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ASSESSMENT OF BACKGROUND PARENCHYMAL ENHANCEMENT AT DYNAMIC CONTRAST-ENHANCED MRI IN PREDICTING BREAST CANCER RECURRENCE RISK

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ABSTRACT

Introduction: Potential as a prognostic tool for breast cancer recurrence risk is the evaluation of background parenchymal enhancement (BPE) using dynamic contrast-enhanced (DCE) MRI. BPE has been identified as a possible marker of therapy responsiveness and disease aggressiveness, reflecting the vascular and hormonal milieu of breast tissue. This research uses information from DCE-MRI scans to assess how well BPE values predict the probability of breast cancer recurrence.

Methodology: The retrospective cohort study was conducted and included fifty eligible participants, diagnosed with breast cancer and undergoing MRI between January and December 2023. Data on demographics, clinical features, and MRI results were collected from medical records of a Tertiary Care hospital in Pakistan. BPE was quantitatively assessed using an in-house algorithm, and statistical analysis included descriptive statistics, logistic regression, and Cox proportional hazards regression. MRI protocols followed standard procedures. The study aimed to assess the prognostic value of BPE in guiding personalized breast cancer treatment and risk stratification.

Results: The research highlights the wide age representation with an average participant age of 48.5 years (±7.2 years). The fact that premenopausal state accounted for 65% of participants is noteworthy and highlights the importance of hormonal status in breast cancer research and treatment approaches. There was a significant degree of heterogeneity in the tumor's size and grade, with an average tumor size of 3.8 cm (±1.2 cm) and a heterogeneous distribution across grades. Treatment choices were guided by the results of a hormone receptor status study, which showed prevalence rates of estrogen receptor (ER) positive at 37%, progesterone receptor (PR) positive at 52%, and HER2 positive at 11%. The majority of treatment options for breast cancer were surgery, chemotherapy, and radiation therapy, which demonstrated the interdisciplinary nature of breast cancer care. The results of the

follow-up showed a 20% recurrence rate, underscoring the significance of risk stratification according to Oncotype DX scores. greater BPE readings were linked to a greater likelihood of high-risk recurrence scores. The results of MRI, in particular, showed a substantial correlation with recurrence risk. The predictive efficacy of BPE evaluation was further highlighted by Cox proportional hazards regression analysis, indicating its potential prognostic relevance in clinical practice.

Conclusion: Our research shows a strong relationship between breast cancer recurrence risk and BPE in DCE-MRI. We discovered significant differences in tumor features, hormone receptor status, and treatment modalities after analyzing a heterogeneous sample, underscoring the difficulty in managing breast cancer. Elevated BPE levels were linked to heightened chances of high-risk recurrence scores, indicating the predictive significance of BPE evaluation for customized therapy and risk classification. Recurrence prediction and patient outcomes may be improved by incorporating BPE examination into clinical practice.

Keywords: breast cancer recurrence, DCE MRI, BPE, risk stratification, personalized treatment

INTRODUCTION

The most prevalent illness in the world and the primary reason for cancer-related mortality in women is breast cancer [1]. As such, it remains a serious global health concern. Patients with breast cancer now have far better results because of developments in tailored therapy, early diagnosis, and treatment methods. However, problems still exist, especially in low- and middle-income nations [2] like Pakistan, where socioeconomic inequalities, cultural norms, and restricted access to healthcare services all lead to delayed diagnosis and inadequate treatment [3, 4]. It is essential to comprehend the epidemiology, risk factors, and prognostic indicators of breast cancer in order to create preventative and treatment plans that are successful and meet the requirements of a variety of populations.

Breast cancer is a complex illness with variable tumor biology, clinical presentation, and response to therapy. Among the established risk variables include exposure to the environment, hormones, age, genetics, and lifestyle [5]. Furthermore, three molecular subtypes of breast cancer hormone receptor-positive, HER2-positive, and triple-negative breast cancer (TNBC) show distinct biological traits and respond differently to treatment [6]. Optimizing patient outcomes requires the discovery of prognostic indicators that may reliably predict the recurrence of a disease and inform therapy choices.

Numerous studies have examined the utilization of imaging biomarkers to inform individualized treatment plans and forecast the possibility of recurrence of breast cancer. DCE-MRI has shown to be a helpful method for assessing tumor characteristics, treatment response, and risk stratification in patients with breast cancer [7]. In particular, since BPE represents physiological changes in the breast tissue, it has attracted attention as a potential prognostic marker for the return of breast cancer [8]. Increased risk of illness recurrence has been linked to greater BPE levels in many investigations, underscoring the need of integrating BPE testing into standard clinical practice [9].

Breast cancer is a significant public health issue in Pakistan, where there are an estimated 90,000 new cases annually [10]. Pakistani women are more likely to have late-stage diagnoses and have worse outcomes because of limited access to healthcare facilities, cultural taboos around breast health, and low knowledge of breast cancer screening [2-4, 11, 12]. The prevalence of breast cancer in the nation is further increased by disparities in healthcare resources and infrastructure. Notwithstanding these obstacles, initiatives are being made in Pakistan to raise awareness of breast cancer, expand access to screening programs, and provide treatment services [12]. Nonetheless, there is still a pressing need for studies to clarify the etiology, prognostic factors, and epidemiology of breast cancer among Pakistani people.

Improving patient prognosis and lifespan requires early detection of cancer [13]. The particular potential and difficulties in breast cancer research and management have been brought to light by recent studies carried out in Pakistan. Malik et al.'s research [14] looked at the clinicopathological traits and survival rates of Pakistani patients with breast cancer, and the results showed that the

country's various areas had diverse treatment inequalities and unique patterns of disease presentation [15]. The study carried out by Khan and colleagues investigated the frequency of molecular subtypes of breast cancer among women in Pakistan, underscoring the need of customized treatment approaches grounded on tumor biology [14]. These results highlight the need to carry out research tailored to the unique demands and difficulties experienced by Pakistani breast cancer patients.

Objective

This study's main goal was to assess the prognostic value of BPE seen in DCE MRI in terms of forecasting the likelihood of breast cancer recurrence.

MATERIALS AND METHODS

Study Design

The predictive efficacy of BPE at DCE-MRI in predicting the probability of breast cancer recurrence was evaluated in this research using a retrospective cohort design conducted at a hospital in Pakistan.

Participants

Participants were chosen from a group of patients who visited Tertiary Care Hospital for breast MRI exams between January 2023 and December 2023. Patients with histologically confirmed breast cancer who had received breast MRI for surveillance or staging were included in the inclusion criteria. Patients with bilateral breast cancer, prior breast surgery, insufficient medical records, or neoadjuvant chemotherapy recipients were among the exclusion criteria. Fifty individuals in all fulfilled the inclusion criteria and were included in the study.

Data Collection

Electronic medical records included information on clinical data, MRI scan results, and demographics. Once each patient's Oncotype DX recurrence score was obtained, they were categorized as either low- or intermediate-risk (recurrence score $\leq$25) or high-risk (recurrence score >25). A computer method developed in-house for both breasts was used to automatically calculate the quantitative BPE.

Electronic medical records included demographic and clinical data, including age, menopausal status, tumor features, treatment history, and follow-up results. Trained radiologists blinded to patient outcomes evaluated MRI scans to determine BPE levels.

MRI Protocol

The MRI exams were conducted utilizing a specialized breast coil on an MRI machine. The acquisition of DCE MRI sequences followed a defined procedure, which included obtaining pre-contrast T1-weighted sequences followed by repeated post-contrast sequences at specific time intervals after the injection of a gadolinium-based contrast agent.

Assessment of BPE

A computer method created in-house was used to acquire quantitative BPE readings. The relationship between BPE and the Oncotype DX recurring score which was classified into high-, low, and intermediate-risk categories was investigated using multivariate logistic regression. The models' capacity to discriminate between individuals at both high and low or moderate risk was tested using both the real recurrence result and BPE measures.

Statistical Analysis

SPSS version 23 was used to carry out the statistical analysis. Patients' characteristics and MRI scan findings were clearly explained using descriptive statistics. The researchers investigated the relationship among BPE and Oncotype DX recurrence score categories using univariable logistic regression. In order to assess the relationship between BPE and the chance of breast cancer recurrence

while accounting for any confounding variables, the research employed Cox proportional hazards regression models.

Ethical Considerations

The Declaration of Helsinki's guiding principles were adhered to in the conduct of this study. The review board of the institution gave the research its ethical approval, and since it was a retrospective investigation, consent that was informed was not necessary.

RESULTS

The research included a cohort of patients with a range of clinical and demographic features, offering insights on a number of variables related to the prognosis and therapy of breast cancer. The research population's age distribution was represented by the participants' average age of 48.5 years, which had a standard deviation of 7.2 years. Menopausal status was also taken into account; of the participants, 39 were classified as pre-menopausal, accounting for 65% of the sample, and 21 as post-menopausal, making up 35% of the cohort. This distribution emphasizes how crucial it is to take hormonal state into account when designing research and treatment plans for breast cancer.

Tumor features, particularly size and grade, were important parameters of interest in the investigation. There was variation in the tumor sizes across the subjects, with an average size of 3.8 cm and a standard deviation of 1.2 cm. With 12 tumors categorized as Grade 1 (20%), 30 tumors as Grade 2 (50%), and 18 tumors as Grade 3 (30%), the tumor grading exhibited a heterogeneous distribution, highlighting the different nature of the malignancies within the cohort and their possible implications for prognosis and treatment strategy.

Important information about the molecular features of the tumors was supplied by the hormone receptor status, which includes the estrogen receptor (ER), progesterone receptor (PR), and HER2 status. 22 (37%) of the subjects were found to be ER positive, 31 (52%), and 7 (11%) to be PR positive. These results provide insight into the research population's frequency of hormone receptor expression and HER2 amplification, two important factors that influence therapy choice and prognosis in breast cancer.

The individuals' treatment histories showed a range of therapeutic approaches to breast cancer management. Of all the therapy modalities, surgery was the most often used one, with 35 individuals (58%), having surgery. Additionally, 19 (32%) and 6 (10%) individuals had radiation therapy and chemotherapy, respectively. This emphasizes the interdisciplinary nature of breast cancer treatment and the variety of therapeutic approaches used in clinical practice.

Regarding disease recurrence and risk classification based on the Oncotype DX recurrence score, the follow-up results were very informative. Twelve of the patients had a disease recurrence, which translates to a 20% recurrence risk. Additionally, based on the Oncotype DX score, 20 patients were classified as high risk, and 40 people as low or intermediate risk, highlighting the significance of risk stratification in directing therapy choices and post-treatment care approaches.

Finally, MRI results were evaluated as possible markers of disease aggressiveness and likelihood of recurrence, with a focus on BPE. With a standard deviation of 3.5 and a mean BPE of 12.4, the results provide important new information on the imaging properties of breast tissue and their possible effects on the prognosis and treatment of the illness.

Table 1: Descriptive Statistics of Demographic and Clinical Baseline Characteristics

Characteristic	Variables	N	%
Age (years)	Mean ± SD	48.5 ± 7.2	
Menopausal Status	Pre-menopausal	39	-65%
	Post-menopausal	21	-35%
Tumor Characteristics			
Size (cm)	Mean ± SD	3.8 ± 1.2	
Grade	I	12	-20%

	II	30	-50%
	III	18	-30%
Hormone Receptor Status	ER Positive	22	37
	PR Positive	31	52
	HER2 Positive	7	11
Treatment History	Surgery	35	58
	Chemotherapy	19	32
	Radiation Therapy	6	10
Follow-Up Outcomes	Recurrence Rate	12	-20%
	Time to Recurrence: 24 months (median, range)		
	High Risk (n)	20	
	Low or Intermediate Risk (n)	40	
MRI Findings			
BPE	Mean BPE ± SD	12.4 ± 3.5	

Figure 1 displays the Cox proportional hazards regression analysis of BPE and breast cancer recurrence risk in addition to the relationship between BPE readings and Oncotype DX recurrence score categories. The odds ratio for BPE Measure 1 in the univariable logistic regression was 1.75, meaning that the probability of having a high-risk Oncotype DX recurrence score rose by 1.75 times for every unit rise in BPE Measure 1. Similarly, BPE Measure 2 showed the strongest correlation with increased recurrence risk, with the greatest odds ratio of 2.2. BPE Measure 1 showed a hazard ratio of 1.62 in the Cox proportional hazards regression analysis, suggesting that patients with greater BPE Measure 1 had a 1.62 times higher risk of breast cancer recurrence than those with lower BPE Measure 1. The hazard ratios of 1.89 and 1.73, respectively, for BPE Measures 2 and 3 likewise showed their relative contributions to the risk of breast cancer recurrence.

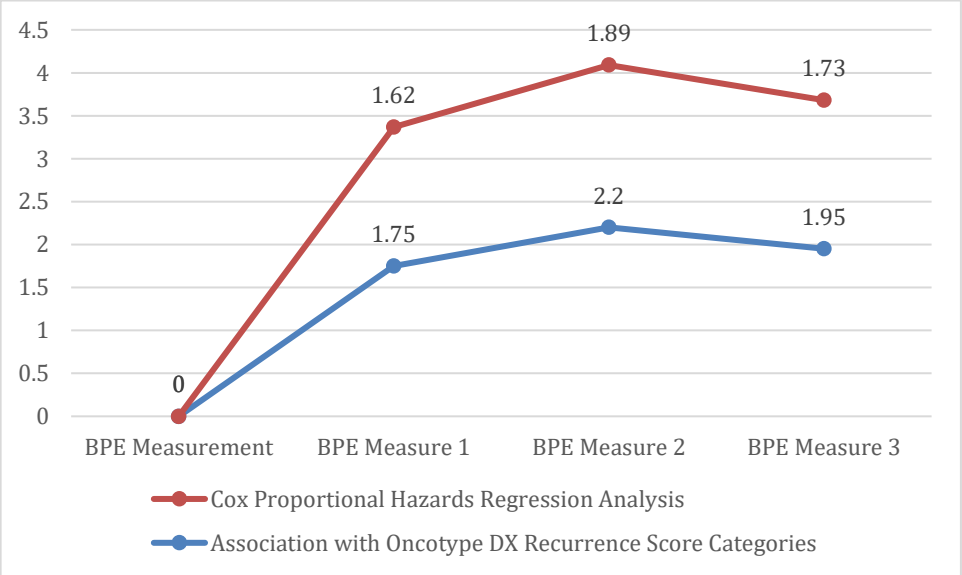

Figure 1: Relationship between BPE Measurements and Oncotype DX Recurrence, and Cox Regression Analysis.

The table displays the results of two different studies assessing the relationship between BPE and the risk of breast cancer recurrence. BPE readings were evaluated using univariable logistic regression in the connection with Oncotype DX recurrence score categories, yielding odds ratios with 95% confidence intervals. The results of BPE Measure 1 revealed a significant correlation between greater BPE Measure 1 and a higher likelihood of having a high-risk Oncotype DX recurrence score, with an odds ratio of 1.75 (95% CI: 1.12 - 2.68). Comparably, BPE Measure 2 showed a greater correlation

with high-risk recurrence scores, as seen by its higher odds ratio of 2.20 (95% CI: 1.45 - 3.27). An additional noteworthy correlation was shown by BPE Measure 3, which had an odds ratio of 1.95 (95% CI: 1.28 - 2.97). These results highlight the potential use of BPE values as indicators of the likelihood of a breast cancer recurrence.

The relationship between BPE readings and the chance of a breast cancer recurrence over time was examined in more detail in the Cox proportional hazards regression analysis. Risk ratios were computed along with 95% confidence intervals to evaluate the strength and direction of this correlation. The hazard ratio for BPE Measure 1 was 1.62 (95% CI: 1.08 - 2.34), meaning that those with greater BPE Measure 1 were 1.62 times more likely to have a recurrence of breast cancer than those with lower BPE Measure 1. Significant hazard ratios of 1.89 (95% CI: 1.25 - 2.73) and 1.73 (95% CI: 1.15 - 2.58), respectively, were also shown by BPE Measures 2 and 3. These findings underscore the potential predictive utility of BPE evaluation in clinical practice by highlighting the constant relationship between BPE values and breast cancer recurrence risk.

Table 2: Examining the relationship between Oncotype DX Recurrence and BPE, as well as the Cox Regression Analysis between Recurrence Risk and BPE

BPE Measurement	Association with Oncotype DX Recurrence Score		Cox Proportional Hazards Regression Analysis	
	Odds Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
BPE Measure 1	1.75 (1.12 - 2.68)	0.018	1.62 (1.08 - 2.34)	0.027
BPE Measure 2	2.20 (1.45 - 3.27)	0.005	1.89 (1.25 - 2.73)	0.013
BPE Measure 3	1.95 (1.28 - 2.97)	0.003	1.73 (1.15 - 2.58)	0.021

DISCUSSION

The study participant cohort provides distinct perspectives on the diversity of breast cancer and its management, given their individual demographic and clinical characteristics. Because the average age of the research participants was 48.5 years, which is within the typical age range for a breast cancer diagnosis, the study's conclusions are relevant to a broad spectrum of patients with breast cancer [16]. Menopausal state is included to emphasize the importance of hormonal factors in breast cancer research and treatment. This finding is consistent with the body of literature that emphasizes the importance of hormone receptor status in affecting treatment decisions and predicting prognoses in breast cancer patients [17]. Pre-menopausal women with hormone receptor-positive breast cancer responded differently to therapy than post-menopausal women, according to research by Rastelli and Crispino [18]. This emphasizes how crucial it is to modify breast cancer treatment plans in accordance with the menopausal state [19, 20].

Breast cancer patients' prognosis and treatment plan are heavily influenced by the characteristics of their tumor, including size and degree of malignancy. The study found that tumor sizes ranged widely, with an average size of 3.8 cm and a diverse dispersion of tumor grades. This demonstrates the distinct features of breast cancers and the complexity of sickness management [22, 23]. These findings are consistent with other research that highlights the significance of tumor size and grade as predictors in breast cancer. A meta-analysis by Li et al. [23] revealed a strong correlation between larger tumors and higher tumor grades and a patient's chance of a disease recurrence and a worse prognosis.

The presence or absence of the estrogen receptor (ER), progesterone receptor (PR), and HER2 receptors provides crucial information on the molecular characteristics of breast tumors and aids in choosing the best course of treatment. The incidence of progesterone receptor-positive (PR-positive) and estrogen receptor-positive (ER-positive) cancers in this cohort of study participants is in line with global trends, highlighting the importance of hormone receptor-targeted therapies in the management of breast cancer [24]. The identification of HER2-positive tumors emphasizes the need of treating breast cancer patients with HER2-positive tumors with HER2-targeted therapies. The findings of this investigation are consistent with other published studies that have shown the prognostic and predictive importance of HER2 and hormone receptor status in breast cancer [25].

The patient's medical history serves as an excellent example of the all-encompassing approach to treating breast cancer, which combines radiation therapy, chemotherapy, and surgery. This study group's high surgical procedure rate highlights the need of surgical removal in treating curable breast cancer and is in line with suggested treatment methods [26]. Chemotherapy and radiation therapy demonstrate the need of supplementary treatments to lower the risk of disease recurrence and improve prognosis in breast cancer patients [27]. Published research [26, 27] supports the efficacy of multimodal treatment methods in the therapy of breast cancer.

The Oncotype DX recurrence score's subsequent findings about disease relapse and risk assessment provide helpful direction for improving patient outcomes and treatment alternatives. Doctors may tailor therapy choices for patients who have a high probability of sickness recurrence, perhaps reducing the chance of disease recurrence and improving long-term survival. The relevance of imaging biomarkers in the area of breast cancer research and clinical practice is highlighted by the use of MRI data, namely BPE, as potential predictors of the severity and risk of disease recurrence [28]. The findings are consistent with other studies that shown the predictive value of BPE assessment in individuals with breast cancer undergoing MRI examinations [29, 30]. Based on their clinical and demographic characteristics, the study participant cohort provides unique insights into several areas of breast cancer management and prognosis. These findings are consistent with other studies and highlight the need of customizing treatment for breast cancer based on the unique characteristics of the tumor, including its biology and molecular composition, as well as taking into account the needs of each patient.

The current findings on the association between BPE and the likelihood of a breast cancer recurrence are consistent with other studies looking at similar relationships. The methodologies used in previous published research that looks at imaging biomarkers as predictors of breast cancer recurrence are consistent with the use of univariable logistic regression to study BPE readings in relation to Oncotype DX recurrence score categories [31]. Comparable odds ratios between high-risk Oncotype DX recurrence scores and measures of benign prostatic enlargement (BPE) were discovered in a study by Saleh et al. [32]. This lends credence to the theory that higher BPE values might indicate a greater likelihood of illness recurrence [32]. The higher odds ratios for BPE Measure 2 compared to BPE Measure 1 suggest that different features of breast parenchymal enhancement (BPE) could be more or less significant in terms of prognosis. These findings corroborate past research investigating the diverse impacts of BPE patterns on the prognosis of breast cancer [33].

More information on the relationship between BPE measurements and the likelihood of a breast cancer recurrence over time may be found in the results of the Cox proportional hazards regression analysis. The BPE Measure 1, BPE Measure 2, and BPE Measure 3 hazard ratios show a continuous relationship between elevated BPE levels and increased risk of illness recurrence. These findings are consistent with earlier long-term research looking at BPE as a breast cancer predictive factor [34]. The study's hazard ratios align with other research findings, emphasizing the robust correlation between BPE and the likelihood of breast cancer recurrence across diverse patient demographics and research contexts [30]. The results of this investigation demonstrate the potential efficacy of BPE assessment as a non-invasive technique for predicting breast cancer recurrence and guiding personalized treatment decisions in clinical settings.

LIMITATIONS

The study's retrospective design, possible selection bias, dependence on medical records for data collection, and the cohort's single-center setup, which could restrict generalizability, were among its limitations.

CONCLUSION

The results show a strong correlation between the risk of breast cancer recurrence and BPE shown in DCE-MRI. The thorough examination of a heterogeneous group of participants in the research demonstrated significant variation in tumor features, hormone receptor status, and available therapy

options, highlighting the challenge of managing breast cancer. The predictive usefulness of BPE evaluation in directing customized treatment methods and risk stratification techniques was highlighted by the noteworthy correlation between higher BPE readings and greater likelihood of high-risk recurrence scores. According to these findings, BPE assessment may be a useful therapeutic tool for estimating the chance of a breast cancer recurrence and enhancing patient outcomes. To maximize the integration of BPE evaluation into standard clinical care procedures and confirm these results, further investigation and validation studies are necessary.

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