



## What is the Role of Two-Dimensional Speckle Tracking Echocardiography in the Diagnosis and Management of Anthracycline-Induced Cardiotoxicity?

Isabela Bispo Santos da Silva Costa<sup>1</sup> and Ludhmila Abrahão Hajjar<sup>1,2</sup>

Instituto do Câncer do Estado de São Paulo - Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (ICESP-HC-FMUSP), São Paulo, SP - Brazil¹

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (INCOR - HC-FMUSP) São Paulo, SP - Brazil<sup>2</sup>

The increasing number of patients with neoplasms and survivors<sup>1,2</sup> has raised the interest of the scientific community in the diagnosis and early management of the effects of neoplasms and/or their treatments on patients. In that scenario, the injury caused to the cardiovascular system belongs to a spectrum and can impair all cardiovascular system structures in a clinically variable way, ranging from asymptomatic forms to cardiovascular death. Most studies on cardiotoxicity have focused on ventricular dysfunction because of its presentation severity and because it is the major cause of late non-oncologic mortality of neoplasm survivors.<sup>3</sup>

In oncologic patients, the drugs most commonly related to ventricular dysfunction are anthracyclines. A Recent studies have reported that the damage related to those drugs, if not identified and treated early, evolves continuously from cell injury to ventricular dysfunction. In the past decade, several studies showed that the subclinical detection of cardiotoxicity, by use of biomarkers, such as troponin and BNP, might be an opportunity to prevent cardiovascular injury, allowing for early treatment and more appropriate individualized follow-up. 5-8

Another current challenge regarding cardiotoxicity is to understand the natural history of neoplasm survivors. Little is known about the prevalence of cardiovascular disease

## **Keywords**

Neoplasms; Cardiotoxicity; Anthracyclines / toxicity; Ventricular Dysfunction; Troponin; Natriuretic Peptides; Echocardiography; Speckle-Tracking.

Mailing Address: Ludhmila Abrahão Hajjar •

Endereço: Av. Dr. Arnaldo, 251 10 andar. Postal Code 01246-000, Cerqueira César, São Paulo, SP - Brazil

E-mail: ludhmila@usp.br

**DOI:** 10.5935/abc.20180047

in those patients, and, thus, no long-term follow-up strategy has been defined for them.

In this issue of the *Arquivos Brasileiros de Cardiologia*, Kang et al.<sup>9</sup> make a relevant contribution to the diagnosis of anthracycline-induced cardiotoxicity. In a cohort of survivors of non-Hodgkin's diffuse large B cell lymphoma treated with anthracyclines, those authors have shown that, as compared to healthy controls, those patients have lower values of circumferential and longitudinal strains on echocardiography in a population with normal ejection fraction. Such findings have been evidenced mainly by changes in the subendocardial segments. In accordance with previous studies, <sup>10</sup> those authors have emphasized the radial strain measure to be of little importance in that population. Inter- and intraobserver analyses reinforce that data obtained can be safely reproducible.

Kang et al.<sup>9</sup> have not observed a direct relationship between anthracycline doses and strain values, suggesting that the myocardial damage, reflected on impaired myocardial deformation, can occur even at doses considered non-cardiotoxic (lower than 240 mg/m²), provided that the population studied used doses ranging from 150.94 mg/m² to 440.00 mg/m².

That was an observational study with a small sample, but its finding is clinically relevant and should be explored. It is yet to be defined whether that finding is only a marker of chemotherapeutic response or whether it represents the beginning of the pathophysiology of the clinically manifest cardiovascular lesion. Further studies are required to clarify whether the neoplasm itself, through its endothelial changes, could be related to changes in strain.

Even without definite responses, the study by Kang et al.<sup>9</sup> contributes to reinforce the importance of combining the clinical practice with a sensitive non-invasive method to aid the management of oncologic patients during and after chemotherapy.<sup>10,11</sup>

## **Short Editorial**

## References

- Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Estimativa 2018: incidência de câncer no Brasil. Rio de Janeiro; 2017.
- Siegel R, DeSantis C, Virgo K, Stein K, Mariotto A, Smith T, et al. Cancer treatment and survivorship statistics, 2012. CA Cancer J Clin. 2012;62(4):220-41. Erratum in: CA Cancer J Clin. 2012;62(5):348.
- Reulen RC, Winter DL, Frobisher C, Lancashire ER, Stiller CA, Jenney ME, et al; British Childhood Cancer Survivor Study Steering Group. Long-term cause-specific mortality among survivors of childhood cancer. JAMA. 2010;304(2):172-9.
- Smith LA, Cornelius VR, Plummer CJ, Levitt G, Verrill M, Canney P, et al. Cardiotoxicity of anthracycline agents for the treatment of cancer: systematic review and meta-analysis of randomized controlled trials. BMC Cancer. 2010 Jun 29;10:337.
- Cardinale D, Colombo A, Bacchiani G, Tedeschi I, Meroni CA, Fabrizio V, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation. 2015;131(22):1981-8.
- Cardinale D, Colombo A, Sandri MT, Lamantia G, Colombo N, Civelli M,et al. Prevention of high-dose chemotherapy-induced cardiotoxicity in highrisk patients by angiotensin-converting enzyme inhibition. Circulation. 2006;114(23):2474-81.

- Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, et al. Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies: the OVERCOME trial (preventiOn of left Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive ChemOtherapy for the treatment of Malignant hEmopathies). J Am Coll Cardiol. 2013;61(23):2355-62.
- Gulati G, Heck SL, Ree AH, Hoffmann P, Schulz-Menger J, Fagerland MW, et al. Prevention of cardiac dysfunction during adjuvant breast cancer therapy (PRADA): a 2 × 2 factorial, randomized, placebo-controlled, double-blind clinical trial of candesartan and metoprolol. Eur Heart J. 2016;37(21):1671-80.
- Kang Y, Xiao F, Chen H, Wang W, Shen L, Zhao H, et al. Subclinical Anthracycline-Induced Cardiotoxicity in the Long-Term Follow-Up of Lymphoma Survivors: A Multi-Layer Speckle Tracking Analysis. Arq Bras Cardiol. 2018; 110(3):219-228.
- 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.
- Yu W, Li SN, Chan GC, Ha SY, Wong SJ, Cheung YF. Transmural strain and rotation gradient in survivors of childhood cancers. Eur Heart J Cardiovasc Imaging 2013;14(2):175-82.



This is an open-access article distributed under the terms of the Creative Commons Attribution License