

REPLY: Impact of Cardiac Rehabilitation on Cardiotoxicity Reduction

We thank Dr Coma and colleagues for their interest in the TITAN trial.¹ Regarding baseline risk of our study population, the European Society of Cardiology Heart Failure Association risk was moderate in 43% and high in 5%,² with 73% meeting criteria for referral to cardio-oncology rehabilitation. The lack of observed effect of exercise training (ET) on resting left ventricular ejection fraction in the TITAN trial is consistent with other similar studies (Figure 1),³ including a recent randomized controlled trial of 104 patients with breast cancer receiving anthracycline chemotherapy.⁴ Nevertheless, ET remains a key component of care for cancer survivors, given that many have reduced cardiorespiratory fitness following their treatment. Foulkes et al⁴ reported a 6% decrease in VO_{2peak} following 3 months of treatment, similar to the 9% decrease in TITAN participants, despite undertaking twice the ET volume. However, unlike other ET intervention studies, we did not observe improved cardiorespiratory fitness at 12 months, likely attributable to the lower exercise dose in TITAN. Overall, we believe that the TITAN trial highlights the need for health care providers to broaden their approach to cardiovascular risk in patients with cancer. Indeed, we have shown that cancer survivors are also at high risk for nonheart failure-related outcomes, including myocardial infarction, cerebrovascular disease, thromboembolism, and cardiovascular death up to 10 years from cancer diagnosis.⁵ We therefore agree with Coma et al that larger studies with long-term follow-up are needed to understand the potential benefits of

rehabilitative programs on overall cardiovascular health in patients with cancer.

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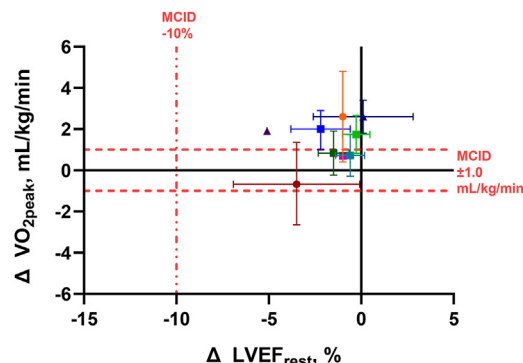
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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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FIGURE 1 Exercise Training and Resting Left Ventricular Ejection Fraction

- Hornsby et al. 2014
- Howden et al. 2019
- Scott et al. 2023 (Concurrent)
- Scott et al. 2023 (Sequential)
- Scott et al. 2023 (Continuous)
- Foulkes et al. 2023
- Kirkham et al. 2023
- ▲ Haykowsky et al. 2009
- ▲ Jacquinet et al. 2022