Original Article

Role of Shearwave Elastography in the Search of Unknown Primary Cancer in Breast and Abdominopelvis

Binafsha Manzoor Syed, Jawaid Naeem Qureshi, Ahmed Khan Sangrasi, Bikha Ram Deverajani, Noshad A. Shaikh, Munir Ahmed Junejo

ABSTRACT

OBJEVTICES: Shearwave elastography has recently got approval for its use in clinical imaging. It has got its established accuracy in assessing liver fibrosis, where biopsy for the staging of cirrhosis has been minimized. There is emerging data showing its superiority in detecting breast and other cancers as compared to conventional imaging methods. This study aimed to analyse role of shearwave elastography in detection of primary impalpable lesions in breast and abdomino-pelvic regions and those missed on conventional imaging modalities.

SETTING: Shearwave Elastography Unit, Liaquat University of Medical & Heath Sciences, Jamshoro, Pakistan

DESIGN & METHODS: The study is an observational pilot project including the patients presented to surgery and oncology departments with metastatic cancer suggested on conventional imaging or cytology of the metastatic site but primary sites were not known and suspected to be in the region of breast, abdomen or pelvis. Shearwave elastography was applied as supplementary tool to re-do B-mode ultrasound. Aixplorer Ultrasound System Multiwave version 8.2.0 (Supersonic Imagine S.A., Aix-en-Provence, France) was used in this study. This study selectively includes the patients who were called on experimental basis to see the effectiveness of the system on trial basis, the calculation of the sensitivity, specificity, positive predictive value and negative predictive values were not determined.

RESULTS: There were seven patients including four with axillary lymph nodes and three having liver metastases. In patients with axillary lymph nodes mammogram and conventional ultrasound failed to show primary breast lesions, histopathology of the axillary lymph nodes suggested infiltrating ductal carcinoma. In patients with liver metastases conventional ultrasound abdomen and CT scan failed to reveal primary lesions. Shearwave assisted B- mode ultrasound suggested a solid mass in a complex cyst in the kidney in one patient and in the other there were multiple benign cysts and a solid mass however the third patient with liver mass found to have primary from gall bladder. These findings were later confirmed on histopathology or cytology.

CONCLUSION: Shearwave elastography is an emerging non invasive technology showing potential role to supplement B-mode ultrasound in detecting unknown primary cancerin breast and abdomino-pelvic region.

KEY WORDS: Unknown Primary Cancer, Shearwave Elastography, cancer imaging.

This article may be cited as: Syed BM, Qureshi JN, Sangrasi AK, Deverajani BR, Shaikh NA, Junejo MA. Role of Shearwave Elastography in the Search of Unknown Primary Cancer in Breast and Abdominopelvis. J Liaquat Uni Med Health Sci. 2016;15(03):152-7.

INTRODUCTION

Shearwave elastography is a recent and evolving technology in the diagnostic imaging. The technology recently (ie 2013) got FDA approval for its utilisation in the measurement of tissue stiffness. Tissue stiffness is one of the parameters observed in a diseased organ. During palpation medical practitioners make an assessment of the tissue architecture. This method had been in practice for over 5000 years,(ie during the era of pharaoh) palpation and assessment of the stiffness and the architecture of the tissue was probably the sole method of making a diagnosis. In the modern era there has been evolution in the medical diagnostics including the use of radiology. There has been tremendous improvement in radiology/ medical imaging in the past few decades including the use of Computed tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) scan. However given all these techniques there remain an area including a small population of patients who present with metastatic disease and all conventional

techniques fail to find the primary cancer. They eventually die undiagnosed even in the developed countries with high tech imaging modalities.

Unknown primary cancer attribute to 2% of all cancers[1]. Although the number of patients who present with metastases at the first encounter is more, but their primary site of the cancer is found without any issue. However a few remain unknown of the primary site which was suspected to be 31000 in USA only in the year 2014[1]. The pattern of the presentation of these cancers remains same all around the globe. However reliable statistics are not available from other parts of the world. Regardless of their number these patients pose a clinical dilemma. Usual modes of making a diagnosis to search the primary cancer are the Ultrasound, X-ray, mammogram CT and MRI. When they fail to detect the site of primary cancer these patients are labelled as unknown primary cancers. These patients are then referred for more advanced technologies such as MDCT.

Shearwave elastography is a non-invasive method of assessment of the tissue stiffness. Most of the cancers are solid tumours and are usually stiff. There are studies available suggesting the role of shearwave elastography in detecting the cancers/ solid tumours in breast, liver, prostate and thyroid[2-8]. These studies have shown high rates of accurate cancer detection when B-mode ultrasound was supplemented by shearwave elastography having high rates of sensitivity and specificity. Given the non-invasive and patient friendly technique we hypothesized that this technique may have potential role in detecting primary site of the cancer in patients presenting with metastases with potential suspected site of the primary in the breast or abdominopelvis, therefore we prospectively conducted this pilot study to assess the potential role of shearwave elastography in patients presenting with unknown primary cancer.

METHODOLOGY

This study was conducted during the period of March 2014 to September 2015 at Shearwave elastography unit, Medical Research Centre, Liaquat University of Medical & Health Sciences Jamshoro in collaboration with the Departments of Surgery and Radiology.

Patient selection:

Patients with unknown primary cancers where conventional methods of imaging failed to identify the primary site of the tumours were included. All patients had metastatic disease suspected on imaging and confirmed on cytology/ histopathology, however the primary site was not known.

Shearwave elastography

Elastography was performed by using Aixplorer Ultrasound System Multiwave version 8.2.0 (Supersonic Imagine S.A., Aix-en-Provence, France). Shearwave measures the tissue stiffness and displays it in quantitative and qualitative mode. The qualitative mode displays change in colour which ranges from blue to red in ascending order of stiffness. Where soft tissues give blue colour impression and very hard give red colour. In very stiff lesions beyond the range of penetration shearwave gives a punched out area (ie signal void area). The quantitative assessment is given in the numbers with calculation of the mean, median and the standard deviation of the assessment of the stiffness in the Region of Interest (ROI). The results are given in Kilo Pascals (KPa). A mean KPa was taken as the final score for that area.

Scanning:

The examination was carried out with patients in supine position and they were asked to hold their breath for a few second when shearwave configure the measurements. All patients had baseline grey scale ultrasound of the abdomen, breast and axilla respectively for gathering the primary information. During grey scale assessment of the suspected organ was done for any abnormality. The hard area in suspected region is then measured by placing the ROI at the area of interest. We used ROI of 20mm diameter for this study. Qualitative as well as quantitative results were counted.

Breast: For breast Superlinear™ (SL15-4* 50 mm Super Linear Array) was used. For examination purpose the breast was divided into five regions (Figure 1a). Each region was assessed by shearwave elastography. The color scale as well as quantitative assessment was done. For color scale blue was considered normal/ soft tissue of the breast while red was stiff area, however the quantitative assessment was done by the scale of 180 as the upper limit of the normality and the lower limit of the suspected malignancy. Any area with red color code, showing mean KPA >180 with and without punched out lesion was biopsied.

Liver, gall bladder and kidney scanning:

For abdominal scanning Supercurved™ (SC6-1 64mm Super Curved Array) was used. For liver, gall bladder and kidney color code was the same as for the breast where blue was considered normal parenchyma while red suggests stiff tissue. The lower limit for the quantitative assessment was 30 mean KPA for liver and gall bladder while 90 mean KPA was consider ednormal upper limit for kidney.

RESULTS

A total of 7 patients were identified to have unknown primary cancers where conventional imaging failed to

locate the primary site of the cancer. Four patients had axillary lymphadenopathy and 3 presented with liver metastases.

Assessment of the breast lesions

In patients with axillary lymph adenopathy mammogram and ultrasound were not helpful in locating the lesion in the breast. Shearwave elastography suggested site in the breast and histopathology confirmed the presence of invasive ductal carcinoma There were non palpable lesions in the breast nor there were any visible lesions on B-mode ultrasound. Shearwave elastography was very carefully applied in the breast in all five regions (Figure Ia). There was abrupt change in the color at certain areas (Figure 1b, 1c, 1d and Ie). The quantitative measurement also raised more than 200 mean KPA. The histopathology confirmed presence of invasive ductal carcinoma. The benign breast lesions are shown here for comparison where a blue color and the quantitative measurement <200 mean KPA as in (figure If) suggestive of benign breast lesion and (Figure 1g) shows fibrocystic disease.

Assessment of liver metastases

Patients with liver metastases were assessed for any suspected intra-abdominal lesion. Two were found to have complex cysts in their right kidney and the third patient had gall stones. Application of shearwave elastography helped in localising the hard area within the complex cyst which was later confirmed as renal cell carcinoma. Figure 2a and 2b shows the imaging taken of the patients, figure 2c shows a normal kidney for comparison. The third patient had two metastatic lesions in the liver with additional finding of the gall stones. There was very stiff lesion in the bed of gall bladder which was then confirmed on histopathology as malignancy. Figure 3a shows the gall bladder images of the patient and 3b shows normal gall bladder appearance on shearwave elastography.

FIGURE I. BREAST LESIONS APPEARANCE ON SHEARWAVE ELASTOGRAPHY

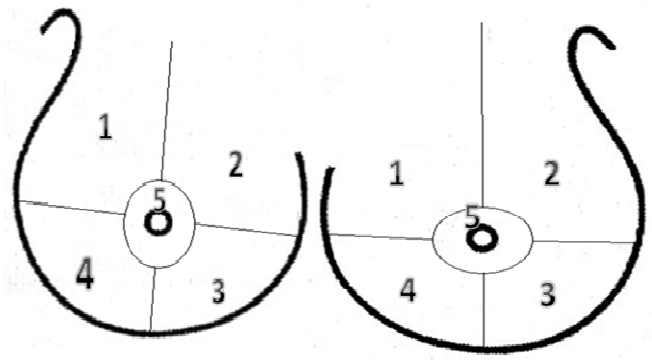

Figure Ia: Breast regions for application of shearwave elastography

Figure Ib: Appearance of Breast cancer in patient 1 presenting with axillary lymphadenopathy

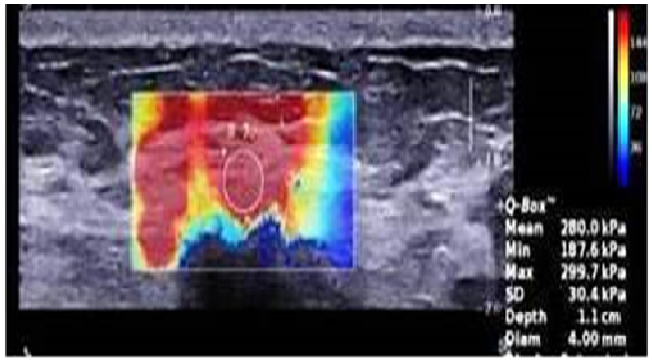

Figure Ic: Appearance of Breast cancer in patient 2 presenting with axillary lymphadenopathy

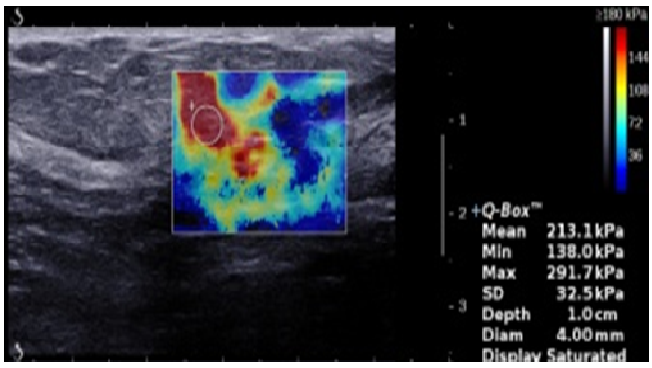

Figure Id: Appearance of Breast cancer in patient 3 presenting with axillary lymphadenopathy

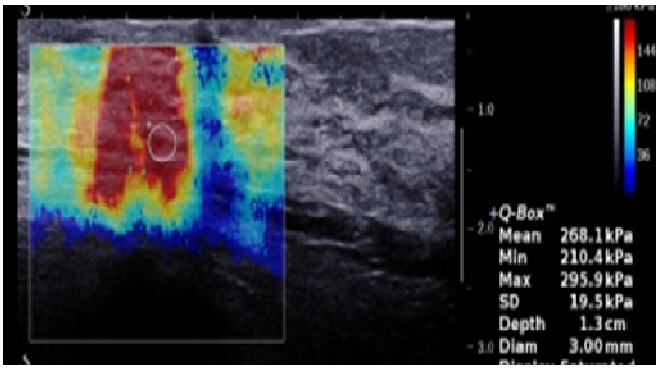

Figure Ie: Appearance of Breast cancer in patient 4 presenting with axillary lymphadenopathy

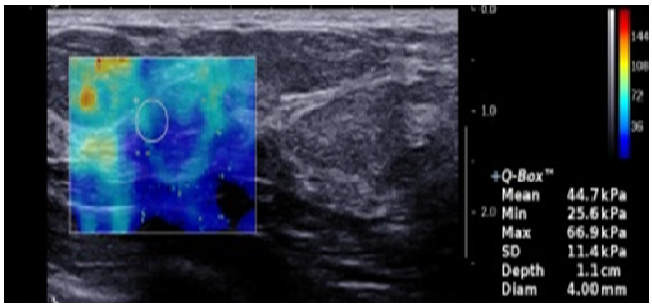

Figure If: Appearance of Benign Breast disease in a patient presenting with breast lump

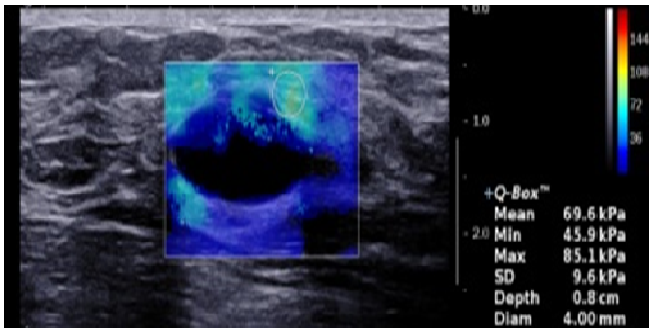

Figure Ig: Appearance of Fibrocystic disease in a patient presenting with breast lump

FIGURE II: APPEARANCE OF KIDNEY LESIONS ON SHEARWAVE ELASTOGRAPHY

Figure IIa: Appearance of carcinoma in right kidney in patient 1 presenting with liver metastases

Figure IIb: Appearance of carcinoma in right kidney in patient 2 presenting with liver metastases

Figure IIc: Appearance of normal kidneyon shearwave elastography

FIGURE III: APPEARANCE OF GALL BLADDER LESION ON SHEARWAVE ELASTOGRAPHY

Figure IIIa: Appearance of carcinoma gall bladder in patient 3 presenting with liver metastases

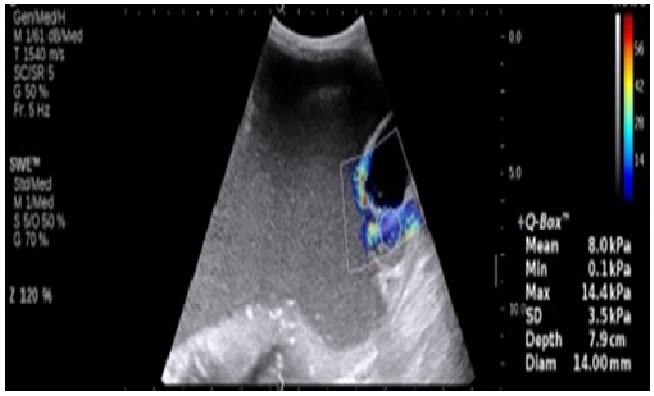

Figure IIIb: Appearance of normal gall bladder on shearwave elastography

DISCUSSION

Shearwave elastography is a new emerging technology in medical diagnostics. It has its established role in staging liver fibrosis in cases of chronic liver diseases such as viral hepatitis. There is also literature available suggesting its role with high sensitivity and specificity in characterising lesions in breast, prostate, thyroid and musculoskeletal. However there is little

literature available suggesting its utilisation in cases of unknown primary cancers. This study involved patients having metastases in axillary lymph nodes and liver.

The Assessment of the Clinical Value of SuperSonic Shear Wave Elastography in the Ultrasonic Evaluation of Breast Lesions (BE1 trial) was conducted including 614 benign and 144 malignant breast lesions[8]. They concluded that the addition of the shearwave elastography to the B-mode ultrasound increases the specificity of the ultrasound and detected more malignant lesions which were then wrongly reported as benign lesions on BI-RAD scoring. Other studies including from different parts of the world also suggested that the application of shearwave elastography is highly reproducible and detects more cancers as compared to conventional breast imaging modalities[7, 9-11]. However all these studies included palpable breast masses, while in our study we included patients with impalpable lesions which were also missed on conventional imaging. The findings in our study suggest potential role of shearwave elastography in screening purpose as well. The younger age group of patients where mammogram has limited role as screening tool, addition of shearwave elastography may provide a substantial mean to detect cancer earlier. However data on a large series of younger (<40 years) patients is needed to support this statement.

The role of shearwave elastography has already been reported in solid organs like thyroid, liver and prostate, where it was reported to be highly sensitive in characterising the nature of lesions[2, 3, 6, 12, 13]. There is limited information available in assessing its utilisation in cases where the suspicious area is masked. Our study showed a potential of this technique to differentiate between the benign and malignant component of the complex mass. The complex cysts were although reported on conventional ultrasound and CT scan so the gall stones were also reported, however the thickening of the gall bladder wall and the bed was not observed nor the solid lesions within the complex cysts were considered. When shearwave elastography was applied over these areas there was abrupt change in the qualitative as well as in quantitative measurements. This finding is highly valuable in cases where there is malignant transformation in a benign mass. This role can also be utilized to assess the progression and early detection of the cancers having high risk of malignant transformation.

The shearwave elastography is a non invasive technique with no risk of radiation and no absolute contraindication and the results are reproducible[14]. The probe is used in the same way as the conventional ultrasound without causing any remarkable discomfort to the patient.

This study is a novel finding however we appreciate its limitation of a small sample size. This was a pilot study to understand the potential role of the technique. Further studies with larger sample size in individual organs will help to establish guidelines in this regard. There is also need for the establishment of proper scoring system to differentiate benign and malignant lesions in different organs. There is also need to understand the limitations of the technique and its sensitivity and specificity in soft tissue tumours.

CONCLUSION AND RECOMMENDATIONS

The shearwave elastography appears to have a potential role in characterising solid tumours present in breast and abdomen. It showed its potential role in searching the primary cancer in patients with unknown primary. However there is need to understand indications and limitations of shearwave elastography. Studies with large sample size are required to formulate the scoring system and validate these findings.

Summary statement

Shearwave elastography is a recently introduced imaging technique, which measures tissue stiffness and displays results in quantitative and qualitative mode. Literature is available showing its role in assessing liver stiffness in cirrhotic patients and its role in differentiating benign and malignant lesions in breast, thyroid, prostate etc. In cancer imaging conventionally used modes are X-ray, Ultrasound, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) scan. However in a small group of cancer patients these modalities fail to identify the risk of primary tumour. In this study we applied shearwave elastography technique in patients having unknown primary cancer. There were seven patients including 4 with axillary lymphadenopathy and 3 with liver metastases. Shearwave elastography successfully identified the four breast lesions, 2 primary cancers in kidney and one in gall bladder. This preliminary data warrants further research in this regard.

Conflict of interest:

Authors declare no conflict of interest.

Advances in knowledge

This is the first report suggesting a role of shearwave elastography to locate unknown primary cancer. Given its non-invasive and patient friendly technique this can be utilised in this regard and warrants further research to make specific guidelines.

REFERENCES

1. Americn Cancer Society [Internet]. Cancer-Unknown Primary. (1 ed) 2014. Available from:

http://www.cancer.org/cancer/ cancerofunknown-primary/
2. Akcay MA, Semiz-Oysu A, Ahiskali R, Aribal E. The value of ultrasound elastography in differentiation of malignancy in thyroid nodules. Clin Imaging. 2014;38(2):100-3.
3. Mansor M, Okasha H, Esmat S, Hashem AM, Attia KA, El-din Hussein H. Role of ultrasound elastography in prediction of malignancy in thyroid nodules. Endocr Res. 2012;37(2):67-77.
4. Szczepanek-Parulska E, Wolinski K, Stangierski A, Gurgul E, Biczysko M, Majewski P, et al. Comparison of diagnostic value of conventional ultrasonography and shear wave elastography in the prediction of thyroid lesions malignancy. PLoS One. 2013;8(11):e81532.
5. Zhang B, Ma X, Wu N, Liu L, Liu X, Zhang J, et al. Shear wave elastography for differentiation of benign and malignant thyroid nodules: a meta-analysis. J Ultrasound Med. 2013;32(12):2163-9.
6. Barr RG, Memo R, Schaub CR. Shear wave ultrasound elastography of the prostate: initial results. Ultrasound Q. 2012;28(1):13-20.
7. Klotz T, Boussion V, Kwiatkowski F, Dieu-de Fraissinette V, Bailly-Glatre A, Lemery S, et al. Shear wave elastography contribution in ultrasound diagnosis management of breast lesions. Diagn Interv Imaging. 2014;95(9):813-24.
8. Schafer FK, Hooley RJ, Ohlinger R, Hahne U, Madjar H, Svensson WE, et al. ShearWave Elastography BE1 multinational breast study: additional SWE features support potential to downgrade BI-RADS(R)-3 lesions. Ultraschall Med. 2013;34(3):254-9.
9. Chang JM, Won JK, Lee KB, Park IA, Yi A, Moon WK. Comparison of shear-wave and strain ultrasound elastography in the differentiation of benign and malignant breast lesions. AJR Am J Roentgenol. 2013;201(2):W347-56.
10. Ko KH, Jung HK, Kim SJ, Kim H, Yoon JH. Potential role of shear-wave ultrasound elastography for the differential diagnosis of breast non-mass lesions: preliminary report. Eur Radiol. 2014;24(2):305-11.
11. Lee SH, Chang JM, Kim WH, Bae MS, Seo M, Koo HR, et al. Added Value of Shear-Wave Elastography for Evaluation of Breast Masses Detected with Screening US Imaging. Radiology. 2014;273(1):61-9.
12. Bota S, Peck-Radosavljevic M. Non-invasive evaluation of patients with viral hepatitis. Minerva Gastroenterol Dietol. 2014;60(1):39-54.
13. Stoian D, Cornianuz M, Dobrescu A, Lazar F. Nodular thyroid cancer. Diagnostic value of real time elastography. Chirurgia (Bucur). 2012;107 (1):39-46.
14. Mun HS, Choi SH, Kook SH, Choi Y, Jeong WK, Kim Y. Validation of intra- and interobserver reproducibility of shearwave elastography: Phantom study. Ultrasonics. 2013;53(5):1039-43.

AUTHOR AFFILIATION:

Dr. Binafsha Manzoor Syed *(Corresponding Author)*
Department of Surgery
Liaquat University of Medical & Health Sciences
(LUMHS), Jamshoro, Sindh-Pakistan.
Email: binafsha.syed@lumhs.edu.pk
drbinafsha@hotmail.com

Prof. Jawaid Naeem Qureshi
Department of Surgery
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Ahmed Khan Sangrasi
Department of Surgery
LUMHS, Jamshoro, Sindh-Pakistan.

Prof. Bikha Ram Deverajani
Department of Medicine
LUMHS, Jamshoro, Sindh-Pakistan.

Prof. Noshad A. Shaikh
Department of Surgery
LUMHS, Jamshoro, Sindh-Pakistan.

Prof. Munir Ahmed Junejo
Department of Radiology
LUMHS, Jamshoro, Sindh-Pakistan.