



Prevalence of Incidental Gynecomastia by Chest Computed Tomography in Patients with a Prediagnosis of COVID-19 Pneumonia

Özge Aslan, Selen Bayraktaroğlu, Akın Çinkooğlu, Naim Ceylan, Recep Savaş, Ayşenur Oktay

Department of Radiology, Ege University Faculty of Medicine, İzmir, Turkey

ABSTRACT

Objective: In this study, we aimed to determine the prevalence of gynecomastia by evaluating computed tomography (CT) images of male patients who were admitted to our hospital during the coronavirus disease-2019 (COVID-19) pandemic.

Materials and Methods: This study included a total of 1,877 patients who underwent chest CT for prediagnosis of COVID-19 pneumonia between March 15th and May 15th, 2020. All images were evaluated for the presence of gynecomastia. Gynecomastia patterns were evaluated according to morphological features, and diagnoses were made by measuring the largest glandular tissue diameter. Statistical analysis was performed with IBM SPSS software version 25.0.

Results: The prevalence of gynecomastia was 32.3%. In terms of pattern, 22% were nodular, 57% were dendritic, and 21% were diffuse glandular gynecomastia. A significant correlation was found between age and gynecomastia pattern ($p < 0.001$). The incidence of nodular, dendritic, and diffuse glandular gynecomastia increased with advancing age. A significant difference was found in the correlation between age groups and glandular tissue diameters ($p < 0.001$). With an increase in glandular tissue diameter, the gynecomastia pattern changed from a nodular to a diffuse glandular pattern.

Conclusion: In our study, gynecomastia diagnosis was made through axial CT images. Although CT should not replace mammography and ultrasonography for clinical diagnosis of gynecomastia, chest CT scans can be used to evaluate patients with suspected gynecomastia.

Keywords: Male breast, gynecomastia, CT, nodular pattern, dendritic pattern, diffuse glandular pattern, COVID-19

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Key Points

- The most common benign breast lesion in men is gynecomastia.
- Gynecomastia is a benign enlargement of male breast tissue resulting from an imbalance of estrogen and testosterone levels.
- Gynecomastia may be physiological or idiopathic or caused by concomitant systemic disease or hormone use.
- If gynecomastia is detected with computed tomography, the patient should be evaluated clinically.

Introduction

The normal male breast consists mainly of adipose tissues and several subareolar ductal structures located on the pectoral muscle. Owing to these anatomical features, male breast diseases differ from female breast diseases in terms of frequency and radiological findings (1). Lobule formation is not usually seen during male breast development (1, 2). Fibroadenoma, cyst, and lobular carcinoma of lobular origin are extremely rare pathologies of male breasts (2). Invasive ductal carcinoma, ductal carcinoma in situ, and papillary neoplasm, which are related to ductal and stromal proliferation, as in gynecomastia, occur in men (2).

Benign breast lesions found in men include infection, abscess, tuberculosis, fibrocystic changes, hematoma, lipoma, sebaceous cyst, ductal ectasia, and diabetic mastopathy, but the most common benign breast lesion in men is gynecomastia (1, 3). Gynecomastia can be defined as the development of fibroepithelial structures in the male breast, giving it an appearance similar to healthy female breast. Glandular tissue of ≥ 2 cm in the subareolar area is generally accepted as gynecomastia (4-7).

The reported prevalence of gynecomastia ranges between 32% and 65% (4). Gynecomastia may be physiological or idiopathic or caused by concomitant systemic disease or hormone use (4, 6). Physiological gynecomastia occurs during the neonatal period, puberty, and old age

(6). Neonatal gynecomastia is caused by estrogen from the mother. In puberty, nearly half of boys have temporary gynecomastia (6). In other cases, gynecomastia is often idiopathic, where the cause is unclear. Gynecomastia is caused by the imbalance between estrogen and testosterone levels (3, 8).

Gynecomastia has three characteristic patterns: nodular, dendritic, and diffuse fibroglandular (2, 8). On mammographic evaluation, nodular gynecomastia has a fan-like appearance extending from the nipple to the back. If nodular gynecomastia is correlated with a pathological classification, the early phase is called gynecomastia, but this stage is reversible. Dendritic gynecomastia appears as retroareolar soft tissue density with radial extension to deep fatty tissues. It is the equivalent of fibrous gynecomastia in pathological classification. Diffuse glandular gynecomastia appears similar to the female breast. Nodular and dendritic forms can occur together. This is especially common in male patients receiving estrogen. In terms of pathological classification, it corresponds to proliferative epithelial changes accompanied by lobule formation in some cases (1).

The diagnosis of gynecomastia is important for patients to know that they do not have a malignant lesion and, if the cause of gynecomastia is found, to plan treatment (2). In patients presenting with complaints such as breast tenderness, swelling, and mass, ultrasonography (US) is used to diagnose young patients, and mammography is used in older and young patients, if necessary (1). Differential diagnosis of gynecomastia includes malignant tumors. In some cases, gynecomastia and malignancy cannot be easily differentiated. If gynecomastia is detected with computed tomography (CT), the patient should be evaluated clinically and imaged with mammography, if necessary. Pseudogynecomastia, another reason for an increase in breast tissue, is also included in the differential diagnosis of gynecomastia. It is caused by benign diffuse proliferation of adipose tissue (adipomastia) and is seen in overweight or obese people. Generally, pseudogynecomastia can be distinguished from gynecomastia based on the absence of a palpable, suspicious lesion under the areola upon clinical examination; if required, it can also be evaluated by US and mammography (2, 9).

Gynecomastia treatment is evaluated by age group. Hormonal imbalance should be investigated in the adolescent period; usually, gynecomastia regresses spontaneously during adolescence. In a patient with an established cause, discontinuing the drug that causes gynecomastia or treating the underlying medical condition typically results in regression unless the process reaches the irreversible fibrotic phase. Androgens, selective estrogen-receptor modulators, and aromatase inhibitors may provide some benefits for patients whose disease is secondary to other hormonal or medical treatments (9). Reduction mammoplasty can be performed in cases where drug treatment is not appropriate, or if patients are not responsive to other treatments (9).

The rate of gynecomastia in the general population is unknown because most cases are asymptomatic and routine breast imaging is not performed in men. Gynecomastia is a common incidental finding in chest CT (4). However, the prevalence of gynecomastia in Turkey by CT has not been reported.

During the coronavirus disease-2019 (COVID-19) pandemic, chest CT, CT angiography, and high-resolution CT (HRCT) examinations were performed in a large number of patients admitted to our hospital

with a preliminary diagnosis of viral pneumonia. In this study, we aimed to evaluate the breast tissue and determine the prevalence of gynecomastia in male patients who were admitted to our hospital and had a chest CT for prediagnosis of COVID-19.

Materials and Methods

This retrospective study was approved by our institutional ethics committee (approval no: 20-8.1T/40) and the Republic of Turkey Ministry of Health, COVID-19 Scientific Research Committee. A total of 4,047 chest CTs were performed in our hospital between March 15th and May 15th, 2020, for preliminary diagnosis of COVID-19 pneumonia. Our study included a total of 1,877 male patients. The mean age was 51.28 years, which ranged from 10 to 95 years (Table 1). Female cases were excluded from the study.

Of the total 1,877 CTs, 1659 (88.3%) were HRCT, 175 (9.3%) were CT angiography, and 43 (2.2%) were non-contrast-enhanced chest CT. Images were taken using a 160-slice CT scanner (Aquilion Prime, Toshiba Medical Systems). Axial images were acquired craniocaudally at shallow inspiration from the thoracic inlet to the diaphragm. HRCT images were taken at a high-resolution CT protocol with 120 kVp, 100–200 mA, and 80 mm × 0.5 mm collimation and reconstructed at 0.5 mm slice thickness with a sharp reconstruction kernel. Chest CTs were performed at a CT protocol with 120 kVp, 100–200 mA, 80 mm × 0.5 mm collimation and reconstructed at 1-mm slice thickness. Chest CT angiography was performed using a CT angiography protocol with 120 kVp, 100–200 mA, and 80 mm × 0.5 mm collimation and reconstructed at 1-mm slice thickness. A bolus of 1 mL/kg body weight of nonionic contrast material (Iopromide, Ultravist 370, Bayer Schering Pharma, Berlin, Germany) was injected intravenously in the antecubital vein at the rate of 4 mL/s by using an automatic injector. The bolus-tracking method was used to optimize pulmonary artery opacification. After termination of contrast agent administration, 50 ml of saline was injected. Diagnoses were determined by using the Sectra IDS-7 program.

All CT images were evaluated for the presence or absence of gynecomastia by a board-certificated radiologist with 14 years of experience. Cases with glandular tissue diameter of ≥ 2 cm at the nipple level in the axial plane were diagnosed as gynecomastia (Figure 1). When the axial diameter of the glandular tissue was 1–2 cm with a vertical growth and demonstrated characteristics that were consistent with gynecomastia, cases were also diagnosed as gynecomastia (Figure 2). In contrast, cases with glandular tissue diameter of 1–2 cm, but with atretic tissue pattern and density, were considered normal.

Gynecomastia patterns and axial diameter measurements were made separately for the right and left breasts. Gynecomastia pattern was evaluated as nodular, dendritic, or diffuse glandular gynecomastia (Figure 3). Nodular gynecomastia has a fan-like appearance, extending from the nipple to the posterior. Dendritic gynecomastia appears as retroareolar soft tissue density with radial extension to deep fatty tissues. Diffuse glandular gynecomastia appears similar to the female breast. At the same time, the presence of adipomastia was evaluated. In this study, adipomastia was defined as adipose tissue thickness of ≥ 2.5 cm in the breast tissue at the nipple level in the vertical plane. The presence of chronic diseases such as malignancies, liver cirrhosis, and chronic kidney failure were evaluated from CT images and clinical information records.

Table 1. Distribution of cases according to age and gynecomastia pattern

Age (years)	Gynecomastia pattern				No Gynecomastia	Total
	Nodular	Dendritic	Diffuse glandular	Total		
10–19	5	7	3	15 (1%)	18 (1%)	33 (2%)
20–29	16	47	11	74 (4%)	171 (9%)	245 (13%)
30–39	49	58	13	120 (6%)	215 (12%)	335 (18%)
40–49	17	49	6	72 (4%)	212 (11%)	284 (15%)
50–59	13	56	22	91 (5%)	211 (11%)	302 (16%)
60–69	16	52	23	91 (5%)	194 (10%)	285 (15%)
70–79	14	53	31	98 (5%)	162 (9%)	260 (14%)
80–89	4	22	12	38 (2%)	83 (4.5%)	121 (6.5%)
90–95	1	3	3	7 (0.3%)	5 (0.2%)	12 (0.5%)
Total	135	347	124	606 (32.3%)	1,271 (67.7%)	1,877 (100%)

Values are expressed as n (%).

n: Number

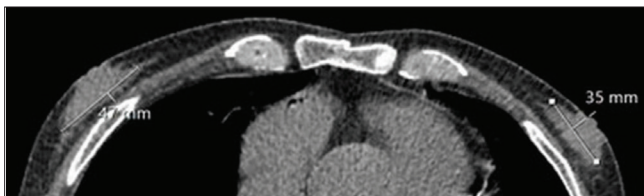


Figure 1. Computed tomography (CT) images showing axial diameter measurement of an 81-year-old patient with bilateral gynecomastia

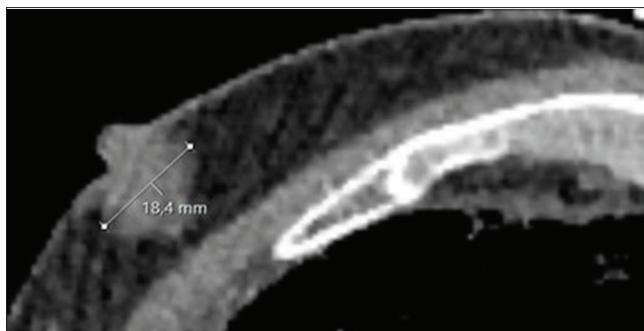


Figure 2. Computed tomography images showing vertical growth of glandular tissue density with an axial diameter of 1–2 cm

Statistical analysis

The distribution of cases in age groups, separated by decade, was determined. Continuous data were expressed as mean and standard deviation, and categorical data were expressed as counts (n) and percentages (%). All statistical analyses were performed with SPSS software version 25.0 (IBM). Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess normal distribution of data. Pearson's chi-square and Fisher's exact tests were employed to compare gynecomastia patterns and age. Student's t-test was utilized to compare differences of continuous variables in independent

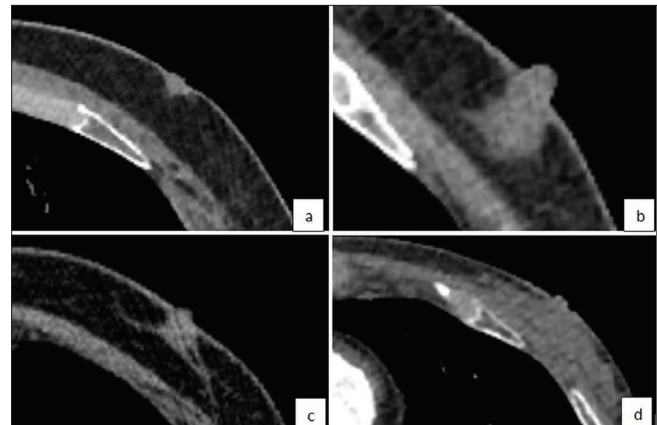


Figure 3. CT images showing patterns of gynecomastia in the male breast. Examples of non-gynecomastic normal retroareolar area (a), nodular pattern (b), dendritic pattern (c), and diffuse glandular pattern (d) of gynecomastia

CT: Computed tomography

groups. Spearman's correlations were used to evaluate the relationship between gynecomastia patterns and breast glandular measurements.

Results

Gynecomastia was detected in 606 (32.3%) of the 1,877 patients, and of those 606 gynecomastia cases, 454 (74.9%) were bilateral and 152 (25.1%) were unilateral (Table 2). Out of the 152 unilateral gynecomastia cases, 75 were observed on the right side and 77 on the left side. Of the 606 gynecomastia cases, 22% had nodular pattern, 57% had dendritic pattern, and 21% had diffuse glandular pattern (Table 1-2). Adipomastia was detected in 84 (4.5%) of 1877 patients.

In cases with axial diameter measurements of 1–2 cm and considered gynecomastia, the enlargement of the glandular density was evident

in the vertical plane. Of the glandular tissue diameter measurements performed in the axial plane of the right breast, 398 (75.3%) cases had a diameter of ≥ 2 cm and 131 (24.7%) cases had a diameter of 1–2 cm (Table 3). Of the glandular tissue diameter measurements performed in the axial plane of the left breast, 374 cases (70.4%) had a diameter of ≥ 2 cm; however, 157 cases (29.6%) had a diameter that was 1–2 cm (Table 3).

No significant difference was found in age between the groups with and without gynecomastia ($p = 0.495$) or between groups with unilateral and bilateral gynecomastia ($p = 0.674$). A significant correlation was found between age groups by decade and gynecomastia patterns with Kruskal-Wallis and Dunn's tests ($p < 0.001$) (Figure 4). As age advanced, an increase was seen trending from nodular pattern to diffuse glandular pattern.

When gynecomastia patterns were compared according to age group, significant differences were found between nodular and dendritic ($p = 0.002$), nodular and diffuse glandular ($p < 0.001$), and dendritic and diffuse glandular gynecomastia patterns ($p = 0.003$) with chi-square

tests (Figure 5). Nodular, dendritic, and diffuse glandular patterns increased with advancing age.

Kruskal-Wallis tests indicated a significant difference in the correlation between age group and glandular tissue diameter for the right breast ($p = 0.004$) and left breast ($p = 0.006$) (Figure 6). Spearman's rho nonparametric correlation test revealed a positive relationship between age and glandular tissue diameter ($p < 0.001$; $r = 0.235$).

Gynecomastia cases were divided into two tissue diameter groups: 1–2 cm and >2 cm. The relationship between these two groups was determined according to the tissue diameter and age by independent samples Kruskal-Wallis tests. When evaluated with paired comparisons, a significant difference was found between age and tissue diameter for the right breast ($p = 0.018$) and left breast ($p = 0.012$). Tissue diameter increased in direct proportion with increasing age.

A significant difference was found between glandular tissue diameter and gynecomastia patterns in the chi-square test for the right breast ($p < 0.001$) and left breast ($p < 0.001$). With an increase in glandular

Table 2. Gynecomastia pattern distribution

Gynecomastia pattern	Bilateral	Unilateral	Total
Nodular	84	51	135 (22%)
Dendritic	251	96	347 (57%)
Diffuse glandular	119	5	124 (21%)
Total	454 (75%)	152 (25%)	606

Values are expressed as n (%).
n: Number

Table 3. Glandular tissue diameter of the right and left breasts

Glandular tissue diameter	Right breast	Left breast
1–2 cm	131 (24.8%)	157 (29.6%)
>2 cm	398 (75.2%)	374 (70.4%)
Total	529	531

Values are expressed as n (%).
n: Number

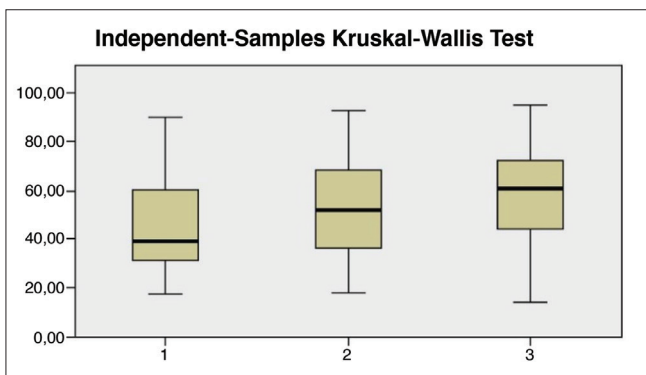


Figure 4. Distribution of age according to gynecomastia pattern (1, nodular pattern; 2, dendritic pattern; 3, diffuse glandular pattern)

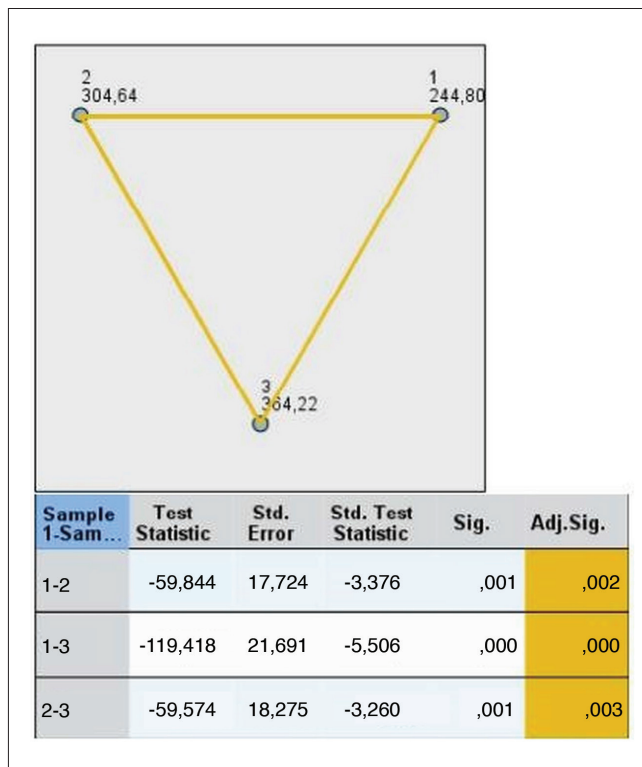


Figure 5. Pairwise comparisons of gynecomastia pattern (1, nodular pattern; 2, dendritic pattern; 3, diffuse glandular pattern)

Std: Standard; Sig: Significance; Adj Sig: Adjusted significance

tissue diameter, the gynecomastia pattern changed from nodular pattern to diffuse glandular pattern. Nonparametric Spearman's rho correlation test indicated a strong positive correlation between both breast glandular tissue diameters and age groups, and this relationship was significant ($p < 0.001$) (Table 4).

Discussion and Conclusion

Male and female breasts are structurally the same until adolescence. During puberty, lobular proliferation occurs following dilatation and branching of the ducts in the female breast. In contrast, usually, no changes occur in the male breast.

Gynecomastia is the most common pathology in the male breast and a common incidental finding in chest CT (3). However, the prevalence of gynecomastia with CT has not been reported in previous studies in Turkey. In this study, the prevalence of gynecomastia by CT images was 32.3%. Breast screening in men is not routinely performed. In symptomatic gynecomastia cases, US and mammography are the preferred imaging methods. Although CT is not superior to mammography in the evaluation of gynecomastia, it may help diagnose asymptomatic cases if reported by radiologists.

Gynecomastia occurs as a result of benign proliferation of ductal and stromal tissues and can be unilateral or bilateral (9). It is caused by the imbalance of testosterone and estrogen levels (3, 8). Other causes

include hormone-secreting tumors, endocrine disorders, liver cirrhosis, obesity, drug use, and drug addiction (3, 10). Approximately 20% of gynecomastia cases are caused by drug side effects, but definitive causes are often not detected (10).

Physiological gynecomastia is caused by normal changes in the balance of hormones. Gynecomastia prevalence is 75% in the neonatal period and 50% in adolescent boys, but it usually regresses within 6 months. Gynecomastia peaks during the neonatal period, adolescence, and old age (4, 6). Between these ages, gynecomastia is usually pathological and depends on various diseases, syndromes, drug treatments, or conditions that cause impaired balance of estrogen and testosterone levels (2, 4, 8).

Gynecomastia is found in about half of older men and is usually asymptomatic (2). A study reported a rise in the prevalence of gynecomastia with increased Body Mass Index (4). Gynecomastia is more common in older obese men owing to increased estrogen levels from peripheral adipose tissue and decreased testosterone due to decreased testicular function (6). Previous studies in elderly men have reported gynecomastia in 55% of autopsies, 57% in healthy cases, and 70% in hospitalized patients (11, 12).

Of the cases in our study, 48% were <50 years old, and 52% were ≥50 years old (Table 1). In our study, no significant difference was noted between groups with and without gynecomastia in terms of age ($p = 0.495$). Considering the distribution of our cases according to age

Table 4. Glandular tissue diameters and age group statistics of nonparametric correlations

Correlations		Age	Right breast glandular tissue diameter	Left breast glandular tissue diameter	
Spearman's rho	Age	Correlation coefficient	1	0.235*	
		p-value	-	<0.001	
		n	1,877	529	
	Right breast glandular tissue diameter	Correlation coefficient	0.235*	1	0.769*
		p-value	<0.001	-	<0.001
		n	529	529	454
Left breast glandular tissue diameter	Correlation coefficient	0.219*	0.769*	1	
	p-value	<0.001	<0.001	-	
	n	531	454	531	

*Correlation is significant at the 0.01 level (2-tailed).
n: Number

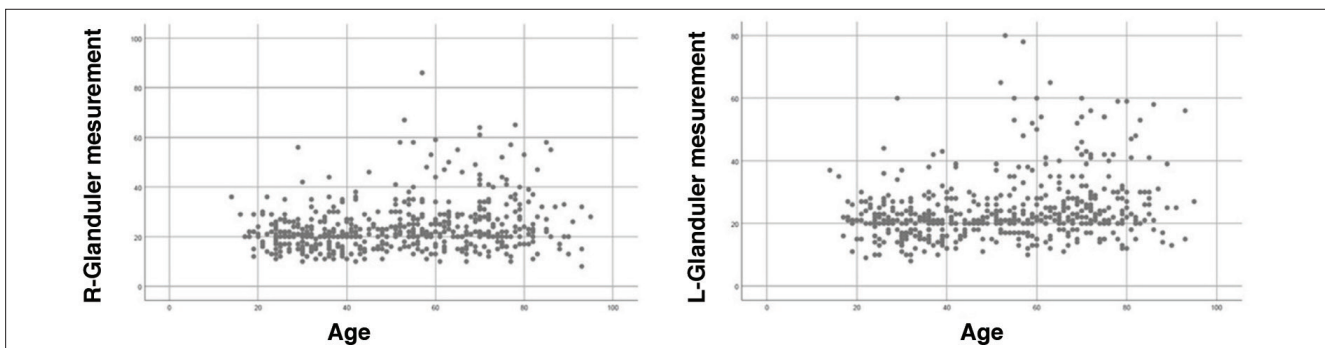


Figure 6. Relationship between age and glandular tissue diameter of right and left breast

decade group, a number of cases were close to each other in all decades. This may be one reason why the prevalence of gynecomastia in this study was different from other reports in the literature.

In our study, accompanying diseases included liver cirrhosis, chronic kidney failure, congestive heart failure, benign prostatic hyperplasia, prostate cancer, lung cancer, and stomach cancer. However, full statistical analysis between these diseases and gynecomastia was not performed because we could not obtain medical records and histories of all cases with and without gynecomastia.

Sonnenblick et al. (13) identified high correlation between CT sectional imaging of gynecomastia and mammography findings. In our study, cases with gynecomastia were not evaluated by mammography. Moreover, gynecomastia cases, especially those with diffuse glandular pattern, were specified in CT reports, and clinical directions were made to determine the underlying cause.

Klang et al. (4, 5) reported that a 2.2 cm breast tissue diameter represents the 90th percentile in the general male population by CT (14). Glandular gynecomastia is defined as the presence of tissue more than 2 cm diameter in the subareolar region in axial CT images. Because a small amount of breast tissue is accepted as a normal finding, we used a 2 cm threshold value, according to definitions in the radiological literature (3-7). As mentioned in the literature, significant growth of glandular tissue was observed in the vertical plane in some gynecomastia cases (25% and 29% on the right and left breasts, respectively). Therefore, although axial diameter measurements are <2 cm, these cases were also considered as gynecomastia, according to their appearance. Conversely, cases with a measurement of 0–2 cm, with characteristics similar to atretic ductal structures, were not considered gynecomastia.

Gynecomastia is mostly asymptomatic, and there is no conclusive evidence to suggest a link between cancer and gynecomastia (6). However, the presence of gynecomastia may mask breast cancer in some cases (8). The prevalence of gynecomastia and breast cancer increases in Klinefelter syndrome (6). The incidence of breast cancer in men is very low; it accounts for just 0.6% of total breast cancers and 1% of male cancers (15). Moreover, 40% of male breast cancers are associated with microscopic gynecomastia (13). In excised specimens from patients who underwent surgical treatment for gynecomastia, the rates of invasive carcinoma and in situ carcinoma were 0.11% and 0.18%, respectively (14). The mismatch between rates of symptomatic breast cancer and cancer prevalence in materials excised from men suggests that the rate of asymptomatic breast cancer in men is higher than reported. If necessary, US and mammography should be done. In our study, suspicious breast lesions were not found in any of the patients who underwent CT. Clinical guidance was recommended for cases with diffuse glandular type, as indicated in CT reports.

Our study has some limitations because it is a retrospective study. Some of our cases were admitted only during the pandemic period, and because they were examined for a preliminary diagnosis of COVID-19 pneumonia, there may be some missing information in the patients' hospital records. In terms of gynecomastia, there was no physical examination, US, or mammography of the patients. Therefore, concomitant diseases and drug information may be missing. To improve determination of gynecomastia causes, new studies should be conducted with all data, including current diseases and drugs taken.

In conclusion, we detected gynecomastia by CT in 32.3% of patients with a prediagnosis of COVID-19 pneumonia. Although gynecomastia is diagnosed primarily with mammography and US, we suggest that chest CT may help diagnose patients with suspected gynecomastia if CT was performed within the last 6 months.

Ethics Committee Approval: This retrospective study was approved by our institutional ethics committee (approval no: 20-8.1T/40) and the Republic of Turkey Ministry of Health, COVID-19 Scientific Research Committee.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: Ö.A., A.O., R.S.; Design: Ö.A., A.O.; Supervision: Ö.A., A.O., R.S., S.B., N.C.; Materials: Ö.A., R.S., S.B., N.C., A.Ç.; Data Collection or Processing: Ö.A.; Analysis or Interpretation: Ö.A., A.O.; Literature Search: Ö.A., A.O., R.S., S.B.; Writing: Ö.A., A.O.; Critical Review: Ö.A., A.O., R.S.

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