Remote Ischemic Conditioning Reduces Myocardial Infarct Size in STEMI Patients Treated by Thrombolysis

In many developing nations, where primary percutaneous coronary intervention (PPCI) is not widely available, ST-segment elevation myocardial infarction (STEMI) patients are still treated by thrombolysis (1). However, because thrombolytic therapy is less effective than PPCI at restoring blood flow in an infarct-related coronary artery, thrombolyzed STEMI patients experience larger myocardial infarcts and are more likely to develop heart failure. As such, there is an urgent need for an innovative, easily applied, and low-cost cardioprotective therapy. In this regard, the heart can be protected against MI by simply applying cycles of brief ischemia and/or reperfusion to the arm or leg, which is termed remote ischemic conditioning (RIC) (2). Therefore, we hypothesized that RIC initiated on arrival at the hospital and before thrombolysis could reduce enzymatic MI size in STEMI patients (ERIC-LYSIS [Effect of Remote Ischemic Conditioning in Heart Attack Patients] Study; NCT02197117).

We performed a multicenter, single-blinded, randomized controlled trial in the developing nation of Mauritius. The Mauritian Ministry of Health and Quality of Life provided ethical approval of the study. All patients gave informed consent before entering the study. Adult patients presenting with a STEMI were randomly assigned to receive either RIC (4/5-min cycles of upper arm cuff inflation to 200 mm Hg and deflation) or to the control group (uninflated cuff placed on the upper arm for 40 min) on immediate arrival at the hospital. Exclusion criteria included contraindications for thrombolysis, previous MI, cardiac arrest, arteriovenous shunts, and pre-existing treatment with nicorandil or glibenclamide. Thrombolysis was achieved using streptokinase at a dose of 1.5 million units over 60 minutes. The RIC or control protocols were initiated before and continued during thrombolysis, and did not delay the onset of reperfusion. The pre-defined primary endpoint was enzymatic MI size as assessed by 24-h area under the curve (AUC) serum troponin T and creatine kinase-myocardial band (CK-MB), measured at 0, 6, 12, and 24 h.

Between March 2011 and November 2013, 519 STEMI patients were randomly assigned to receive either RIC \((n = 258)\) or the control protocol \((n = 261)\). The 2 groups had similar patient characteristics. AUC troponin T data were available for 414 patients, and AUC CK-MB data were available for 407 patients. Median enzymatic MI size was 32% smaller by 24-h AUC troponin T and 19% smaller by 24-h AUC CK-MB in patients who received RIC compared with the control patients (Table 1).

The ERIC-LYSIS study was the first to investigate the effect of RIC in STEMI patients reperfused by...
thrombolytic therapy in a developing nation. We found that those patients who were randomized to receive RIC upon arrival at the hospital and before thrombolytic therapy experienced a significant reduction in enzymatic MI size compared with the control group. The size of this cardioprotective effect was comparable to that observed in STEMI patients treated by PPCI, for which studies have reported 25% to 30% reductions in MI size as measured by myocardial single-photon emission computed tomography and cardiac magnetic resonance imaging (3–5). The limitations of our study include the following: 1) although tissue plasminogen activator (t-PA) is the most commonly used thrombolytic agent in developed countries, streptokinase (which costs 10-fold less than t-PA) continues to be used in developing nations; and 2) conducting a randomized control trial in a developing nation with very limited resources was challenging and explains in part why we were only able to obtain data on enzymatic MI size.

In conclusion, we have shown that RIC reduced MI size in STEMI patients treated with thrombolysis, making this noninvasive, easily applied, low-cost therapy an attractive option in developing nations where health care resources are limited and current therapy is not optimal.

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REFERENCES

Are Phytosterols Responsible for the Low-Density Lipoprotein-Lowering Effects of Tree Nuts?
A Systematic Review and Meta-Analysis

Intake of tree nuts is associated with a lower risk of cardiovascular events in prospective cohorts and the PREMIDED (Prevención con Dieta Mediterránea) trial (1). Previous meta-analyses indicated that tree nut intake lowered low-density lipoprotein (LDL) cholesterol (2,3). However, few trials (≤13 studies) were included in these meta-analyses; pooled effects were not standardized to a common dose, which prevented conclusions about the magnitude of effects for a given intake of nuts, and specific constituents in tree nuts were not examined for their contributions to this LDL-lowering effect. Tree nuts are rich in phytosterols that displace cholesterol from intestinal micelles and reduce the pool of absorbable...