Unnecessary Biopsy For Fibroadenomas, How Can We Decrease Its Rate?

Fibroadenomlara Yapılan Gereksiz Biyopsiler, Nasıl Oranlarını Düşürebiliriz?

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Abstract

Fibroadenoma (FA) is benign form of tumors of the breast with a very low risk of transformation to malignity. It is very common among young women and incidence drops with age. Diagnosis is often made by ultrasonography (US). Instead of excision for diagnosis, following is made by imaging. Currently, FA amount for about half of the biopsies of breast. The objective of our study is to find by which mean we can decrease the rate of unnecessary biopsies. We made a retrospective study on 39 patients labelled as FA (mean age 48.8±7.7 years). We analyzed the features of lesions in US: size, localization, contour, orientation, homogeneity, echogenicity, single or multiple, presence or absence of calcifications. We classified our masses according to BIRADS categorization and also calculated the rate of masses according to indications of biopsies. Concerning the ultrasonographic description of FA's features, all of our findings were compatible with literature. Except one patient, all of them were classified as less suspicious according to BIRADS categorization. 2/3 of biopsies in our sample were made in the first examination and 1/3 presented suspicious features. A high amount of biopsy is indicated in the first contact with patients because there is no previous examination to refer to. We suggest to not wait for patient to be aware of the mass or for systematic examination set at the age of 40 and to make earlier US in purpose to have a documented reference of masses' features which are well established according to literature in order to avoid unnecessary biopsies.

Keywords: Breast, Fibroadenoma, Tru-cut Biopsy, Ultrasonography

Öz

Fibroadenoma malign transformasyon riski çok düşük olan benign formda bir meme tümörüdür. Genç yaşta daha yaygındır ve insidansı yaş ile düşer. Tanısı sıklıkla ultrasonografi ile konur. Eksizyon yerine genellikle radyolojik izlem yapılır. Buna rağmen meme biyopsilerinin yarısı fibroadenomlara yapılmaktadır. Araştırmamızın konusu fibroadenomlara yapılan gereksiz biyopsilerin nasıl düşürülebileceği hakkındadır. Araştırma Fibroadenom tanısı almış 39 hastayı kapsayan retrospektif bir çalışmadır. (ortalama yaş 48.8±7.7). Ultrasonografi ile lezyonların özellikleri analiz edildi. Boyut, lokalizasyon, kontür, oryantasyon, homojenite, ekojenite, tek ya da multipl olması, kalsifikasyon özelliklerine göre sınıflandırıldı . Ayrıca lezyonların BIRADS grupları belirtildi. Son olarak lezyonlar biyopsi yapılma nedenlerine göre sınıflandırıldı. Lezyonların ultrasonografik özellikleri ile ilgili tüm bulgular literatürle uyumluydu. Bir hasta hariç tüm hastalar BIRADS grubuna göre düşük riskli gruptaydı. Araştırmamızda biyopsi yapılan hastaların 2/3'ü ilk kez ultrasonografik takibe giren hastalardı ve 1/3'ü şüpheli özelliklere sahipti. Literatürde belirtilen biyopsi endikasyonlarına göre hasta 40 yaşına gelmeden ya da kitle ele gelmeden yapılan bir ultrasonografik muayene ile lezyona ait referans bir döküman bulunduğunda fibroadenomlara yapılan gereksiz biyopsi oranı azaltılabilir.

Anahtar Kelimeler: Fibroadenoma, Meme, Tru-cut Biyopsi, Ultrasonografi

Başvuru Tarihi / Received: 03.05.2018
Kabul Tarihi / Accepted : 28.06.2018

Introduction

Fibroadenoma (FA) is a form of benign breast mass. It consists of both stromal and epithelial elements (1). These lesions typically present as solid, well-circumscribed masses. Fibroadenomas tend to grow slowly, reaching maximum diameters of 2–3 cm in size (2). They are generally unique but 20 % can be multiple (3). They are more prevalent in younger patients and incidence drops with aging (4). Fibroadenomas are more frequent among women in higher socioeconomic classes (5,6) and in dark-skinned populations (7).

The age of menarche, the age of menopause, and hormonal therapy, including oral contraceptives were shown not to alter the risk of these lesions (6-10) also no genetics factors are known to alter the risk of fibroadenoma. However, a family history of breast cancer in first-degree relatives was reported by some investigators as related with an increased risk of developing these tumors (2,11). Conversely, body mass index and the number of full-term pregnancies were found to have a negative correlation with the risk of fibroadenomas (5,6,9, 12). Moreover, consumption of large quantities of vitamin C and cigarette smoking were found to be associated with reduced risk of a fibroadenoma (6).

The risk of malignant transformation is extremely low and has been reported to a range of around 0.0125-0.3% (13-15).

Mammograms are limited in term of differentiation of FA masses from other pathologies (cysts and carcinomas) as the quality of mammogram decreases in younger patients with denser breast tissues. Thus, ultrasound (US) is a useful alternative for mammographic studies (2).

Often diagnosed sonographically, fibroadenomas appear as hypoechoic, oval solid masses with smooth contours and weak internal echoes in a uniform distribution (16). The typical imaging features of fibroadenoma on mammography and ultrasound (US) are well known, and in the majority of cases,

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no further characterization (histologic/cytologic sampling, breast magnetic resonance imaging (MRI)) is required (17,18). Since the 1990s, with the increasing use of core biopsy rather than excision to diagnose these lesions, it has became common to follow these lesions with imaging. Fibroadenomas account for about half of all breast biopsies (13-15). The objective of our study is to find by which mean we can decrease the rate of unnecessary biopsies.

Material and Method

This retrospective study was conducted in breast department of Muğla Sıtkı Koçman University Educational and Research Hospital. The cases were selected from patients admitted in our hospital between April 2017 and September 2017. 39 patients labelled as having FA were retained for this study. For the ultrasonographic examination, Toshiba S 300 ultrasonographic device and high resolution 10 MHz breast probe were used. After obtaining the patient's consent and filling the acceptance form, the biopsies were performed with tru-cut biopsy technic. Minimum 3 samples were obtained and then were evaluated in pathology department. Thus all of the patients had full description of breast masses in US and detailed anatomo-pathology reports. Characteristics of the masses seen in US were carefully evaluated. We assessed the size. Dimensions were measured in millimetre. Small diameter and big diameter were used in our study. Index of circularity which is defined as big diameter on the small one had been calculated. We specified place of the mass according to right or left breast and its localization (central or peripheral) in the same breast. We also described the lesions according to shape:

-contour: If they have more than 4 lobulations it is labelled as micro lobulated, if less than 4 or smooth border like macrolobulated and if the border is incompletely irregular like partially irregular.

-homogeneity: Homogeneous or heterogeneous. If there is a remarkable difference of echogenicity inside the lesion, it was accepted as heterogeneous.

-echogenicity: Isoechoic or hypoechoic

-orientation: Oblique, parallel or vertical

-single or multiple character of the mass

-presence or absence of calcifications: calcific or non-calcific lesions

The data are presented as percentage for the qualitative variables and as mean ± standard deviation for the quantitative variables. The SPSS statistical software (IBM, SPSS statistics 20, Armonk, NY, USA) was used for data analysis.

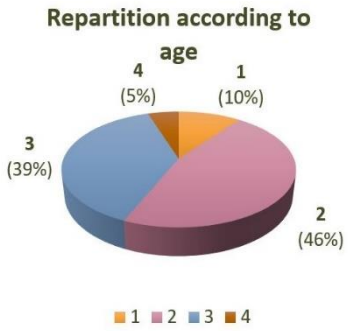
Results

I. Age of patients

The mean age of patients is 48.8±7.7 years. The maximum age was 71 and the minimum was 30. We devided our sample into 4 small groups. We report that most of FA were found in the 40/50-year-old group.

Table 1. Number and percentage of FA according to interval of age

Repartition according to age	Number	Percentage
1. Less than 40 years	4	10.3
2. Between 40-50 years	18	46.2
3. Between 50-60 years	15	38.5
4. More than 60 years	2	5.1



Graphic 1. Repartition according to age

II. Dimensions of the mass

The mean of big diameter is 15.7 mm; the mean of small diameter is 8 mm. 64% of the mass that were biopsied had a size between 10 and 20 mm. The mean of the circularity index obtained (circularity index is defined as big diameter on the small one) is 1.9. 7.6% had a remarkable circularity index less than 1.4.

Table 2. Minimum, maximum, mean and standard deviation of size parameters

Size parameters	Min	Max	Mean ± SD
Big diameter	6	50	15.78 ± 7.87
Small diameter	3	24	8±3.84
Circularity index	1.3	3	1.98±0.41

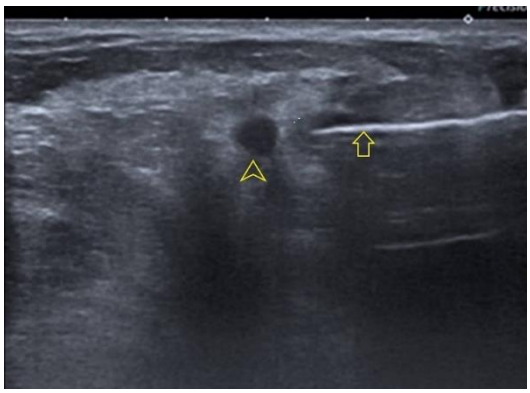
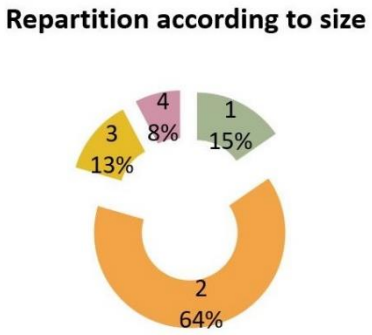


Figure 1. The Smallest FA with tru-cut biopsy (Arrow Head: Fibroadenoma, Arrow: Needle)

Table 3. Number and percentage of FA according to size

Repartition according to size	Number	Percentage
1. Less than 10 mm	6	15.4
2. Between 10-20 mm	25	64.1
3. Between 20-30 mm	5	12.8
4. More than 30 mm	3	7.7



Graphic 2. Repartition according to age

III. Localization of the mass

1. Place of tumor according to right or left breast:

We noticed a non-significant difference about emplacement of tumor according to right and left breast. 46.2 % of masses were found in the left breast while 53.8% of masses were found in the right breast.

2. Place of tumor inside the same breast:

Almost 74.4% of tumors were in the center of the breast. 25.6% were peripheral.

IV. Characteristics of the mass

1. Contour of the mass:

The masses were classified according to shape of borders as following:

Table 4. Classification according to borders' shape

Shape of contour	Number	Percentage
Microlobulated	3	7.7%
Partially irregular	3	7.7%
Macrolobulated-regular	33	84.6%

2. Homogenity of the mass:

Heterogeneous shape was found in 30.8% of the tumors. 69.2% were homogeneous (Figure 2).

3. Echogenicity of the mass:

Almost ¾ (74.4%) of tumors were hypoechoic while the others were isoechoic.

4. Orientation of the mass:

All of the masses were oblique or parallel. None was vertical.38 cases were parallel to long axis, only one case was oblique (Figure 3).

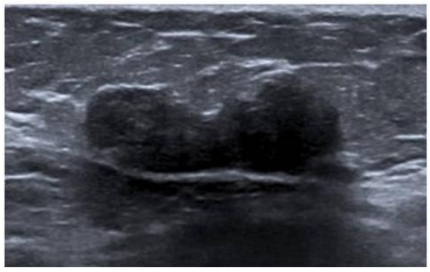


Figure 2. Homogen, macrolobulated, hypoechogenic FA

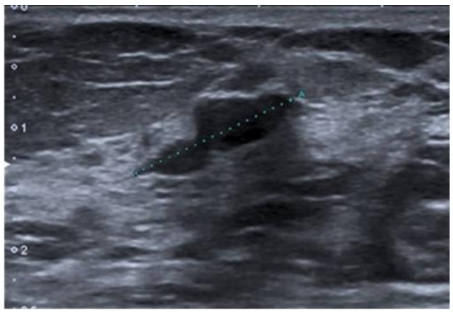


Figure 3. Oblique FA

5. Single or multiple character of the mass:

Multiple tumors had been found in 30.8% of our patients.

6. Presence or absence of the calcifications:

The biggest majority of the masses were non-calcific. Calcifications had been found in only 3 patients (7.7%).

7. BIRADS classification of masses:

According to BIRADS classification of FA, only 1 patient was BIRADS 4B, the rest were 4A.

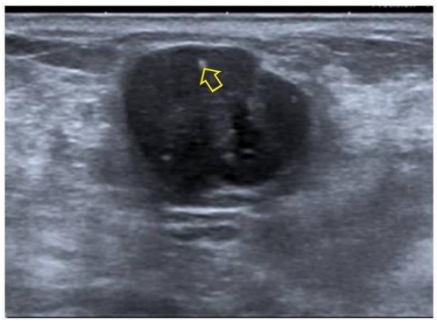


Figure 4. The lesion described BIRADS 4 B with microcalcifications and less circularity index (Arrow: Microcalcification)

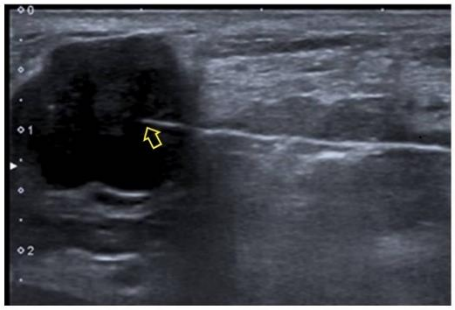


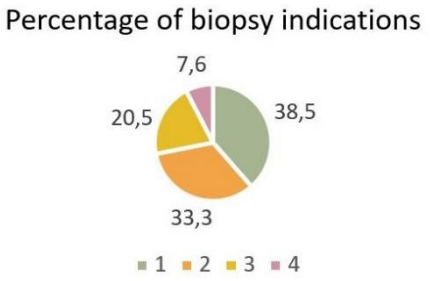
Figure 5. Tru-cut biopsy on the lesion quoted above (Arrow: Needle inside fibroadenoma)

V. Indications of the biopsy:

The reasons of biopsies were classified as following:

Table 5. Classification according to the reasons of biopsies

Indication of biopsy	Number	Percentage
1. Suspicious shape	15	38.5%
2. Increasing size	13	33.3%
3. Social reasons	8	20.5%
4. First examination after 40 years old + size >2.5 cm.	3	7.6%



Graphic 3. Percentage of biopsy indications

Discussion

Fornage et al. conducted a retrospective study on the sonographic patterns of 101 FA in 92 consecutive patients whose ages ranged from 13 to 80 years. The mean age was 39±13 years. In the study made by Namazi et al. where 92 patients were enrolled, the mean age was 40.4 ± 9.2 years (17,19). The mean age of our group (48.8±7.7 years) was a little bit higher according to literature. This can be easily explained by the large samples of the other studies or by the fact that systematic consultation has been set at 40 years. Anyway, the mean age of old investigations may suggest the idea that further examinations should be done earlier.

In our study, the mean of the big diameter was 15.7±7 mm and the mean of small diameter was 8±3 mm. In Fornage et al., big and small diameter were also measured and they were respectively 18±1 mm and 12±6 mm (17).

According to literature, size is a variable but circularity index is more important. Nishimura used an original concept of using circularity index threshold value to distinguish fibroadenomas (L/AP>1.4) from carcinomas (L/AP<1.4) (20). Among our patients, only 7.6% of the patients presented a circularity index inferior to 1.4, which was considered as a suspicious feature. In our study 84.6% of the masses were well circumscribed macrolobulated or with regular contour and 15.4 %were non circumscribed. This last group included 2 groups: microlobulated and partially irregular with an equal rate of 7.7%.

Namazi et al. simply divided masses into circumscribed and non-circumscribed. The rates were respectively 60% and 40%. Fornage et al. proceeded to another classification. In his study the majority of the lesions had regular (57%) or lobulated (16%) contours whereas 27% were irregular (17, 19). In other studies, irregularity of contour has been reported as 6%-58% of cases (21-23).

It is obvious that FA are generally well circumscribed however there is not a negligible percentage of irregular FA which may lead to confusion because it is considered as suspicious feature. In despite of different percentages, our results do not contradict previous studies.

Fornage et al. found that 71% percent of the lesions were homogeneous in echotexture, whereas 29% showed a variable degree of non-homogeneity. Jackson et al. reported a heterogeneous internal echo-pattern in 28%-52% of FA (17, 23) while other studies reported a homogeneous echotexture in 48%-89% of FA (21-23). Globally the heterogeneous shape is observed in 1/3 of FA. In our sample, it was found in 30.8% of the tumors while 69.2% were homogeneous. Our findings are similar to the study of Fornage et al. and close to literature.

In the evaluation of the masses content by US, Fornage et al. reported that the majority of the lesions (92%) were hypoechoic in comparison with the adjacent fibro glandular tissue; 4% were hyperechoic, 2% showed a mixed pattern containing markedly hyper- and hypoechoic areas, 1% were anechoic, and 1% were isoechoic. Namazi et al. were quite similar to Fornage et al. with a percentage of 91.3% for hypoechoic lesions. In the series of Cole-Beuglet et al. and Heywang et al. hypoechogenity was 80% and 96% respectively (17, 19, 21, 22) our study revealed that almost ¾ (74.4%) of tumors were is hypoechoic while the others were isoechoic. Our results are far from the number observed in the other investigations however it stays compatible with literature since the majority of our patients had homogenous masses.

In Fornage's study, only one mass was vertical to axis. There was no another classification about orientation of the mass while in our study there was no vertical mass, all of the patient cases were parallel to long axis and only one cases was oblique (17). In the literature, FA are multiple in approximately 15%-25% of patients (24, 25). Our results are near the highest rate with 30.8 % of multiple FA.

Calcifications can be associated with fibroadenomas and can have a wide spectrum of radiologic appearances (26). Namazi et al. found 9.8% of calcific FA and our rate (7.7%) didn't excess his percentage (19).

Guidelines from the U. S. Department of Health and Human Services, the American Medical Association and the American College of Radiology

(ACR) recommend screening mammography every year for women, beginning at age 40 (27). BI-RADS classification reflects the radiologist's level of suspicion for malignancy, and these assessment categories have been shown to be correlated with the likelihood of malignancy (28).

Namazi et al. used BI-RADS classification to assess mammography of his patients. 88% of the masses were classified as 4A, 8.7% and 3.3% of the masses were categorized as 4B and 4C, respectively (19). In our study, only one patient was BI-RADS 4B, the rest were 4A which means that almost all of our FA were spotted in the less suspicious BIRADS category (27). Our findings resemble to the literature, since the biggest majority of FA show low suspicion features.

Even if the risk of malignant transformation is extremely low (0.0125-0.3%) (13-15). It has been established in the literature that clinical diagnosis of FA does not exclude malignancies (1). Ultrasound imaging in young patients and its combination with mammogram in older patients provide further evidence for a more accurate diagnosis; however, there are reports of overlapping features in the results with other diagnosis (29, 30).

Thus biopsy is necessary during the following of FA or if lesions lead to confusion, for the early diagnosis of a possible cancer. According to literature, the indications for biopsy of FA-Like lesions include:

-Enlarging lesion

-Atypical findings on ultrasound

-A lesion above 2.5-3.0 cm where there are no previous studies for comparison

-Patient peace of mind: some patients are simply not happy with a palpable mass in the breast without a histological diagnosis; this is a valid and reasonable indication for biopsy (14).

In our study, 33.3% of biopsies were made for an increasing size of the mass, which means that only 1/3 of FA lesions were followed and had previous US. A total of 66.6% of biopsies were performed in patients who came for their first examination. 38.5% biopsies were indicated for suspicious features; 20.5% for social reasons as explained above, and finally 7.6% for patients older than 40 years (age where we start a systematical detection of lesions) and size of the mass was over 2.5 cm.

In our department during the same period, 300 biopsies had been made, 98 biopsies were indicated in the first examination and a total of 39 of confirmed FA obtained. In other words FA represent only 6.4% (13/202) of the masses which had been biopsied during the routine following of breast masses while 26.5% (26/98) were biopsied directly in the first contact with the patient because of the recommended indications.

Our findings suggest that more than 2/3 of the total number of discovered FA were biopsied during their first coming because there was no previous examination that could orientate the diagnosis and this number represents ¼ of all the total masses newly discovered in a period of 6 months. Numbers are talking by themselves, even in a small sample, the biopsies of a benign tumor are frequent and one of the main reasons is simply the doubt due to absence of any old information. We won't say that these biopsies were abusive because it is wiser to make a biopsy by excess than to miss out on a cancer but we think that we must not wait until the patient is coming with a palpable mass or is attending the systematic consultation at the age of 40.

Many skeptical may consider our study incomplete because of the absence of a control group and the small size of our sample. However it is with intend that we collected our data from only 6 months to show that FA is frequent even in a short interval. This will attract your attention to the fact that FA is a common mass in the biopsy of breast and this was largely reported in literature. As we know, biopsy is not free of risk, is psychologically constraining and generates additional costs. From this perspective, it became obvious that our efforts should concentrate on how we can reduce its rate. This paper's purpose is not to compare prevalence or to find new features of FA, it is the opposite. FA is a frequently seen mass, with clear, known characteristics and after comparison to literature, in our group of study FA's features were quite similar to old studies and this independently of age or biopsy indications. In fact an early diagnosis of this mass based on clinic examination, US and a simple follow of patients would greatly decrease future biopsies and the resulting constraints.

Scientific reasoning is not based only on results or comparisons, it englobes new ideas and different points of view. So instead of new findings, we will suggest a new concept that may open the door for further studies. Women should benefit from an early breast consultation including US examination before 40 years old, even if mass is not discoverable by the patient. Indications of biopsy should be reviewed. To wait until the patient is aware of its mass means a higher probability of making a biopsy. Our study is the proof that many unnecessary biopsies would had been avoided if only previous images of US were present as a reference. Indeed, it seems illogical to wait until 40 years old for systematic consultation while we need to take a decision on we should or not make a biopsy for patients who come for the first time to breast examination for an FA- like shape's lesions.

Future studies including a bigger size of sample and early examinations with a long term following of patients labelled as having FA will be interesting to clarify the dark zones of these recommendations.

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