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Saitama Municipal Hospital, Japan

Postconditioning with lactate-enriched blood for cardioprotection in patients with ST-segment elevation myocardial infarction

y colleagues and I recently reported a new approach, postconditioning with lactate-enriched blood (PCLeB), for preventing reperfusion injury in patients with ST-segment elevation myocardial infarction (STEMI). This approach targets reperfusion-induced hypercontracture, which compresses the microvasculature and mechanically disrupts myocardial cell skeletons. PCLeB comprises intermittent reperfusion and timely coronary injections of lactated Ringer's solution (Figure 1), aiming to achieve controlled reperfusion with tissue oxygenation and minimal lactate washout. This approach was designed based on the results of our previous experimental study. We have reported that abrupt lactate washout during reperfusion after simulated ischemia induced contracture in guinea-pig myocytes despite a substantial decrease in intracellular Ca²⁺ concentrations ([Ca²⁺]i), which were elevated during simulated ischemia. This reperfusion-induced contracture developed in association with resensitization of



Overview of the protocol for postconditioning with lactate-enriched blood. The duration of each brief reperfusion was prolonged from 10 to 60 s in a stepwise manner. At the end of each brief reperfusion, lactate was supplied by injecting lactated Ringer's solution into the culprit coronary artery. Each brief ischemic period lasted 60 s. After 7 cycles of balloon inflation and deflation, full reperfusion was performed, followed by stenting. LCA, left coronary artery; RCA, right coronary artery. (Reprinted from Koyama et al. (2))

myofilaments to Ca^{2+} . We therefore attempted to create a transition period between ischemia and reperfusion through our new approach. During this transition period, the elevated $[Ca^{2+}]i$ was allowed to resume its normal level safely, while restoration of vigorous myocardial contraction was suspended by keeping tissue lactate concentrations high, which otherwise might lead to hypercontracture. We have treated 76 consecutive patients with STEMI (age, 65.5 ± 14.1 years; 77.6% men; 43.4% anterior STEMI) using percutaneous coronary intervention and PCLeB within 12 h of symptom onset since late 2011. No patient experienced ventricular tachycardia or fibrillation during reperfusion. After PCI, corrected TIMI frame count was 20.4 \pm 11.1 (normal value, 21). Peak creatine kinase and creatine kinase-MB levels were 2707 \pm 2099 and 264 \pm 170 IU/L, respectively. No patient died or experienced worsening/new-onset heart failure at 30 days. Only one patient required oral diuretic therapy at discharge. In conclusion, PCLeB induced augmented microcirculation recovery, abolished reperfusion arrhythmia, and led to zero mortality and no worsening/new-onset heart failure at 30 days in 76 consecutive patients with STEMI.

Related publications

- 1. Koyama T, Shibata M, Moritani K. Ischemic postconditioning with lactate-enriched blood in patients with acute myocardial infarction. *Cardiology* 2013; 125: 92-93.
- 2. Koyama T, Niikura H, Shibata M, Moritani K, Shimada M, Baba A, Akaishi M, Hideo M. Impact of ischemic postconditioning with lactate-enriched blood on early inflammation after myocardial infarction. *IJC Metab Endocr* 2014; 2: 30-34.

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- 3. Koyama T, Niikura H, Shibata M, Munakata M, Kageyama T, Akima T, Kanki H, Moritani K, Ishikawa S, Mitamura H. Possible creatine kinase washout mechanism revealed by postconditioning with lactate-enriched blood in patients experiencing ST-elevation myocardial infarctions. *Int J Cardiol* 2014; 177: 492-493.
- 4. Koyama T, Kageyama T, Munakata M, Nagaoka M, Akima T, Kanki H, Ishikawa S. Muscle squeezing of the culprit coronary artery in a patient with ST-elevation myocardial infarction after postconditioning with lactate-enriched blood. *Int J Cardiol* 2015; 182: 77-78.
- 5. Koyama T, Munakata M. Akima T, Kanki H, Ishikawa S. An extensive discrepancy in myocardial uptake of thallium-201 and iodine-123 BMIPP in a patient with ST-segment elevation myocardial infarction treated using postconditioning with lactateenriched blood. *Int J Cardiol* 2015;198:51-52.
- 6. Munakata M, Koyama T, Akima T, Kanki H, Ishikawa S. Minimum ischemia-reperfusion injury in a STEMI patient treated using postconditioning with lactate-enriched blood. *Int J Cardiol* 2016; 202:282-284.
- 7. Koyama T, Munakata M, Akima T, Kageyama T, Shibata M, Moritani K, Kanki H, Ishikawa S, Mitamura H. Impact of postconditioning with lactate-enriched blood on in-hospital outcomes of patients with ST-segment elevation myocardial infarction. *Int J Cardiol* 2016;220:146-148.
- 8. Akima T, Koyama T, Munakata M, Shibata M, Moritani K, Kanki H, Ishikawa S, Mitamura H. Absence of reperfusion-induced arrhythmia in patients with ST-segment elevation myocardial infarction treated using postconditioning with lactate-enriched blood. *Int J Cardiol* 2016;222:780-781.
- 9. Koyama T. Lactated Ringer's solution for preventing myocardial reperfusion injury. Int J Cardiol Heart Vasc 2017;15:1-8 (review).

Biography

Koyama is currently a vice director of the Saitama Municipal Hospital in Saitama, Japan. He has expertise in research in myocardial reperfusion injury. He has recently developed a new treatment strategy for myocardial reperfusion injury in patients with ST-segment elevation myocardial infarction (STEMI), based on the results of his previous experimental study using guinea-pig myocytes that was published in Am J Physiol in 1991. He is basically a clinical cardiologist, performing percutaneous coronary intervention himself. But his experiences not only in STEMI treatment but also in animal experiments inspired him to develop a new treatment strategy for myocardial reperfusion injury, i.e. postconditioning with lactate-enriched blood. He has already published a review paper on this new approach in IJC Heart & Vasculature, claiming that the new approach may be effective against all four types of myocardial reperfusion injury.

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