POTENTIAL OF ONCOCARDIOLOGY

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We read the recent review by Yeh and Chang with interest and congratulate them for reinforcing the role of cardio-oncology (oncocardiology), an emergent discipline in the cardiology field. This article is timely in the context of the proliferation of new cancer therapies and the increase in the number of cancer survivors. Cardiovascular care for cancer patients has become challenging because they live longer and are at greater risk of cardiovascular events. Yeh and Chang pointed out the well-known toxic effects of anthracyclines, but they also underlined the cardiovascular toxicity resulting from the anti-HER2 and anti-VEGF antibodies, inhibitors of tyrosine kinases and of other intracellular signals. This description is very important because it aims at educating the cardiology community about the growing issue of cardiotoxicity in cancer patients.

However, the authors did not address the potential cardiovascular effects of the emergent immune checkpoint-modulating immunotherapy. To our knowledge, this therapy, including anti-PD-1 and anti-CTLA-4 antibodies, represents the most promising therapeutic approach against cancer. These treatments have revolutionized cancer therapy, but their application is also associated with a spectrum of immune-related adverse events, including heart failure due to dysimmune acute myocarditis or dilated cardiomyopathy with fibrosis. Although the rate of left ventricular dysfunction was low in clinical trials, safety signals were issued and selected cases of cardiotoxicity were recently published. A 2016 article reported on patients with cardiotoxicity observed during immune checkpoint-blocking therapy in 6 large clinical American and European cancer centers. These adverse events were sometimes fatal and occurred mostly in patients who had previous cardiovascular diseases or risk factors. Most of these therapies act by blocking PD-1 or CTLA-4 receptors on T cells and then stimulating their antitumor effect. The mechanisms of their cardiotoxicity have not been fully elucidated, but many years before their use, PD-1 deficiency was described to predispose for spontaneous myocarditis and cardiomyopathy in mice. Severe myocarditis also occurred in a model of CTLA-4-deficient mice. Interestingly the epidemiologic data presented in a white population showed evidence for an association of the CTLA-4 +49A>G polymorphism with dilated cardiomyopathy. The authors of this work suggested that upregulated immune reactions in the myocardium induced by CTLA-4 modulation might contribute to inflammatory responses and favor reparative fibrosis. This example of cardiotoxicity induced by the new immunotherapies strengthens the importance of cardio-oncology for patient care and development of cancer and cardiovascular basic research.