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Impact of Supervised Exercise Training on HDL Cholesterol Efflux Capacity in Post-Myocardial Infarction Patients

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Abstract

A reduced incidence of cardiovascular events has been linked to high-density lipoprotein (HDL), with patient prognosis additionally shaped by its functional properties. While physical training is a vital measure for improving outcomes in the post-infarction (MI) cohort, the extent to which exercise modulates HDL function remains poorly defined. Sixty-two individuals suffering from acute MI were allocated at random to either a 12–14 week supervised exercise regimen (exercise group—EG) or a control condition (CG). The central goal of the investigation was to assess the impact of exercise on the movement of esterified cholesterol (EC) and unesterified cholesterol (UC) into HDL. Across the full cohort, the starting average velocity of EC transfer to HDL was 2.53 ± 0.83, rising to 2.74 ± 0.64 (P = 0.03) by the conclusion of follow-up. For UC, the analogous readings were 4.08 ± 1.2 initially and 4.4 ± 1.06 subsequently (P = 0.02). The net shift (follow-up less baseline) in EC equaled 0.15 ± 0.84 in the control arm and 0.27 ± 0.69 in the exercise arm (P = 0.53); regarding UC, the shifts came to 0.28 ± 1.14 and 0.35 ± 0.96 (P = 0.80) for the control and exercise arms, respectively. Among post-MI subjects, a 12–14-week course of supervised physical training failed to improve HDL function.

Keywords: Acute myocardial infarction, HDL functionality, Supervised exercise, Cardiac rehabilitation

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Introduction

Globally, myocardial infarction (MI) represents a principal source of morbidity and mortality, markedly diminishing patients' life quality and physical performance [1-3]. In the aftermath of an MI, the organism undergoes pronounced biochemical and physiological adjustments, including alterations in lipid handling [4]. High-density lipoprotein (HDL) is widely recognized for its capacity to counteract atherosclerosis, an effect predominantly driven by its role in reverse cholesterol transport and plasma esterification of cholesterol, coupled with several other positive effects, including the dampening of inflammation [5, 6]. In a study of approximately 3000 cardiovascular disease-free subjects, Rohatgi *et al*. [7] documented a robust negative correlation between cholesterol efflux capacity and incident cardiovascular events, with a median follow-up of 9.4 years. Even so, an MI can disrupt HDL functionality, thereby elevating the threat of repeat cardiovascular occurrences and both short- and long-term fatality [8-12]. Beyond the uptake of unesterified cholesterol (UC) from peripheral tissues—a step in the pathway known as reverse cholesterol transport—HDL within the intravascular space engages in a persistent acquisition of UC and esterified cholesterol (EC) from lipoproteins that contain apo B. This dynamic modifies the composition and function of HDL particles, is critical for maintaining plasma cholesterol homeostasis, and is itself an integral component of the

reverse cholesterol transport system. The UC assimilated by HDL undergoes esterification via lecithin–cholesterol-acyl-transferase (LCAT) in partnership with apo A-I, and a portion may subsequently be relocated to lipoproteins containing apo B [13].

While the elevated hazard of recurrent ischemic episodes following an MI is not entirely elucidated [14, 15], cardiac rehabilitation (CR) centered on physical exercise has proven effective in bettering cardiovascular results through gains in physical conditioning, symptom mitigation, and enhancements in autonomic control, vascular endothelial performance, and inflammatory status, collectively diminishing the odds of subsequent cardiovascular events [16-18]. Cardiorespiratory fitness indeed acts as a strong quantitative predictor of death from all causes [19]. Yet, the existence of a dose–response relationship linking the quantity and duration of exercise to the degree of cardiovascular risk and mortality reduction has not been firmly established [20]. Consequently, while moderate, exercise-based CR remains a pillar of post-MI care, with its well-characterized merits extending past gains in cardiovascular stamina alone, the particular channels through which it exerts influence over lipid metabolism—HDL functionality especially—are still largely uncharted, with contradictory findings concerning the ability of consistent aerobic training to augment cholesterol efflux capacity [21, 22]. Tellingly, a broad review examining how exercise training affects cardiovascular well-being omitted any reference to HDL and its functional parameters, features increasingly regarded as more consequential than a standalone HDL–cholesterol (HDL-C) measurement when gauging cardiovascular risk [23].

Given that modern cardiovascular disease therapies are increasingly emphasizing HDL function rather than mere HDL-C levels, clarifying how exercise-based CR might shape this dimension of lipid metabolism is of considerable importance [6, 24].

In the work reported here, we advanced the hypothesis that engagement with a structured CR protocol could bolster HDL functionality in individuals recovering from an MI, thereby yielding further justification for the deployment of exercise training to curtail cardiovascular risk in ways that surpass conventional lipid regulation.

Materials and Methods

Study design and participants

The present work constitutes a pre-planned secondary analysis of a prospective randomized trial that examined the effect of exercise on platelet reactivity after myocardial infarction (NCT 02958657). An exhaustive account of the methodology and core findings has been laid out in a prior publication [25]. In summary, patients diagnosed with type I MI [26] who were not habitually undertaking structured exercise before the index episode, who exhibited a left ventricular ejection fraction no lower than 45%, a hematocrit value spanning 32% to 52%, who were on dual antiplatelet therapy, and who were neither slated for operative coronary revascularization nor prescribed oral anticoagulation, were prospectively allocated via randomization to a supervised training protocol (exercise group) or to a control group. At hospital discharge, the deployment of guideline-directed treatments and lifestyle counseling, including recommendations to engage in physical activity, remained uniform across individuals regardless of group assignment. All participants enrolled in the trial had previously provided informed consent and underwent a cardiopulmonary exercise test at the initial study encounter (30 ± 5 days post-MI) and again upon completion of the follow-up window (12–14 weeks after the initial encounter).

Of the 65 patients whose data appeared in the principal publication [25], 62 had HDL-transfer readings at both baseline and follow-up. It was therefore retained in the current analysis (31 in each arm: exercise or control). The three remaining patients lacked both HDL-transfer measurements due to logistical or technical obstacles.

Exercise training program

Following the first study encounter, patients assigned to the intervention arm began a supervised exercise-based cardiac rehabilitation program at the Cardiovascular Rehabilitation and Exercise Physiology Unit of InCor/HCFMUSP. The training blueprint entailed 2-3 sessions per week, contingent on each participant's schedule. Every session included 5 minutes of warm-up, 40 minutes of aerobic work on a cycle ergometer, 10 minutes of localized resistance exercises, and 5 minutes of cool-down stretching. The aerobic workload was calibrated using heart rate aligned with the anaerobic threshold, set at 10% below the respiratory compensation threshold identified during the baseline cardiopulmonary exercise test. Participants who could commit to thrice-weekly training completed a 12-week follow-up, while those limited to twice-weekly attendance finished a 14-week follow-up. By adopting this framework, the cumulative training dose remained identical for all subjects within the exercise arm. Blood draws were performed at baseline and at the terminal follow-up visit for the exercise arm, and both at baseline and after a 12–14 week interval for the control arm.

Laboratory analyses

Blood specimens were obtained after an overnight fast of 12 hours to permit quantification of cholesterol transfer to HDL, along with other assays. The simultaneous movement of esterified cholesterol (EC) and unesterified

cholesterol (UC) out of a synthetic nanoparticle and into HDL was measured in vitro, following the protocol described by Lo Prete *et al*. [13]. Concisely, a donor lipid nanoparticle loaded with ^{3}H-cholesteryl oleate and ^{14}C-phosphatidylcholine or ^{3}H-triolein and ^{14}C-cholesterol was introduced to plasma under agitation and allowed to incubate for 1 hour at 37 °C. Upon chemical precipitation of the nanoparticle along with Apo B-containing lipoproteins, the supernatant housing the HDL fraction was subjected to radioactivity enumeration within a scintillation cocktail. The proportion of each lipid class that had migrated from the nanoparticle to HDL was subsequently computed.

Study purpose

The central thrust of this work was to probe how exercise shapes the movement of EC and UC into HDL particles. Secondary explorations targeted the role of exercise in modulating other lipid-related indices and inflammatory status.

Statistical analyses

Categorical data are presented as raw frequencies or proportions, with the chi-square test or Fisher's exact test used for group comparisons, depending on the context. Continuous measures are summarized as mean ± standard deviation (when normally distributed) or median ± interquartile range (when the distribution is nonnormal). Conformity to a Gaussian curve was verified through the Shapiro–Wilk procedure. For contrasts drawn between the study arms, the Independent-samples Student's t-test (parametric) or the Mann–Whitney approach (non-parametric) was selected accordingly. Within-group shifts in HDL transfer from baseline to the follow-up time point were examined, for the aggregate sample as well as for each arm in isolation, by way of the Paired Student's t-test (parametric) or the Wilcoxon Signed Rank Test (non-parametric). To explore group-by-category interactions involving HDL transfer expressed as a dichotomous variable, a binary logistic regression framework was implemented. The McNemar test, designed for paired-sample proportions, was applied to assess baseline-to-follow-up discrepancies in the HDL transfer endpoints. Every statistical evaluation used a two-tailed approach, with $p < 0.05$ as the threshold for significance. Computational procedures were performed using IBM SPSS Statistics 28.0.

Results and Discussion

Figure 1 outlines the study's participant flow. One month after the index MI, enrolled patients were randomly assigned to either the exercise or the control condition and followed for 12–14 weeks thereafter.

Figure 1. Flowchart of the study.

A summary of the cohort's clinical features is presented in **Table 1**. Participants averaged 59 years of age, with a male predominance of 74%, and the two study arms were well matched for prior medical history, GRACE score, ST-elevation MI presentation, renal function, troponin levels, left ventricular ejection fraction, and adherence to guideline-endorsed post-MI therapeutic regimens.

Table 1. Clinical characteristics of the population.

Parameter	P-value	Exercise intervention group (n = 31)	Standard care group (n = 31)
Mean age ± SD (years)	0.60	59.8 ± 9	58.5 ± 10.8
Proportion of males (%)	1.00	74.2%	74.2%

History of hypertension (%)	0.12	48.4%	67.7%
History of diabetes mellitus (%)	0.10	22.6%	41.9%
Prior stroke (%)	0.39	6.5%	12.9%
Prior myocardial infarction (%)	1.00	12.9%	12.9%
Previous coronary artery bypass grafting (%)	1.00	6.5%	6.5%
Previous percutaneous coronary intervention (%)	1.00	12.9%	12.9%
Active smoking (%)	0.15	35.5%	19.4%
ST-elevation myocardial infarction (%)	0.30	64.5%	51.6%
GRACE risk score (mean ± SD)	0.30	138.4 ± 24.3	130.3 ± 31.1
Left ventricular ejection fraction (%)	0.27	55.7 ± 6.3%	54.7 ± 7.3%
Serum creatinine (mg/dL, mean ± SD)	0.24	1.01 ± 0.2	1.09 ± 0.2
MDRD estimated GFR (mL/min, mean ± SD)	0.18	82.87 ± 23.57	74.81 ± 23.5
Ultrasensitive troponin I (pg/mL, median [IQR])	0.23	38.4 (11.8–50)	25 (2.9–50)
Dual antiplatelet therapy (%)	1.00	100%	100%
Statin therapy (%)	0.31	100%	96.8%
Beta-blocker use (%)	0.14	83.9%	66.7%
ACE inhibitor or ARB use (%)	0.40	77.4%	67.7%

Captured at randomization (30 days after the index MI). All P-values = NS. Abbreviations: ACEI = Angiotensin-converting Enzyme Inhibitor, ARB = Angiotensin Receptor Blocker, CABG = Coronary Artery Bypass Graft, DAPT = Dual Antiplatelet Therapy, DM = Diabetes Mellitus, GRACE = Global Registry of Acute Coronary Events, HTN = Hypertension, us-Troponin I = Ultra-sensitivity Troponin I, LVEF = Left Ventricular Ejection Fraction, MDRD = Modification of Diet in Renal Disease, MI = Myocardial Infarction, PCI = Percutaneous Coronary Intervention, and STEMI = ST-Elevation Myocardial Infarction.

The mean velocities at which EC and UC were transferred to HDL, recorded at study entry and again at the close of the monitoring phase for the full set of participants, are collated in **Table 2**; both measures rose to a statistically meaningful degree by the end of the observation window. A per-group breakdown of this same analysis is provided in **Table 3 and Figure 2**. A meaningful upswing was detected in the exercise arm alone, with the control arm showing no such change; that said, the delta (follow-up reading minus baseline reading), though numerically superior within the exercise arm, fell short of statistical significance. Turning to categorical endpoints, the groups did not differ meaningfully in EC (interaction P-value = 0.783). For UC, the fraction of individuals positioned above the median at both the initial and concluding assessments was indistinguishable across the two arms (96.8%). When scrutinizing within-group shifts in the proportion of patients surpassing the mean from the start to the end of follow-up, the observed changes remained statistically nonsignificant **(Table 4; Figure 3)**.

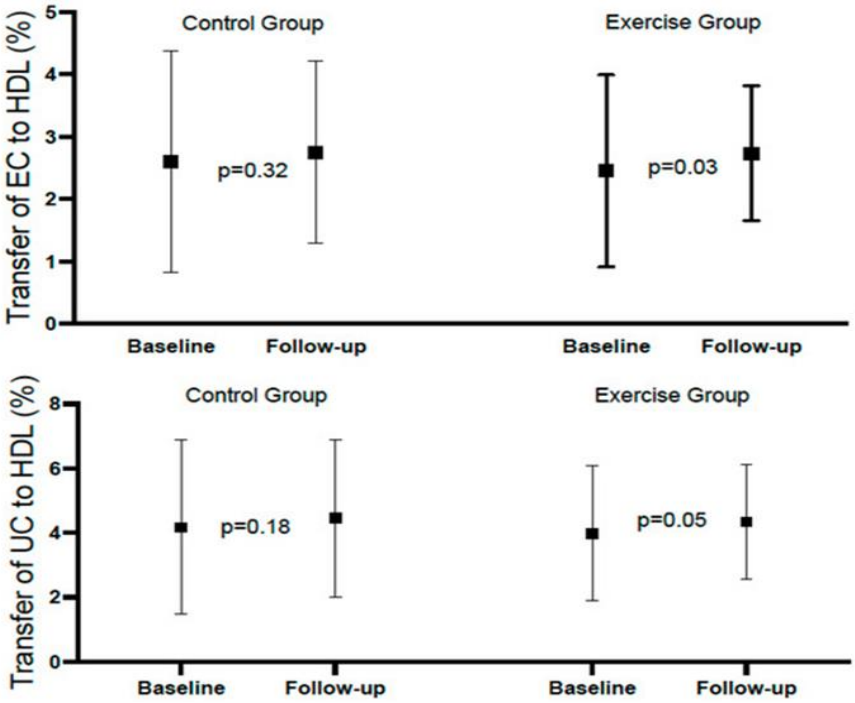

Figure 2. Forest plot of esterified and unesterified cholesterol to HDL in the control and exercise group.

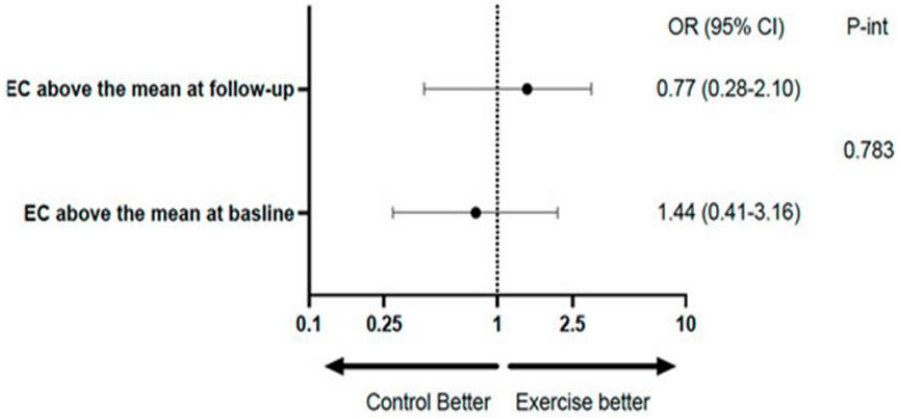

Figure 3. Forest plot showing the effect of exercise on the transfer process involving HDL.

Table 2. Average velocities at which esterified (EC) and unesterified (UC) cholesterol relocate to HDL, measured initially and at the conclusion of the surveillance interval for the aggregate subject pool.

Measure	P-value	Follow-up evaluation	Initial assessment
Esterified cholesterol transfer to HDL (mean ± SD)	0.032	2.74 ± 0.64	2.53 ± 0.83
Unesterified cholesterol transfer to HDL (mean ± SD)	0.021	4.40 ± 1.06	4.08 ± 1.2

Every figure shows the mean ± SD.

Table 3. Average velocities at which esterified cholesterol (EC) and unesterified cholesterol (UC) relocate to HDL, presented separately for the control and intervention arms.

Parameter	P-value	Exercise intervention group (n = 31)	Standard care group (n = 31)
EC transfer to HDL at baseline (mean ± SD)	0.480	2.45 ± 0.77	2.60 ± 0.89
EC transfer to HDL at follow-up (mean ± SD)	0.863	2.73 ± 0.54	2.75 ± 0.73
Within-group p-value* (EC transfer)	—	0.034	0.32
UC transfer to HDL at baseline (mean ± SD)	0.559	3.99 ± 1.05	4.17 ± 1.35
UC transfer to HDL at follow-up (mean ± SD)	0.678	4.34 ± 0.89	4.45 ± 1.22
Within-group P-value* (UC transfer)	—	0.053	0.18
Change from baseline to follow-up in EC (mean ± SD)	0.533	0.27 ± 0.69	0.15 ± 0.84
Change from baseline to follow-up in UC (mean ± SD)	0.804	0.35 ± 0.96	0.28 ± 1.14

P-value derived from testing the baseline against follow-up measurements. Every figure shows the mean ± SD.

Table 4. The impact of physical training on HDL transfer, as reflected in categorical parameters.

Parameter	Interaction P-value	Odds ratio (95% CI)	P-value	Exercise intervention group (n = 31)	Standard care group (n = 31)
EC levels above mean at baseline (%)	0.783	0.77 (0.28–2.10)	0.610	41.9	48.4
EC levels above mean at follow-up (%)	—	1.44 (0.41–3.16)	0.796	61.3	58.1
Within-group P-value* (EC)	—	—	—	0.083	0.366
UC levels above the mean at baseline (%)	NA	1.00 (0.23–4.41)	1.000	87.1	87.1
UC levels above mean at follow-up (%)	—	1.00 (0.06–16.74)	1.000	96.8	96.8
Within-group P-value* (UC)	—	—	—	0.058	0.083

P-value derived from testing the baseline against follow-up measurements. Abbreviations: EC = esterified cholesterol; UC = unesterified cholesterol; p-int = p for interaction.

Regarding other lipid parameters, both groups experienced a notable rise in HDL–cholesterol and LDL–cholesterol over the course of follow-up, yet no meaningful differences emerged between the groups **(Table 5)**. Within a subset consisting of 12 individuals from the control arm and 18 from the exercise arm, the average apolipoprotein A1 concentrations at the end of follow-up were recorded as 1.11 ± 0.19 and 1.13 ± 0.21, respectively (P = 0.844); for apolipoprotein B within this same subset, the corresponding values stood at 0.66 ± 0.04 and 0.69 ± 0.16, respectively (P = 0.598).

Table 5. The influence of exercise on lipid parameters.

Measure	P-value	Exercise intervention group (n = 31)	Standard care group (n = 31)
HDL cholesterol at baseline (mg/dL)*	0.891	38 ± 8	38 ± 10
HDL cholesterol at follow-up (mg/dL)*	0.713	42 ± 10	40 ± 10
Change from baseline to follow-up (HDL)*	0.109	4.54 ± 6.70	0.92 ± 9.43
Within-group P-value+ (HDL)	—	<0.001	<0.001
LDL cholesterol at baseline (mg/dL)*	0.422	71 ± 24	66 ± 26
LDL cholesterol at follow-up (mg/dL)*	0.634	76 ± 27	79 ± 34
Change from baseline to follow-up (LDL)*	0.306	59.93 ± 42.99	46.63 ± 53.05
Within-group P-value+ (LDL)	—	< 0.001	0.017
Total cholesterol at baseline (mg/dL)*	0.373	135 ± 30	129 ± 30
Total cholesterol at follow-up (mg/dL)*	0.488	141 ± 32	148 ± 39
Change from baseline to follow-up (total cholesterol)*	0.876	69.78 ± 48.70	67.37 ± 65.11
Within-group P-value+ (total cholesterol)	—	0.138	0.016
Triglycerides at baseline (mg/dL)⊥	0.720	98 (78–168)	94 (75–150)
Triglycerides at follow-up (mg/dL)⊥	0.499	103 (71–149)	120 (74–201)
Change from baseline to follow-up (triglycerides)⊥	0.046	18.5 (−23.5–61)	52 (7–139)
Within-group P-value+ (triglycerides)	—	0.806	0.276

+ P-value corresponding to the comparison between baseline and follow-up assessments. Mean ± SD; ⊥ Median (25th–75th percentiles).

Table 6 presents the effect of exercise on C-reactive protein (CRP) and peak VO_2. A numeric reduction in CRP was observed following the exercise intervention, though the change did not reach statistical significance (P = 0.06). As for peak VO_2, a meaningful elevation was detected within the exercise arm (P = 0.005) that was absent in the control arm, accompanied by a trend (P = 0.092) toward statistical significance when comparing the two groups against one another.

Table 6. The effect of exercise on inflammatory markers and maximal oxygen uptake.

Variables	Control group (n = 31)	Exercise group (n = 31)	P-value
CRP at baseline ⊥ (mg/dL)	1.80 (0.64–3.33)	1.26 (0.46–3.99)	0.607
CRP at follow-up ⊥ (mg/dL)	1.58 (0.74–2.91)	1.00 (0.35–4.04)	0.184
p-value +	0.719	0.060	
Peak VO_2 at baseline ⊥ ($mL \cdot kg^{-1} \cdot min^{-1}$)	20.00 (16.75–24.55)	22.1 (17.20–26.20)	0.459
Peak VO_2 at follow-up * ($mL \cdot kg^{-1} \cdot min^{-1}$)	21.58 ± 4.98	24.25 ± 6.76	0.092
p-value +	0.176	0.005	

Mean ± SD; ⊥ Median (25th–75th percentile). + P-value for the comparison of baseline and follow-up.

The findings of this randomized trial revealed that, in subjects suffering an acute MI, the movement of EC and UC into HDL underwent a decline during the earliest post-MI period, then rebounded to a significant degree after a 12–14 week interval, with this trajectory unfolding in a nearly identical manner irrespective of whether individuals were enrolled in a supervised exercise-based rehabilitation protocol or not.

A meta-analysis published by Salzwedel *et al*. [27] that scrutinized the contribution of cardiac rehabilitation following ACS (spanning > 50,000 patients) found a meaningful reduction in all-cause mortality in retrospective (HR = 0.64) and prospective (HR = 0.37) cohort studies. However, the lone randomized controlled trial, which recruited more than 1800 participants, showed neutral results (HR = 1.01).

Earlier work has established that exercise training accelerates the delivery of UC or EC to HDL in individuals with metabolic syndrome [28] and across both normal-weight young and older healthy volunteers [29]. Moreover, our research group previously reported that EC transfer to HDL was blunted in patients assessed on day five following MI, compared with those examined within 24 hours of the onset of MI symptoms. In contrast, no such discrepancy in UC transfer to HDL was observed between the groups [9].

That said, as underscored by Ruiz-Ramie *et al*. [22] upon concluding an exhaustive literature review: “there is mixed evidence that regular aerobic exercise improves

cholesterol efflux capacity". The inconsistencies may trace back to a host of variables, including exercise dosage and the baseline characteristics of study subjects, with only a handful of studies specifically probing this question in populations with myocardial infarction or acute coronary syndromes (ACS). In a retrospective investigation of post-ACS patients who participated in a 6-month outpatient cardiac rehabilitation initiative, Koba *et al*. [30] compared 57 program completers with 11 individuals who withdrew before completion. The central insight was that those who completed the full 6-month rehabilitation course showed a significantly greater HDL-mediated efflux capacity. A subsequent report from the same team, grounded in the same retrospective framework, pitted a 5-month outpatient rehabilitation program against 15 patients who either never joined or abandoned it prematurely and revealed a significant 9.4% surge in cholesterol efflux capacity. This benefit held regardless of the statin agent used [31].

In contrast, Sarzynski *et al*. [32], in dissecting the effects of exercise intensity and total volume on HDL function, observed a rise in HDL efflux capacity exclusively in the subgroups that underwent high-volume/high-intensity regimens.

To our knowledge, this study is the first of its kind to deploy a randomized design to evaluate a myocardial infarction cohort exposed to, or not, a supervised exercise rehabilitation curriculum, and it did not detect meaningful differences between the intervention and control arms. This null result may be a function of the comparatively short training window (12–14 weeks) in our cohort, compared with the studies referenced earlier (6 and 5 months), and/or reflect the particular intensity and modality of exercise we prescribed. It is worth noting that, within our sample. However, statistical significance was not reached; the delta between baseline and follow-up measurements for both EC and UC was numerically larger in the intervention arm. The within-group baseline-to-follow-up comparison for EC transfer to HDL attained statistical significance ($P = 0.03$) in the exercise arm alone—a finding absent in the control arm.

The body of literature examining how routine physical activity shapes circulating HDL-C concentrations has produced a patchwork of discordant findings. Sources of this variability may lie in the heterogeneity of the interventions deployed, the diversity of patient phenotypes studied, and the range of concurrent pharmacotherapies in use, with the preponderance of reports addressing the role of exercise in clinically stable populations and lacking either a comparator arm or random assignment [33, 34].

The current work, centered on post-MI subjects, identified a notable increase in mean HDL-C across both the control and intervention limbs, with no appreciable difference between them. On a separate note, rigorous LDL-C management is of the utmost importance in this elevated-risk post-MI group, including those classified as MINOCA [35]. Our data revealed a significant increase in LDL concentrations from baseline to the end of follow-up in both study limbs, without any meaningful separation between them. Given that every patient, save one, was on a high-potency statin at baseline and that the entire cohort was receiving statin therapy by the conclusion of follow-up, this upward shift might be ascribed to the LDL decrement typical of the initial MI phase, and/or to nutritional adjustments adopted during the follow-up interval.

Turning to the inflammatory dimension, a meta-analysis performed by Zheng *et al*. [36], encompassing 1250 healthy middle-aged and elderly individuals drawn from randomized controlled clinical trials, brought to light a pronounced reduction in CRP levels ($P = 0.0002$) among those randomized to aerobic exercise relative to control counterparts, with parallel patterns surfacing for other inflammatory indices, interleukin 6 being a case in point. Within the narrower domain of secondary prevention, a review by Lavie *et al*. [37] concluded that cardiac rehabilitation led to meaningful reductions in CRP concentrations, with greater reductions in patients with excess weight or who met criteria for obesity. Consistent with this line of evidence, the present investigation, focusing on post-MI patients, documented a numerical decrease in CRP from baseline to follow-up in both the exercise and control arms, with P-values of 0.06 and 0.72, respectively.

Regarding peak VO_2, the capacity of aerobic training to enhance this metric has been widely accepted for decades [17]. A published study [38] examined 126 MI patients participating in a cardiac rehabilitation initiative (without a control group) and found a substantial increase in peak VO_2 after a 3-month training period in this high-risk group. Beyond that, a meta-analysis pooling 12 investigations into the impact of post-MI cardiac rehabilitation on peak VO_2 set 855 control subjects against 827 intervention subjects and generated markedly favorable outcomes in support of the exercise cohort ($P < 0.0001$) [39]. The data reported here reveal a numerically larger improvement in peak VO_2 in the exercise arm, coupled with a borderline drift toward statistical significance (P-value = 0.092). One should note, however, that even though it fell short of significance, the share of current smokers within the exercise arm was 83% greater than in the control arm, a circumstance that may well have left an imprint on the findings, given the established adverse impact of smoking on VO_2 max [40].

Several limitations temper the present study. To begin with, because the rates of EC and UC transfer to HDL served as a secondary endpoint derived from the parent trial, the current observations must be viewed strictly as

hypothesis-generating. Compounding this, the fairly small sample size was likely underpowered to yield a more robust conclusion. Secondly, it is plausible that the length of supervised physical conditioning (12 to 14 weeks) was insufficient to produce a measurable effect on the endpoints of interest. Thirdly, other variables capable of swaying the outcomes—oxidative stress being a prime example—went unmeasured. Lastly, although indices of cholesterol transfer to HDL may bear a relationship to atheroprotection, whether shifts in this proxy marker can be concretely converted into clinical gains remains unverified.

Conclusion

Drawing on data from post-myocardial infarction subjects, our results suggest that a supervised physical training period spanning 12–14 weeks does not yield a statistically significant augmentation in EC and UC transfer to HDL compared with a non-exercising control condition. Across the entire cohort under study, a steady, parallel upswing in both EC and UC transfer to HDL occurred during the observation window, a pattern suggesting a transient dampening of these transfer rates at the earliest stage following MI. Given this pattern, it is appealing to propose that future research evaluate EC and UC transfer kinetics as surrogate indicators of myocardial recovery in the post-MI setting.

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Conflict of interest: None

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Ethics statement: Protocol approved by the Research Ethics Committee of the Clinical Hospitals, University of Sao Paulo Medical School (SDC 4086/14/066).
Informed consent was obtained from all subjects involved in the study

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