

## Use of 2D Strain Imaging for Detecting Left Ventricular Dysfunction in Patients Receiving Pre and Post Chemotherapy with Anthracyclines

Suresh V Patted<sup>1</sup>, Sanjay C Porwal<sup>2\*</sup>, Sameer S Ambar<sup>3</sup>, Nikhil Basavanagowda<sup>4</sup>, Rohan Bhise<sup>5</sup>, Prasad MR<sup>6</sup>, Vishwanath Hesarur<sup>6</sup> and Vaibhav Patil<sup>6</sup>

<sup>1</sup>Professor and HOD, Department of Cardiology, J.N. Medical College, Belgaum, Karnataka, India.

<sup>2</sup>Professor, Department of Cardiology, J.N. Medical College, Belgaum, Karnataka, India.

<sup>3</sup>Associate Professor, Department of Cardiology, J.N. Medical College, Belgaum, Karnataka, India.

<sup>4</sup>Senior Resident, Department of Cardiology, J.N. Medical College, Belgaum, Karnataka, India.

<sup>5</sup>Associate Professor, Department of Oncology, J.N. Medical College, Belgaum, Karnataka, India.

<sup>6</sup>Assistant Professor, Department of Cardiology, J.N. Medical College, Belgaum, Karnataka, India.

### \*Correspondence:

Sanjay C Porwal, Professor, Department of Cardiology, J.N. Medical College, Belagavi, 590010, Karnataka, India, E-mail: drsanjayporwal@gmail.com.

Received: 30 March 2018; Accepted: 28 April 2018

**Citation:** Suresh V Patted, Sanjay C Porwal, Sameer S Ambar, et al. Use of 2D Strain Imaging for Detecting Left Ventricular Dysfunction in Patients Receiving Pre and Post Chemotherapy with Anthracyclines. *Cardiol Vasc Res.* 2018; 2(2); 1-4.

### ABSTRACT

**Introduction:** Cancer is a major public health and economical concern. Chemotherapy induced LV Dysfunction hinders the applicability of these agents. Anthracycline chemotherapy plays a major role in many cancer treatments, especially breast cancer. Cardiotoxicity is a major concern in this group as it can have early onset or late onset, clinically apparent or subclinical. Echocardiography is the non-invasive technique of choice in the imaging of patients before, during and after undergoing chemotherapy. Speckle tracking echocardiography gives an objective and qualitative assessment of LV function. This study was done to assess the risk factors associated with chemotherapy induced LV Dysfunction along with the feasibility of 2D speckle tracking strain imaging.

**Methods:** 54 consecutive patients above the age of 18 years diagnosed to have breast cancer from November 2015 to October 2016 were included in this study. The patients were further divided into LV Dysfunction group and Non LV Dysfunction group at the end of the follow up. The baseline clinical, echocardiographic parameters and follow up parameters were compared in the 2 groups.

**Results:** Anthracycline induced LV Dysfunction was found in 14.8% of the study population. Advanced age, low BMI, Diabetes, advanced cancer stage, number of chemotherapy cycles were all found to be associated with increased risk of developing chemotherapy induced LV dysfunction. 2D strain imaging was helpful in early detection of LV Dysfunction in 25% of the LV Dysfunction group. Among the patients who had LV Dysfunction at the end of the chemotherapy regimen, 75% had persistent LV Dysfunction during follow-up where as 25% recovered their LV Function.

**Conclusion:** Chemotherapy induced LV Dysfunction remains a major public health concern and it is not uncommon. The development of LV Dysfunction in this group of patients should be carefully monitored by 2D strain imaging as it can help in detection of early onset of LV Dysfunction.

## Keywords

Anthracyclines, 2D speckle tracking, Chemotherapy, LV Dysfunction, Global Longitudinal Strain.

## Introduction

Cancer is a major public health and economical concern. Multidisciplinary approach with surgery, radiotherapy and chemotherapy has resulted in significant reduction in the mortality [1]. Treatment for cancer has improved significantly over the years and has proved to reduce recurrences as well as increase the rate of cure. Chemotherapy is one of the principle areas of development in the history of cancer treatment. However, the applicability of these drugs has been limited by their effect of cardiotoxicity [2].

A variety of chemotherapeutic agents have been in use. Current cancer treatments incorporate multiple agents whose deleterious effects may be additive or synergetic. Cytostatic antibiotics of anthracycline class are the most recognized ones for their cardiotoxicity, but other chemotherapeutic agents such as alkylating agents can also cause serious cardiotoxicity. Anthracycline chemotherapy regimens play a major role in many cancer treatments like breast carcinoma, sarcoma, lymphoma, gynecological cancers and childhood cancers [3,4]. Thus, with long term cancer survivorship there will be a substantial group of cancer patients who will remain at risk of early cardiovascular morbidity and mortality due to their anthracycline chemotherapy [5,6].

Cardiotoxicity can appear either early (within days) or late (within months or years later) in the course of the disease and may vary from subclinical myocardial dysfunction to irreversible heart failure or even death. Limited data is available on mechanism of developing cardiac dysfunction and susceptibility of patients for the same [7]. Recent consensus statements define chemotherapy induced cardio toxicity as a decrease in the Left Ventricular Ejection Fraction (LVEF) of more than 10% to a value less than 55%, confirmed by repeated cardiac imaging [8]. Echocardiography is the technique of choice in the cardiac imaging of patients before, during and after cancer chemotherapy because of its wide availability, easy repeatability, versatility, lack of radiation exposure, and safety in this group of patients. Speckle-tracking echocardiography is a new noninvasive imaging technique of echocardiography that allows an objective and quantitative evaluation of global and regional myocardial function [9]. By tracking the displacement of speckles during the cardiac cycle, speckle-tracking echocardiography allows semi-automated elaboration of myocardial deformation in 3 spatial directions: longitudinal, radial and Circumferential. In addition, speckle-tracking echocardiography offers an evaluation of the occurrence, direction and velocity of left ventricle (LV) rotation [10].

The present study was designed with an aim to assess the Left Ventricular End Diastolic Volume (LVEDV), Left Ventricular End Systolic Volume (LVESV), Left Ventricular Stroke Volume (SV), Left Ventricular Ejection Fraction (LVEF), Left Ventricular Fractional Area Change by using 2D Speckle-

tracking-based left ventricle Global Longitudinal Strain (GLS) and Global Circumferential Strain (GCS) imaging before and after chemotherapy in patients receiving chemotherapy with anthracyclines.

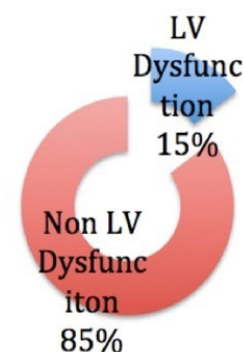
## Methods

The present study was conducted between November 2015 and October 2017. 54 consecutive patients above 18 years of age who were diagnosed to have breast cancer prior to consultation and had been advised anthracycline group of chemotherapy agents were included. Ethical clearance was obtained from ethical committee of J. N. Medical College. Patients who had a previous history of myocardial injury, received radiotherapy and those with LV dysfunction at baseline were excluded. Anthropometric data in regards to height, weight, BMI and baseline characteristics such as cancer variant, chemotherapy regimens were entered in a pre-structured proforma. All subjects underwent a baseline echocardiographic examination which was ECG gated and 2D speckle tracking transthoracic analysis was done offline. Images acquired included all the below mentioned but not limited to a parasternal short axis view at apical, mid and basal levels and an apical 4, 3 and 2 chamber view by real time acquisition. Echocardiographic examination was repeated after each scheduled cycle of anthracycline chemotherapy. In patients who had symptoms or signs of heart failure and/or in those who developed echocardiographically definable LV dysfunction, the chemotherapy was stopped and the patient was followed up. In all the other patients, they underwent an echocardiographic examination at 3, 6 and 12 months intervals.

After offline analysis with automated software installed in EPIQ 7C echo machine on each view of long and short axis views, the left ventricular endocardial borders were manually traced. Longitudinal strain was derived by using apical 2-chamber, 3-chamber, 4-chamber views whereas circumferential by parasternal Short Axis at basal, mid and apical level and finally global strain of longitudinal and circumferential (Bull's eye) were obtained in every patient during each assessment.

## Results

54 patients were included in the study. The mean age was  $58 \pm 15$  years. The baseline characteristics of the study population are depicted in Table 1. 14.8% (n=8) developed LV dysfunction (Figure 1).



Characteristic	LV Dysfunction group n=8	Non LV dysfunction group n=46	p value
Age	62 ± 10.2	56 ± 9.8	0.01
BMI	19.68 ± 2.1	22.45 ± 1.8	0.01
Hypertension	3	14	0.24
Diabetes	4	10	0.040
Renal failure	2	8	0.47
Cancer Stage III-IV	5	19	0.01
Chemotherapy cycles	6.8 ± 1.2	4.9 ± 1.1	0.01
Doxorubicin	6	31	0.040
Epirubicin	2	15	0.131

### Echocardiographic findings

Baseline and post completion of chemotherapy parameters in both the groups is depicted in Table 2.

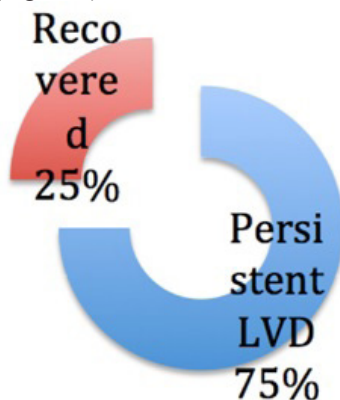
Characteristics	Baseline			Completion		
	LVD	Non LVD	p value	LVD	Non LVD	p value
LV EF (%)	62 ± 4.4	66 ± 4.1	0.05	49 ± 4.2	64 ± 4.3	0.001
GLS	-22.18 ± 2.04	-23.32 ± 2.88	0.22	-18.87 ± 2.12	-22.44 ± 2.59	0.001
GCS	-25.56 ± 4.89	-27.70 ± 2.81	0.04	-24.15 ± 4.28	-27.15 ± 4.15	0.001

### Strain Imaging

Global longitudinal strain and circumferential strain were done during each visit. In 2 patients who had 6% and 8% drop in LV EF post chemotherapy, the Global Longitudinal Strain was reduced by 16% and 18% respectively, which is a significant drop. Moreover the same 2 patients went on to develop definable LV Dysfunction at the end of 3 months post chemotherapy. This shows that strain parameters can detect early onset LV Dysfunction while being easily reproducible.

### Follow up

On follow up, at 3 months out of the 8 patients who had developed LV Dysfunction, 6 patients continued to have persistent LV dysfunction whereas 2 patients recovered. At long term follow up of 12 months; it was found that all the 6 patients who had LV dysfunction at the end of 3 months continued to have LV dysfunction (Figure 2).



### Chemotherapeutic agent

The mean cumulative dosage of doxorubicin in the LV Dysfunction group was 350 ± 46.2 mg/m<sup>2</sup>, where as in the non LV Dysfunction group it was 340 ± 42.2mg/m<sup>2</sup>. With respect to epirubicin, the mean cumulative dose was 132 ± 154mg/m<sup>2</sup> in the LV Dysfunction group and 144 ± 128mg/m<sup>2</sup> in the non LV Dysfunction group. Both were not found to be statistically significant.

### Discussion

In the present, we evaluated chemotherapy induced LV dysfunction in patients undergoing chemotherapy with anthracyclines. Advanced age, low BMI, Diabetes, advanced cancer stage, number of chemotherapy cycles were all found to be associated with increased risk of developing chemotherapy induced LV dysfunction. Chemotherapeutic agent and their cumulative dosage when measured per m<sup>2</sup> of the body surface area did not correlate with the risk of developing LV dysfunction. Among the patients who developed LV dysfunction post chemotherapy, majority (75%) of them had persistent LV dysfunction after 3 months of the onset of LV dysfunction. In those who had LV dysfunction at the end of 3 months, it was found that all of them remained in LV dysfunction even on long-term follow-up. Cancer survival, especially in the initial stages has shown increased survival rates owing to earlier diagnosis. The adverse effects of chemotherapy, such as cardiotoxicity have been on the rise and have become a paramount issue for cancer patient survival and morbidity. Chemotherapy induced cardiomyopathy secondary to Anthracyclines has been known [11]. In our study Anthracycline induced LV dysfunction developed in 14.8% of the study population. Although the study included only 54 patients who are undergoing chemotherapy, similar studies in the Indian subcontinent have not been done and further prospective studies are necessary to evaluate the same.

The present study showed that LVEF and Global strain parameters were reduced not only in the LV Dysfunction group, but also in the Non LV Dysfunction group suggesting subclinical LV Dysfunction even in the Non LV Dysfunction group. This further signifies the importance of early and correct recognition of chemotherapy induced LV Dysfunction in such patients.

The present study had several limitations. The study population was only 54 patients in whom both baseline and follow-up echocardiographic examinations were done, so it cannot be generalized for the whole patient population who receive Anthracyclines. The medication details regarding treatment for chemotherapy induced LV dysfunction were not analysed in the present study which could throw light on why majority of the LV Dysfunction patients failed to recover during follow-up. A routine Coronary angiography was not performed in all patients and hence it was not included in the analysis, however those patients who were found to have coronary artery disease were excluded from the study.

### Conclusion

The study demonstrated the presence of Chemotherapy induced LV Dysfunction in patients receiving Anthracyclines group of

---

chemotherapy. Age, low BMI, diabetes, advanced cancer stage are all associated with higher risk of developing LV Dysfunction post chemotherapy. Careful monitoring with non-invasive modalities such as strain imaging are ideal for early detection of LV dysfunction.

## References

1. Gillespie HS, McGann CJ, Wilson BD. Noninvasive diagnosis of chemotherapy related cardiotoxicity. *Curr Cardiol Rev*. 2011; 7: 234-244.
2. Brana I, Tabernero J. Cardiotoxicity. *Ann Oncol*. 2010; 21: 173-179.
3. Nabhan C, Byrtek M, Rai A, et al. Disease characteristics, treatment patterns, prognosis, outcomes and lymphoma-related mortality in elderly follicular lymphoma in the United States. *Br J Haematol*. 2015; 170: 85-95.
4. Chihara D, Westin JR, Oki Y, et al. Management strategies and outcomes for very elderly patients with diffuse large B-cell lymphoma. *Cancer*. 2016; 122: 3145-3151.
5. Armstrong GT, Chen Y, Yasui Y, et al. Reduction in late mortality among 5-year survivors of childhood cancer. *N Engl J Med*. 2016; 374: 833-842.
6. Patnaik JL, Byers T, DiGiuseppe C, et al. Cardiovascular disease competes with breast cancer as the leading cause of death for older females diagnosed with breast cancer: a retrospective cohort study. *Breast Cancer Res*. 2011; 13: R64.
7. Mercurio G, Cadeddou C, Piras A, et al. Early epirubicin-induced myocardial dysfunction revealed by serial tissue Doppler echocardiography: correlation with inflammatory and oxidative stress markers. *The Oncologist*. 2007; 12:1124-1233.
8. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). *Eur Heart J*. 2016; 21; 2768-2801.
9. Dandel M, Lehmkuhl H, Knosalla C, et al. Strain and strain rate imaging by echocardiography: basic concepts and clinical applicability. *CurrCardiolRev* 2009; 5: 133-148.
10. Shaw SM, Fox DJ, Williams SG. The development of left ventricular torsion and its clinical relevance. *IntJCardiol*2008; 130: 319-25.
11. Swain SM, Whaley FS, Ewer MS. Congestive heart failure in patients treated with doxorubicin: a retrospective analysis of three trials. *Cancer* 2003; 97: 2869-2879.