suspicious, biopsy should not be delayed.	3

Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Bernardi D, Ciatto S, Pellegrini M, et al. Application of breast tomosynthesis in screening: incremental effect on mammography acquisition and reading time. Br J Radiol. 2012;85(1020):e1174-1178.	Observational-Dx	10 cancers and 90 negative controls	To supplement the paucity of information available on logistical aspects of the application of three-dimensional (3D) mammography in breast screening.	Average acquisition time (measured from start of first-view breast positioning to compression release at completion of last view) for seven radiographers, based on 20 screening examinations, was longer for 2D+3D (4 min 3 s; range 3 min 53 s-4 min 18 s) than 2D mammography (3 min 13 s; range 3 min 0 s-3 min 26 s; $p<0.01$). Average radiologists' reading time per screening examination (three radiologists reading case-mix of 100 screens: 10 cancers, 90 controls) was longer for 2D+3D (77 s; range 60-90 s) than for 2D mammography (33 s; range 25-46 s; $p<0.01$). 2D+3D screen-reading was associated with detection of more cancers and with substantially fewer recalls than 2D mammography alone.	2
40. Hofvind S, Hovda T, Holen AS, et al. Digital Breast Tomosynthesis and Synthetic 2D Mammography versus Digital Mammography: Evaluation in a Population-based Screening Program. Radiology. 171361, 2018 Mar 01.	Observational-Dx	98,927 women	To compare the performance of digital breast tomosynthesis (DBT) and two-dimensional synthetic mammography (SM) with that of digital mammography (DM) in a population-based mammographic screening program.	Recall rates were 3.4% for DBT and SM screening and 3.3% for DM screening ($P = .563$). DBT and SM screening showed a significantly higher rate of screen-detected cancer compared with DM screening (9.4 vs 6.1 cancers per 1000 patients screened, respectively; $P < .001$). The rate of detection of tumors 10 mm or smaller was 3.2 per 1000 patients screened with DBT and SM and 1.8 per 1000 patients screened with DM ($P < .001$), and the rate of grade 1 tumors was 3.3 per 1000 patients screened with DBT and SM versus 1.4 per 1000 patients screened with DM ($P < .001$). On the basis of immunohistochemical analyses, rates of lymph node involvement and tumor subtypes did not differ between women who underwent DBT and SM screening and those who underwent DM screening.	2

Breast Pain
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Skaane P, Sebuodegard S, Bandos AI, et al. Performance of breast cancer screening using digital breast tomosynthesis: results from the prospective population-based Oslo Tomosynthesis Screening Trial. Breast Cancer Res Treat. 2018 Feb 10.	Observational-Dx	24,301 women	To investigate the effects of addition of DBT on interval and detected cancers in population-based screening.	24,301 consenting women underwent FFDM + DBT screening over a 2-year period. Results were compared with 59,877 FFDM examinations during prior rounds. Addition of DBT resulted in a non-significant increase in sensitivity (76.2%, 378/496, vs. 80.8%, 227/281, p = 0.151) and a significant increase in specificity (96.4%, 57229/59381 vs. 97.5%, 23427/24020, p < .001). Number of recalls per screen-detected cancer decreased from 6.7 (2530/378) to 3.6 (820/227) with DBT (p < .001). Cancer detection per 1000 women screened increased (6.3, 378/59877, vs. 9.3, 227/24301, p < .001). Interval cancer rate per 1000 screens for FFDM + DBT remained similar to previous FFDM rounds (2.1, 51/24301 vs. 2.0, 118/59877, p = 0.734). Interval cancers post-DBT were comparable to prior rounds but significantly different in size, grade, and node status from cancers detected only using DBT. 39.6% (19/48) of interval cancers had positive nodes compared with only 3.9% (2/51) of additional DBT-only-detected cancers.	2
42. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf.	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	No results stated in abstract.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a. The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b. The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c. The study is an expert opinion or consensus document.
- Meta-analysis
  a. *Good quality* – the study design, methods, analysis, and results are valid and the conclusion is supported.
  b. *Inadequate quality* – the study design, analysis, and results lack the methodological rigor to be considered a good meta-analysis study.

Abbreviations Key

Dx = Diagnostic

Tx = Treatment