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CONCORDANCE BETWEEN RADIOLOGICAL IMAGING MODALITIES AND HISTOPATHOLOGICAL EXAMINATION OF BREAST CANCER

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Abstract

Radiological assessment and histopathological evaluation are among the critical tools for breast cancer diagnosis and staging. This study interrogates the concordance between computed tomography (CT) imaging and histopathological measurements for staging breast cancers. This prospective observational study, conducted at Jinnah Medical Postgraduate Center (JMPC), Karachi, Pakistan, enrolled female patients with a minimum age of 18 years, histologically proven breast carcinoma, no history of recent breast excision or post-neoadjuvant chemotherapy. Among the 293 patients enrolled, ethnicity of majority patients was Urdu Speaking (n = 144, 49.1%), followed by Sindhi (n = 10, 38.6%), Punjabi (n = 27, 9.2%), and Pathan (n = 08, 2.7%). Moreover, 295 (97.3%) patients were married, 176 (60.1%) were postmenopausal, 108 (36.9%) were of age 51-60 years, 281 (95.9%) were house-wives, and 275 (93.9%) patients presented with invasive ductal carcinoma (IDC) breast. The number of breast cancer patients presented with tumor size T1 and T2, as classified with CT and histopathology studies was (107 vs. 95) and (129 vs. 139), while the N0 and N1 nodal status was (207 vs. 118) and (86 vs. 122), respectively. The number of patients with TNM stage of 1A, 2A, 3A, 1B and 2B as evaluated with CT and histopathology was (70 vs. 33), (117 vs. 49), (0 vs. 40), (0 vs. 36) and (10 vs. 115) patients, respectively. These results indicate substantial discordances between CT imaging and histopathology in the assessment of tumor size, nodal status and TNM stage of breast cancer.

Keywords: NCCN, TNM Staging, MRI, Mastectomy, Tumor Size.

1. INTRODUCTION

Radiological assessment and histopathological evaluation are among the critical tools for breast cancer diagnosis and staging. However, these two modalities belong to distinct medical specialities and their findings are independently reported [1]. Specifically, histopathological studies are not only the gold standard for breast cancer diagnosis, but also complement the findings from radiological studies in establishing stage of the disease, partially by providing an acceptable explanation for the imaging features [2]. Moreover, histopathalogy typically evaluates the disease status from a limited/ local tissue sample, while the radiological studies provide extensive characterization of the disease in locoregional organs and beyond [3]. Taken together, these differences between histopathalogy and radiological studies have important clinical implications [4]. To

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exemplify, concordance between histopathalogy and different types of radiological modalities remains a fundamental question, both for the basic research arena and clinical applications. Selection of treatment protocol is governed by the stage of breast cancer, which is, in turn, primarily associated with the size of tumor and status of lymph nodes [5]. However, stage of the disease change with only small decrements/ increments in tumor size. Beside the change in tumor size as *per se*, a significant confusion regarding the measured tumor size may arise from a difference between radiological imaging and histopathological measurements [6]. Such a mismatch in tumor size between the two major tools of tumor size measurement can lead to complication in disease staging and consequently to potential over or under treatment of the patient [7]. This emphasize the need for a high concordance between radiological imaging and histopathological measurements towards reaching an accurate decision for the disease staging and thereby appropriate oncological intervention. This study interrogates the concordance between radiological imaging and histopathological measurements for staging breast cancers. In particular, the radiological imaging employed were computed tomography (CT), because of its high resolution and precise nature. For disease staging purpose, both the tumor size and nodal status were assesses (and compared) with both CT and histopathology. Moreover, the overall CT-pathologic concordance was also evaluated with the TNM stage of the breast cancer.

2. MATERIALS AND METHODS

2.1 Study design

This prospective observational study was conducted at the Medical Oncology Department of Jinnah Medical Postgraduate Center (JMPC), Karachi from January to December, 2022. Institutional Review Board (IRB) of JMPC, Karachi assessed and approved this study. All patients, prior to enrollment, signed an informed consent, with the liberty of consent withdrawal at any time.

2.2 Inclusion and exclusion criteria

Patient’s eligibility criteria for inclusion were composed of: adult Pakistani female population with a minimum age of 18 years, histologically proven invasive breast carcinoma diagnosed via core needle biopsy, surgical excision (lumpectomy or mastectomy), no history of recent excision in the same breast and pre-operative radiological imaging performed at the study institution. The exclusion criteria consisted of: patients with benign lesions or only carcinoma in situ, younger than 18 years, pregnant women, mentally retarded patients, receiving post-neoadjuvant chemotherapy, recurrent disease, and non-availability of preoperative imaging.

2.3 Data collection

OpenEpi was utilized for sample size determination with the following variables: a 5% margin of error, 95% confidence level and 29% expected discrepancy for tumor stage in radiology studies. A non-probability consecutive sampling technique was utilized for

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recruitment of eligible patients, with data of each patient recorded on a predesigned questionnaire. More specifically, the questionnaire contained the following three sections: demographics (i.e., age, parity, gravidity, menopausal status, marital status), radiological imaging findings (i.e., tumor size, nodal status, and distant metastasis), and histopathological findings (i.e., gross tumor size, foci, and pathological staging). For both the radiological imaging and histopathology, the largest tumor dimension were considered and recorded. The above variables from the radiology and pathology were compared to identify any discrepancies.

2.4 Data analysis

Data analyses were performed in SPSS package. Paired t-test and Mann-Whitney test were employed for evaluating differences in tumor size, nodal status, TNM stage and focality as identified between radiological imaging and histopathology, with $p < 0.05$ was considered as statistically significant. Mean and standard deviations were also determined and compared.

3. RESULTS

The total number of patients enrolled were 293, all were female. Demographics of these patients are summarized in Table 1. The ethnicity of majority patients was Urdu Speaking (n = 144, 49.1%), followed by Sindhi (n = 10, 38.6%), Punjabi (n = 27, 9.2%), and Pathan (n = 08, 2.7%). This ethnic distribution of patients is a reflection of general population of Karachi, Pakistan. Moreover, 295 (97.3%) patients were married, 176 (60.1%) were postmenopausal, 281 (95.9%) were house-wives, and 275 (93.9%) patients presented with invasive ductal carcinoma (IDC) breast.

Table 1: Summary of patient's demographics (n = 293)

Demographics		Number of patients (%)
Ethnicity	Sindhi	113 (38.6)
	Urdu speaking	144 (49.1)
	Punjabi	27 (9.2)
	Pathan	08 (2.7)
	Others	01 (0.4)
Marital Status	Married	285 (97.3)
	Unmarried	08 (2.7)
Number of children	0	14 (4.8)
	1	12 (4.1)
	2	30 (10.2)
	3	212 (72.4)
	4	18 (6.1)
	5	6 (2.0)
	6	1 (0.4)
Menopausal	Premenopausal	117 (39.9)
	Postmenopausal	176 (60.1)
Profession	House wife	281 (95.9)
	Employed	12 (4.1)
Histopathology	Invasive ductal carcinoma	275 (93.9)
	Others	18 (6.1)

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The age distribution of patients is shown in Figure 1. It may be noted that the highest number of patients presented in the age group 51-55 years, followed by 56-60 years group. The minimum number of patients were from the young age (i.e., ≤ 30 years), followed by the older patients of >70 years. Overall, the age distribution of patients followed an almost normal distribution.

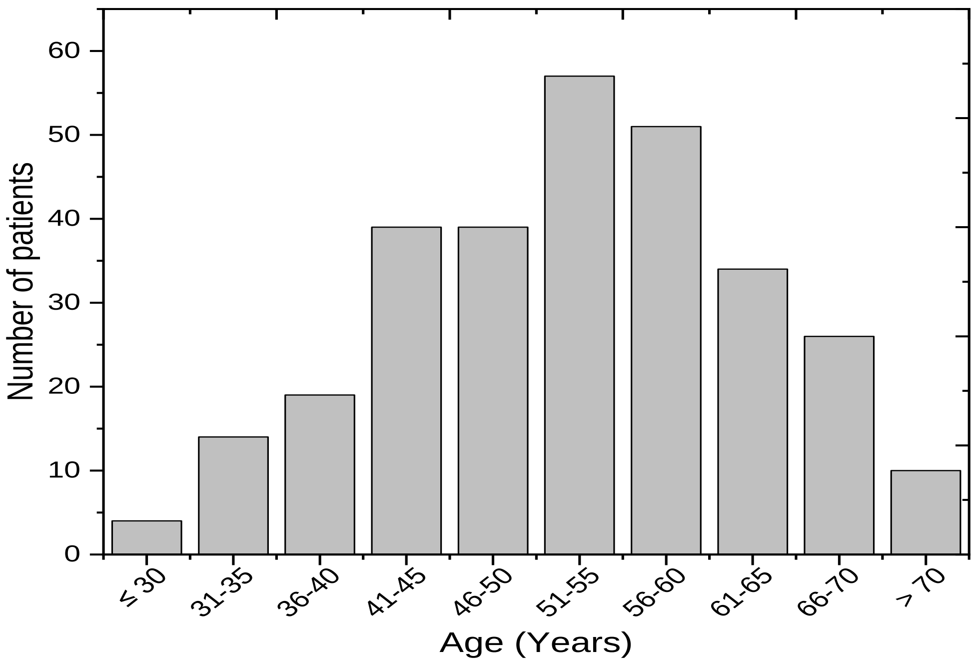

Fig 1: Age distribution of the patients (n = 293)

TNM classification was followed to classify the tumor size (into T1, T2 and T3), nodal status (N0, N1, N1m, and N3), and distant metastasis (M0 and M1), for both the computed tomography and histopathology. This was followed by determining the overall TNM stage of the breast cancer. A comparison of tumor size, nodal status and overall TNM stage of the breast cancer as determined from the radiological imaging (i.e., CT scan) and histopathology is shown in Table 2. Substantial discordances were observed between the two tumor evaluation approaches, both in terms of tumor size and nodal status. Specifically, the number of breast cancer patients presented with tumor size of T1, T2 and T3, as classified with CT and histopathology studies was (107 vs. 95), (129 vs. 139) and (57 vs. 59), respectively. This discordance was significant with $p < 0.001$. The concordance between the CT and histopathology was also determined for involvement of lymph nodes by the disease. The N0, N1, N1m and N2 nodal status was evaluated with CT and histopathology was (207 vs. 118), (86 vs. 122), (0 vs. 37) and (0 vs. 16) patients, respectively. Again, this discordance for nodal infiltration by the disease was highly significant with $p < 0.0001$. These differences in the tumor size and lymph node status rendered contrast in the TNM staging as determined with CT and histopathology. In particular, the number of patients with TNM stage of 1A, 2A, 3A, 1B and 2B as evaluated

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with CT and histopathology was (70 vs. 33), (117 vs. 49), (0 vs. 40), (0 vs. 36) and (10 vs. 115) patients, respectively. In addition to CT imaging, mammography was also performed in 276 (94%) patients. It was interesting to note that all these patient had Breast Imaging Reporting and Data System (BI-RADS) scores ≈ 6.

Table 2: Comparison of tumor size, nodal status and overall TNM stage of the breast cancer as determined from the computed tomography and histopathology

Tumor status	Computed tomography study		Mammography	Histopathology	p value
Tumor size	T1	107	Performed in 276 patients All patient had Breast Imaging Reporting and Data System (BI-RADS) scores ≈ 6	95	0.00098
	T2	129		139	
	T3	57		59	
Nodal status	N0	207		118	<0.0001
	N1	86		122	
	N1m			37	
	N2			16	
Metastasis	M0	293		293	
	M1	0		0	
Overall TNM stage	1A	70		33	<0.001
	2A	117		49	
	3A	0		40	
	1B	0		36	
	2B	10		115	
The tumor size, nodal status and metastasis are given as per TNM staging criteria					

4. DISCUSSION

In this study, we investigated the concordance between radiological and histopathological studies for the quantitative evaluation of TNM stage in patients with breast cancer. Comparisons of tumor size, nodal status and TNM stage from CT imaging and histopathology demonstrated significant discordance, illustrating differences in the capability of the two tumor characterization techniques to detect and measure the spatial extent of tumor in breast cancer patients. Since the tumor size is an integral element for disease staging, these observations have important clinical implications during decision making. Although pathologic assessment is the gold standard, surgical decision for tumor excision (e.g., lumpectomy versus mastectomy) is determined by radiologic tumor size. Moreover, radiological tumor size is imperative for planning and delivery radiation therapy and anticipated cosmetic outcomes.

Although CT imaging is used to evaluate liver and pulmonary metastases in breast cancer [8], [9], limited studies have reported its predictive value for the evaluation of tumor size. This may be attributed to the fact that routine use of CT (chest) imaging in operable patients of breast cancer is not recommend by the present guidelines. Moreover, radiation dose received by the breast and other healthy tissues during CT imaging is also a concern, particularly in younger patients [10]. Studies have documented a radiation dose of 28 mSv for the patient undergoing breast CT examination [11]. To elaborate, the

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radiation dose received during a standard mammography imaging is 2.8 mSv-approximately 10 times lower than that of CT imaging [12].

As opposed to ultrasound and magnetic resonance imaging (MRI), a relatively limited number of studies are available on the use of CT (chest) imaging to determine tumor size in breast cancer. Nevertheless, studies have reported a positive correlation between tumor sizes quantified with pathology (gold standard) and CT (chest) imaging, with 80% of tumors sizes differing by <5 mm [13]. The CT imaging along with a dedicated protocol for breast cancer staging was developed and compared with MRI [14]. The results showed substantial agreement between the two imaging tools, indicated by higher values of Kappa coefficient for evaluation of tumor extension, nipple invasion, multicentricity, presence of multifocality, and skin invasion. Moreover, both methods demonstrated similar correlation with tumor size and T staging on pathology [14]. Other studies have also reported good correlation of tumor size on CT images with pathological tumor size [15]. Despite these studies reporting promising results, the sensitivity of CT imaging to identify the intraductal involvement by breast cancer has been questioned [16].

In addition to CT, findings from other radiological imaging and histopathology of breast tumors have been correlated in multiple studies. In particular, the breast tumor size was assessed and compared with these two techniques. To exemplify, spatial extension of the tumor as determined with MRI was correlated with pathologic size [17]. Concordance of tumor size determined with ultrasound and histopathology has also been assessed in breast cancer [18]. The correlation coefficient for tumor size between ultrasound and pathology ranges in 0.45-0.92 [19], [20]. These studies concluded that tumor size is typically underestimated by ultrasound while overestimated by MRI [21]. Consequently, a combination of utilizing both ultrasound and MRI was suggested to ensure higher accuracy in measuring tumor size [22]. Moreover, ultrasound, MRI and mammography were also compared with histopathology for the assessment of tumor size in breast cancer, which revealed correlation coefficients of 0.76, 0.67, and 0.75, respectively [23], [24]. Comparison of ultrasound and mammography in combination with MRI alone for tumor size measurements showed higher accuracy of MRI alone in 32.9% of patients [25].

5. CONCLUSIONS

This study illustrates a high discordance between CT imaging and histopathology in the assessment of breast cancer. Although CT imaging was capable for characterization of breast cancer tumors, large discrepancies were revealed when compared with histopathology. Specifically, the tumor size, nodal status and TNM stage were determined with both CT imaging and histopathology, followed by an objective comparison. The results showed significant underestimation of tumor size, nodal status and TNM stage by CT imaging. The results indicate that the spatial extent of breast cancer tumor and lymph nodes involvements as determined with CT imaging may significantly under-estimate the TNM staging of the disease, thereby affecting the optimal management.

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