International Journal of Public Health Science (IJPHS)
Vol. 12, No. 1, March 2023, pp. 427~436
ISSN: 2252-8806, DOI: 10.11591/ijphs.v12i1.22525

The diagnostic value of ultrasound and mammography in detection of breast cancer in Albania

Ilirian Laçi[1], Leart Bërdica[1], Helidon Nina[1], Ilir Akshija[1], Alketa Spahiu[2], Ervin Toçi[3]
[1]Radiology and Nuclear Mecicine Service, University Hospital Center "Mother Theresa", Tirana, Albania
[2]Polyclinic of Specialties, Tirana, Albania
[3]Department of Public Health, Faculty of Medicine, University of Medicine, Tirana, Albania

Article Info

Article history:

Received Sep 22, 2022
Revised Nov 10, 2022
Accepted Nov 26, 2022

Keywords:

Breast malignancy
Core needle biopsy
Mammography
Old patient
Ultrasonography
Young patient

ABSTRACT

Early detection of breast cancer is essential for improving patient survival. However, non-invasive imaging test have different diagnostic value. This study aimed to assess the diagnostic accuracy of mammography and ultrasound to detect breast malignancy in Albania. The 234 patients suspected with breast lesions in Albania during 2018-2022 were subjected to both mammograph and ultrasound and then to core needle biopsy (CNB). The BI-RADS classification was used to evaluate breast lesions. The diagnostic value of ultrasound, mammography and their combination were assessed. Mean age of participants was 55.97 years (96.2% females). Ultrasound detected higher proportions of high-risk patients compared to mammography (79.1% vs. 52.6%, respectively) but the combination of the two increased this figure even further (88.9%). The sensitivity of mammography increased quickly with age, peaking to 93.2% among patients >60 years old, whereas ultrasound has better sensitivity among younger participants (<45 years and 45-60 years); overall, the combined tests had the highest sensitivity (95.1%), followed by ultrasound (87.4%) and mammography (59.3%). In conclusion, the sensitivity of mammography is best among older patients whereas ultrasound seems to be more accurate among younger patients. The combination of mammography and ultrasound seems to increase the diagnostic accuracy of breast tumors among Albanian patients.

Corresponding Author:

Ervin Toçi
Department of Public Health, Faculty of Medicine, University of Medicine
Rr. Dibers, Nr. 371, Tirana, Alania
Email: ervintoci@yahoo.com

1. INTRODUCTION

Breast cancer is the most common cancer in females. Every year, there are 2.3 million new cases diagnosed worldwide [1]. Initial diagnostic methods through screening programs using mammography and ultrasound have extraordinary value in early diagnosis of this disease [2]. The early diagnosis of breast cancer is extremely important and shows invaluable as the five year survival rate of women diagnosed with localized breast cancer is 99%, but it drops to 86% if the cancer is regional and to 29% for the distant forms [3].

The increase of new cases of breast tumor diagnosed necessitates the collaboration of radiologists, surgeons, oncologists, family physicians, anatomic pathologists, for the treatment of the mounting number of patients. With regard to breast cancer, the American College of Radiology standardized the system of reporting the data of breast imagining according to the breast imaging reporting and database system (BI-RADS) score [4]. The BI-RADS system, currently in its fifth edition, is an important part of the radiological report. It includes seven categories from 0 to 6 with the suspicion of malignancy increasing with the increasing

BI-RADS category [4]–[6]. Besides mammography, the BI-RADS score applies to ultrasound and MRI as well [7]. The BI-RADS score aims to support health care professionals and breast tumor patients for the diagnosis of breast lesions and pathologies through the use of a unique standardized system.

On the other hand, core needle biopsy (CNB) is considered the gold standard procedure for the diagnosis of palpable and non-palpable breast lesions [8]. However, the invasive CNB procedure requires considerably higher-level patient preparation and laboratory and medical infrastructure to be carried out compared to the non-invasive imaging examinations such as mammography and ultrasound. Therefore, any effort to assess and improve the diagnosis accuracy of non-invasive imaging could result in more resources available for other priorities and avoidance of invasive procedure for the patients.

While breast mammography and ultrasound have been identified as effective screening tools for breast lesions in the international arena, there is no information on these issues in Albania, a small post-communist country located in southeastern Europe. The country is experiencing a prolonged transition period, unavoidingly affecting the health system and health information system as well. In this context, the aim of this study was to compare the effectiveness of mammography and ultrasound in detecting breast lesions with the results of CNB in order to assess their value as screening tools for breast tumors' early detection and prevent unnecessary surgery, contributing to the more effective follow up and increased quality of care for patients with breast tumor in Albania.

2. RESEARCH METHOD

2.1. Study design

This is a study of a series of patients being referred to the University Hospital Center "Mother Theresa" in Tirana, Albania, by the radiologist doctor or at the request of the surgeon, for radiological examinations of ultrasound or mammography, or referred by the oncologist for core needle biopsy (CNB). The recruitement of patiens occurred between 2018 and 2022. During this period, a total of 234 patients (225 females and 9 males) showed up.

2.2. Radiographic imaging

All patients were submitted to ultrasound or mammography before CNB. Breast lesions were evaluated according to the BI-RADS score. CNB was carried out when requested by the surgeon, oncologist, radiologist or when disconcerting tumoral masses were noted. CNB was mandatory for the patients in the BI-RADS categories 4 and 5; however, there were cases of lower BI-RADS categories when the CNB was carried out at the request of the surgeon. All patients were applied the CNB for the first time. Besides radiological examination, all patients were submitted to clinical examination and the disease history was obtained, including breast pain, nipple discharge, breast tumoral masses, breast asymmetry, nipple retraction, adenopathy and skin change.

Mammography examinations were done using both analogue and digital mammography devices. Ultrasound examinations were also conducted using varying type of ultrasound appliances. Patients who came with an already conducted mammography where not submitted a second mammography, while the patients who came with an ultrasound were submitted to a mammography examination. The ultrasound was repeated for each patient before the biopsy procedure. Based on ultrasound, there has been an evaluation of malign tumors if it had these features: irregular contours, microlobulated, posterior shades longer than wider, irregular shape, hypoechogenic and heterogeneous lesions [5], [9], [10]. Based on mammography, the following features were considered doubtful: spiculated, microlobulated, microcalcifications and hyperdense lesions [5], [9], [10]. The BI-RADS classification was defined as follows [11]: i) BI-RADS 3 (maybe benign): ≤2% danger of malignancy; ii) BI-RADS 4A (low suspicion): >2% to ≤10% danger of malignancy; iii) BI-RADS 4B (moderated suspicion): >10% to ≤50% danger of malignancy; iv) BI-RADS 4C (high suspicion): >50% to <95% danger of malignancy; v) BI-RADS 5 (maybe malign): ≥95% danger of malignancy.

When mammography and ultrasound readings were combined, the test with the highest BI-RADS score was taken as a reference. For example, if in a patient mammography had a BI-RADS of 3 and ultrasound had a BI-RADS of 4B, then the combined BI-RADS score for this patient was set at 4B. CNB of breast tumors were conducted by the radiologist and anatomopathological evaluations were conducted by the anatomic pathologists. The CNB procedure was conducted under ultrasound guidance under the protocols of asepsis and local anesthesia using lycodine 1%. CNB was conducted with linear probe 7-12 MHz, using automatic and semi-automatic needles of 14 G. Four shots were taken, and the material was saved in 10% formalin and then sent to the laboratory of pathological anatomy. After the anatomopathological results, indications for surgery were based on the reports of CNB, radiological examinations and the recommendations of the surgeon and oncologist.

Each patient signed a consent form before the procedures, explaining in understandable language the purpose and the procedures themselves. Each patient was allocated an adequate amount of time to read the form before signing it. Every patient signed the informed consent form.

2.3. Statistical analysis

A case was regarded as True Positive when the radiology was suggestive of malignancy and the CNB also confirmed malignancy; a case was regarded as true negative (TN) when the lesions was regarded as benign in radiology and CNB; a case was regarded as false positive (FP) when radiology was suggestive for malignancy, but the CNB did not confirm it; finally, a case was regarded as false negative (FN) when radiology suggested a benign tumor, but CNB confirmed malignancy. These parameters were used to calculate sensitivity, specificity, positive predictive value and negative predictive value of the tests.

In addition, the analysis of receiver operating characteristic (ROC) was utilized to assess the effectiveness of using only mammography, only ultrasound, and mammography combined with ultrasound to predict the malignity of the breast, as indicated by the area under the curve (AUC). In addition, the precision-recall curve (PRC) was constructed in order to further check the validity of the imaging tests.

The Spearman’s rho coefficient was used to assess bivariate correlations. The students t-test was used to compare the mean values of a numeric variable across categories of categorical variables. All analysis has been carried out through the IBM SPSS Statistics, version 26.

3. RESULTS AND DISCUSSION

In total 234 patients with breast lesions were included: 225 females (96.2%) and 9 males (3.8%). The average age of patients was 55.97 years ±13.51 years, ranging from 23.9 years to 83.5 years. No gender differences were noticed with regard to age (mean age of females: 55.91 years ±13.48 years, mean age of males 57.54 years ±14.71 years, P=0.722). About one quarter of patients were younger than 45 years old at the moment of the examinations, 30.8% were 45-60 years old and 44% were older than 60 years. The average tumor size was 29.04 mm ±11.62 mm, ranging from 10 mm to 62 mm. All patients were subjected to mammography, ultrasound and then CNB as presented in Table 1. CNB was positive for malignant tumors in 182 patients or 77.8% of all participants.

Table 1. Basic characteristics of participants

Variable	Number	Percentage
Total	234	100.0
Sex		
Female	225	96.2
Male	9	3.8
Age in years (mean ± standard deviation)	55.97±13.51	
Age-group		
<45 years old	59	25.2
45-60 years old	72	30.8
>60 years old	103	44.0
Tumor size in mm (mean ± standard deviation)	29.04±11.62	
Mammography Yes	234	100.0
Ultrasound Yes	234	100.0
Core needle biopsy Yes	234	100.0

Table 2 shows the distribution of BI-RADS scoring from mammography and ultrasound examination of breast among participants. If we consider BI-RADS scores of 3-4A as indicating low malignancy risk and BI-RADS scores of 4B-4C-5 as indicating a high malignancy risk, then it can be noted that ultrasound results in higher proportions of high-risk scores compared to mammography (79.1% vs. 52.6%, respectively) and these differences are significant. However, the combination of mammography with ultrasound yields even higher proportions of high-risk scores (88.9%), which exceeds the respective figures produced by ultrasound alone and mammography alone. A significant positive moderate correlation was noticed between the two methods of examination, based on Spearman`s rho coefficient of 0.325; p<0.001. This result was further confirmed by a low level of agreement beyond chance between mammography and ultrasound (Kappa statistic=0.182; p<0.001), indicating slight yet significant agreement.

Table 2. Mammography and ultrasound BI-RADS score among participants

Variable	Number	Percentage
Mammography BI-RADS score		
3	79	33.8
4A	32	13.7
4B	6	2.6
4C	54	23.1
5	63	26.9
Ultrasound BI-RADS score		
3	26	11.1
4A	23	9.8
4B	10	4.3
4C	67	28.6
5	108	46.2
Mammography + Ultrasound		
3	11	4.7
4A	15	6.4
4B	12	5.1
4C	76	32.5
5	120	51.3

Table 3 shows the sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of mammography, ultrasound and the mammography-ultrasound combination compared to CNB results. It can be noticed that the sensitivity of ultrasound is superior compared to that of mammography (87.4% vs. 59.3%, respectively) in diagnosing malignant lesions in patients with BI-RAIDS score of 4B-4C-5. However, the sensitivity of mammography increases rapidly and considerably with age, ranging from 2.6% among patients younger than 45 years old, to 44.6% among those aged 45-60 years old and peaking to 93.2% among patient older than 60 years; ultrasound has its highest sensitivity (100%) among patients aged 45-60 years old and it diminishes with increasing age. The specificity of mammography is always higher than ultrasound whereas PPV of both tests are similar among patients of all ages. When mammography is combined with ultrasound, then the sensitivity is highest (95.1%), but the specificity results very low (at 32.7%), whereas the PPV and NPV are comparable to mammography and ultrasound alone, among all patients.

Table 3. Diagnostic value of mammography and ultrasound for malignant breast lesions

Imaging test	Age	Sensitivity (%, 95% CI) *	Specificity (%, 95% CI)	Positive predictive value (%, 95% ci)	Negative predictive value (%, 95% ci)
Mammography	All ages	59.3 (51.8-66.5)	71.2 (56.9-82.9)	87.8 (80.7-93.0)	33.3 (24.7-42.9)
	<45 years	2.6 (0.7-13.8)	85.7 (63.7-96.9)	25.0 (0.6-80.6)	32.7 (20.7-46.7)
	45-60 years	44.6 (31.3-58.5)	75.0 (47.6-92.7)	86.2 (68.3-96.1)	27.9 (15.3-43.7)
	>60 years	93.2 (85.8-97.5)	46.7 (21.3-73.4)	91.1 (83.3-96.1)	53.8 (25.1-80.8)
Ultrasound	All ages	87.4 (81.6-91.8)	50.0 (35.8-64.2)	85.9 (80.1-90.6)	53.1 (38.3-67.5)
	<45 years	84.2 (68.8-94.0)	42.9 (21.8-66.0)	72.7 (57.2-85.0)	60.0 (32.3-83.7)
	45-60 years	100.0 (93.6-100)	50.0 (24.6-75.4)	87.5 (76.9-94.5)	100.0 (63.1-100)
	>60 years	80.7 (70.9-88.3)	60.0 (32.3-83.7)	92.2 (83.8-97.1)	34.6 (17.2-55.7)
Mammography and ultrasound	All ages	95.1 (90.8-97.7)	32.7 (20.3-47.1)	83.2 (77.4-88.0)	65.4 (44.3-82.8)
	<45 years	84.2 (68.8-94.0)	28.6 (11.3-52.2)	68.1 (52.3-80.9)	50.0 (21.1-78.9)
	45-60 years	100.0 (93.6-100)	37.5 (15.2-65.6)	84.8 (73.9-92.5)	100.0 (54.1-100)
	>60 years	96.6 (90.4-99.3)	33.3 (11.8-61.6)	89.5 (81.5-94.8)	62.5 (24.5-91.5)

*Mammography and ultrasound BI-RADS dichotomized into low malignancy risk (score 3-4A) and high malignancy risk (score 4B-4C-5).

There was a strong positive significant correlation between the age of the patients and mammography BI-RADS score (Spearman's rho 0.813, p<0.001), whereas this association was moderate for the combined mammography-ultrasound BI-RADS score (Spearman's rho 0.411, p<0.001) and weaker for ultrasound BI-RADS score (Spearman's rho 0.237, p<0.001). The size of the tumor was moderately positively and significantly associated with mammography, ultrasound and combined BI-RADS scores (Spearman's rho 0.451, 0.368, 0.371, respectively, p<0.001 in all cases) as presented in Table 4.

Table 4. Bivariate correlations between age and tumor size with BI-RADS scores of imaging tests

Test	Mammography BI-RADS	Ultrasound BI-RADS	Mammography + Ultrasound BI-RADS
Age (years)	0.813 (<0.001) *	0.237 (<0.001)	0.411 (<0.001)
Tumor size (mm)	0.451 (<0.001)	0.368 (<0.001)	0.371 (<0.001)

*Spearman's rho coefficient and p-value (in parentheses)

In order to better understand the diagnostic value of mammography and ultrasound and their combination, receiver operating characteristic (ROC) curve was run and the results are shown in Table 5. Judging from the area under the curve, the combination of mammography and ultrasound seems a better test compared to mammography alone or ultrasound alone.

Table 5. Area under the ROC curve

Test result variable	Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
Mammography BI-RADS	0.710	0.036	<0.001	0.639	0.782
Ultrasound BI-RADS	0.825	0.032	<0.001	0.763	0.888
Mammography + Ultrasound BI-RADS	0.846	0.030	<0.001	0.786	0.906

The ROC curve as shown in Figure 1 confirms that ultrasound is better than mammography, and both tests can distinguish affected patients significantly better than just guessing. A mammography BI-RADS score higher than 4A is associated with a 59.3% sensitivity and 71.2% specificity; the corresponding sensitivity and specificity for ultrasound are 87.4% and 50%, whereas for the combination of both tests the respective figures are 95.1% and 32.7%. A mammography BI-RADS score higher than 4B is associated with a 57.7% sensitivity and 76.9% specificity; the corresponding sensitivity and specificity for ultrasound are 86.3% and 65.4%, whereas for the combination of both tests the respective figures are 94% and 51.9%.

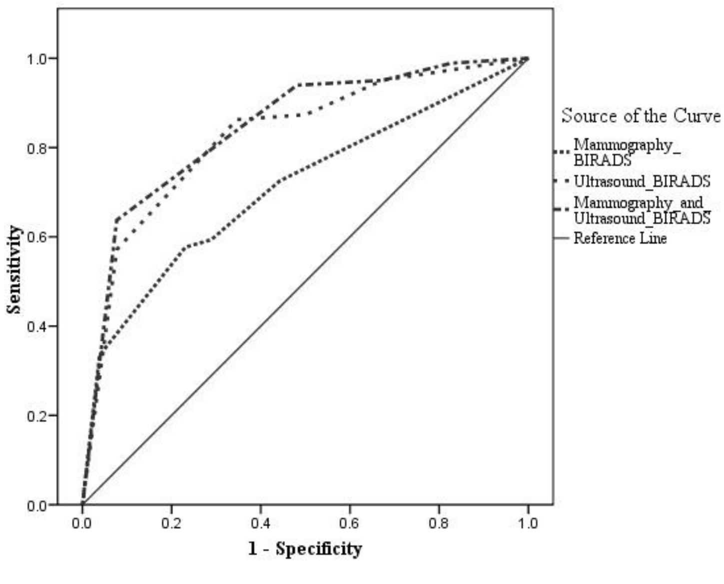

Figure 1. ROC Curve for mammography, ultrasound and mammography + ultrasound of malignant breast lesions

Based on coordinates of the precision-recall curve (PRC), again it seems that the combination of mammography with ultrasound is superior to both ultrasound and mammography alone since the mammography-ultrasound PRC is closer to the upper right corner compared to the separate ultrasound and mammography PRCs as shown in Figure 2. A mammography-ultrasound BI-RADS score higher than 4A is associated with a 95.1% sensitivity and 83.2% precision (PPV). The corresponding sensitivity and PPV for ultrasound are 87.4% and 85.9% and for mammography 59.3% and 87.8%.

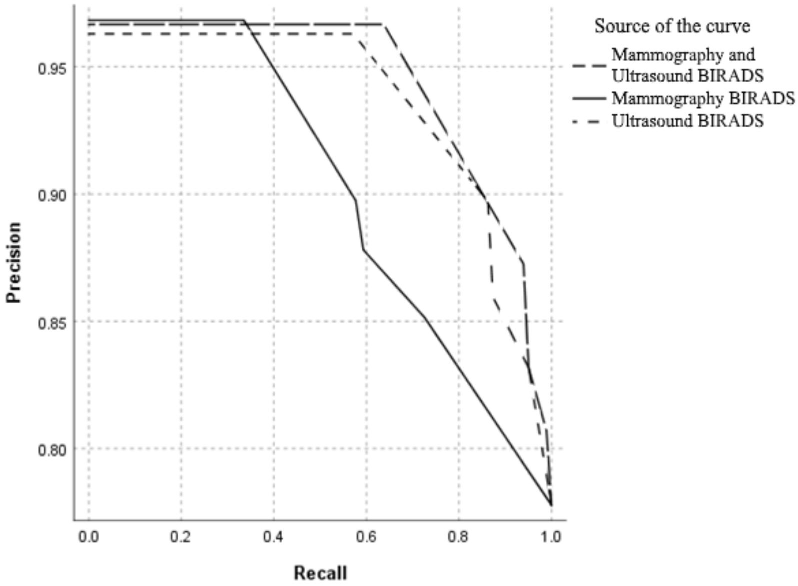

Figure 2. Precision-recall curve for mammography, ultrasound and mammography + ultrasound of malignant breast lesions

During breast tissue biopsy, minor complications (such as pain) were detected in three patients or 1.3% of all participants. Pain was controlled with the application of analgesics, orally administered, and these patients were kept under observation for about one hour. This is the first study reporting the validity parameters (sensitivity, specificity, positive predictive value and negative predictive value) of mammography, ultrasound and the combination of both methods in patients (both men and women) with breast symptoms and lesions in Albania. The actual findings suggest that, overall, the combination of mammography with ultrasound, provides the highest sensitivity (95.1%) compared to ultrasound alone (87.4%) or mammography alone (59.3%) for the correct detection of high-risk breast lesions (BI-RADS score 4B-4C-5); however, combining mammography and ultrasound results in a much lower specificity (32.7%) compared to ultrasound (50%) or mammography (71.2%) alone. Sensitivity of the tests varies significantly with age, with ultrasound having higher sensitivity among younger patients (<45 years and 45-60 years) whereas mammography had a higher sensitivity in patients >60 years old. The combination of mammography and ultrasound resulted in a higher sensitivity than each separate test for any age group. However, the specificity of ultrasound and especially of the combined test, was lower than that of mammography. There was a moderate significant correlation between mammography and ultrasound (Spearman's rho 0.325) and a slight, yet significant, agreement beyond chance (Kappa statistic 0.182, p<0.001) between the two tests. The mammography BI-RADS score was strongly positively and significantly increased with age, whereas the associations of ultrasound and combined test BI-RADS scores with age were weak to moderate. The associations with the tumor size were moderate, positive and significant for all the three tests. Overall, the findings of this study suggest that the combination of mammography and ultrasound is more useful in diagnosing malign breast tumors compared to each method separately.

Our findings are in general in concordance with previously published literature. For example, a study in Kosovo that compared the accuracy of mammography and ultrasound among 546 women with breast symptoms, reported that ultrasound had a higher sensitivity than mammography in younger women (<45 years) whereas mammography's sensitivity was superior to ultrasound in women older than 60 years [12]. In Kosovo the sensitivity of ultrasound and mammography was 72.6% and 52.1%, respectively [12], findings that are similar to our figures (87.4% and 59.3%, respectively). However, the specificity of ultrasound and mammography in the Kosovo study was 88.5% and 73.9%, respectively [12], whereas the corresponding figures in our study were lower: 50% and 71.2%, respectively.

In another study of 210 patients with breast masses, the sensitivity of mammography, ultrasound and their combination were 72.6%, 68.9% and 84.9%, respectively, whereas the corresponding specificity was

43.9%, 48.6% and 43% [13]. The especially low specificity of ultrasound in our study could be explained by a number of factors but, to our opinion, the most important factor could be the insufficient training of the professionals conducting ultrasound examinations in Albania. The specialization in diagnostic imaging is limited to a few seats per academic year at the premises of University Hospital Center "Mother Theresa"; for example, only five seats were available during the 2018-2019 academic year, even though lately this number has increased to about 10 per year. On the other hand, there is no information on how individuals get such training abroad or other certified (or not) providers within the country, and the quality of later trainings is also unknown.

As explained in the methodology section, the patients included in our study came with already conducted mammography and ultrasound, and only CNB was performed in the premises of UHC "Mother Theresa". Since ultrasound and mammography tests have been conducted largely by different professionals, then the low specificity of these tests (especially ultrasound) could reflect the inter-observer differences: the professionals conducting ultrasound examination might have been too "eager" to detect a breast cancer or they might have been in doubt about the mass detected by ultrasound and marked it as "positive" in order to be definitively checked by needle biopsy. Other reasons for the low specificity of ultrasound might include the body composition of patients, i.e. in obese patients ultrasound could be more problematic [12], [14]. Another reason for the low ultrasound specificity could be the advanced stage of the patients examined: among 234 patients, 77.8% of them had a CNB confirmation of malignancy; this means that the prevalence of the disease is very high among our study population. Given that generally the specificity tends to be lower when the prevalence of the disease is higher [15], then this could partly explain the low specificity of ultrasound in our study. As a conclusion to this point, more research is needed to highlight the reasons behind the low specificity of breast lesions ultrasound in Albania. For example, a qualitative study could be designed to explore in depth why and based on what criteria the imaging professionals refer a woman (or a man) for diagnostic imaging tests, including subjective and personal dimensions involved in the process; this could be accompanied by a quantitative study that might compare readings of different such professionals and assess the inter-observer reliability.

On the other hand, the fact that a considerable proportion of patients with breast lesions in Albania are relatively young (<45 years old) might point out to the inadequateness of prevention efforts, a sub-optimal effectiveness of information and awareness raising campaigns in Albania as well as an inadequate training of health care staff at all levels of the heatlh system to suspect and/or detect breast lesions. These elements constitute a serious clinical and public health concern with a high impact on affected individuals in Albania.

One the most important challenges of researchers is determining which method is most effective to examine breast tumors. Currently, protocols recommend women over 40 to undergo mammography. However, this method has its own limitations. For example, mammography is insufficient for women with more dense breasts, because the sensitivity during examination diminishes due to the increased density of the glandular tissue, while women with increased glandular tissue have higher risk to breast cancer [10], [16]; in these cases, the doctor that interprets the mammography plays a crucial role [17], [18]. Therefore, the recommendation is to combine mammography with ultrasound to be able to better detect breast tumors, including those not detected by mammography [14], [19]–[21].

Other studies confirm that the combination of ultrasound and mammography increases the diagnostic accuracy of breast tumors [13], [22]. Combining mammography and ultrasound in breast cancers increased the sensitivity from 62% (mammography only) to 81% in women with dense breasts [22]. Meanwhile, in the patients that had had a mammography, but also had an ultrasound, it was noted that the sensitivity jumped from 74% to 79 % [19], [22].

The accuracy of the BI-RADS is debatable. The BI-RADS system is useful to discern malign and benign tumors, but its scale of accuracy is still debatable given the varied experience of radiologists. The classification itself has differences [22]. In essence, BI-RADS is a radiological classification and as such it does not take into account some important clinical or prognostic factors [23]. Furthermore, the BI-RADS system of classification has a high level of inter- and intra-observer variability, especially with regard to BI-RADS 3-4 categories, with the BI-RADS category 3 showing the most inter-observer variability [23]–[25]. Such errors could result from the inability to detect a lesion, especially in dense breast, the mis-interpretation of a detected lesion, and the tendency to classify benign changes as BI-RADS category 4 or 5 or wrongly considering suspicious lesions as benign [24]. The actual study highlighted some of these issues, given the variations of validity parameters (sensitivity, specificity, positive and negative predictive value) across imaging tests. Despite these fluctuations, this study suggested that the combination of both breast mammography with breast ultrasound increases the diagnostic accuracy of breast tumors. Lastly, even though it has its own limitations, the BI-RADS classification system constitutes and important element of quality assurance in imaging examination and for the interpretation and communication of the results (through the standardization of mammographic reports) [23], [26].

The use of ultrasound evaluation helps distinguishing malign and benign lesions of the breast by limiting the number of CNBs. In BI-RADS 3 lesions, where the danger of malignity is under 2%, there is a recommendation of a six-month follow up with ultrasound, but also mammography when that is deemed reasonable [27], [28]. In the case of BI-RADS 4 lesions, which are doubtful, CNB is recommended. CNB is also recommended for BI-RADS 5 lesions, spiculated lesions and/or lesions with pleomorphic calcification [29]. Complications during the CNB procedure are minimal and very rare [30], when the procedure is done by experienced interventional radiologists.

4. CONCLUSION

The combination of mammography and ultrasound seems to increase the diagnostic accuracy of breast tumors among Albanian patients. It is indispensable to further train the radiologists in Albania and strengthen their skills in reading radiological images and standardize the language they use to classify breast lesions. In addition, there is need for comprehensive interventions to raise the awareness of the public and health professionals about prevention and early detection of breast lesions.

REFERENCES

[1] H. Sung *et al.*, "Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries," *CA: A Cancer Journal for Clinicians*, vol. 71, no. 3, pp. 209–249, 2021, doi: 10.3322/caac.21660.

[2] C. Duggan *et al.*, "The Breast Health Global Initiative 2018 Global Summit on Improving Breast Healthcare Through Resource-Stratified Phased Implementation: Methods and Overview," *Cancer*, vol. 126, no. S10, pp. 2339–2352, 2020, doi: 10.1002/cncr.32891.

[3] A. C. Society, "Survival Rates for Breast Cancer," *American Cancer Society*, 2019. https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-survival-rates.html.

[4] K. Pesce, M. B. Orruma, C. Hadad, Y. B. Cano, R. Secco, and A. Cernadas, "BI-RADS terminology for mammography reports: What residents need to know," *Radiographics*, vol. 39, no. 2, pp. 319–320, 2019, doi: 10.1148/rg.2019180068.

[5] D. A. Spak, J. S. Plaxco, L. Santiago, M. J. Dryden, and B. E. Dogan, "BI-RADS ® fifth edition: A summary of changes," *Diagnostic and Interventional Imaging*, vol. 98, no. 3, pp. 179–190, Mar. 2017, doi: 10.1016/j.diii.2017.01.001.

[6] T. V. Bartolotta *et al.*, "S-Detect characterization of focal solid breast lesions: a prospective analysis of inter-reader agreement for US BI-RADS descriptors," *Journal of Ultrasound*, vol. 24, no. 2, pp. 143–150, 2021, doi: 10.1007/s40477-020-00476-5.

[7] American College of Radiology, "Breast imaging reporting and data system (BI-RADS)," *American College of Radiology*. https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Bi-Rads.

[8] G. Sauer *et al.*, "Ultrasound-guided large-core needle biopsies of breast lesions: Analysis of 962 cases to determine the number of samples for reliable tumour classification," *British Journal of Cancer*, vol. 92, no. 2, pp. 231–235, 2005, doi: 10.1038/sj.bjc.6602303.

[9] V. Y. Park, E. K. Kim, H. J. Moon, J. H. Yoon, and M. J. Kim, "Evaluating imaging-pathology concordance and discordance after ultrasound-guided breast biopsy," *Ultrasonography*, vol. 37, no. 2, pp. 107–120, 2018, doi: 10.14366/usg.17049.

[10] P. E. Freer, "Mammographic breast density: Impact on breast cancer risk and implications for screening," *Radiographics*, vol. 35, no. 2, pp. 302–315, 2015, doi: 10.1148/rg.352140106.

[11] R. M. Strigel *et al.*, "Utility of BI-RADS assessment category 4 subdivisions for screening breast MRI," *American Journal of Roentgenology*, vol. 208, no. 6, pp. 1392–1399, 2017, doi: 10.2214/AJR.16.16730.

[12] E. Devolli-Disha, S. Manxhuka-Kërliu, H. Ymeri, and A. Kutllovci, "Comparative accuracy of mammography and ultrasound in women with breast symptoms according to age and breast density," *Bosnian Journal of Basic Medical Sciences*, vol. 9, no. 2, pp. 131–136, 2009, doi: 10.17305/bjbms.2009.2832.

[13] N. Ghaemian, N. H. G. Tehrani, and M. Nabahati, "Accuracy of mammography and ultrasonography and their BI-RADS in detection of breast malignancy," *Caspian Journal of Internal Medicine*, vol. 12, no. 4, pp. 573–579, 2021, doi: 10.22088/cjim.12.4.573.

[14] D. Thigpen, A. Kappler, and R. Brem, "The role of ultrasound in screening dense breasts - A review of the literature and practical solutions for implementation," *Diagnostics*, vol. 8, no. 1, 2018, doi: 10.3390/diagnostics8010020.

[15] M. M. G. Leeflang, A. W. S. Rutjes, J. B. Reitsma, L. Hooft, and P. M. M. Bossuyt, "Variation of a test's sensitivity and specificity with disease prevalence," *CMAJ. Canadian Medical Association Journal*, vol. 185, no. 11, 2013, doi: 10.1503/cmaj.121286.

[16] A. S. Tagliafico *et al.*, "Adjunct screening with tomosynthesis or ultrasound in women with mammography-negative dense breasts: Interim report of a prospective comparative trial," *Journal of Clinical Oncology*, vol. 34, no. 16, pp. 1882–1888, 2016, doi: 10.1200/JCO.2015.63.4147.

[17] A. Fanizzi *et al.*, "Ensemble Discrete Wavelet Transform and Gray-Level Co-Occurrence Matrix for Microcalcification Cluster Classification in Digital Mammography," *Applied Sciences*, vol. 9, no. 24, p. 5388, Dec. 2019, doi: 10.3390/app9245388.

[18] L. Losurdo *et al.*, "Radiomics analysis on contrast-enhanced spectral mammography images for breast cancer diagnosis: A pilot study," *Entropy*, vol. 21, no. 11, 2019, doi: 10.3390/e21111110.

[19] W. Buchberger, S. Geiger-Gritsch, R. Knapp, K. Gautsch, and W. Oberaigner, "Combined screening with mammography and ultrasound in a population-based screening program," *European Journal of Radiology*, vol. 101, pp. 24–29, 2018, doi: 10.1016/j.ejrad.2018.01.022.

[20] W. A. Berg *et al.*, "Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk," *Jama*, vol. 307, no. 13, pp. 1394–1404, 2012, doi: 10.1001/jama.2012.388.

[21] M. Rebolj, V. Assi, A. Brentnall, D. Parmar, and S. W. Duffy, "Addition of ultrasound to mammography in the case of dense breast tissue: Systematic review and meta-analysis," *British Journal of Cancer*, vol. 118, no. 12, pp. 1559–1570, 2018, doi: 10.1038/s41416-018-0080-3.

[22] J. M. Lee *et al.*, "Performance of Screening Ultrasonography as an Adjunct to Screening Mammography in Women Across the Spectrum of Breast Cancer Risk," *JAMA Internal Medicine*, vol. 179, no. 5, pp. 658–667, 2019, doi:

10.1001/jamainternmed.2018.8372.
[23] C. Balleyguier, S. Ayadi, K. Van Nguyen, D. Vanel, C. Dromain, and R. Sigal, "BIRADS™ classification in mammography," *European Journal of Radiology*, vol. 61, no. 2, pp. 192–194, 2007, doi: 10.1016/j.ejrad.2006.08.033.
[24] B. Boyer, S. Canale, J. Arfi-Rouche, Q. Monzani, W. Khaled, and C. Balleyguier, "Variability and errors when applying the BIRADS mammography classification," *European Journal of Radiology*, vol. 82, no. 3, pp. 388–397, 2013, doi: 10.1016/j.ejrad.2012.02.005.
[25] W. A. Berg *et al.*, "Does training in the breast imaging reporting and data system (BI-RADS) improve biopsy recommendations or feature analysis agreement with experienced breast imagers at mammography?," *Radiology*, vol. 224, no. 3, pp. 871–880, 2002, doi: 10.1148/radiol.2243011626.
[26] L. Levy, M. Suissa, J. F. Chiche, G. Teman, and B. Martin, "BIRADS ultrasonography," *European Journal of Radiology*, vol. 61, no. 2, pp. 202–211, 2007, doi: 10.1016/j.ejrad.2006.08.035.
[27] J. Heinig, R. Witteler, R. Schmitz, L. Kiesel, and J. Steinhard, "Accuracy of classification of breast ultrasound findings based on criteria used for BI-RADS," *Ultrasound in Obstetrics & Gynecology*, vol. 32, no. 4, pp. 573–578, 2008, doi: 10.1002/uog.5191.
[28] K. A. Lee, N. Talati, R. Oudsema, S. Steinberger, and L. R. Margolies, "BI-RADS 3: Current and Future Use of Probably Benign," *Current Radiology Reports*, vol. 6, no. 2, 2018, doi: 10.1007/s40134-018-0266-8.
[29] E. Elverici *et al.*, "Nonpalpable BI-RADS 4 breast lesions: Sonographic findings and pathology correlation," *Diagnostic and Interventional Radiology*, vol. 21, no. 3, pp. 189–194, 2015, doi: 10.5152/dir.2014.14103.
[30] W. Bruening, J. Fontanarosa, K. Tipton, J. R. Treadwell, J. Launders, and K. Schoelles, "Systematic review: Comparative effectiveness of core-needle and open surgical biopsy to diagnose breast lesions," *Annals of Internal Medicine*, vol. 152, no. 4, pp. 238–246, 2010, doi: 10.7326/0003-4819-152-1-201001050-00190.

BIOGRAPHIES OF AUTHORS

Ilirian Laçi is a radiologist working in the University Hospital Center "Mother Theresa" in Tirana, Albania. He has a long experience in radiological imaging and applying of new imaging techniques. He can be contacted at email: ilirianlaci@yahoo.com.

Leart Bërdica is anatomopathologist working in the University Hospital Center "Mother Theresa" in Tirana, Albania. He can be contacted at email: leartberdica@gmail.com.

Helidon Nina is an oncosurgeon working in the University Hospital Center "Mother Theresa" in Tirana, Albania. He can be contacted at email: ninahelios@yahoo.com.

Ilir Akshija is a bioinformatician and biostatistician working in the University Hospital Center "Mother Theresa" in Tirana, Albania. He can be contacted at email: iakshija@yahoo.com.

Alketa Spahiu currently works in the Polyclinic of Specialities No. 3, in Tirana, Albania. She can be contacted at email: keti.spahiu@yahoo.com.

Ervin Toçi is a medical doctor trained in public health. Actually, he works in the Department of Public Health, Faculty of Medicine, University of Medicine in Tirana, Albania. He can be contacted at email: ervintoci@yahoo.com.