

## Subclinical Ventricular Dysfunction Detected by Speckle-Tracking Two Years after Use of Anthracycline

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### Dear Editor

We would like to congratulate the authors for the publication of their article "Subclinical Ventricular Dysfunction Detected by Speckle-Tracking Two Years after Use of Anthracycline", considering the great practical applicability of the theme. Cardiotoxicity secondary to chemotherapy drugs is a reality that imposes, on cardiologists and oncologists, the challenge of prevention and/or early detection of this complication, which has high morbidity and mortality<sup>1</sup>.

In this regard, we read with interest the abovementioned article, which highlights the usefulness of speckle-tracking to attain an early diagnosis of subclinical ventricular dysfunction,

although this finding does not directly imply in implementing treatment due to the lack of current scientific evidence, which makes studies in this area even more important.

However, we would like to point out some aspects to add to the scientific information brought on by this article. In the Results section, the authors demonstrate that almost 80% of patients had also received cyclophosphamide as a chemotherapy drug, an alkylating agent that may be associated with ventricular dysfunction rates of up to 25% of the cases<sup>2,3</sup>, which cannot be minimized in the Discussion and Conclusion sections of this study. This same rationale can be applied to the more than 50% of patients receiving radiotherapy in the mediastinal region, regardless of the treated hemithorax, since the incidence of coronary heart disease in these patients is a side effect of significant incidence<sup>4</sup>.

We also observed a high rate of hypertension in both groups of patients and controls and that the systolic and diastolic BP levels were higher in the latter than in the first group. We would like to know if there was any difference between the groups regarding the class of antihypertensive drug used, as data in the literature suggest some protective effect of ACE inhibitors and beta-blockers on the incidence of ventricular dysfunction and major clinical outcomes<sup>5</sup>.

### Keywords

Heart Failure; Ventricular Dysfunction Left/chemically induced; Echocardiography; Anthracyclines/adverse effects.

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## Reply

### Dear authors

We appreciate your interest and comments about our article.

Cyclophosphamide-associated cardiotoxicity presents as a syndrome of heart failure, myocarditis, pericarditis, or their association and can lead to death. It has an acute onset, with signs and symptoms occurring within one to ten days after the first dose, lasting for approximately one week<sup>1</sup>. Delayed cardiotoxicity development (> 3 weeks) is very rare in patients that survive the initial event<sup>2-4</sup>. In our sample, patients were assessed after a median of two years after the end of chemotherapy, making it unlikely that the obtained results can be attributed to the use of cyclophosphamide.

The observation about the increased incidence of coronary artery disease (CAD), as a side effect of radiotherapy in patients with breast cancer is absolutely pertinent. This increase is proportional to the number of cardiovascular risk factors the patients have and the mean dose of radiation to the heart. Previous data demonstrated that CAD development after radiation therapy occurred after a longer period of follow-up: 82 months, on average<sup>5</sup>.

Recently, Darby et al<sup>6</sup> showed an increase of 16.3% (per Gray of radiation) in the rate of major coronary events in the first four years after radiation therapy in women with breast cancer<sup>6</sup>. This increase begins in the first five years after radiotherapy and persists for at least 20 years<sup>6</sup>. The development of new technologies in the field of radiation therapy has shown to be favorable to reduce this side effect<sup>7</sup>.

In our study, however, none of the patients had coronary event during the study period.

Although there was no difference in the percentage of participants considered hypertensive in both groups ( $p = 0.71$ ), the controls had higher levels of systolic and diastolic BP at the time of evaluation. As stated in the Discussion section, we attribute this fact to greater adherence to antihypertensive therapy among patients who were undergoing more stringent medical follow-up in the post-chemotherapy period. The increase in blood pressure levels tends to compromise strain values<sup>8</sup>. However, despite these higher blood pressure levels in the control group, the strain values were more compromised in the group using doxorubicin (DOX), which reinforces the importance of this drug as an independent predictor of reduced  $\epsilon$ LL and  $\epsilon$ CC in our patients.

There was no significant difference between the groups regarding the class of antihypertensive drug used: fourteen patients (34%) from the control group used angiotensin-converting enzyme inhibitors or Angiotensin II-receptor blockers vs. ten patients (25%) in the group treated with DOX ( $p = 0.367$ ). One (2.4%) participant from the control group used a beta-blocker vs. five (12.5%) in the DOX group ( $p = 0.109$ ).

Sincerely,

André L C Almeida

Edval Gomes dos Santos Júnior

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