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Original Article

The evaluation of breast biopsy results before and after the inception of COVID-19 pandemic: Single center retrospective study

COVID-19 pandemisi başlangıcından önce ve sonra yapılan meme biyopsilerinin değerlendirilmesi: Tek merkezli retrospektif çalışma

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Abstract

Aim: This study aimed to evaluate breast biopsy procedures performed in radiology unit before and after COVID-19 pandemic initiation, and compare breast cancer diagnosis.

Material and Methods: Breast biopsies performed two years before and after March 2020 were retrospectively analyzed. Patient demographics, referral reason (screening/diagnostic), biopsy type and region, tumor size, BI-RADS category and pathology were evaluated. Statistical analysis was made using chi-square test, independent samples t-test and Mann-Whitney U test.

Results: Among 903 biopsies, the mean age was 51 (range 15 to 88 years). Biopsy volume decreased in the early six months of the pandemic, but accelerated soon after, with numbers even more than the pre-pandemic era. Screening intention on patient referral decreased significantly in the pandemic period, where diagnostic purposes arised ($p<0.05$). The prominent imaging modality used for diagnosis was mammography before pandemic and ultrasonography after pandemic ($p<0.05$). There was no statistical difference regarding biopsy type, biopsy region, tumor size, axillary lymph node invasion and pathology results by period.

Conclusion: Despite the sudden decrease of breast biopsy volume in the early pandemic, demand of screening reduced and diagnostic referrals increased dramatically afterwards . Therefore, the interruption of cancer screening programmes should be avoided to prevent cancer burden.

Keywords: Imaging aided breast biopsy, COVID-19, breast cancer

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Öz

Amaç: Bu çalışma ile COVID-19 pandemisi öncesi ve pandemi sırasında radyoloji biriminde yapılan meme biyopsilerini değerlendirmek ve bu dönemlerdeki meme kanseri teşhislerini karşılaştırmak amaçlanmıştır.

Gereç ve Yöntemler: Mart 2020 öncesi ve sonrasındaki 2 yıl boyunca yapılan meme biyopsileri retrospektif olarak incelendi. Hastaların demografi bilgileri, başvuru sebebi (tarama/tanısal), biyopsi tipi ve bölgesi, kitle boyutu, BI-RADS kategorisi ve patolojisi değerlendirildi. İstatistiksel analiz için ki-kare testi, bağımsız örneklem t-testi ve Mann-Whitney U testi kullanıldı.

Bulgular: Toplam 903 biyopsi hastasında ortalama yaş 51 (15-88) bulundu. Biyopsi sayısının pandeminin erken ilk 6 ayında düşüp hemen sonrasında, pre-pandemi döneminden de fazla olmak suretiyle, yükselmeye başladığı izlendi. Pandemi döneminde tarama başvuruları ile ilişkili biyopsi sayıları anlamlı olarak düşerken tanısal başvurularla gelen biyopsi sayılarının arttığı görüldü ($p<0.05$). Tanısal amaçlı en sık kullanılan görüntüleme yöntemi pandemi öncesi mamografi iken pandemi sonrası ultrason olmuştur ($p<0.05$). Biyopsi tipi, bölgesi, kitle boyutu, aksiller lenf nodu tutulumu ve patoloji sonuçlarında dönemsel olarak anlamlı farklılık saptanmadı.

Sonuçlar: Erken pandemi döneminde meme biyopsisi sayısında izlenen ani düşüşe rağmen, hemen izleyen dönemde tarama ilişkili biyopsi sayısında azalma ve tanısal başvurulara bağlı yapılan biyopsi sayısında belirgin artış saptandı. Bu sebeple, olası kanser kanser yoğunluğunun önüne geçebilmek amacıyla kanser tarama programlarının sekteye uğramaması için gerekli önlemler alınmalıdır.

Anahtar kelimeler: Görüntüleme eşliğinde biyopsi, COVID-19, meme kanseri

Introduction

In the spring of 2020, the coronavirus disease 2019 (COVID-19) disrupted daily life, including preventive health care services worldwide. Cancer screening programmes were interrupted yielding to a temporary decrease in cancer diagnoses (1, 2). Many professional organizations and cancer societies recommended asymptomatic individuals to postpone their routine cancer screening appointments (3). This health issue brought out the consequences of its own, where an abrupt increment of newly diagnosed cancers arised due to extended delays, with additional burden on the health care system (4).

It has been reported that during the initial pandemic outbreak and lockdowns, many hospitals closed outpatient clinics and postponed or cancelled elective surgeries as precaution against COVID-19 spread (5). In parallel with the reduction of hospital visits of patients, radiological imaging utilization also markedly decreased (6, 7). Screening mammography programmes were paused internationally in the spring of 2020, due to the governmental advisory about avoiding nonurgent demand of health care (1, 8). This sharp decrease in monthly screening volumes returned to normal when recalls were started by the following summer (3, 8).

It is predicted that these delays in cancer screening programmes will impact the outcomes of breast cancer (9-11). With regard to breast cancer, during the lockdowns, the number of diagnosed malignancy rates decreased in certain countries (9, 12). On the other hand, in Finland, oncological surgery rates were not affected from postponed elective surgeries (11). In this context, we aimed to evaluate breast biopsies performed in out breast imaging unit of radiology department and compare their results before and after the initiation of COVID-19 pandemic.

Material and Methods

This retrospective study was conducted between March 2018 and March 2022, after being approved by the Research and Ethics Committee of a private University School of Medicine. All breast biopsy procedures recorded in the breast imaging unit of the radiology department between the indicated dates were scanned. The total sum was divided into two groups, where referrals before March 2020 were noted as the pre-pandemic group and after March 2020 were defined as the pandemic group.

The imaging modality used to diagnose, breast imaging reporting and data systems (BI-RADS) category of the lesion, biopsy procedure features, pathology results and the demographics of the patient population were noted. Imaging modalities used to guide biopsies consisted of breast ultrasound (US) and mammography. All patient data at the time of the referrals were scanned through the database system of the hospital and the cases were categorized upon intention of the imaging; rather screening or diagnostic

purpose. Screening group was defined as annual or biannual examinations with no symptoms or already known breast cancer patients attending to their scheduled oncologic examination. Diagnostic group was related to patients visiting the hospital for a new breast symptom. The radiologic type of the breast intervention for tissue sampling was noted, including US-guided fine needle biopsy, core-needle biopsy, wire localization or stereotactic biopsy. Ultrasound-guided core-needle biopsies were performed with 9 cm 16-gauge biopsy device (Argon medical devices SuperCore Biopsy Instrument, TX, USA) and stereotactic biopsies were performed with 10 cm long 20-gauge guide wire (Argon medical devices, Accura BLN, TX, USA). Patients who had more than one type of biopsy procedure for the same lesion were not repeatedly included in the study. Only one biopsy data was accounted for such patients: either excisional biopsy or the procedure finalized in malignancy, if present.

Data analysis was performed with statistical software (SPSS, version 20.0, IBM Company, Chicago, IL). Descriptive statistics were computed for all demographic data. Group differences were calculated by using chi-square test, independent samples t-test and Mann-Whitney U test. Statistical significance was accepted for $p < 0.05$.

Results

In total, 903 biopsy procedures were conducted in four years. The mean age was 51 (range 15 to 88 years) and women with age below 40 made 15% of the patient population. The demographics of the patients are shown in Table 1. Thirteen men were evaluated during pre-pandemic period and eight in the pandemic period, all of whom were all sampled of axillary lymph node. About 38% (n=344) of all biopsies were diagnosed malignant, where the rest 62% (n=559) was concluded in benign pathology. Seventeen lesions were reported ductal carcinoma in situ (DCIS) in the pre-pandemic group, against twenty preinvasive malignant lesions in the pandemic group (Table 2). We observed an increase in the number and ratio of malignant breast lesions during COVID-19 pandemic. However, this difference in biopsy results among two periods was not statistically significant.

The mean dimension of the breast lesions was 18 mm in the pre-pandemic period and 23 mm in the pandemic period. Biopsies scheduled due to screening referrals was 307 in the pre-pandemic period, and 261 in the pandemic period, whereas diagnostic referrals was 130 and 205, respectively. The number of ultrasound procedures used as the first step diagnosis tool was significantly higher that mammography in the pandemic period. In 12 patients US-guided fine-needle biopsy and 379 patients core-needle biopsy was performed, where the remaining had excisional biopsy including 419 patients with US-guided wire localization and 93 cases with stereotactic biopsy. The biopsy and tumor related features of the breast lesions are summarized in Table 2.

The maximum reduction in the number of biopsies during the pandemic period was observed in April 2020 (n=3), followed by May 2020 (n=15). Despite the number of reduced breast biopsies, the ratio of malignancy did not decrease (Table 3). In the first 6 months of the pandemic period, the malignancy rate was 39% and it had tendency to increase in the following intervals. When compared to the pre-pandemic era, the total number of malignant breast biopsies increased, and the malignancy rate was higher (34% vs. 39%).

Table 1. Comparison of patient demographics, referrals and imaging modalities by period

	Period		P Value
	Pre-pandemic (n=437)	**Pandemic (n=466)**	
Age (years) (mean ± SD)	52.1 ± 10.9	50.6 ± 10.1	0.528
Gender (n) (%)			
Female	424 (97%)	458 (98%)	0.072
Male	13 (3%)	8 (2%)	
Patient referral (n) (%)			
Screening	307 (70%)	261 (56%)	<0.05
Annual/biannual examination	197 (44%)	162 (35%)	
Oncological follow-up	110 (26%)	99 (21%)	
Diagnostic	130 (30%)	205 (44%)	
Imaging modality that first diagnosed the breast lesion (n) (%)			
Mammography			
Ultrasound (US	184 (38%)	131 (28%)	<0.05
	253 (57%)	335 (66%)	

Table 2. Comparison of biopsy and tumor related data by period

	Period		P Value
	Pre-pandemic (n=437) (48%)	**Pandemic (n=466) (52%)**	
Biopsy type (n) (%)			0.380
US-guided			
Fine needle aspiration	10 (2%)	2 (0.5%)	
Core-needle biopsy	179 (41%)	200 (43%)	
Wire localization	207 (47.5%)	212 (45.5%)	
Stereotactic biopsy	41 (9.5%)	52 (11%)	
Biopsy localization			
Breast tissue	412 (94%)	428 (92%)	0.151
Axilla	25 (6%)	38 (8%)	
BI-RADS category			
BI-RADS 4A	161 (37%)	98 (21%)	
BI-RADS 4B	52 (12%)	49 (10.5%)	
BI-RADS 4C	114 (26%)	135 (29%)	<0.05
BI-RADS 5	66 (15%)	119 (25.5%)	
BI-RADS 6	44 (10%)	65 (14%)	
Tumor size (mean ± SD)	18 mm (± SD)	23 mm (± SD)	0.217
Axillary lymph node invasion (n) (%)	106 (24%)	137 (29%)	0.082
Pathology (n) (%)			0.634
Benign	274 (63%)	285 (61%)	
Malignant	163 (37%)	181 (39%)	
DCIS	17 (10%)	20 (11%)	

Table 3. Biopsy volume by 6 months period in pre-pandemic and pandemic era

	Period					
	Pre-pandemic (n=437, 48%)			**Pandemic (n=466, 52%)**		
	Total	**Malignant (34%)**	**DCIS**	**Total**	**Malignant (39%)**	**DCIS**
1st 6M	94	30 (32%)	3			
2nd 6M	108	42 (38%)	5			
3rd 6M	114	44 (38%)	7			
4th 6M	121	38 (31%)	3			
5th 6M				81	32 (39%)	2
March 2020				17	5 (29%)	0
April 2020				3	1 (33%)	0
May 2020				15	7 (46%)	0
June 2020				19	7 (37%)	0
July 2020				10	4 (40%)	2
August 2020				17	6 (35%)	0
6th 6M				91	37 (40%)	4
7th 6M				144	56 (38%)	6
8th 6M				150	63 (42%)	8

* 6M: six months period

Discussion

The COVID-19 pandemic related breast cancer mortality is unknown yet and will be unclear for at least a decade. However, collateral outcomes, including pandemic-related diagnostical delays regarding breast cancer, are being reported up to date and providing insight of a probable picture of future results. In this analysis of data collected from a single center breast imaging unit of a university hospital, diagnosis of breast cancer is observed to reduce initially with the onset of COVID-19 pandemic outbreak, when compered to two years' registries prior to the pandemic and took a rapid increase after the two months of the early pandemic era.

In our study, the number of breast biopsies and diagnosed breast cancers increased soon after the spring of 2020 and got even higher than the pre-pandemic era. This finding was in line with similar published studies concerning the volume of breast cancer (3, 9). Nyante et al. reported that the reduction of biopsy volume in the pandemic period was associated with the decline in screening mammography numbers (3). We did not retrospectively evaluate the mammography size of both era before and after the pandemic initiation. However, we analyzed the medical history of patients at the time of referral and found that diagnostic intention was significantly higher in the early pandemic era compared to screening purposes.

Previous studies have shown that the impact of pandemic on delayed breast cancer diagnosis is predominantly due to interrupted screening rather than diagnostic imaging (3, 13). This would be the reason of a probable decline in the volume of early-stage breast cancer (14, 15). Our results are in opposite with the literature regarding the diagnosed early breast cancer volume, which decreased only in the early months of the COVID-19 pandemic and increased in overall 2 years' period of pandemic, compared to the pre-pandemic era. This might be the consequence of imbalance between diagnostic and screening imaging, that could have elevated the number of more advanced tumors, which presents with marked clinical symptoms, in the early pandemic and the total volume of breast cancer which showed a rapid increase right after the first summer of the pandemic. However, this is another subject to analyze that should be focused on in future studies.

Nyante et al. reported in their study that the decrease in the number of breast biopsies lagged behind the decrease in screening and diagnostic mammography (3). This might be the reason that the biopsy volume of our study in the pandemic period is higher than we expected. In the early period of the pandemic era, especially in the first 6 months, the number of breast biopsies reduced. However, in the following months an abrupt rise is observed in the biopsy volume, and the increase continued with an acceleration. Therefore, we think that the decrease of biopsies in the initial pandemic period will have consequences concerning advanced breast cancer and cancer related deaths. We don't have data to evaluate this subject, which would be a new topic of future studies.

The biopsy procedures in our breast screening unit also included axillary lymph node sampling. Axillary lump is an important referral reason of advanced breast cancer or metastasis, apart from benign etiology. Advanced disease in the pandemic period, including axillary lymph node invasion or greater tumor size, had a higher ratio in the present study. Reported delayed diagnoses in literature were not only due to postponed screening appointments or surgeries, but also pandemic related anxiety and concerns of women to undergo any procedure at the hospital, even though they had obvious clinical symptoms (9, 16). However, our results do not represent the whole patient population biopsied for axillary lymphadenopathy, because a part of this biopsy group is evaluated in our interventional radiology department. This split might be the reason of insignificant axillary lymph node related results in our study . Also, unilateral axillary lymphadenopathy reported after COVID-19 vaccination during pandemic (17) would be another reason of our insignificant but relatively higher number of axillary lymph node biopsy in the pandemic group.

We hypothesized that the total breast biopsy volume would not decrease dramatically in our hospital compared to the pre-pandemic period. The reason of this assumption was that our hospital was not declared as one of the "COVID-19 pandemic hospitals" by the national ministry of health and was assigned as one of the few "non-pandemic hospitals" in the whole city, where health services can be maintained for non-COVID patients. But our results of early pandemic period demonstrated an abrupt decrease in the number of breast biopsies. We thought that this is related to the national lockdowns, recommendations of different cancer societies and community organizations to stay home together with the fear and anxiety of hospital visits during the initiation of the pandemic.

The impact of lockdowns was prominent on the reduced rates of patient referrals to hospitals, especially for elective surgeries, non-oncological procedures and follow-up programmes. Postponing elective surgeries due to the pandemic had an effect on the relative decrease of oncological surgery rates in many countries (11). The ratio of BI-RADS 4C, BI-RADS 5 and 6 diagnoses in overall breast imaging modalities of our study presented a significant increase in the pandemic period, compared to the pre-pandemic period. This might be attributed to the decrease in screening referrals due to the will of patients to postpone their screening programmes until after the pandemic, and the increase of diagnostic presentations instead. Together with insignificant but greater size of tumor presented in the pandemic period and increased rate of axillary lymph node invasion, the number of significantly elevated BI-RADS category could be the early signs of upcoming advanced disease. Besides, the rate of oncological patients' attendance to their scheduled hospital visit had a minimal reduction in the pandemic, but with no significant difference between the two periods. We thought that this would be owing to the fact that our hospital was declared as a non-pandemic center, so that the oncology patients were encouraged to attend their follow-ups accordingly.

Major limitation of our study was the fact that the COVID-19 pandemic is still ongoing and its longterm outcomes on breast cancer cannot yet fulfilly be discussed. Future studies, especially focused on COVID-19 pandemic associated advanced breast cancer and breast cancer related deaths, should be the topics in agenda. Another limitation was the inhomogenity of the two compared groups, pre-pandemic and pandemic periods, due to the diversity of patient volume in the pandemic group that has changed with the unstable course of the disease.

Conclusion

In conclusion, this study shows that the COVID-19 pandemic had an obvious effect on the breast biopsy numbers, both in the early pandemic and later on, conversely. The implementation of our center to become a non-pandemic hospital provided some advantages, but still the breast biopsy volume decreased, especially in the lockdown period, and dramatically increased afterwards. Therefore, complete shutdown of healthcare services should be avoided in case of any future pandemic disease for routine cancer screening programmes to be maintained.

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