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Anti-ischemic effect of 2-week cycle of heparin plus exercise-to-ischemia twice daily in patients with "no-option" angina: the CARHEXA trial

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Background: Coronary collateral circulation (CCC) exerts protective effects on myocardial ischemia due to coronary artery disease (CAD), but the anti-ischemic, pro-CCC effects of exercise (E) with or without heparin (H) co-administration remain unclear.
Purpose: To establish the anti-ischemic functional efficacy of 2-week cycle of E-to-ischemia twice daily, with or without unfractionated i.v. H immediately before E, in patients with "no-option" CAD
Methods: In a prospective, single-center, parallel group study design we recruited 32 "no-option" patients (27 males; mean age of 61±8 years) with at least one chronically occluded coronary artery and stable angina, refractory to optimal medical management, not suitable for revascularization therapy and with E-induced ischemia. All underwent a 2-week cycle of E (2 E test per day, 5 days a week, for 2 weeks) and were randomized, with a double-blind design, to i.v. placebo (0.9% saline) versus unfractionated H (100 IU/kg up to a maximum of 5.000 IU iv, 10 min prior to E). Seattle stable angina questionnaire (SAQ), 12-lead E-ECG for time-to-ischemia (treadmill exercise testing), and MDCT angiography for CCC imaging (Rentrop score, from 0= absent to 3= full opacification of occluded vessel) were assessed at entry and re-assessed after treatment for symptomatic, ECG, and anatomic end-points respectively.
Results: In H+E group (n=16), time to 1 mm ST segment depression (ST-D) increased, and CCC improved, $p<0.05$. On the contrary, no difference was observed in E group (n=16) in the pre-specified end-points ($p>0.05$) (see table). Clinically important change of more 10 points in SAQ was observed regarding physical limitation, angina stability and disease perception in H+E patients, and in only angina frequency in E group.
Conclusion: A 2-week, 10 E test cycles are well tolerated and effective particularly with H in ameliorating symptoms, E-induced ischemia and CCC in "no-option" CAD patients with refractory angina.

The ECG and angiographic results

	Heparin + Exercise	Placebo + Exercise
Rentrop baseline	0.73±0.88	1.06±1.06
Rentrop 2-week	1.6±0.99*	1.19±1.05
Time to ST-D base (s)	269±64	273±176
Time to ST-D 2-week (s)	328±65*	306±151

*$p<0.05$.