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Correlation of Size of Lump by Clinical Examination, Ultrasonography and Mammography with Size of Pathalogical Specimen in Carcinoma Breast

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Abstract

Background: Breast cancer is among the top three cancers affecting women across the world and its incidence is increasing worldwide. The size of lump at the time of initial treatment has a direct bearing on the prognosis. Therefore accuracy in detecting the exact size of lump with clinical assessment,imaging modalities like ultrasound and mammography are important tools of management. Neoadjuvant chemotherapy has become an accepted part of breast cancer treatment.Accurate assessment of lump before and after chemotherapy will indicate the response to treatment. The size of lump found in pathological specimen is the gold standard of exact dimension of the lump. Clinical examination, ultrasonography and mammography have all been used to assess the size of the lump and correlate their accuracy in assessing the actual size of lump in pathological specimen after surgery. There are conflicting reports about the accuracy of these tests in various studies conducted so far. *Aim:* The aim of the study is to identify the best modality, among Clinical examination, ultrasonography and mammography to assess the size of lump by correlating it to the actual size as found in the pathological specimen after surgery. *Methods:* This is a retrospective study of 53 cases of confirmed of breast cancer treated at Adichunchcnagiri hospital and research center BG Nagara over a period of five years from Feb 2011 to Feb 2016. These patients had undergone Physical examintion, ultrsonography and mammography before surgery. Patients who had not undergone both imaging tests in addition to clinical examination were excluded. The data was compiled and correlation of the size of the breast lump was compared with that found after surgical removal of the lump. *Results:* Mean age of the study group was 53.5 years. The mean tumour size measured on clinical assessment was 10.77cm, 8.49cm on , mammography and 7.43cm on ultrasonography. Mean histopathological tumour size was 8.66cm. *Conclusion:* Mammographic size correlated closest to the size of the lump found in pathological specimen. Clinical examination underestimated and ultrasonography tended to overestimate the size.

Keywords: Breast Carcinoma; Correlation; Clinical; Ultrasonography; Mammography.

Introduction

Breast cancer is now the most common cancer in Indian women having recently overtaken cervical cancer in this respect. With increasing incidence of breast carcinoma all over the world the stress is being laid on early diagnosis and conservative breast surgery alongwith chemotherapy and radiotherapy. In India, 144,937 women were newly detected with breast cancer in 2012 and 70,218 women died of breast cancer, approximately alternate woman with breast dying due to the disease [1,2,3]. The need for early diagnosis with screening programmes and early treatment of breast cancers cannot be overemphasized. Ultrasound and mammography have shown to increase the detection rate of cancer by almost 15%[4]. Various studies have been done to find out the best imaging modality to detect the size [5]. Combined assessment have been found to be more

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accurate than individual tests [6]. Neoadjuvant chemotherapy (NACT) has played an important role in better management by shrinking the size of locally advanced breast cancers [7].

Tumour response to NACT needs to be assessed early on in the course of the disease so that non responders can be changed over to a more effective regime. This would reduce unnecessary toxic effects on the patient and also help to plan the timing of surgery. Imaging techniques used in the routine clinical practice to assess the size of breast tumours are a matter of concern regarding their accuracy [9,10].

There are many studies found in the literature which assess the accuracy of clinical assessment (clinical breast examination, (BE), mammography (MMG) and ultrasonography (USG) in delineating the actual size of primary breast tumour before and after NACT, but the results of these studies are contradictory. Most of these studies suggest that mammography and clinical assessment overestimate while USG underestimate the breast tumour size as compared to the actual size of pathological specimen [11,12,13,14].

This study has been undertaken to determine the most optimal and accurate modality among clinical assessment, mammography and ultrasonography to determine the preoperative tumour size in breast cancer patients.

Materials and Methods

After approval by the Ethical Committee, a retrospective study of 53 patients diagnosed as primary breast cancer by FNAC was conducted at Adichunchanagiri Institute of Medical Sciences, from February 2011 to February 2016.

The patients were subjected to clinical examination, ultrasonography and mammography preoperatively and the largest tumour diameter obtained by these modalities was recorded and findings were compared with postoperative histopathological specimen size.

Inclusion Criteria

a. Primary breast cancer confirmed by FNAC.
b. Patients undergoing BCS or MRM with or without adjuvant chemotherapy, hormonal therapy or radiotherapy.

Exclusion Criteria

a. Presence of distant metastasis
b. Patients who had undergone neoadjuvant chemotherapy
c. Inflammatory breast cancer and Paget's breast disease
d. Inoperable tumours

Initial Assessment of Tumour Size

All 53 patients underwent clinical assessment, ultrasonography and mammography and the data was recorded. BE, MMG and USG were performed by experienced surgeons and radiologists. Measurements of tumour size were taken along the long axis of the tumour and noted down.

Clinical Assessment

A thorough clinical assessment of all patients was carried out at the out-patient block and for those with a palpable breast mass a single estimate of the maximum diameter of the tumour between two palpating fingers was recorded. In the rare case of more than one lump in the breast, then the largest lump measurement was taken into consideration.

Ultrasonography

Diagnostic ultrasound was performed in all patients at the radiodiagnosis department by a single radiologist. GE Voluson S6 Pro was the ultrasound unit and a probe frequency of 7.5 MHz was used. The same ultrasound machine was used throughout the study.

Mammography

All patients underwent mammography using the Siemens Mammomat 3000 NOVA mammography unit. A measurement of the single largest tumour diameter on any projection was recorded. Routine medio-lateral and cranio-caudal projections were examined. Lumps with Spiculation and microcalcification were excluded from the study.

Assessment of Histopathological Tumour Size

Patients underwent either BCS or MRM and the specimen was sent for histopathological examination. A single pathologist was assigned to measure the histopathological tumour size in all specimens. The specimen was cut along its longest axis and a single measurement of the largest tumour diameter was made using a metal scale. For tumours which were very small to be measured using the scale, a Vernier

caliper was used.

Statistical Analysis

Statistical analysis of the study was performed using the MS Excel and SPSS version 22computer software.Mean, median and mode of different tumour sizes were calculated. Pearson correlation coefficient was used to establish the correlation between BE, MMG and USG with that of tumour size after surgery.

Bland and Altman analysis was done.A graph was plotted showing the difference between the preoperative size estimated by each modality and size on histopathology, on Y- axis and the average of the two estimates on X- axis. The mean difference between preoperative and histopathological measurement, the standard deviation of the differences and the 95% limits of agreement (95% confidence interval) were calculated for each of the preoperative modality.

To increase the validity of the study, another statistical test, the 'Z' test was used to establish the correlation between the pre and postoperative measurement techniques.

Results

Mean age of the cohort was 53.5 years (range: 38-76) with a standard deviation (SD) of 10.6. The mean tumour size measured on clinical assessment, MMG and USG were 10.77cm, 8.49cm and 7.43cm respectively. Mean histopathological specimen tumour size was 8.66cm.

The standard deviation for clinical assessment was 5.26 for USG, 7.06 for MMG, 8.88 for USG and 8.82 for histopathology (Table 1).

The correlation coefficients between tumour size measurement by histopathology and tumour size measurement by clinical assessment, USG and mammography are shown (Figure 1).

Significant positive correlation was observed between HPE and other methods. i.e. with increase in HPE tumour size there was significant increase in tumour size measured by MMG, USG and BE. Both MMG and USG underestimated the histopathological tumour size (r=0.976, p=<0.001 and r=0.813, p=<0.001), however MG was closer to the histopathological tumour size. BE overestimated the histopathological tumour size (r=0.623, p=<0.001) (Table 2).

The mean of difference for clinical assessment was 2.11, 1.23 for USG and 0.18 for MMG.

Standard deviation of difference for clinical assessment was 6.90,5.13 for USG and 1.94 for mammography 1.94 (Table 3).

The 95% confidence limit for clinical assessment (mean size ±2 SD) was 5.51, for USG 0.37-14.49 cm,

Table 1:

	Mean	SD	Z Score	P value
HPE	8.66	8.82		
Mammography	8.49	8.88	-0.659	0.513
USG	7.43	7.06	-1.750	0.086
Clinical Assessment	10.77	5.26	2.225	0.03*

Table 2: Pearson correlation between specimen tumour size and lump size by other tests

		HPE	Mammography	USG	Clinical assessment
HPE	Pearson Correlation	1	0.976**	0.813**	0.623**
	P value		<0.001*	<0.001*	<0.001*
	N	53	53	53	53

Table 3: Correlation between BE,MMG,USG and actual tumour size

	Mean	SD	95% Confidence Interval (Mean ± 2SD)
Difference between Mammography and HPE	-0.18	1.94	- 4.06 to 3.7
Difference between Ultrasonography and HPE	-1.23	5.13	- 11.49 to 9.03
Difference between Clinical Assessment and HPE	2.11	6.90	- 15.91 to 11.69

	Mean	SD	95% Confidence Interval (Mean ± 2SD)
Average of Mammography and HPE	8.58	8.79	9 to 26.16
Average of Ultrasonography and HPE	8.05	7.56	7.07 to 23.17
Average of Clinical Assessment and HPE	9.72	6.39	3.06 to 22.5

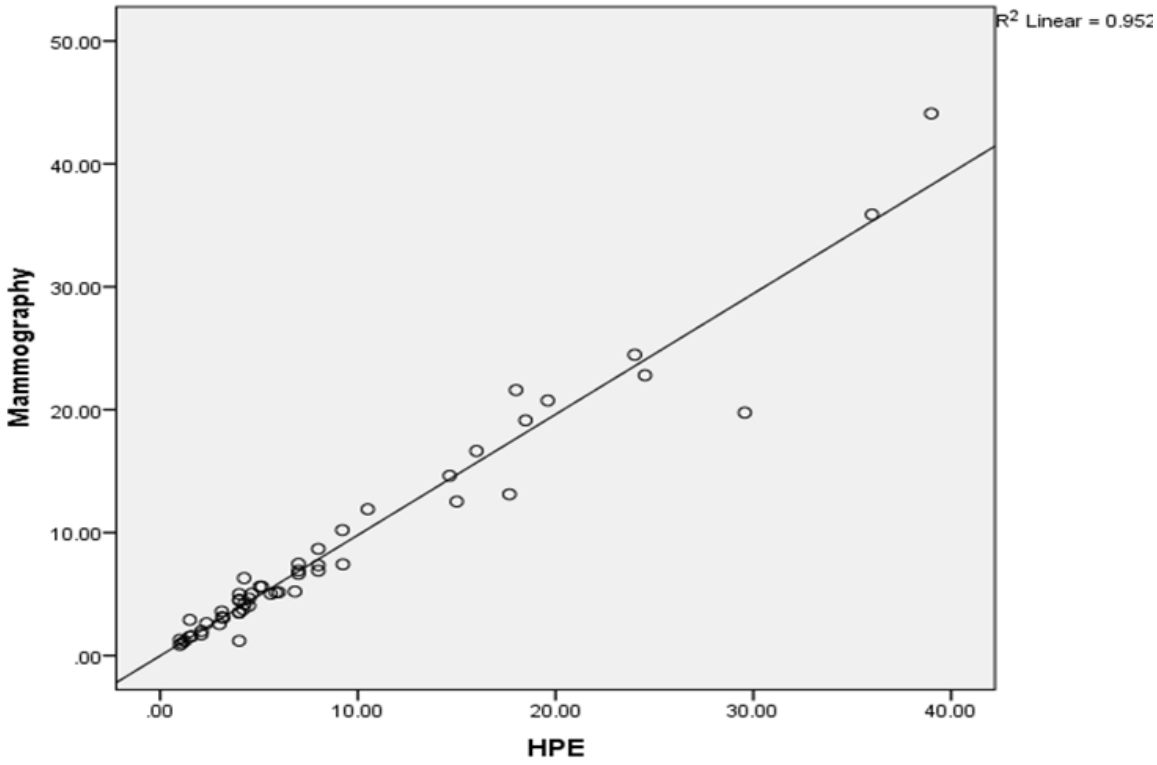

Fig. 1: Scatter plot showing Positive correlation between HPE and Mammography

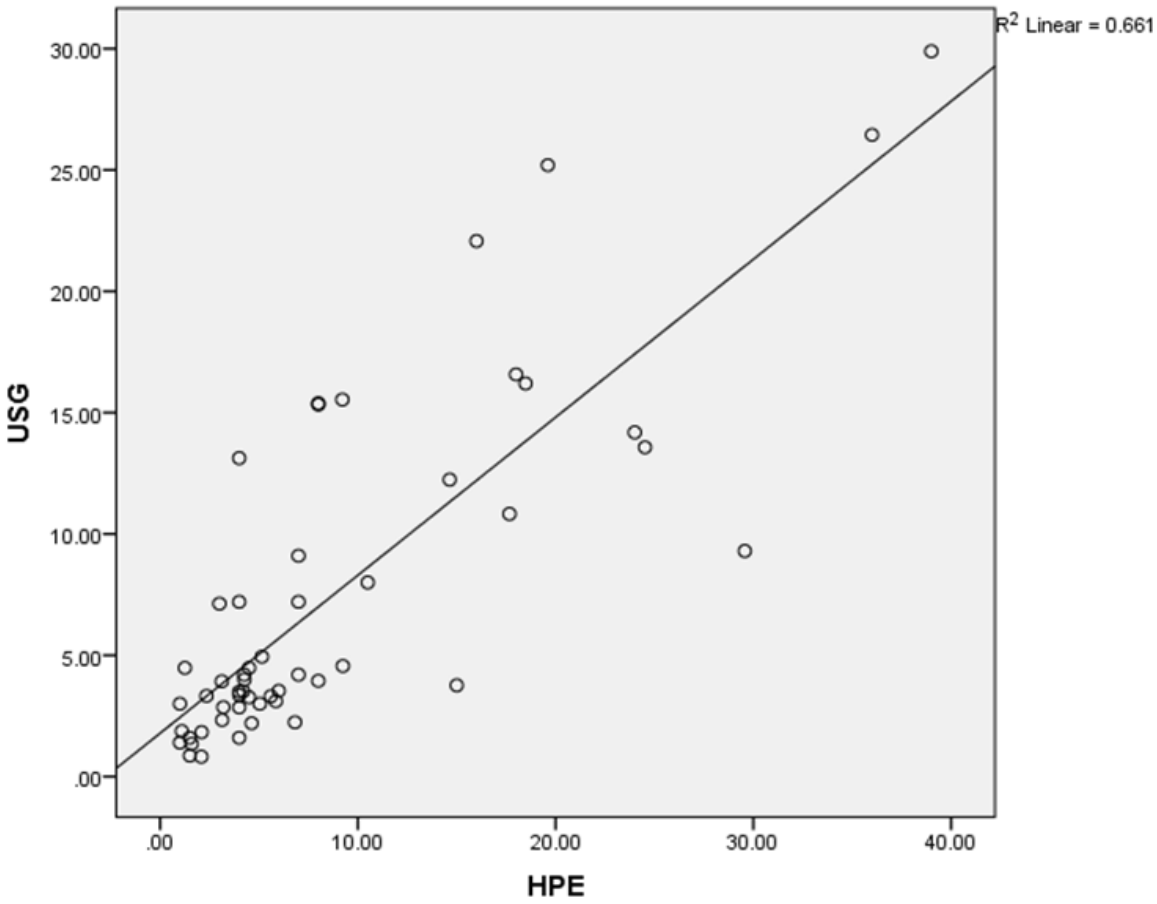

Fig. 2: Scatter plot showing Positive correlation between HPE and USG

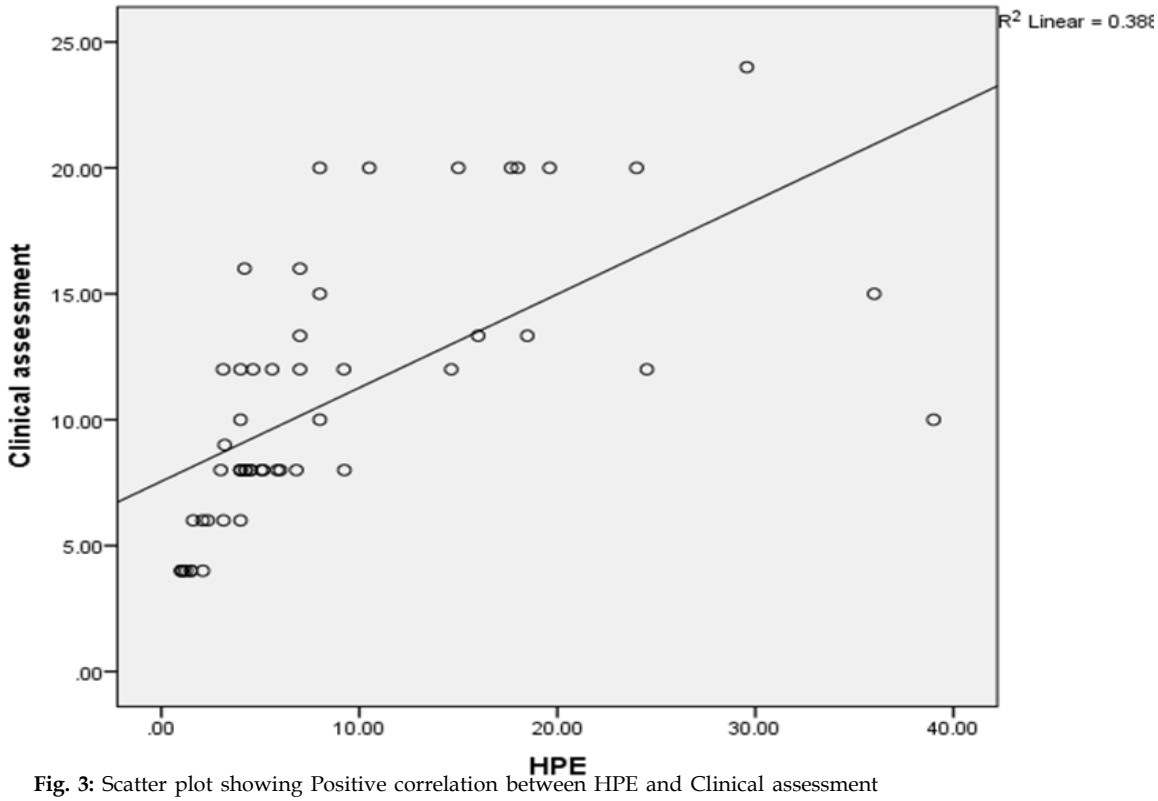

Fig. 3: Scatter plot showing Positive correlation between HPE and Clinical assessment

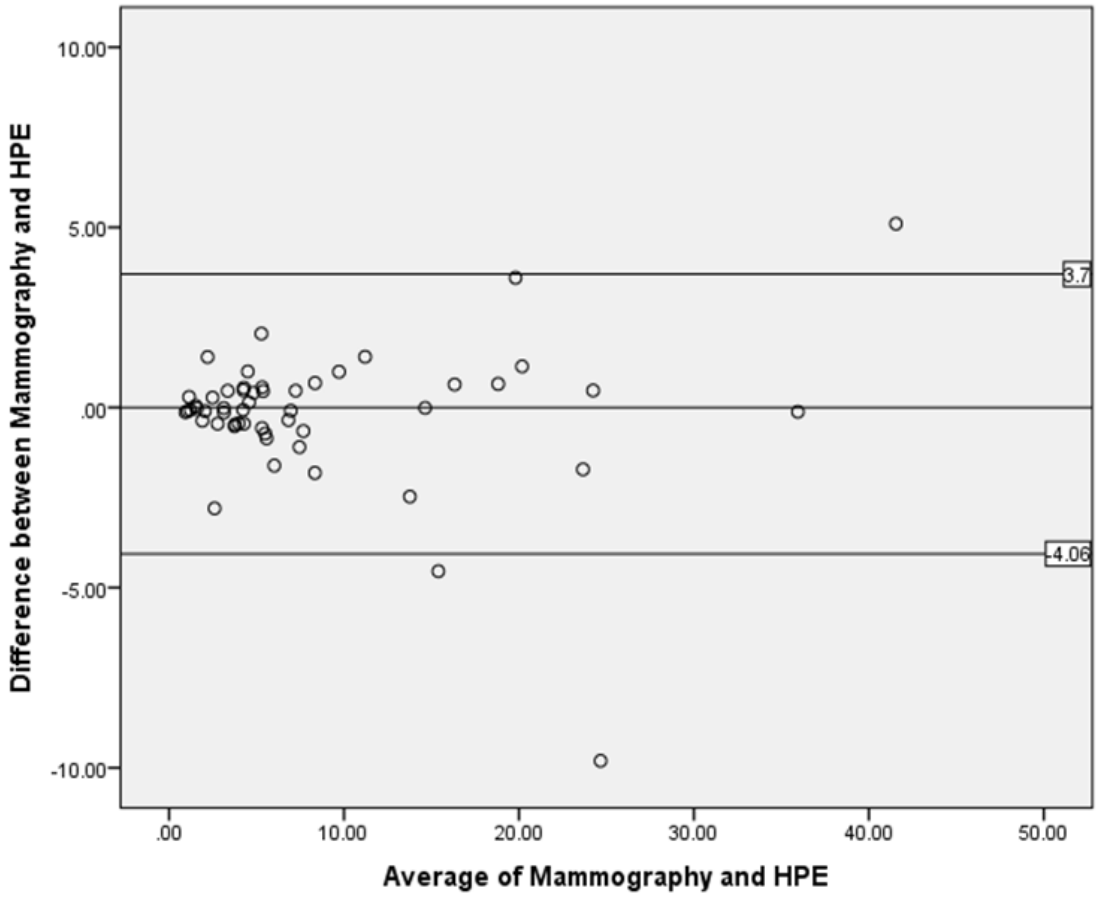

Fig. 4: Bland Altman plot of Difference between Mammography – HPE compared to the mean of the two

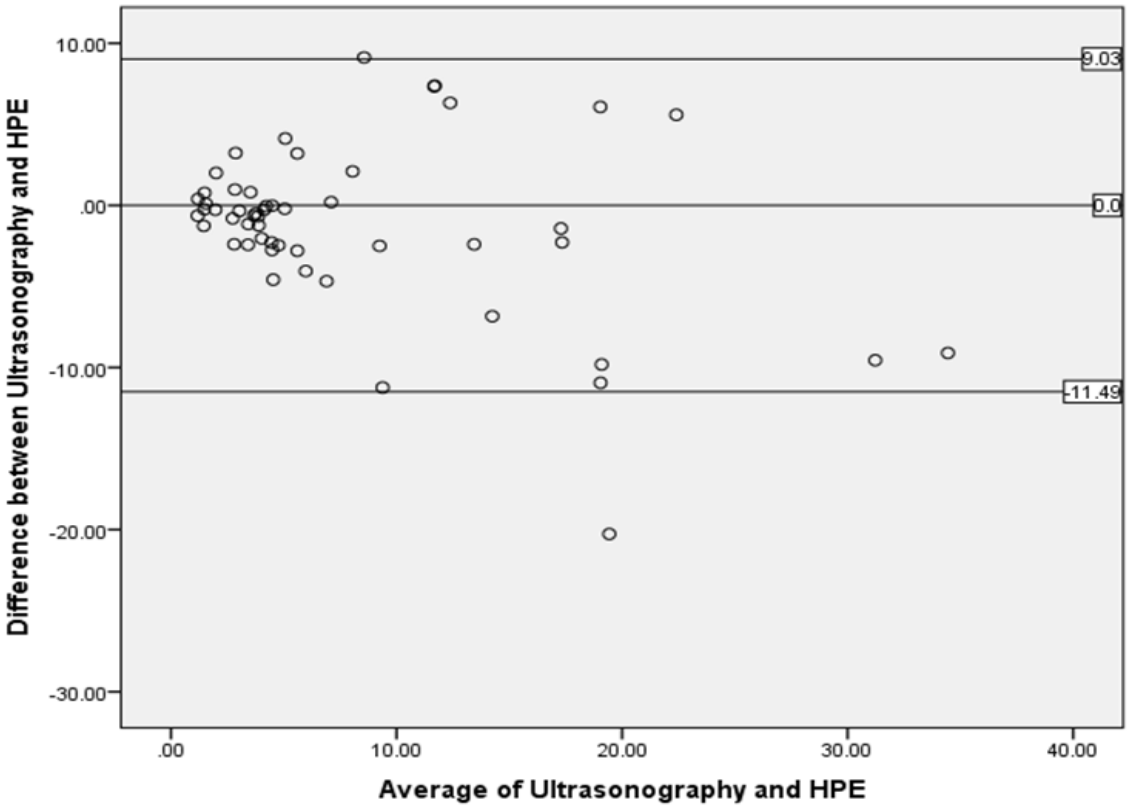

Fig. 5: Bland Altman plot of Difference between USG & HPE compared to the mean of the both

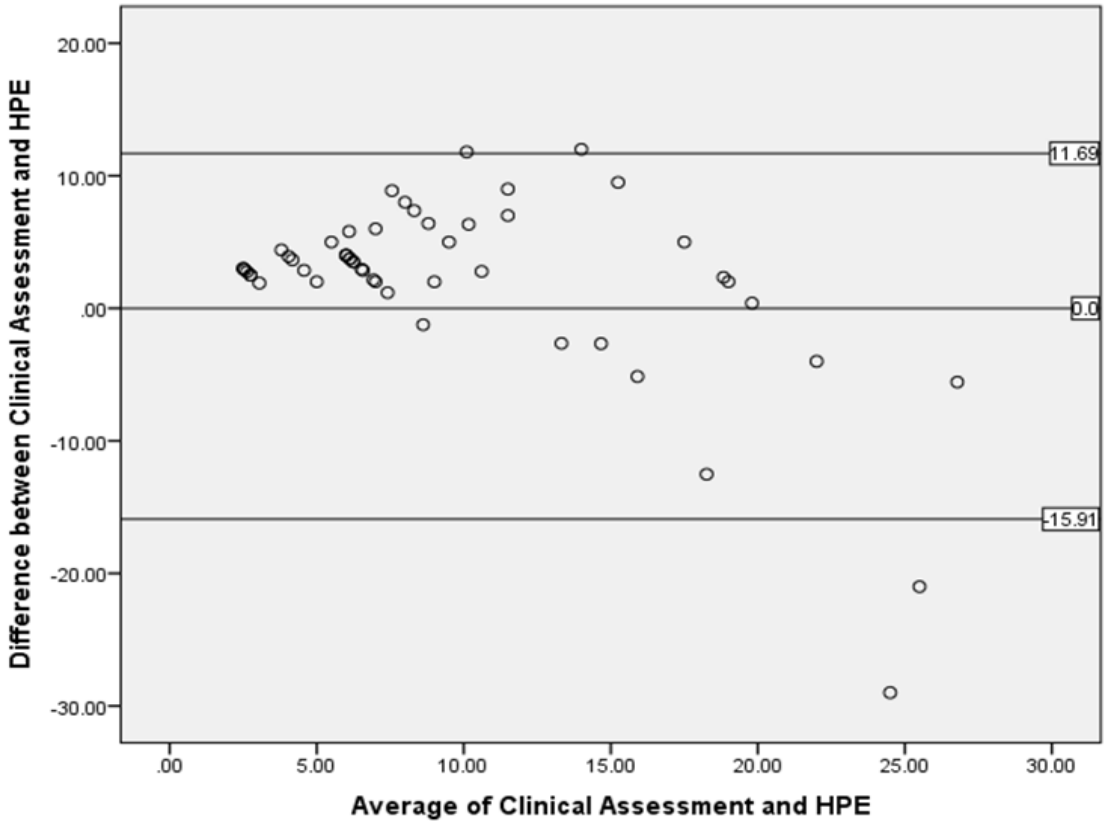

Fig. 6: Bland Altman plot of Difference between Clinical – HPE compared to the mean of both

for MMG was 0.39-17.37 cm, and for pathology specimen was 0.16-17.48.

To increase the validity of the study another statistical test, the 'Z' test was used. The Z-test value for clinical assessment was 2.225, for USG 1.750 and for MMG 0.659 showing that there was significant statistical difference between size assessment by BE and histopathological specimen size. The Z test values show that there was no significant difference in tumour size measurement by MMG and Pathology specimen size. Although there was no significant difference in tumour size measurement by USG and histopathology, USG tended to underestimate the tumour size when compared to MMG. MMG values of tumour size measurement were found to be the closest to histopathologic tumour size.

Discussion

Tomas Cortadellas et al and many other similar studies in the past while comparing clinical assessment, MMG and USG in accurately assessing the breast tumour size have found conflicting results in their findings [15,16]. Many of them consider USG as the best preoperative modality in assessing the size which was found closest to actual tumour size found in the specimen [17,18]. Whereas few other studies including that by Goverdhan HB et al, conclude that mammography is better than CBE and USG [19,20,21,22].

Kald B, Boiesen P, Ronnow K, Jonsson P and Bisgaard Tin, in their study of Preoperative Assessment of Small Tumours in Women with Breast Cancer and in another study by Alsaeed E, Tunio M,of Prediction of Postoperative Tumor Size in Breast Cancer Patients by Clinical Assessment, Mammography and Ultrasonography [23,24], they are of the same opinion as that of our study in that ultrasonography tended to underestimate postoperative histological tumour size. This may be the result of difficulty in recognising the tumour margins accurately on ultrasonography. Anees B Chagpar et al in their retrospective study of 189 patients had moderate to high correlation accuracy and concluded that interpretation of preoperative size should be done with caution.They found USG correlation with pathological size only in small lumps less than 02cms size [25].

In a study done at the Royal Marsden Hospital, London, it was found that the tumours in which ultrasound overestimated the size of the breast tumour, the tumour was surrounded by either a region of desmoplastic response or DCIS. Both these conditions increase the size of the abnormality visualised by ultrasound. The tumours in which ultrasound tended to underestimate the tumour size were often histologically diffuse or multifocal [26,27,28].

In a study by Herrada et al,among the three noninvasive tests physical examination correlated best with the pathological tumour size (p=0.0003), followed by USG (p=0.0005) and MMG (p=0.132)[29]. Forouhi et al found there was moderate correlation between size of tumour by CBE and pathological tumour size($p<0.0001$) and even closer correlation with USG and MMG. Rashmi et al also found strong correlation between USG and pathological tumour size. In a study by Heiken et al,USG and MMG underestimated the size.

Other studies conclude that histological tumour size was underestimated by mammography. Other studies conclude that.This variability in the results of mammography suggests the subjective nature of mammographic observations, a finding supported by Simpson et. al [30,31,32,33].

According to our study mammography is the most precise preoperative modality of predicting postoperative histological tumour size. Although ultrasonography produced almost similar results as mammography, it did tend to underestimate tumour size to a some extent than did mammography.

In our study we also found that clinical assessment overestimates the final histopathological tumour size, a finding similar to many other studies. This might be due to inter-observer variations and may also be due to considering the overlying skin and healthy breast tissue during clinical assessment. A report from the Yorkshire breast cancer group has shown that inter-observer variability is a major field of concern in measuring breast tumour size by clinical assessment [34].

According to a study done by Thomlinson, a better method to overcome this problem is to use calipers [35]. In our study use of calipers has been minimised as its use caused discomfort and found patients less compliant.

In another similar study by Vriens B, de Vries B, Lobbes M, van Gastel S, van den Berkmortel F, Smilde T et al,they compared the accuracy of MRI, mammography and USG in assessing histological tumour size preoperatively and they found MRI superior to the others.This however has not been highlighted in our studies as MRI as a routine modality of investigation in our setup was not feasible and hence not done [36,37].

Most of the studies addressing this research question consider histological tumour size as the gold standard reference to compare the results of other methods. The UK National Health Service Breast Screening Programme (NHSBSP) external quality assurance scheme in breast histopathology has made an attempt to monitor and improve the quality of pathology reports in this regard [38].

Conclusion

According to this study preoperative mammographic findings were more predictive of the postoperative histopathological tumour size. Clinical assessment overestimated the tumour size and gave the largest standard deviation of the difference and ultrasound tended to underestimate tumour size. Although there was little difference between the accuracy of ultrasonography and mammography in assessing tumour size preoperatively, we consider mammography as the most accurate modality for measuring primary breast tumour size. Both ultrasonographic and mammographic observations being subjective in nature, there are chances of inter-observer variability which could alter the results. This is one of the areas of concern for future studies. Based on our experience we recommend the use of both mammography and ultrasonography to plan the management of invasive breast cancers. In case there is wide variability in the results obtained by these two modalities, a repeat measurement by a second radiologist can be helpful. Further studies on newer techniques like CT, MRI and PET-CT of the breast is needed to accurately predict the postoperative tumour size in breast cancer patients.

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