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Short communication

Muscle squeezing immediately after coronary reperfusion therapy using postconditioning with lactate-enriched blood

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ABSTRACT

Background: We recently reported a new approach for cardioprotection, postconditioning with lactate-enriched blood (PCLeB), and a patient with ST-segment elevation myocardial infarction (STEMI), in whom muscle squeezing of the culprit coronary artery was observed immediately after reperfusion with PCLeB. In this study, we examined the prevalence of muscle squeezing immediately after reperfusion in patients with anterior STEMI treated using PCLeB.

Methods and results: PCLeB is a modified postconditioning protocol that comprises intermittent reperfusion and timely coronary injections of lactated Ringer's solution. We treated 30 consecutive patients with anterior STEMI using PCLeB. Among the 30 patients, 4 patients exhibited muscle squeezing of the left anterior descending artery (LAD) immediately after reperfusion. We performed follow-up coronary angiography in 23 patients and found another patient who exhibited muscle squeezing of the LAD. Thus, of 30 patients, 5 were confirmed to have myocardial bridging and 4 exhibited muscle squeezing immediately after reperfusion with PCLeB. No patient died or experienced re-hospitalization for heart failure or recurrent ischemic events at 6 months except for one patient with malignancy.

Conclusion: Muscle squeezing immediately after reperfusion therapy is not a rare phenomenon in patients with anterior STEMI treated using PCLeB.

1. Introduction

Myocardial reperfusion injury attenuates the beneficial effects of reperfusion therapy for ST-segment elevation myocardial infarction (STEMI). No approach has proven successful in preventing myocardial reperfusion injury in the clinical setting. Recently, we reported a new approach for cardioprotection, namely, postconditioning with lactate-enriched blood (PCLeB), in patients with STEMI [1,2]. This modified postconditioning protocol comprises intermittent reperfusion and timely coronary injections of lactated Ringer's solution, aimed at achieving controlled reperfusion with cellular oxygenation and minimal lactate washout from the cells. This approach specifically targets reperfusion-induced hypercontracture, which mechanically disrupts myocardial cell skeletons. We have already reported that PCLeB yielded excellent in-hospital outcomes in patients with STEMI [3]. We have also reported a patient with STEMI, in whom we could see muscle contraction by coronary angiography (CAG) immediately after reperfusion with PCLeB, through muscle squeezing of the culprit coronary artery [4]. This case suggests attenuation of myocardial stunning by PCLeB, at least in the epicardial portion of the reperfused myocardium. In this study, we examined the prevalence of muscle squeezing immediately after reperfusion in patients with STEMI who were treated using PCLeB.

2. Methods

Only patients with STEMI who had proximal occlusion of the left anterior descending artery (LAD) (anterior STEMI) were considered eligible for inclusion in this study because myocardial bridging is observed predominantly in the LAD [5]. Consecutive patients with anterior STEMI who were treated using percutaneous coronary intervention (PCI) and PCLeB within 12 h of symptom onset in our hospital between March 2014 and January 2018 were included in this study. Follow-up CAG was recommended for all patients; this is usual practice in Japan to determine if restenosis is present or not, and this was performed 6 to 12 months later in this study if the patient returned for the test. Anterior STEMI was defined as prolonged chest pain (duration > 30 min) and >1 mm of ST-segment elevation in ≥2 adjacent anterior leads. Patients with LAD with a thrombolysis-in-myocardial-infarction flow grade II or III or those with failed recanalization of the LAD during the postconditioning procedure were excluded.

Fig. 1 shows an overview of the protocol for PCLeB. In our modified postconditioning protocol, the duration of each brief reperfusion was prolonged stepwise from 10 to 60 s. This approach sought to prevent the rapid and abrupt washout of lactate during the very early phase of reperfusion. Lactated Ringer's solution (30 mL) containing 28 mM of

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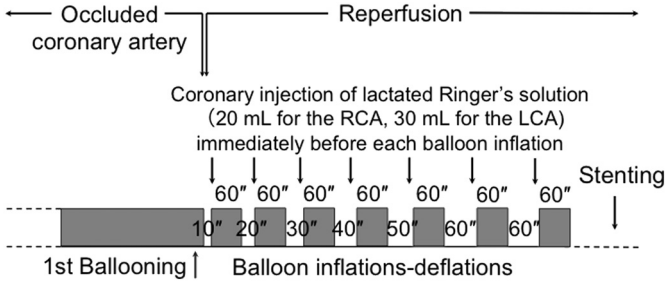

Fig. 1. Overview of the protocol for postconditioning with lactate-enriched blood. The duration of each brief reperfusion was prolonged from 10 to 60 s in a stepwise manner. At the end of each brief reperfusion, lactate was supplied by injecting lactated Ringer's solution into the culprit coronary artery. Each brief ischemic period lasted for 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. [1]).

lactate was injected directly into the culprit coronary artery at the end of each brief reperfusion, and the balloon was rapidly inflated at the lesion site to trap the lactate inside the ischemic myocardium. Each brief ischemic episode lasted 60 s. After seven cycles of balloon inflation and deflation, complete reperfusion was performed. Stenting was performed thereafter, and the PCI was completed.

This study was approved by the Ethics Review Board of the Saitama Municipal Hospital. All patients provided written informed consent for participation in the study.

3. Results

We treated 30 consecutive patients with anterior STEMI using PCLeB during the study period (mean age, 59.8 ± 15.2 years, 80.0% men; ischemia time, 3.5 ± 1.7 h; peak creatine kinase level, 3687 ± 2576 IU/L). Of 30 patients, 4 (mean age, 56.8 ± 12.6 years, all men; ischemia time, 2.3 ± 0.7 h; peak creatine kinase level, 5168 ± 4091 IU/L) exhibited muscle squeezing of the LAD immediately after reperfusion (Fig. 2). Follow-up CAGs were performed in 23 patients. Of the 4 patients who exhibited muscle squeezing immediately after reperfusion, 3 patients underwent follow-up CAGs and muscle squeezing was confirmed also in the follow-up CAGs in these patients. Besides these three patients, we found another patient who exhibited muscle squeezing of the LAD. In this patient, we could not observe muscle squeezing immediately after reperfusion. Thus, of the 30 patients, at least 5 patients were confirmed to have myocardial bridging, and 4 of them exhibited muscle squeezing immediately after reperfusion.

With respect to the outcomes of the 30 study patients, after excluding one patient who had died because of cancer 4 months after myocardial infarction, none of the 29 patients died or experienced re-hospitalization for heart failure or recurrent coronary ischemic events 6 months after myocardial infarction.

4. Discussion

Myocardial bridging is observed in 5–12% of patients, and it usually involves the LAD [5]. In this study, despite no follow-up CAG in 7 patients, 5 of 30 study patients were found to have myocardial bridging in primary PCI, in the follow-up CAG, or in both. In this study, some patients might possibly permanently lose muscle squeezing due to myocardial infarction, and others were unnoticed to have myocardial bridging because of no follow-up CAG. Nevertheless, 5 of 30 patients were confirmed to have myocardial bridging (prevalence, 16.7%), which is higher than that mentioned above. Therefore, in most, if not all, patients who originally had myocardial bridging, muscle squeezing was observed in primary PCI, in the follow-up CAG, or in both.

The prevalence of muscle squeezing immediately after reperfusion in patients who originally had myocardial bridging and were treated using PCLeB seems considerably high (4 of 5 or some more patients?). Furthermore, the definite prevalence of muscle squeezing immediately after reperfusion among the 30 study patients still seemed high (13.3%, i.e., 4 of 30 patients). Although no study has revealed the prevalence of muscle squeezing in patients treated with conventional reperfusion therapy, the overall incidence in these patients should be very low owing to myocardial stunning or infarction. Thus, the results of this study suggest the cardioprotective effects of PCLeB against myocardial stunning or lethal reperfusion injury; this was supported by good 6-month outcomes of the study patients.

Our new approach specifically targets reperfusion-induced hypercontracture, which mechanically disrupts myocardial cell skeletons, resulting in irreversible myocardial cell injury. In contrast, less severe form of hypercontracture, i.e., contracture may cause less severe myocardial cell injury. If the mechanical force generated by contracture is not strong enough to disrupt myocardial cell skeletons, myocardial cell injury can possibly be reversible, leaving reversible functional alterations behind in the myocardium, such as myocardial stunning. The precise mechanisms responsible for myocardial stunning remain to be elucidated. Therefore, the mechanism of the possible protective effects of PCLeB against myocardial stunning cannot be specifically stated; instead, generalize explanation might be possible as stated above. This question needs to be addressed in the future studies.

In conclusion, muscle squeezing observed immediately after reperfusion therapy is not a rare phenomenon in patients with anterior STEMI treated using PCLeB.

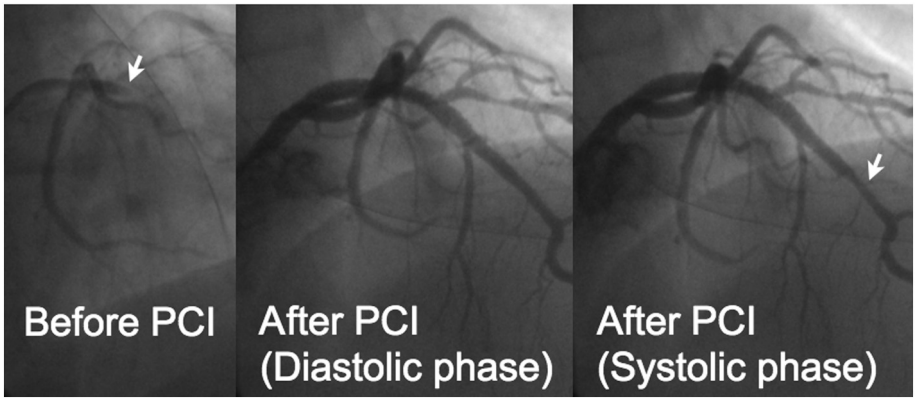

Fig. 2. Coronary angiography (CAG) of a representative patient before and after primary coronary intervention (PCI). Left panel: CAG before PCI. The proximal left anterior descending artery (LAD) is completely occluded (arrow). Middle panel: Diastolic phase of the final CAG view after PCI. Right panel: Systolic phase of the same CAG view as shown in the middle panel. The mid-portion of the LAD shows segmental narrowing caused by muscle squeezing (arrow).

Funding source

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Conflicts of interest statement

The authors declare no conflict of interest relevant to this work.

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