Clinics in Oncology

Editorial
Published: 30 Jul, 2021

Echocardiographic Strain Analysis: Is it Vital to Rule out Very Low Doses of Anthracyclines Related Cardiotoxicity?

*Rafael B Piveta[1], Samira Saady Morhy[1] and Marcelo Luiz Campos Vieira[1,2]**

[1]Hospital Israelita Albert Einstein, Brazil

[2]Heart Institute (InCor), Sao Paulo University Medical School, Brazil

Keywords

Echocardiography; Strain; Cardiotoxicicity

Editorial

New advances in oncology therapy increased cancer patient's survival. However, those patients are exposed to the damaging effects of anticancer treatment, especially chemotherapy-related cardiotoxicity leading to heart failure which represents a significant cause of morbidity and mortality [1-4]. Anthracyclines have a high efficacy in the treatment of solid tumors, including breast cancer, however, they can cause irreversible cardiac damage and affect the prognosis of those patients .Heart failure in the setting of anthracycline therapy has a 2-year mortality rate of up to 60% [1,3,4]. Thus, earlier and more sensitive parameters to identify patients at risk for future heart failure are very important, once these patients may benefit from early medical intervention with cardioprotective regimens. While many patients tolerate standard doses of chemotherapy without long-term complications, cardiomyocytes damaging can occur after the first dose in other patients. Therefore, early detection of cardiotoxicity and a cardioprotection therapy are fundamental and cornerstones for the best prognosis of those patients [1-4].

Left Ventricular Ejection Fraction (LVEF) is the recognized method to diagnose, follow and monitor cardiotoxicity. However, it has shown low sensitivity, changing just in later phases when the majority of the patients do not very appropriately respond to treatment [3]. Thus, it has worldwide dramatically increased the interest in identifying early markers of cardiotoxicity that could predict the subsequent decrease in LVEF and progression to Heart Failure (HF).

Subclinical cardiotoxicity can be detected by the analysis of myocardial deformations assessed by 2-Dimensional Speckle Tracking Echocardiography (2DSTE), especially Global Longitudinal Strain (2DGLS) [4-6]. In this sense, Sawaya et al. [1] in a prospective investigation comprising 81 patients, demonstrated that 2DGLS measured at the end of treatment (3 months after a cumulative dose of 240 mg/m^2 doxorubicin or 300 mg/m^2 epirubicin) was the best predictor of subsequent development of cardiotoxicity. In a similar study, Negishi et al. [2] followed up 81 women treated with trastuzumab, 37 of whom received anthracyclines simultaneously (cumulative dose of 240 mg/m^2 of doxorubicin or 300 mg/m^2 of epirubicin) and 2DGLS, evaluated after 6 months of treatment, was the best predictor of cardiotoxicity. A relative fall greater than 11% from its baseline value had a sensitivity of 65% and a specificity of 94% to identify patients with subsequent left ventricular systolic dysfunction. A systematic review involving 1,504 patients during or after the end of chemotherapy demonstrated the important value of analyzing myocardial deformation using 2DSTE in the early recognition of cardiotoxicity. The best parameter for this evaluation was the 2DGLS, with a reduction of 10% to 15% in relation to its pre-chemotherapy value being the best predictor of cardiotoxicity [6]. Thus, recent international guidelines suggest that the relative percentage reduction of 2DGLS >15% from baseline is very likely to be abnormal [3,4].

Currently it is possible to study myocardial mechanics employing 3D technology (3DSTE). 3DSTE enables myocardial deformation quantification offering the advantage of a complete analysis of the left ventricle from a single rendered volumetric data (from a single and same heart beat, under the same loading conditions), presenting the potential to overcome intrinsic limitations of 2DSTE (foreshortening of left ventricle and geometrical assumptions) [5]. 3DSTE may be employed to study longitudinal, radial or circumferential myocardial fibers (as with 2DSTE) or a combination of those fibers in different spatial distributions (area strain, area tracking). Thus, 3DSTE myocardial analysis enables a higher proximity to the cardiac anatomy and demonstrates many similar results to

OPEN ACCESS

Correspondence:
Marcelo Luiz Campos Vieira, Hospital Israelita Albert Einstein, Laboratory of Echocardiography, Av. Albert Einstein, 627/701, São Paulo, 05651-901, Brazil, Tel: (+55)-11-3747-0440/(+55)-11-981888301;
E-mail: mluiz766@terra.com.br

Received Date: *05 Jul 2021*
Accepted Date: *27 Jul 2021*
Published Date: *30 Jul 2021*

Citation:
Piveta RB, Morhy SS, Vieira MLC. Echocardiographic Strain Analysis: Is it Vital to Rule out Very Low Doses of Anthracyclines Related Cardiotoxicity?. Clin Oncol. 2021; 6: 1840.

ISSN: 2474-1663

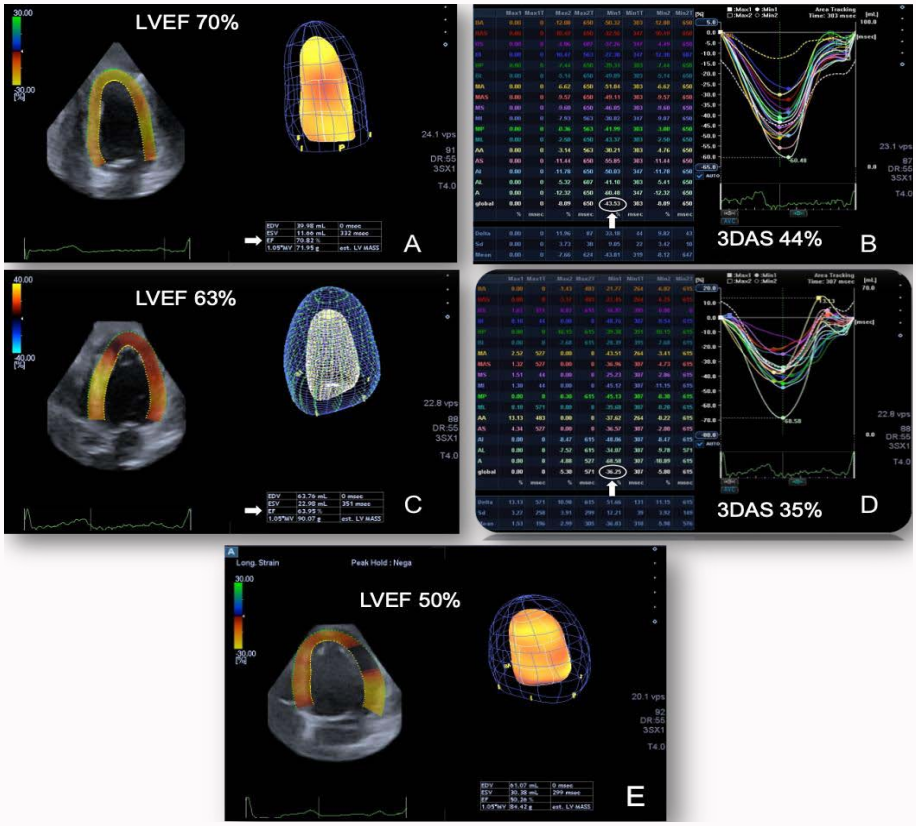

Figure 1: Patient with breast cancer undergoing chemotherapy. In **A, B**: baseline evaluation showing LVEF of 70% and 3DAS of 44%. In **C, D:** early revaluation, after low dose of anthracycline (120 mg/m^2), showing LVEF of 63% and 3DAS of 35%. In **E:** revaluation 6 months after the end of chemotherapy, showing an LVEF of 50%. Note that after low dose of anthracycline (120 mg/m^2), although LVEF did not changed, 3DAS dropped significantly. Also, 6 months later, LVEF dropped significantly. Thus, 3DAS can represent an earlier marker of cardiotoxicity.
LVEF: Left Ventricular Ejection Fraction; 3DAS: area strain calculated by Three-Dimensional Speckle Tracking

cardiac magnetic resonance, being more consistent when compared to 2DSTE analysis in different clinical conditions. However it has not been much studied in cardiomyopathy associated with chemotherapy scenarios.

Miyoshi et al. [6] evaluated the left ventricular mechanics through 2DSTE and 3DSTE in 55 patients with preserved LVEF after chemotherapy treatment with anthracyclines and observed that the 3D Area Strain (3DAS) and 3D Circumferential Strain (3DCS) were the most altered parameters compared to a control group. In this study, AS3D was independently associated with the cumulative dose of anthracycline. However, there was no assessment of patients at baseline (before chemotherapy), limiting the analysis of the method as an early marker of cardiotoxicity. Santoro et al. [7] evaluated 100 patients with breast cancer undergoing treatment with anthracyclines and demonstrated potential superiority of 3DSTE in relation to other echocardiographic parameters in the subclinical diagnosis of cardiotoxicity, with a greater effect observed in 3DCS and 3DAS. However, these patients were evaluated after a higher cumulative dose of anthracycline (mean of 505 mg/m^2 of epirubicin). Other recent study, Song et al. [8] evaluated 89 patients with lymphoma and demonstrated potential superiority of 3DSTE over 2DSTE in the early identification of cardiotoxicity, however, changes were observed after a mean cumulative dose of 263 mg/m^2 of epirubicin.

Despite very important investigations, these studies involving 2DSTE and 3DSTE did not evaluated patients earlier, after exposure to a lower dose of anthracycline.

In a recent study involving 86 patients with non-Hodgkin's lymphoma, Hodgkin's disease and acute leukemia, 2DGLS was evaluated after cumulative dosage of 150 mg/m^2 of doxorubicin and was a predictor of cardiotoxicity in the 6 patients (7%) who had a fall in LVEF after one year of the cancer treatment [9].

Piveta et al. [10] evaluated patients with breast cancer at 3 clinical moments: Baseline and after cumulative doses of 120 mg/m^2 and 240 mg/m^2 of anthracyclines. LVEF, 3DSTE, 2DSTE and ultrasensitive troponin I were evaluated. The only parameters that changed very early, after exposure to low dose anthracycline (120 mg/m^2) were 3DCS and 3DAS. These findings using 3DSTE are unprecedented and promising, suggesting that these parameters could represent earlier markers of myocardial injury induced by anthracyclines (Figure 1).

Thus, the assessment of ventricular mechanics with echocardiographic speckle tracking, especially three-dimensional technique, at an earlier time, after very low doses of anthracyclines, may be important and of vital clinical value. We hypothesize that this technique could provide additive information to clinical risk stratification and identify a subset of patients at higher risk for future development of heart failure. In this sense, it could be decisive for the introduction of cardioprotection at earlier clinical time.

References

1. Sawaya H, Sebag IA, Plana JC, Januzzi JL, Ky B, Tan TC, et al. Assessment

of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. Circ Cardiovasc Imaging. 2012;5(5):596-603.

2. Negishi K, Negishi T, Hare JL, Haluska BA, Plana JC, Marwick TH. Independent and incremental value of deformation indices for prediction of trastuzumab-induced cardiotoxicity. J Am Soc Echocardiogr. 2013;26(5):493-8.
3. Zamorano JL, Lancellotti P, Muñoz RD, Aboyans V, Asteggiano R, Galderisi M, et al. 2016 ESC position paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. Eur Heart J. 2016;37(36):2768-801.
4. Plana JC, Galderisi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: A report from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2014;27(9):911-39.
5. Kleijn SA, Pandian NG, Thomas JD, De Isla LP, Kamp O, Zuber M, et al. Normal reference values of left ventricular strain using three-dimensional speckle tracking echocardiography: Results from a multicentre study. Eur Heart J Cardiovasc Imaging. 2015;16(4):410-6.
6. Miyoshi T, Tanaka H, Kaneko A, Tatsumi K, Matsumoto K, Minami H, et al. Left ventricular endocardial dysfunction in patients with preserved ejection fraction after receiving anthracycline. Echocardiography. 2014;31(7):848-57.
7. Santoro C, Arpino G, Esposito R, Lembo M, Paciolla I, Cardalesi C, et al. 2D and 3D strain for detection of subclinical anthracycline cardiotoxicity in breast cancer patients: A balance with feasibility. Eur Hear J Cardiovasc Imaging. 2017;18(8):930-6.
8. Song FY, Shi J, Guo Y, Zhang CJ, Xu YC, Zhang QL, et al. Assessment of biventricular systolic strain derived from the two-dimensional and three-dimensional speckle tracking echocardiography in lymphoma patients after anthracycline therapy. Int J Cardiovasc Imaging. 2017;33(6):857-68.
9. Charbonnel C, Convers-Domart R, Rigaudeau S, Taksin AL, Baron N, Lambert J, et al. Assessment of global longitudinal strain at low dose anthracycline-based chemotherapy, for the prediction of subsequent cardiotoxicity. Eur Heart J Cardiovasc Imaging. 2017;18(4):392-401.
10. Piveta RB, Rodrigues ACT, Vieira MLC, Fischer CH, Afonso TR, Daminello E, et al. Early changes in myocardial mechanics detected by 3-dimensional speckle tracking echocardiography in patients treated with low doses of anthracyclines. JACC Cardiovasc Imaging. 2018;11(11):1729-31.