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The intriguing issue of genetic predisposition and the importance of identification of pre-clinical markers of endothelial damage in radiotherapy-induced cardiotoxicity

We have read with great interest the article ‘Expert consensus for multi-modality imaging evaluation of cardiovascular complications of radiotherapy in adults: a report from the European Association of Cardiovascular Imaging and the American Society of Echocardiography’ by Lancellotti et al.1 Late cardiovascular complications after chest radiotherapy (RT), even modern RT techniques, are a remarkably increasing problem. Care of cancer survivors is becoming an emergent and topic issue especially after chest irradiation and more so for left breast cancer patients.2 In this subset of patients, RT should be addressed a risk factor for coronary artery disease (CAD) and since vascular endothelium seems to be the first target of radiation, it should be our duty to detect early marker of endothelial damage long before clinical coronary events. In our institution, we are enrolling early left breast cancer patients in a protocol study to estimate coronary flow reserve ( CFR) by Tc-99m-Tc-sestamibi SPECT Myocardial Perfusion Imaging before and after RT. Regional CFR is defined as the ratio between dipyridamole and baseline myocardial blood flow.3 In preliminary data, we have found ST segment and T wave of ventricular repolarization abnormalities registered soon after RT, coupled with myocardial perfusion defects (mostly in the apical region of the left ventricle) and with reduction of estimated values of CFR even in patients with no other risk factors for (CAD) besides chest RT. Our patients were all treated according to the Quantecc constraints.4 We do not know yet the predicting role of CFR reduction for clinical coronary events, but while following up very closely our patients, we are aggressively treating their risk factors for CAD.

We are also intrigued by the genetic issue of RT-induced cardiotoxicity, and we are also trying to identify the genetic marker of increased risk. We have read the editorial by Kelsey et al.5 and the paper by Hilbers et al.6 about the association between genetic variants in Transforming Growth Factor β-1 and Plasminogen activator inhibitor-1 and an increased risk for cardiovascular diseases after RT for breast cancer. The authors say that, for the great majority of individuals, the normal tissue toxicity is influenced by the cumulative effect of multiple genetic polymorphisms. If these assumption are proved to be true, then we will be able to predict which patient are more exposed to toxicity and we can improve our ‘tailored therapies’ maximizing the therapeutic ratio of cancer therapies.

We would like to ask two questions:

(1) What is your opinion on genetic determinants of RT-induced toxicity? The search for polymorphisms should be encouraged in Oncology Departments to modify therapeutic strategies. (For example, left mastectomy instead of breast-conserving surgery plus adjuvant RT if the risk of RT-induced cardiotoxicity is genetically increased.)

(2) Do you think it is worthy to search for a suitable early marker of endothelial damage? And do you think CFR reduction could be such a preclinical marker? Would you suggest an ECG recording soon after RT to screen high-risk patients?

Conflict of interest: None declared.

References


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The intriguing issue of genetic predisposition and the importance of identification of pre-clinical markers of endothelial damage in radiotherapy-induced cardiotoxicity: reply

We thank Dr Gallucci for her letter about the joint EACVI/ASE expert consensus for multi-modality imaging evaluation of cardiovascular complications of radiotherapy in adults.1 As underlined, there is compelling evidence that chest radiotherapy can increase the risk of heart disease. Although modern radiotherapy techniques are likely to reduce the prevalence and severity of radiation-induced heart disease (RIHD), the incidence of RIHD is expected to