# An Approach to Gynecomastia in Primary Care Clinics

*Kavya Bharathidasan, MD, Jordan Curl, BS, Vedesh Kumar Babu, MD, Shaili Felton, MD, and Kenneth Nugent, MD*

**Abstract:** Gynecomastia is a more common finding in primary care clinics than is recognized. Because this finding can be easily overlooked, appropriate investigation and management often are missed. The workup of gynecomastia is highly individualized, based on the patient's presentation and related factors. It should be guided by thorough history taking and physical examination. Unless the patient has associated symptoms, or there is suspicion for an underlying clinical disorder causing the gynecomastia, the patient need not be investigated further. A breast ultrasound is not routinely recommended. Gynecomastia is a benign finding that will spontaneously regress in most patients; however, patients who are concerned with their physical appearance can be treated either medically or surgically. Patients who have had gynecomastia for more than 1 year tend to have fibrosis, which may be more difficult to treat. Management of gynecomastia is highly patient centered, following a detailed discussion about treatment goals and should be started early. Gynecomastia is not considered a premalignant condition; routine screening is not cost-effective, and imaging studies should be pursued only if physical examination findings suggest malignancy.

**Key Words:** androgen deficiency, breast carcinoma, estrogen excess, gynecomastia

Gynecomastia is a more common finding in primary care clinics than is recognized. Approximately 40% to 55% of men have gynecomastia on autopsy.[1] Because this finding can be easily overlooked, appropriate workup and management often are missed. According to the American Society of Andrology and European Academy of Andrology guidelines for the management of gynecomastia published in 2019, 45% to 50% of cases are caused by an underlying pathology when properly investigated.[2] Based on age at onset, gynecomastia can be loosely divided into infantile, prepubertal, adult onset, and senile. In this article, we focus on breast swelling in the adult and geriatric populations, when a case of gynecomastia requires more workup, which laboratory tests and imaging studies should be ordered, and who should be treated.

For this discussion, we classify patients with gynecomastia into three broad categories: patient A, with no medication history or pertinent medical history other than concern over his breast swelling; patient B, who has an underlying medical disorder and has noticed a new onset increase in breast size; and patient C, who presents for a well visit with no complaints or medical history of gynecomastia and was incidentally found to have enlarged breasts on examination.

## Epidemiology

In healthy men, the prevalence of gynecomastia is estimated to be between 36% in nonhospitalized patients in the age range of 17 to 58 years[3] and 65% in hospitalized patients in the age range of 27 to 92 years.[4] It occurs commonly in both breasts.[4,5] The natural history of this condition suggests that there are three peaks with increased prevalence: puberty, early adult life, and middle age,[3] but there are an insufficient number of studies to determine age-related prevalence rates in the typical population. In hospitalized patients, the highest prevalence occurred in men 50 to 69 years old[4]; however, in computed tomography (CT) studies of patients with preexisting disease and health checkups, the prevalence was highest between 10 to 19 years and older than 70 years of age. In comparison with controls, the main predisposing factors were liver and kidney disease.[6] One study showed a positive correlation between prevalence and diameter of breast tissue in patients with higher body mass indices,[4] but when analyzing incidental gynecomastia on CT films, the correlation was not observed.[6] Although the prevalence of true gynecomastia has

### Key Points

- The prevalence of gynecomastia has three peaks: puberty, early adult life, and middle age.
- Gynecomastia has been identified in 65% of hospitalized patients in the age range 27 to 92 years.
- The causes include excess estrogen, androgen deficiency, and reduced androgen-to-estrogen ratio.
- Gynecomastia is benign and regresses in many patients; medical treatment can include discontinuation of culprit drugs, the use of tamoxifen, and/or surgery.

From the Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock.
Correspondence to Dr Kavya Bharathidasan, Department of Internal Medicine, Texas Tech University Health Sciences Center, 3601 4th St, Lubbock, TX 79430. E-mail: kavya.bharathidasan@ttuhsc.edu. 
S.F. has received compensation from AstraZeneca. The remaining authors did not report any financial relationships or conflicts of interest.
Accepted February 1, 2022.
0038-4348/0–2000/115-597

DOI: 10.14423/SMJ.0000000000001425

been described in various populations in several studies, the prevalence of pseudogynecomastia, identified by physical examination or ultrasound findings, has not been reported in the literature.

## Etiology

The pathophysiological basis for gynecomastia usually involves a hormonal imbalance, resulting in either excess estrogens or a deficiency of androgens. Estrogens promote the proliferation of breast tissue, whereas androgens counteract this process. It is important to note that gynecomastia can occur even in males with normal testosterone levels when there is excess estrogens. Endogenous causes include disease states affecting the metabolism of estrogens, increased sensitivity of the breast tissue to circulating estrogens, decreased sensitivity to androgens, impaired production/release of androgens, increased binding of testosterone to sex hormone–binding globulin, and/or increased peripheral aromatization of androgens into estradiol. Hyperprolactinemia is a commonly observed cause of gynecomastia.[5,7] High prolactin levels suppress gonadotropic-releasing hormone, which leads to central hypogonadism and alters the androgen:estrogen ratio. Adolescent gynecomastia is a normal physiological phenomenon during puberty in which surges of luteinizing hormone, follicle-stimulating hormone, growth hormone, and insulin-like growth factor 1 cause an initial increase in estrogen levels followed by an increase in testosterone levels. As androgen levels rise and the testosterone:estrogen ratio is restored, there is spontaneous regression of breast hyperplasia associated with virilization.[2] Senile gynecomastia results from the physiologic decline in androgens and increase in aromatase activity with increasing age.[8] Exogenous causes can be dietary or medication related through similar mechanisms as endogenous causes acting either directly or indirectly (Table). Drug-induced gynecomastia accounts for 10% to 25% of all cases of gynecomastia.[9] Treatment with gonadotropic-releasing hormone antagonists in androgen-deprivation therapy, such as with leuprolide in the management of prostate cancer, is associated with hypogonadism and subsequently can cause breast enlargement. Not all patients with true gynecomastia have an attributable cause, because roughly 25% of cases are idiopathic.[10,11]

Breast enlargement can be unilateral or bilateral and asymptomatic or painful. The time of onset and changes since onset should be reviewed carefully during history taking. Rarely, pubertal gynecomastia can persist into adulthood and is called essential gynecomastia.[9]

## Diagnosis

After gynecomastia is suspected, the first step is to differentiate true gynecomastia from pseudogynecomastia (lipomastia or adipomastia) (Fig. 1). On physical examination, the two can be distinguished by palpating the retro-areolar area between the examining index finger and thumb in a pincer grasp to identify the consistency of the breast tissue. If it is smooth and resembles the consistency of adipose tissue, then these findings are consistent with pseudogynecomastia. Glandular tissue is more suggestive of true gynecomastia and is characterized as a soft discoidal lesion below the nipple, usually 2 to 4 cm in diameter.[10] Other important physical findings include tenderness, discharge, mobility, and skin changes over the swelling. A fixed hard mass with irregular borders, bloody discharge, with ulceration or skin changes (peau d'orange), a retracted nipple, and associated lymphadenopathy are highly suspicious for malignancy. Galactorrhea can occur in patients with gynecomastia secondary to hyperprolactinemia.

The workup of gynecomastia is highly individualized based on the patient's presentation and related factors. It should be guided by thorough history taking and physical examination. Unless the patient has pain or associated symptoms or there is suspicion for underlying disease causing the gynecomastia, the patient need not be investigated further. Although obesity increases the incidence of pseudogynecomastia because of excess adipose

**Table. Causes of gynecomastia**

| Causes | Endogenous causes | Exogenous causes |
|---|---|---|
| Excess estrogen | Leydig cell tumors, Sertoli cell tumors, feminizing adrenocortical tumor, hCG- secreting tumor (large cell carcinoma of lung, gastric, or renal tumor), aromatase excess syndrome | Anabolic steroids aromatized to estrogen in athletes<br>Phytoestrogens: soy, hops, ginseng<br>Environmental estrogens: paint/cleaning products, lavender/tea tree oil, consuming excessive poultry containing diethylstilbesterol[5]<br>Drugs: digitoxin, hCG, phenytoin, clomiphene, diazepam |
| Androgen deficiency | Primary or secondary hypogonadism due to disease (HIV, Klinefelter syndrome, hemochromatosis, mumps orchitis, MEN), trauma, radiation, drugs | Androgen receptor antagonists: spironolactone, cimetidine, bicalutamide, flutamide, marijuana, alcohol, heroin, amphetamines<br>Absent/defective androgen receptors<br>Drugs: ketoconazole, metronidazole, antineoplastics (busulfan, vincristine, vinblastine), methotrexate, omeprazole, penicillamine, ranitidine |
| Reduced serum androgen:estrogen ratio | Increased aromatization of androgens to estrogens: refeeding, aging, hepatic cirrhosis, renal failure, dialysis, hyperthyroidism | Increased prolactin: domperidone, haloperidol, phenothiazines, metoclopramide, verapamil<br>Other drugs: isoniazid, amiodarone, finasteride, antidepressants, human growth hormone, HAART, PPIs |

*HAART, highly active antiretroviral therapy; hCG, human chorionic gonadotropin; HIV, human immunodeficiency virus; MEN, multiple endocrine neoplasia; PPIs, proton pump inhibitors.*

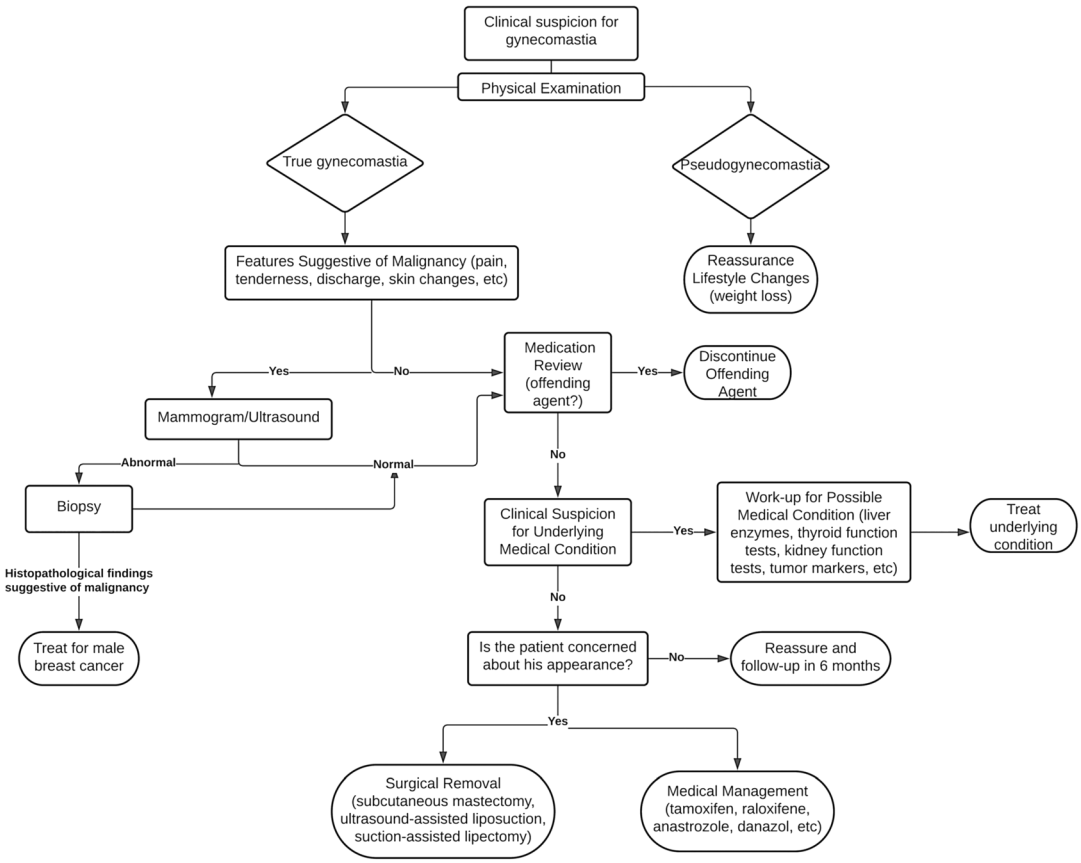


**Fig. 1.** **Diagnostic flowchart showing suggested approach to gynecomastia in the primary care clinic.**

deposition, high circulating levels of leptin also promote aromatization of androgens to estrogens, causing true gynecomastia.[11]

With patient A, if he is obese, then lifestyle changes and weight reduction can be tried before a workup is started. Otherwise, the treating physician can reassure the patient and follow up biannually to monitor regression. The psychological component of gynecomastia should be addressed during the encounter, because patients often are embarrassed about their body image and fear developing breast cancer in the future.[11] For patients B and C, a thorough review of medications is essential before investigating for underlying medical conditions. The most prescribed medications in primary care clinics that can cause gynecomastia are cimetidine, spironolactone, ketoconazole, and phenytoin (Table). The most common drugs known to cause gynecomastia in nearly 40% to 70% of patients are testosterone-lowering medications, such as bicalutamide, flutamide, or nilutamide, used to treat prostate cancer.[9]

A thorough dietary history should be obtained along with a history of over-the-counter supplement use. Increased consumption of soy (greater than 300 mg/day) has been associated with gynecomastia because of phytoestrogens; other herbal remedies such as ginseng and dong quai also can cause gynecomastia.[11,12] Environmental estrogens from paints and cleaning supplies and consumption of excess poultry treated with diethylstilbestrol have been described to cause gynecomastia.[10] Fifty percent of bodybuilders taking high-dose anabolic steroids develop gynecomastia as a result of peripheral aromatization.[13] Use of anabolic steroids, marijuana, heroin, or amphetamines can lead to irreversible gynecomastia.[11]

If no potential offending agent is identified, then the next step is to screen for hyperthyroidism (thyroid function tests), chronic liver disease (liver enzymes), end-stage renal disease (kidney function tests), and testicular tumors (by tumor markers such as β-human chorionic gonadotropin and α-fetoprotein for germ cell tumors). Feminizing or estrogen-producing tumors can present with breast enlargement and proliferation. If a mass cannot be found on examination, then a testicular ultrasound can be ordered to screen for tumors that are too small to be palpated. Approximately 7% to 11% of men with testicular tumors develop gynecomastia before a mass is physically palpable.[14] Sudden, painful gynecomastia can be a helpful clue in the diagnosis of recurrent testicular cancer.[9] An abdominal CT scan or pituitary magnetic resonance image can detect adrenal or pituitary tumors if clinically suspected.

A hormonal workup can be performed if the preliminary laboratory values are inconclusive. Hypogonadism should be ruled out by testing for serum levels of morning testosterone, morning luteinizing hormone, follicle-stimulating hormone, and estradiol. Other tests of slightly lesser significance include sex hormone–binding globulin and prolactin. Hyperprolactinemia

has been identified in some patients with gynecomastia, but most patients with elevated prolactin do not tend to develop enlarged breasts. High prolactin levels can inhibit luteinizing hormone and follicle-stimulating hormone, which in turn causes hypogonadism leading to gynecomastia.[9]

Occasionally, the patient has preexisting conditions, such as Klinefelter syndrome, which alerts the clinician to this possible diagnosis. Human immunodeficiency virus also has been associated with gynecomastia. Although it is unclear whether antiretroviral drugs contribute to the pathogenesis, hypogonadism caused by the disease process is a plausible explanation.[9] Evans et al describe a direct mammotropic effect of antiretroviral drugs on breast tissue.[15]

A breast ultrasound is not routinely recommended and does not influence the course of management unless the patient presents with symptoms or signs suspicious for malignancy. Ultrasonography usually reveals a hypoechoic irregular mass without associated axillary adenopathy (Fig. 2).[16] Mammography and fine-needle aspiration cytology/biopsy can help diagnose breast cancer but are not essential for every patient who presents with gynecomastia. Normal histological findings show dilated ducts with periductal fibrosis, stromal hyalinization, and increased subareolar fat. If the breast enlargement is associated with pain and tenderness, then hyperplasia of the ductal epithelium with infiltration by inflammatory cells may occur.[17] Patients who have had gynecomastia for more than 1 year tend to have more fibrous tissue, which may be difficult to treat with medical management.

## Treatment

Gynecomastia is a benign finding that will spontaneously regress in most patients; however, patients concerned with their physical appearance can be treated either medically or surgically. The offending drug (if any) should be discontinued, and the underlying disease treated appropriately. Patients should note improvement within 1 to 2 months and complete resolution in 6 to 7 months.[9] Patients with proven testosterone deficiency or hypogonadism can be started on testosterone therapy.

Although there are no US Food and Drug Administration–approved treatment options for the treatment of gynecomastia, tamoxifen has been widely used with documented success. Partial regression of breast swelling occurs in 80% of patients taking tamoxifen and complete regression in 60%.[7,14] The American Society of Andrology and the European Academy of Andrology still did not endorse tamoxifen in their 2019 management guidelines, however, because of the limited evidence regarding efficacy. Tamoxifen is useful in painful gynecomastia for rapid symptomatic relief.[2] Raloxifene also has been successful in reducing breast size, but the data are limited.[18] Other drugs, including danazol and anastrozole, have been tried but with less efficacy.[17] Anastrozole is particularly helpful in treating gynecomastia secondary to familial aromatase excess, feminizing Sertoli cell tumors, and gynecomastia induced by testosterone therapy caused by increased aromatization to estrogen.[8] For gynecomastia that has been present for greater than 1 year or has failed to respond to medical therapy, cosmetic surgery (subcutaneous mastectomy, ultrasound-assisted liposuction, suction-assisted lipectomy) can be used to remove the excess tissue. Particularly with adolescents and young adult males for whom their physical appearance may be distressing, the primary care physician should be empathetic and may need to consider treatment modalities beyond reassurance. Management of gynecomastia should be patient centered and started early following a detailed discussion about treatment goals.[11]

For patient A, because he presents with concern over his breast swelling, treatment with tamoxifen at 20 mg/day for 3 months can be offered. Cosmetic surgery also is an option;

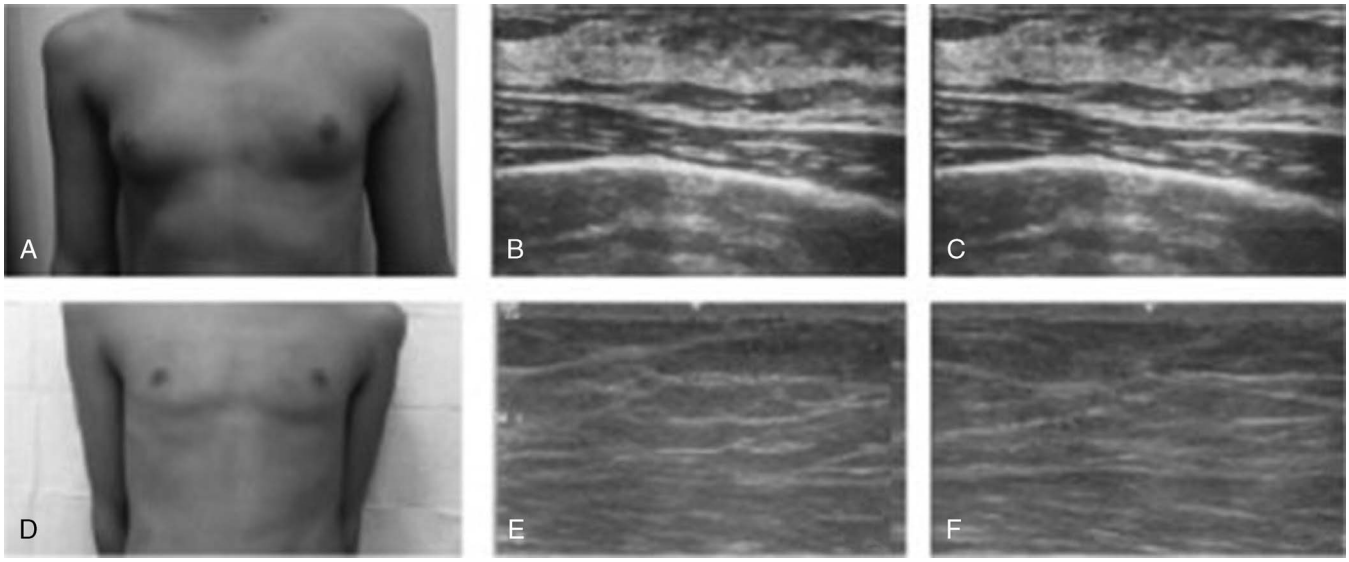


**Fig. 2.** **Clinical preoperative breast view (*a*) and breast ultrasound (*b* and *c*) scan showing bilateral gynecomastia. No solid nodular or cystic formations are present on either side; clinical postoperative breast view (*d*) and breast ultrasound (*e* and *f*) scan 1 year after surgery showing a total absence of glandular parenchyma, with muscle planes well represented. Reproduced from Springer Nature.[16]**

however, many patients decide to wait for the swelling to regress spontaneously once they have been reassured that it is a benign condition.[9] For patient B, his underlying medical condition and/or medication use must be addressed first. The gynecomastia should spontaneously regress after treating the disease state or stopping the offending agent. For patient C, it is at the discretion of the physician to decide whether further workup is needed. After reviewing the patient's medication list, if the physician suspects a common medical condition, such as hyperthyroidism, cirrhosis, or renal disease, then the appropriate laboratory tests should be ordered. Cancer screening for testicular and adrenal tumors also is recommended if clinically suspected. If physical findings suggesting malignancy are present, then the physician should at least order a diagnostic mammogram. If a mass is detected or suspected, then ultrasonography and/or biopsy of the lesion are recommended.[19] If the gynecomastia has been present for more than 1 year in any of the above patients, it is less likely that the swelling will regress completely with or without medical management from fibrosis. Surgical options are more likely to be successful in these cases.

Gynecomastia is one of the most common reasons that men withdraw from hormonal therapy in the management of prostate cancer.[10] Tamoxifen can be used as prophylaxis in these patients. Breast enlargement was observed in only 10% of patients taking tamoxifen 20 mg/day versus 51% taking anastrozole 1 mg/day, and 73% on placebo in a large randomized controlled trial receiving high-dose (150 mg) bicalutamide for prostate cancer at 48 weeks.[20] Tamoxifen has also shown greater efficacy when compared to low-dose prophylactic radiotherapy for patients receiving bicalutamide therapy.[21]

## Gynecomastia and Breast Cancer

Most patients with gynecomastia will not develop breast cancer in their lifetimes. Conditions associated with a higher risk include Klinefelter syndrome; a history of cryptorchidism, orchitis, or orchiectomy; a family history of breast cancer, particularly with BRCA1/BRCA2 mutations; and previous radiation exposure. Men who have a BRCA2 gene mutation are at an 8% to 10% increased risk of developing male breast cancer.[22] Sub-Saharan Africans and Ashkenazi Jews also have a slightly higher risk than the general population.[23] Patients with Klinefelter syndrome have a 10- to 30-fold increased risk of developing breast cancer.[10,11]

Although gynecomastia with or without preexisting conditions, other than those previously mentioned, has not been considered an isolated risk factor for cancer on its own, a large pooling project by Brinton et al showed a 10-fold higher risk for male breast cancer in patients with gynecomastia; however, this result may be attributed to greater chances of detection by medical attention, among other confounding factors.[24] Gynecomastia is not considered a premalignant condition.[2] Routine screening is not cost-effective, and imaging studies such as mammography or ultrasonography should be pursued only if physical examination findings suggest malignancy.[8] Given the increased risk of developing breast cancer, routine screening of individuals with a known diagnosis of Klinefelter syndrome should be considered, however.

The increased awareness and screening for breast cancer in women can detect cancer at an early stage; male breast cancer tends to be detected much later with worse outcomes in comparison.[25,26] Most cases of male breast cancer are hormone receptor positive and can be treated with adjuvant hormonal therapy (tamoxifen for a total of 5–10 years). Chemotherapy is indicated only in rapidly growing tumors or severe organ dysfunction.[27]

## Conclusions

Public awareness and clinical research on gynecomastia and male breast cancer have increased significantly during the past several decades. The number of yearly breast reduction surgeries performed for gynecomastia has increased by 29% from 2000 to 2014.[28] A sense of uneasiness or hesitancy seems to prevail in the primary care physician's practice when he or she encounters a patient with gynecomastia, however. Given the number of underlying conditions that could present as gynecomastia, it is essential to investigate when appropriate to avoid missing significant diagnoses, such as testicular cancer. It also is the responsibility of the primary care physician to openly discuss concerns regarding body image and possible psychosocial stressors and present available treatment modalities to the patient.

## References


1. Williams MJ. Gynecomastia: its incidence, recognition, and host characterization in 447 autopsy cases. *Am J Med* 1963;34:103–112.
2. Kanakis GA, Nordkap L, Bang AK, et al. EAA clinical practice guidelines—gynecomastia evaluation and management. *Andrology* 2019;7:778–793.
3. Nuttall FQ. Gynecomastia as a physical finding in normal men. *J Clin Endocrinol Metab* 1979;48:338–340.
4. Niewoehner CB, Nuttal FQ. Gynecomastia in a hospitalized male population. *Am J Med* 1984;77:633–638.
5. Costanzo PR, Pacenza NA, Aszpis SM, et al. Clinical and etiological aspects of gynecomastia in adult males: a multicenter study. *Biomed Res Int* 2018; 2018:8364824.
6. Kim MS, Kim JH, Lee KH, et al. Incidental gynecomastia on thoracic computed tomography in clinical practice: characteristics, radiologic features, and correlation with possible causes in South Korean Men. *Am J Mens Health* 2020;14:1557988320908102.
7. Ersöz HO, Önde ME, Terekeci H, et al. Causes of gynaecomastia in young adult males and factors associated with idiopathic gynaecomastia. *Int J Androl* 2002;5:312–316.
8. Carlson HE. Approach to the patient with gynecomastia. *J Clin Endocrinol Metab* 2011;96:15–21.
9. Eckman A, Dobs A. Drug-induced gynecomastia. *Expert Opin Drug Saf* 2008;7:691–702.
10. Derkacz M, Chmiel-Perzyńska I, Nowakowski A. Gynecomastia—a difficult diagnostic problem. *Endokrynol Pol* 2011;62:190–202.
11. Dickson G. Gynecomastia. *Am Fam Physician* 2012 Apr 1;85(7):716–22.
12. Messina M. Soybean isoflavone exposure does not have feminizing effects on men: a critical examination of the clinical evidence. *Fertil Steril* 2010;93:2095–2104.
13. de Luis DA, Aller R, Cuéllar LA, et al. Anabolizantes esteroideos y ginecomastia. Revisión de la literatura [Anabolic steroids and gynecomastia. Review of the literature]. *An Med Interna* 2001;18:489–491.
14. Hassan HC, Cullen IM, Casey RG, et al. Gynaecomastia: an endocrine manifestation of testicular cancer. *Andrologia* 2008;40:152–157.

15. Evans DL, Pantanowitz L, Dezube BJ, et al. Breast enlargement in 13 men who were seropositive for human immunodeficiency virus. *Clin Infect Dis* 2002;35:1113–1119.
16. Di Grezia G, Romano T, De Francesco F, et al. Breast ultrasound in the management of gynecomastia in Peutz-Jeghers syndrome in monozygotic twins: two case reports. *J Med Case Rep* 2014;8:440.
17. Braunstein GD. Clinical practice. Gynecomastia. *N Engl J Med* 2007;357: 1229–1237.
18. Lawrence SE, Faught KA, Vethamuthu J, et al. Beneficial effects of raloxifene and tamoxifen in the treatment of pubertal gynecomastia. *J Pediatr* 2004;145:71–76.
19. Chau A, Jafarian N, Rosa M. Male breast: clinical and imaging evaluations of benign and malignant entities with histologic correlation. *Am J Med* 2016;129:776–791.
20. Boccardo F, Rubagotti A, Battaglia M, et al. Evaluation of tamoxifen and anastrozole in the prevention of gynecomastia and breast pain induced by bicalutamide monotherapy of prostate cancer. *J Clin Oncol* 2005;23:808–815.
21. Perdonà S, Autorino R, De Placido S, et al. Efficacy of tamoxifen and radiotherapy for prevention and treatment of gynaecomastia and breast pain caused by bicalutamide in prostate cancer: a randomised controlled trial. *Lancet Oncol* 2005;6:295–300.
22. Evans DG, Susnerwala I, Dawson J, et al. Risk of breast cancer in male BRCA2 carriers. *J Med Genet* 2010;47:710–711.
23. Niewoehner CB, Schorer AE. Gynaecomastia and breast cancer in men. *BMJ* 2008;336:709–713.
24. Brinton LA, Cook MB, McCormack V, et al. Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results. *J Natl Cancer Inst* 2014;106:djt465.
25. Zurrida S, Nolè F, Bonanni B, et al. Male breast cancer. *Future Oncol* 2010; 6:985–991.
26. Kim SH, Kim YS. Ultrasonographic and mammographic findings of male breast disease. *J Ultrasound Med* 2019;38:243–252.
27. Khan NAJ, Tirona M. An updated review of epidemiology, risk factors, and management of male breast cancer. *Med Oncol* 2021;38:39.
28. Ordaz DL, Thompson JK. Gynecomastia and psychological functioning: a review of the literature. *Body Image* 2015;15:141–148.