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Comparison of Internal Mammary Artery and Lateral Thoracic Artery Width in Patients with Benign and Malignant Breast Tumors

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: The main objective of this study was to analyze the differences in ipsilateral and contralateral internal mammary artery (IMA) and lateral thoracic artery (LTA) width in patients with malignant and benign breast tumor.

Materials and Methods: A total of 104 female patients, of which 41 had benign and 63 had malignant tumors, were included in the study. The diameters of the IMA and LTA were measured from the widest point in T1-weighted post-contrast images. Breast magnetic resonance images were evaluated by a breast radiologist.

Results: The ipsilateral IMA diameter of cases in the malignant group was found to be statistically significantly higher when compared with the benign group. In the benign group, the ipsilateral IMA diameter being an average of 0.43±0.87 mm larger than the contralateral IMA diameter was found to be statistically significant, whereas in the malignant cases, the ipsilateral IMA diameter being an average of 0.78±1.08 mm larger than the contralateral IMA diameter was found to be statistically significant. Also, in benign cases, the ipsilateral LTA diameter being an average of 0.31±0.70 mm larger than the contralateral LTA diameter was found to be statistically significant, whereas in malignant cases, the ipsilateral LTA diameter being an average of 0.29±0.68 mm larger than the contralateral LTA diameter was found to be statistically significant.

Conclusion: The IMA and LTA diameters in benign and malignant cases were found to be higher in comparison with contralateral breast, independent of the size of the lesion.

Keywords: Artery, breast, MRI, tumor

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INTRODUCTION

Proliferation in the adjacent vascular network is required in all cancer types to feed the tumor (1, 2). As a result of angiogenic and lymphangiogenic substances released by the tumor cells, new vessels and lymphatic structures are formed (3). This condition is called angiogenesis and lymphangiogenesis, respectively. In this way, the tumor can both grow and metastasize via the lymphatics or vessels to distant tissues. The tumor cell growth and metastatic spread occur in this manner in breast cancer, which is the most common type of cancer seen in women today. There are two main vascular structures feeding the breast called the internal mammary artery (IMA) and lateral thoracic artery (LTA), and the growth and spread of tumor cells occur via these vessels. Benign tumors such as fibroadenomas are frequently seen in the breast in addition to malignant tumors. These benign tumors also require vascular structures to feed. In our study, we measured the widest point of these two vessels using magnetic resonance imaging (MRI), in cases diagnosed with breast cancer or fibroadenoma by biopsy and compared with the vessel diameters of contralateral breast without lesions. We also investigated the relationship between the size of the lesion, the vascular diameter, and the quadrant where the lesion is located. The aim of our study was to demonstrate angiogenesis or increased vascular dimension ipsilateral to the benign or malignant breast lesion when compared with the side without lesion.

MATERIALS and METHODS

This retrospective study was conducted at the radiology department of a tertiary university hospital, between 2013 and 2016. A total of 104 women aged between 21 and 80 years (mean age of 48.91±12.60 years) who had biopsy-proven malignant lesions on breast MRI (BIRADS 6) or had biopsy-proven fibroadenoma on breast MRI (BIRADS 2) were included in this study. The study was approved by the local ethics commity and signed consent was obtained from the patients. Patients who had tumor only on one breast were also included in this study. The contralateral breasts were BIRADS 1. Signed consent was obtained from all participants. MR images of lesions were evaluated by a breast radiologists blind to the breast lesions. Only the largest dimensions of IMA and LTA were measured. If results differed, then the images were re-evaluated together and a consensus was reached. Fol-

lowing the measurement, the breast lesions were evaluated (size, location), and patients were classified as BIRADS 6 and BIRADS 2 according to histopathology results and then the two groups were compared. Before the MRI, the histopathological diagnosis of the lesions was conducted with biopsies taken by our interventional radiologists using 14-G needles, guided by ultrasonography.

Patients were scanned on a 1.5-T MR scanner (Intera, Philips Medical Systems, Best, The Netherlands) using a dedicated double-breast surface coil with the patient in the prone position. An axial three-dimensional high-resolution T1-weighted fast gradient echo fat-suppressed sequence (TE/TR 2.4/4.6 ms; inversion delay spectral presaturation attenuated by inversion recovery (SPAIR) 90 ms; flip angle 10°; FOV 360×360 mm^2, acquired voxel size 0.9×0.9×2.5 mm^3, reconstructed voxel size 0.83×0.83×2.50 mm^3, total acquisition time 60 s) was performed before administration of the contrast agent, followed by repeat performance of this same sequence at 0, 1, 2, 3, 4, 5, and 7 min after administration of contrast agent of 0.1 mmol/kg gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA).

An additional axial T2-weighted fat suppressed spin echo sequence (TE/TR 110/7548 ms; inversion delay SPAIR 80 ms; flip angle 90°; FOV 380×380 mm^2, acquired voxel size 1.06×1.74×3.0 mm^3, reconstructed voxel size 0.94×0.94×3.00 mm^3, total acquisition time 242 s) was performed before the administration of contrast material. Post-contrast three-dimensional T1-weighted fast gradient-echo dynamic MR images were acquired.

On these post-contrast T1-weighted sequences, lesion dimensions and the dimensions of ipsilateral and contralateral IMA and LTA were measured (Figure 1).

Exclusion Criteria

- Prior history of breast cancer and prior history of chemotherapy/ radiotherapy for breast
- Prior history of breast surgery (breast conserving or radical mastectomy/breast augmentation, etc.)
- Prior history of bypass surgery
- Tumors in both the breasts
- Presence of anastomosis with opposite IMA

Statistical analysis

Number Cruncher Statistical System (NCSS 2007, Kaysville, Utah, USA) software was utilized for statistical analysis. When evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, median, frequency, minimum, maximum), Student's t-test was used for the comparison of two groups of quantitative data growing normal distribution. In the comparison of three or more groups not showing normal distribution, Kruskal-Wallis test was used, and in the determination of the group causing the difference, Mann-Whitney U test was used. Paired-samples t-test was used in the comparison of groups with variables showing normal distribution. Wilcoxon signed ranks test was used in comparison of groups without normal distribution. Spearman correlation analysis was used in the evaluation of relationships within variables. Significance was considered at a level of $p<0.01$ and $p<0.05$.

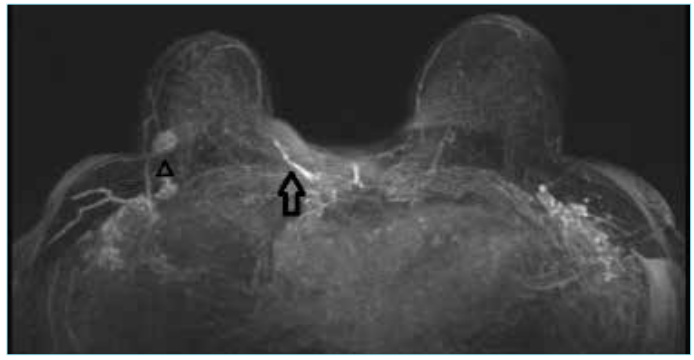

Figure 1. Axial postcontrast MIP T1-weighted MRI sequence. Right breast invasive ductal cancer (arrowhead). Increased dimensions of right internal mammary artery (thick arrow) and lateral thoracic artery (thin arrow)

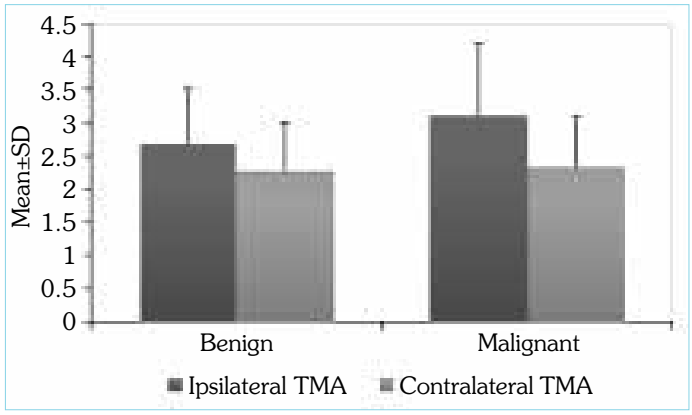

Figure 2. Ipsilateral and contralateral internal mammary artery diameter distributions of benign and malignant lesions

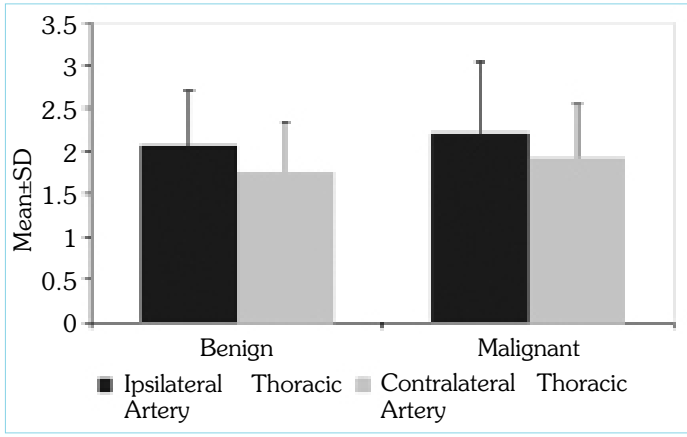

Figure 3. Ipsilateral and contralateral thoracic artery diameter distributions of benign and malignant lesions

RESULTS

Magnetic resonance imaging examinations were carried out on a total of 104 female cases, aged between 21 and 80 years, with a mean age of 48.91±12.60 years.

While 1% (n=1) of lesions of cases were found to be inflammatory cancer, 39.4% (n=41) were fibroadenoma, 4.8% (n=5) were ductal cancer in situ, 47.1% (n=49) were invasive ductal cancer, 2.9% (n=3)

Table 1. Distribution of descriptive characteristics

		Min-Max	Avg±Sd
Age [years]		21-80	48.91±12.60
Lesion size [mm^2]		16-1920	318.52±394.73
Ipsilateral IMA Diameter [mm]:		1.2-5.7	2.94±0.99
Ipsilateral Thoracic Artery Diameter [mm]		0.6-5.0	2.14±0.77
Contralateral IMA Diameter [mm]		0.9-4.6	2.30±0.76
Contralateral Thoracic Artery Diameter [mm]		0.6-3.8	1.84±0.62
		n	%
Lesion	Inflammatory CA	1	1.0
	Fibroadenoma	41	39.4
	Ductal CA In Situ	5	4.8
	Invasive Ductal CA	49	47.1
	Invasive Lobular CA	3	2.9
	Medullar CA	2	1.9
	Papillary CA	2	1.9
	Tubular CA	1	1.0
Location	Lower Outer Quadrant	18	17.3
	Lower Inner Quadrant	7	6.7
	Upper Outer Quadrant	37	35.6
	Upper Inner Quadrant	11	10.6
	Retroareolar area	31	29.8
Breast Side	Right	58	55.8
	Left	46	44.2

IMA: internal mammary artery

were invasive lobular cancer, 1.9% (n=2) medullary cancer, 1.9% (n=2) were papillary cancer, and 1% (n=1] were tubular cancer.

The tumor locations of 17.3% (n=18) cases were lower outer quadrant, 6.7% (n=7) cases were lower inner quadrant, 35.6% (n=37) cases were upper outer quadrant, 10.6% (n=11) cases were upper inner quadrant, and 29.8% (n=31) cases were retroareolar. While 55.8% (n=58) tumor were observed in the right breast, 44.2% (n=46) were observed in the left breast. The lesion size differed between 16 and 1920 mm^2 with a mean of 318.52±394.73 mm^2 (Table 1).

The ipsilateral IMA diameter of cases in the malignant group were found to be statistically significantly higher when compared with the benign group ($p<0.05$) (Figure 2).

No statistically significant difference was determined between contralateral IMA diameters between malignant and benign group cases ($p>0.05$).

In the benign cases, the ipsilateral IMA diameter being an average of 0.43±0.87 mm larger than the contralateral IMA diameter was found to be statistically significant ($p<0.01$), whereas in the malignant cases, the ipsilateral IMA diameter being an average of 0.78±1.08 mm larger than the contralateral IMA diameter was found to be statistically significant ($p<0.01$).

No statistically significant difference were determined between ipsilateral LTA diameters in the malignant and benign group cases ($p>0.05$) (Figure 3) and between contralateral LTA diameters in the malignant and benign group cases ($p>0.05$).

In the benign cases, the ipsilateral LTA diameter being an average of 0.31±0.70 mm larger than the contralateral LTA diameter found to be statistically significant ($p<0.01$), whereas in the malignant cases, the ipsilateral LTA diameter being an average of 0.29±0.68 mm larger than the contralateral LTA diameter was found to be statistically significant ($p<0.01$).

No statistically significant relationship was found between the lesion size and ipsilateral IMA, ipsilateral LTA diameter, contralateral IMA, and contralateral LTA diameter measurements of benign group cases ($p>0.05$) and between the lesion size and ipsilateral IMA, ipsilateral LTA diameter, contralateral IMA, and contralateral LTA diameter measurements of malignant group cases ($p>0.05$).

In the lower outer quadrant lesion cases, the ipsilateral IMA diameter being an average of 1.01±1.17 mm larger than the contralateral IMA diameter was found to be statistically significant ($p<0.01$), whereas in the upper outer quadrant lesion cases, the ipsilateral IMA diameter being an average of 0.56±1.02 mm larger than the contralateral IMA diameter was found to be statistically significant ($p<0.01$). Also, in the retroareolar lesion cases, the ipsilateral IMA diameter being an average of 0.72±0.92 mm larger than the contralateral IMA diameter was found to be statistically significant ($p<0.01$).

In the upper outer lesion cases, the ipsilateral LTA diameter being an average of 0.45±0.70 mm larger than the contralateral LTA diameter was found to be statistically significant ($p<0.01$), whereas in the retroareolar lesion cases, the ipsilateral LTA diameter being an average of 0.38±0.61 mm larger than the contralateral LTA diameter was found to be statistically significant ($p<0.01$).

DISCUSSION

The breast is supplied by two major vascular structures. The most important of these vascular structures is the IMA, which is a branch of the internal thoracic artery and which reaches the medial sides of breasts running along each side of the sternum. The other main vascular structure is the LTA, which is a branch of the axillary artery reaching the breast from the outer half (4). For the tumor cells to grow and metastasize by hematogenesis, adjacent vascular networks must proliferate. From tumor cells, certain angiogenic activators are released, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), angiogenin, transforming growth factor (TGF)-α, TGF-β, tumor necrosis factor (TNF)- α, platelet-derived endothelial growth factor, and epidermal growth factor (5, 6). These provide neoproliferation. Tumors may become necrotic without these substances, and hence sufficient vascular support is needed (7, 8). These vascular networks, allowing the growth of benign tumors and the growth

and metastasis of malignant tumors, can be blocked through various methods. It has been observed in clinical studies that antiangiogenic drugs added to chemotherapy and radiotherapy give positive results (9). In interventional radiology, treatment is also carried out by placing chemotherapeutic agents into these vascular structures or by thrombosing these vascular structures feeding the tumor.

In our study, we have evaluated the lesions dimensions, locations, and ipsilateral and contralateral IMA and LTA diameters of cases with malignant or benign breast lesions in a single breast. Previous studies have been carried out on this subject. Studies comparing whether vascularization in the breast with lesion is increased in comparison with the contralateral breast through subjective methods without measuring vessel diameters are in the majority (10-12). In a study by Kang et al. (11) it has been observed that vascularization has increased globally in the breast with lesion; however, vascular diameter has not been addressed, and only malignant cases were included in the study. In a study by Schmitz et al. (10) the number of patients was relatively small, and again general breast vascularization was considered.

In a study carried out by Schipper et al. (13) in 2012, diameters were measured as in our study. Their study differs from ours in measurements being made of the IMA diameter before reaching the breast through the intercostal space, not considering LTA diameters, and including only malignant lesions in the study.

We included both benign and malignant lesions in our study. We observed that the IMA and LTA diameters were increased on the tumor side compared with contralateral breast in both benign and malignant tumors. This leads us to consider that even benign tumors can proliferate vascular networks to feed.

The diameter increase of IMA is higher in the malignant group than in the benign group. We are aware that angiogenesis is stimulated when tumor tissues require nutrients and oxygen. We are aware that this requirement is higher in malignant cases and carry out more aggressive angiogenesis. We are also aware that angiogenesis rate also shows prognosis (14, 15). Interestingly; no statistically significant difference was determined between ipsilateral LTA diameters between malignant and benign group cases. No matter benign or malignant, all tumors feed from LTA in a certain point, but malignant tumors seem to feed more from IMA than LTA. This could be explained by the relatively small size of LTA. Maybe its increase in size could not be distinguished by current imaging methods, and the small size caused some measurement errors. This could be clarified with higher number of study groups and inter-reader agreement.

No statistically significant difference between diameter increase and lesion size was found. We can see that small lesions can have more pronounced angiogenesis in comparison with larger tumors. This situation may be due to the lesion having a higher likelihood of malignancy or having shown rapid growth. In this context, it is necessary to know how much of a size increase has occurred in a period of time. As follow-up cannot be carried out in malignant cases, this cannot be considered; however, the diameter increase and IMA/LTA diameter increase rate can be compared with MRI examinations carried out at regular intervals.

When considering the lesion location, we can see that lesions in the upper outer quadrant and retroareolar area have an increased diameter of both IMA and LTA. We believe that more significant results can be found with more patients.

Our limitations can be considered as, relatively low number of patients, only vascular dimension evaluation but not the dimension's increase rate in a specific time and relatively small size of LTA which can cause measurement errors. Also, the largest site at which the vessels are measured could be different between readers. It would have been useful to obtain an inter-reader agreement.

CONCLUSION

Benign and malignant tumors grow by proliferation of adjacent vascular networks. In our study, we showed that in cases with breast tumor (no matter benign or malignant), the diameters of main feeding vessels (IMA and LTA) are increased in the side with tumor in comparison with the side without tumor. If these vascular structures that feed the tumors are inhibited through various methods, the growth and metastasis risk of the lesion will decrease. In this context, we believe that antiangiogenetic drugs or vascular interventional methods will have more of a place in treatment in the future.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Maltepe University Hospital.

Informed Consent: Written informed consent was obtained from patients/ who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Conceived and designed the experiments or case: GA.,LÇ. Performed the experiments or case: GA. Analyzed the data: RÇ., LÇ., MMA. Wrote the paper: GA. All authors have read and approved the final manuscript.

Conflict of Interest: No conflict of interest was declared by the authors.

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