

Letters

TO THE EDITOR

Impact of Cardiac Rehabilitation on Cardiotoxicity Reduction



We read the very interesting paper by Kirkham et al¹ about randomized controlled trial evaluating the impact of cardiac rehabilitation (CR)-modeled care on cardiotoxicity reduction and cardiovascular risk improvement in breast-cancer patients undergoing treatment.

Beneficial effects of exercise and structured programs on cardiovascular risk prevention in breast cancer patients have been reported in several studies and reviews.² However, its role in cardiotoxicity prevention remains unknown (Table 1).³⁻⁵ The authors conclude that the CR-modeled intervention had no effect on left ventricular ejection fraction or biomarkers of cardiotoxicity. Nevertheless, no cases of cardiotoxicity were observed in the entire studied cohort, when the reported rate in medical literature with this type of treatment is 15% to 20%. These data suggest that the enrolled population is at very low risk of developing cardiotoxicity, which would considerably limit the conclusions of the study. Furthermore, no improvement was observed in any of the parameters related to the patients' functional capacity, neither with the implementation of the CR-modeled program in the intervention group nor by

comparing the follow-up data with the control arm. Such results are particularly astonishing, given that most of the studies addressing the subject highlight an improvement in physical condition compared to control groups, particularly in those CR programs lasting more than 3 months.

The results of this clinical trial may help to be critical with the systemic generalization of CR-modeled intervention in order to prevent cardiotoxicity in breast cancer. However, considering the limitations of the study, its conclusion seems excessively blunt. It would be reasonable to note that larger studies would be required to confirm whether such types of programs have a potential benefit on cardiotoxicity, especially in high-risk cohorts or with a different training approach.

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TABLE 1 Summary of Clinical Findings From Trials Examining Exercise Intervention for Cardiotoxicity Related to AC and Trastuzumab

First Author, Year	Patient Group	Intervention	Finding
Ma 2018 ³	n = 70 (IG = 31) undergoing AC	Aerobic exercise: 3 sessions weekly for 16 wk	Statistically significant decrease in LVEF in UC patients
Hojan et al ⁴ 2020	n = 47 (IG = 26) undergoing trastuzumab	Aerobic and resistance training Daily sessions for 9 wk	Statistically significant decrease in LVEF in UC patients
Foulkes et al ⁵ 2022	n = 104 (IG = 52) undergoing AC	Aerobic and resistance training 3-4 sessions weekly for 12 mo	Significant greater improvements in cardiac reserve measures (change in CO, SV, and LVEF from rest to peak exercise)

AC = anthracycline; CO = cardiac output; IG = intervention group; LVEF = left ventricular ejection fraction; SV = stroke volume; UC = usual care.

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](#).

REFERENCES

1. Kirkham AA, Mackey JR, Thompson RB, et al. TITAN trial: a randomized controlled trial of a cardiac rehabilitation care model in breast cancer. *JACC: Adv.* 2023;2(6):100424.
2. Coma N, Moral S, Ballesteros E, et al. Current evidence on the benefit of exercise in cancer patients: effects on cardiovascular mortality, cardiotoxicity, and quality of life. *Rev Cardiovasc Med.* 2023;24(6):160.
3. Ma Z. Effect of anthracycline combined with aerobic exercise on the treatment of breast cancer. *Pak J Pharm Sci.* 2018;31:1125-1129.
4. Hojan K, Procyk D, Horyńska-Kęstowicz D, Leporowska E, Litwiniuk M. The preventive role of regular physical training in ventricular remodeling, serum cardiac markers, and exercise performance changes in breast cancer in women undergoing trastuzumab therapy-an REH-HER study. *J Clin Med.* 2020;9:1379.
5. Foulkes SJ, Howden EJ, Haykowsky MJ, et al. The BREXIT study. *Circulation.* 2023;147(7):532-545.