



Treatment for Refractory Cardiogenic Shock Using Traditional Chinese Herbs Combined with Acupuncture: Two Case Reports

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Abstract

Cardiogenic Shock (CS) is a serious complication of Acute Myocardial Infarction (AMI) with a high fatality rate with existing treatment methods. We report two clinical cases in which Traditional Chinese Herbs (TCH) combined with acupuncture successfully improved the prognosis of patients with AMI complicated with refractory CS. The patients with AMI developed CS while undergoing standard Western medicine treatment, including coronary revascularization; hemodynamics were effectively maintained with the assistance of vasoactive drugs even an Intra-Aortic Balloon Pump (IABP). After the implementation of TCHs with similar effects and acupuncture, not only did the patients' status improve but so did the long-term clinical benefits. Given the current high fatality rate of CS, the treatment method used successfully in these two cases offers new opportunities for the effective treatment of CS.

Keywords: ACEI; Percutaneous coronary intervention; Periprocedure myocardial injury

Abbreviations

ACEI: Angiotensin Converting Enzyme Inhibitor; AMI: Acute Myocardial Infarction; ARB: Angiotensin Receptor Antagonist; BP: Blood Pressure; CCU: Cardiac Care Unit; CS: Cardiogenic Shock; DES: drug-Eluting Stent; EF: Ejection Fraction; HR: Heart Rate; IABP: Intra-Aortic Balloon Pump; PCI: Percutaneous Coronary Intervention; PMI: Peri-Procedure Myocardial Injury; TCH: Traditional Chinese Herb; TCM: Traditional Chinese Medicine

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Introduction

Cardiogenic Shock (CS) is severe and persistent hypotension (systolic blood pressure <90 mmHg) accompanied by tissue hypoperfusion (increased resting heart rate, altered state of consciousness, oliguria, wet and cold limbs) under the condition of appropriate cardiac filling. In addition, CS should also be considered in patients who require pressure-boosting/positive inotropic drugs or mechanical circulation aids to maintain a systolic blood pressure of >90 mm Hg [1]. Studies have shown that about 80% of CSs are caused by Acute Myocardial Infarction (AMI) [2], and that AMI has a 5% to 8% probability of triggering CS [3]. Although the continuous development of modern diagnosis and treatment technology has greatly promoted the early reperfusion treatment of AMI and the maintenance of hemodynamics during the shock state, the case fatality rate of CS caused by AMI is still very high (~50%) [4] and it may be as high as 80% if not treated in time [2]. Early implementation of coronary reperfusion therapy is the core strategy to reduce the incidence of CS in AMI patients. For AMI complicated with CS, vasoactive drugs, Intra-Aortic Balloon Pumps (IABP), left ventricular assistance devices, extracorporeal membrane oxygenation systems, and other machines are increasingly used for hemodynamics maintenance. However, these approaches do not play a major role in reducing the case fatality rate [4]. Previous studies have shown that Traditional Chinese Herbs (TCHs) are potentially valuable in improving the clinical prognosis of AMI-induced CS [5]. However, Chinese herbal medicines combined with acupuncture have not been reported as an intervention for CS. This paper introduces two medical cases where the combination of TCHs and acupuncture helped patients with AMI complicated with refractory CS to derive clinical benefits. The treatment modalities reflected in these successful cases may lead to new opportunities for the effective treatment of CS. This report was published with the informed

consent of the two patients involved.

Case Series

Case 1

Patient information and clinical findings: This was a 58-year-old male patient from Beijing who was brought to our emergency department by ambulance with persistent chest pain for one hour. The first electrocardiogram diagnosis of AMI was made in the ambulance (Figure 1), and the chest pain center of our hospital was immediately notified. After arriving at the emergency department, the patient was quickly transferred to the catheterization room for emergency coronary angiography, and the angiography suggested that the left anterior descending branch was 100% occluded at the opening. No obvious obstructive lesion was observed in the left rotary branch and the right coronary artery. Thrombosis aspiration was performed in the anterior descending branch, and a 3.5 mm × 23 mm Firehawk Drug-Eluting Stent (DES) (MicroPort, Shanghai, China) was implanted (Figure 2). The time from entry to guide Wire (Door to Wire) was 53 min. The lowest intraoperative blood pressure of the patient was reduced to about 70/40 mmHg. Cardiogenic shock was considered, and IABP was used to maintain hemodynamics by applying vasoactive drugs. The patient was transferred to the Cardiac Care Unit (CCU) after surgery. Standardized diagnosis and treatment were carried out according to the 'Guidelines for diagnosis and treatment of acute ST-segment elevation myocardial infarction (2019) [1] published by the Cardiovascular Diseases Branch of the Chinese Medical Association. Postoperative ultrasonic cardiogram showed that the motion amplitude of the anterior wall of the left ventricle and the middle apical segment of the ventricular septum decreased, the Ejection Fraction (EF) was 50%, and the left ventricular end-diastolic diameter was 55 mm. Medication included aspirin

(100 mg Qd), ticagrelor (90 mg Bid), atorvastatin (40 mg Qn), low molecular weight heparin (4000 IU Q12h), and dopamine injection 6 ug/min/kg combined with m-hydroxylamine injection 0.13 mg/min. Considering the hemodynamic instability of patients, β-receptor blockers and Angiotensin-Converting Enzyme Inhibitor (ACEI)/Angiotensin Receptor Antagonist (ARB) were not given. Using the above drug therapy and the application of IABP, arterial pressure was maintained at 90-110/50-70 mmHg, but hemodynamics could not be effectively maintained in patients with reduced vasoactive drug dosage or reduced IABP working intensity (adjusting the counter pulsation ratio to 1:3).

Chinese herbs and acupuncture intervention: On day 5 of those mentioned above standardized Western medicine treatment, we decided to give the patient a combination of TCHs and acupuncture combined with Western medicine based on our clinical experience to try to correct the patient's refractory CS state. At that time, the patient felt short of breath, had a dry mouth prompting a desire for a hot drink, drinking water did not quench thirst, limbs were wet and cold, poor appetite and sleep, and stool and stool urine were normal. He was weak-spirited, yellow in complexion, had a pale tongue with white coating, and a heavy and weak pulse. The diagnosis, according to Traditional Chinese Medicine (TCM), was "true pain" and the syndrome differentiation was "exhaustion of Yang in heart and kidney combined with a loss of Qi Yin and floating of the mind with declining of stomach Qi (TCM terminology)." The patient was prescribed *hui jue jiu xin* decoction, three doses, thickly decocted, 100 mL each time, twice a day. The specific composition of TCH prescriptions is shown in Table 1. Moreover, according to the acupuncture theory of TCM, acupuncture treatment was carried out every day. Acupoints were selected as follows: Bilateral *hegu* (LI4), *neiguan* (PC6), *taichong* (LR3), *gongsun* (SP4), *tianshu*



Figure 1: Preoperative and postoperative Electrocardiogram (ECG). (A) Preoperative electrocardiogram suggested that ST segments in leads I, AVL, and V1-V3 were 0.1-0.2 mV elevated, while ST segments in II, III, and AVF were 0.1-0.2 mV depressed. (B) Postoperative electrocardiogram indicated that all the ST segments changed before surgery returned to normal.

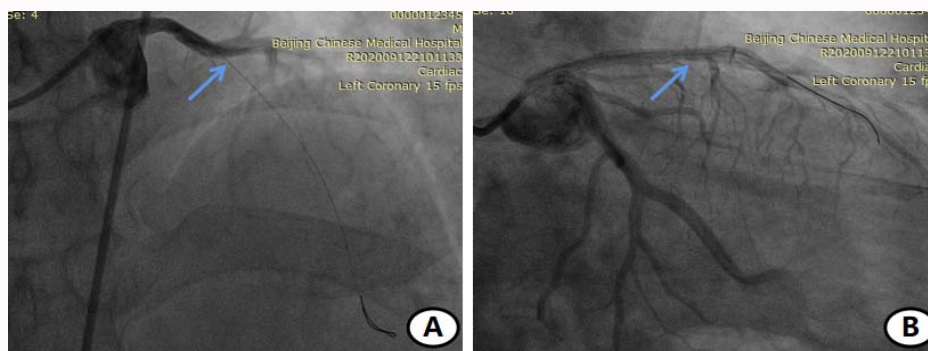


Figure 2: Coronary angiography before and after Percutaneous Coronary Intervention (PCI). (A) Pre-PCI coronary angiography indicated 100% occlusion of the left anterior descending branch opening. (B) Coronary angiography after PCI indicated that the anterior descending branch restored anterior flow.

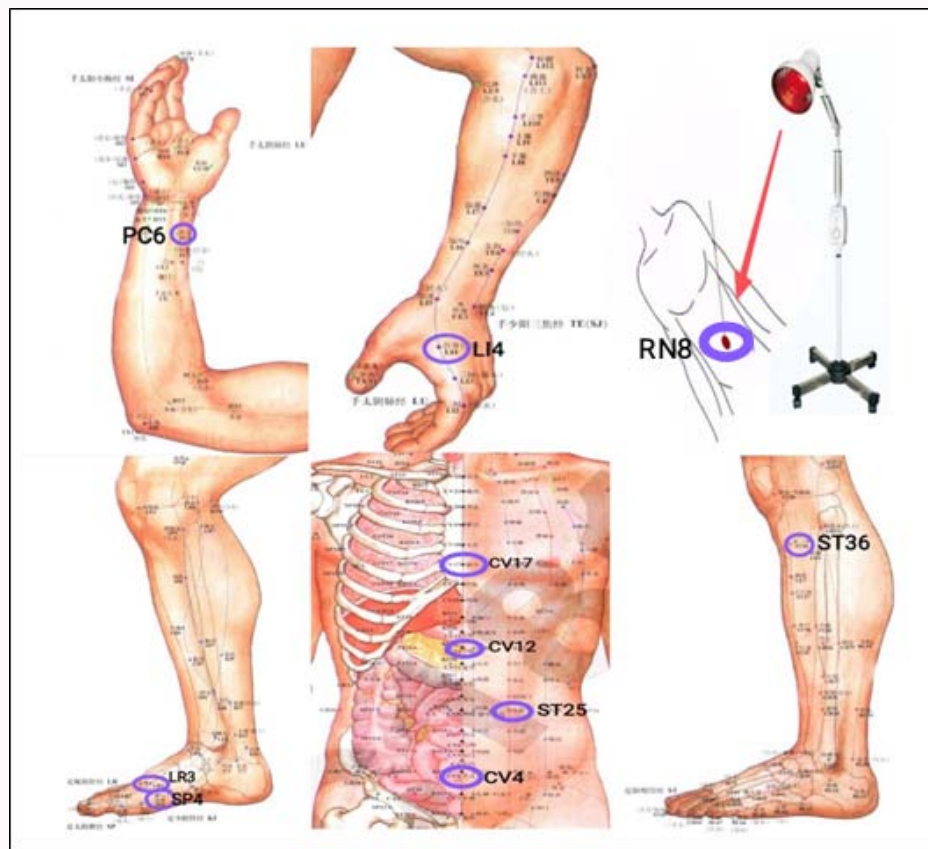


Figure 3: Acupuncture point map of patients.

(ST25), *zusanli* (ST36), *danzhong* (CV17), *zhongwan* (CV12), and *guanyuan* (CV4). Acupuncture manipulations were carried out at *hegu* (LI4), *taichong* (LR3), and *zusanli* (ST36). During the 20-min wake-up period, an infrared therapy apparatus was used (Model 350, XINFENG Instruments Co. Ltd, Guangdong Sheng, China), such that the temperature of the *shenque* (RN8) acupoint was maintained at about 40°C (Figure 3, Table 2).

Outcomes and follow up: Using integrative treatment, the hemodynamics of the patient was gradually stabilized. On day 3 of the combination therapy, we successfully removed the patient's IABP device. After that, the above TCM treatment regimens were continued, and the intensity of vasoactive drug treatment was gradually reduced. On day 6 of combined Chinese and Western medicine treatment, all vasoactive drugs were successfully withdrawn from the patient. In

addition, his previous clinical manifestations, such as shortness of breath, cold and damp limbs, and poor appetite and sleep, significantly improved. Reexamination of echocardiography showed the level of EF was back up to 65%, and the left ventricular end-diastolic diameter fell to 43 mm. After discharge, the patient continued treatment with integrated TCHs and Western medicine for more than six months. Follow-up showed that the patient's vital signs were good and that he could resume normal daily activities.

Case 2

Patient information and clinical findings: This 69-year-old male patient was admitted to the hospital due to paroxysmal chest pain for 10 days. Ten days ago, the patient was admitted to the emergency department of a local hospital with chest pain, which persisted for 13 h and was diagnosed as acute anterior wall myocardial infarction.

Table 1: Specific composition of traditional Chinese herb prescriptions.

| Chinese name | Common name | Dosage | Amount |
|--------------|----------------------------------|--------|--------|
| Hongshen | <i>Radix ginseng rubra</i> | 10g | 4.0% |
| Maidong | <i>Radix ophiopogonis</i> | 15g | 6.1% |
| Wuweizi | <i>Schisandra chinensis</i> | 12g | 4.9% |
| Guizhi | <i>Cassia twig</i> | 45g | 18.2% |
| Shaoyao | <i>Paeony</i> | 15g | 6.1% |
| Zhigancao | Honey-fried licorice root | 10g | 4.0% |
| Fuzi | <i>Radix aconiti carmichaeli</i> | 30g | 12.1% |
| Ganjiang | <i>Rhizoma zingiberis</i> | 20g | 8.1% |
| Muli | Oyster shell | 30g | 12.1% |
| Longgu | Keel | 30g | 12.1% |
| Shanzhuyu | Dogwood | 20g | 8.1% |
| Jiaosanxian | Charred triplet | 10g | 4.0% |

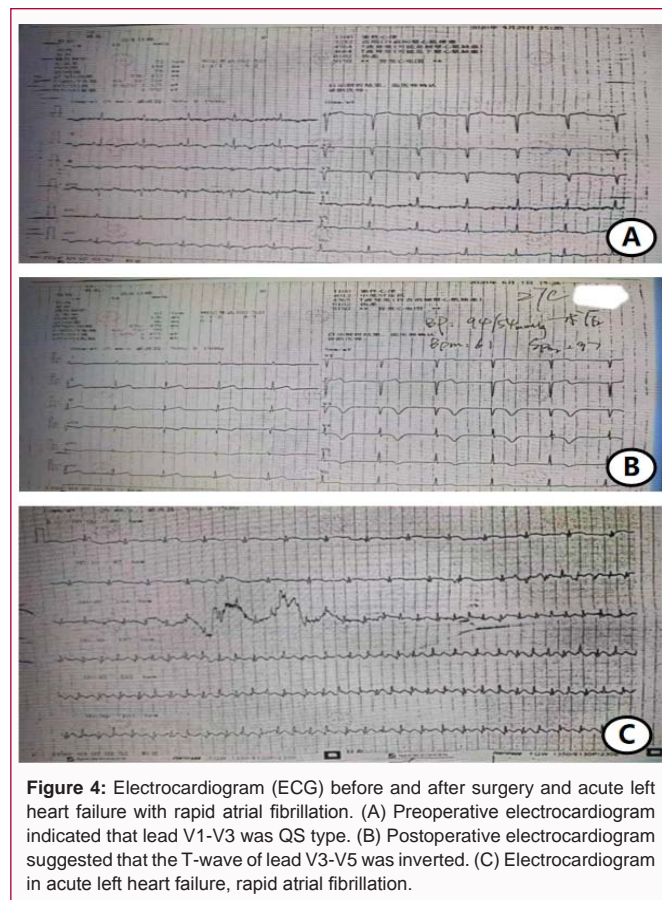


Figure 4: Electrocardiogram (ECG) before and after surgery and acute left heart failure with rapid atrial fibrillation. (A) Preoperative electrocardiogram indicated that lead V1-V3 was QS type. (B) Postoperative electrocardiogram suggested that the T-wave of lead V3-V5 was inverted. (C) Electrocardiogram in acute left heart failure, rapid atrial fibrillation.

Ventricular fibrillation occurred in the emergency room, sinus rhythm was restored after advanced cardiopulmonary resuscitation, and he was transferred to the CCU. Based on the relatively stable vital signs, elective coronary angiography was performed on the ninth day of hospitalization, but coronary interventional therapy was not performed due to the difficulty of such surgery. The patient was transferred by ambulance to our center on May 29th, 2019, for further coronary revascularization. Echocardiography showed left ventricular enlargement, abnormal left ventricular wall movement (left ventricular end-diastolic diameter: 60 mm, EF: 45%). The patient did not report a history of hypertension or diabetes. Elective coronary angiography was performed on June 01st, 2020, based on relatively

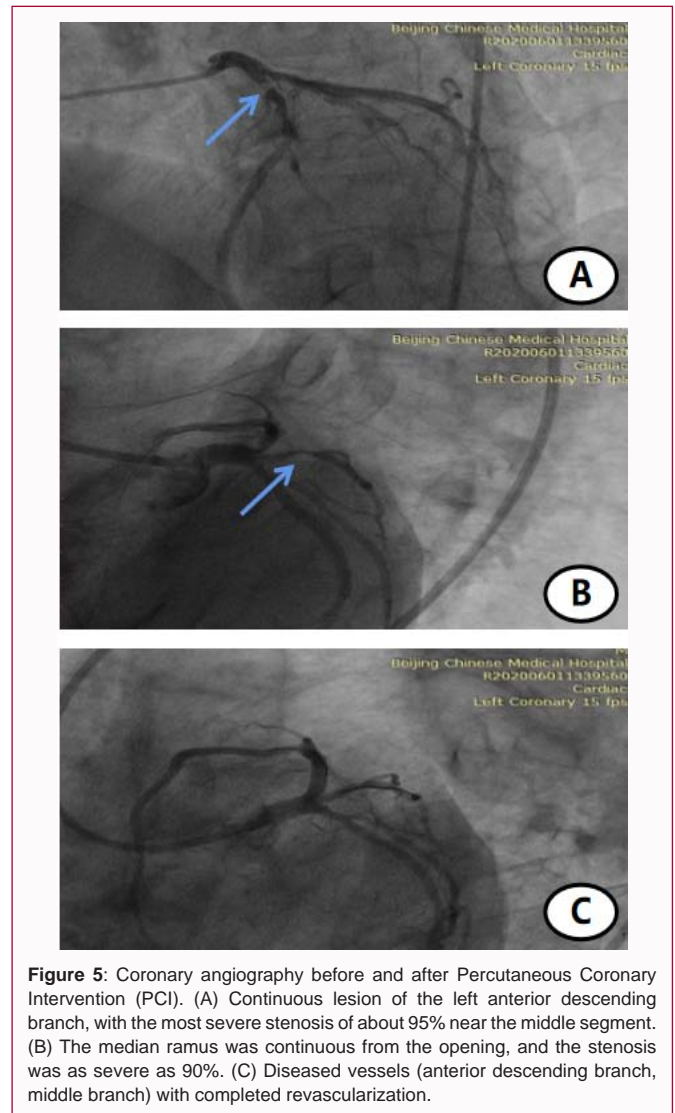


Figure 5: Coronary angiography before and after Percutaneous Coronary Intervention (PCI). (A) Continuous lesion of the left anterior descending branch, with the most severe stenosis of about 95% near the middle segment. (B) The median ramus was continuous from the opening, and the stenosis was as severe as 90%. (C) Diseased vessels (anterior descending branch, middle branch) with completed revascularization.

stable vital signs. Radiography showed a continuous lesion of the left anterior descending branch, and stenosis of the near middle segment was up to 95%. The middle ramus was continuous from the opening, and stenosis was about 90%. The right middle coronary artery stenosis ended up being about 60%. A 3.0 mm × 33 mm and a 2.25 mm × 23 mm Firehawk DES (MicroPort, Shanghai, China) stent were implanted in the anterior descending branch lesion. The operation was successful, and the target vessel revascularization was successful (Figure 4, 5). On a postoperative day 1 (June 02nd, 2020), the patient had sudden dyspnea and sat up to breathe. The extremities were damp and cold, and rales of fine moisture could be heard in both lungs. Acute left heart failure was considered. The dyspnea symptoms were relieved after diuretic treatment, vasodilation, and non-invasive ventilator-assisted ventilation. While undergoing strict fluid management, the patient redeveloped acute left heart failure with rapid atrial fibrillation on day 4 (June 05th, 2020) postoperatively (Figure 3). After symptomatic treatment of acute left heart failure and intravenous infusion with amiodarone, the patient's heart failure was relieved and reverted to sinus rhythm. The patient's limbs were wet and cold, and his mental state was poor. The hemodynamics could be effectively maintained only by applying vasoactive drugs more intensively. At this point, the patient approved of a combination of traditional Chinese herbs and acupuncture combined with a Western

Table 2: Names and locations of acupoints.

| Acupoints | International standard | Location |
|-----------|------------------------|---|
| Hegu | LI 4 | At the back of hand, between the first and second metacarpal bones, and at the midpoint of the radial side of the second metacarpal bone. |
| Neiguan | PC 6 | On the volar side of the forearm, at the line between <i>quchi</i> and <i>daling</i> , there are two inches on the wrist stripe, between the palmaris longus tendon and the radial flexor carpi tendon. |
| Zusanli | ST 36 | On the anterolateral side of the calf, 3 inches below the calf nose, one finger away from the leading edge of the tibia. |
| Taichong | LR 3 | On the dorsal side of the foot, at the depression behind the first metatarsal space. |
| Gongsun | SP 4 | On the medial margin of the foot, at the base of the first anterior and lower metatarsal bone. |
| Tianshu | ST 25 | At the middle of the abdomen, 2 inches from the navel. |
| Danzhong | CV 17 | At the chest, anterior midline, flat fourth intercostal, midpoint between the nipples. |
| Zhongwan | CV 12 | At the upper abdomen, at the anterior midline, 4 inches from the umbilicus. |
| Guan Yuan | CV 4 | Lower abdomen, anterior midline, 3 inches below the umbilicus. |
| Shenque | RN 8 | At the middle of the abdomen, in the center of the umbilicus. |

medicine treatment program.

Chinese herbs and acupuncture intervention: On June 05th, 2020, the patient complained of shortness of breath, dry mouth, prompting a craving for a hot drink, which, however, did not quench thirst; cold and wet limbs; sweating; poor appetite; poor sleep, with stool and urine being normal. Blood pressure: 110/69 mmHg (dopamine: 3 ug/min/kg, m-hydroxylamine: 0.2 mg/min), HR: 69 times/min. He was weak-spirited, lacked energy, showed a dark purple tongue with less coating, and his pulse appeared weak. The TCM diagnosis was "true pain" and the differential diagnosis was "exhaustion of Yang in heart and kidney combined with the loss of Qi Yin, and floating in mind with declining of stomach Qi." We applied exactly the same TCM treatment regimen as in Case 1 to the patient, including TCHs and acupuncture therapy. On June 8th, 2020, the patient's symptoms of chest tightness and poor appetite improved after taking the TCHs, and the patient experienced no particular discomfort. Nevertheless, the patient still felt short of breath and was fatigued, and his limbs were wet and cold. Based on these symptoms, the dosage of cassia twig in the original prescription was adjusted to 60 g, the prescription was one dose, and it was applied in the same manner as before. On June 09th, 2020, the dampness and cold condition of the patient's extremities improved, with morning BP: 101/60 mmHg (dopamine: 2.6 ug/min/kg, m-hydroxyamine: 0.15 mg/min), HR: 81 times/min. The dosage of *radix aconiti carmichaeli* in the original prescription was adjusted to 40 g, and 3 doses were prescribed. The treatment plan of TCHs combined with acupuncture was continued.

Outcomes and follow up: After the above treatment, the patient's mental state and the wet and cold condition of his extremities improved further, and the application intensity of the vasoactive drugs was gradually reduced. On day 6 (June 11th, 2020) after TCHs combined with acupuncture, the patient was discharged successfully. After discharge, the patient received integrated TCHs and Western medicine treatment and was followed up 6 months after discharge. The patient's condition was stable, and he was able to resume normal daily activities.

Discussion

To the best of our knowledge, this is the first case report of TCHs combined with acupuncture in the treatment of refractory CS. The magnitude of the myocardial infarction may have led to CS in Case 1, despite prompt coronary reperfusion therapy. In Case 2, the opportunity of early reperfusion therapy was missed because the duration of chest pain exceeded the time window of emergency

treatment for early coronary reperfusion. The patient developed acute left heart failure after the successful completion of diseased vessel revascularization, and it was considered that myocardial reperfusion injury might have been an important cause of CS for him. The similarities between the two cases were as follows: The two AMI patients developed CS while undergoing standard Western medicine treatment, including coronary revascularization, and both patients' hemodynamics could be effectively maintained with the assistance of vasoactive drugs, even IABP. In this context, the implementation of similar TCHs and acupuncture therapy may help to effectively improve patients' CS status and improve long-term clinical benefits. According to TCM, shock is a syndromic condition, a comprehensive manifestation of severe depletion in Yin, Yang, Qi, "blood," and "body fluid". The pathophysiological mechanisms according to Western medicine were different in the two patients, but the pathogenesis according to TCM theory was similar, both of which were characterized by "exhaustion of Yang in heart and kidney combined with loss of Qi Yin and floating of the mind with declining of stomach Qi". According to TCM, Yang is the foundation of human life. The importance of Yang was mentioned by the "Inner Canon of Huangdi", the most famous classic text of Chinese medicine, over 2,000 years ago. Two patients suffered from myocardial infarction leading to heart Yang loss and showed hemodynamics could not be effectively maintained. The loss of Heart Yang can result in being patients being weak-spirited and lacking in energy. According to TCM theory, Yin, Qi, "blood," and "body fluid" tend to get damaged as a result of exhaustion of Yang. Therefore, while "warming Yang", the emphasis of therapy is to "nourish Qi and Yin and activate blood circulation". When prescribing *hui jue jiu xin* decoction, large doses of *radix aconiti carmichaeli*, *rhizoma zingiberis*, and cassia twig were used to "reverse back to Yang"; *radix ginseng rubra*, *radix ophiopogonis*, *schisandra chinensis*, and dogwood were used to "reinforce Qi and nourish Yin"; and keel and oyster shell were used to "restore Yang". Charred triplet was used to stimulate the appetite and protect the stomach. The TCH prescriptions in these cases included *radix aconiti carmichaeli*, *radix ginseng rubra*, *schisandra chinensis*, and other drugs. Modern studies have shown that ginsenosides can alleviate reperfusion injury of myocardial cells and inhibit apoptosis of ischemia-reperfusion cells [6]. Aconitoid alkaloids are important effective components of aconite, which have been shown to antagonize oxidative damage of myocardial cells and inhibit the expression of myocardial apoptotic proteins [7]. Shenfu injections, made from the extracts of red ginseng and aconite, are widely used in clinical practice and are potentially valuable for recovering cardiac

function in patients with CS [8]. *Shengmai* injection composed of ginseng, *radix ophiopogonis*, and *schisandra chinensis* also widely used in the treatment of CS. Studies have shown that it has a variety of pharmacological effects such as increasing coronary blood flow, preventing myocardial ischemia-reperfusion injury, and improving left ventricular remodeling [9]. Therefore, we speculated that the traditional Chinese herb prescriptions in these medical cases may have played a protective role in the myocardium by inhibiting cell apoptosis and alleviating reperfusion injury and other potential mechanisms and by promoting the recovery of cardiac function of the patients. Acupuncture is widely used to relieve and improve somatic symptoms. A recent multicentre, randomized controlled study showed that acupuncture can effectively relieve angina pectoris symptoms [10]. In the cases reported here *hegu* (LI4) was used together with *taichong* (LR3), *neiguan* (PC6), and *gongsun* (SP4), aimed at "regulating Qi and nourishing blood"; *guanyuan* (CV4), *zhongwan* (CV12) were used simultaneously with *tianshu* (ST25) and *zusanli* (ST36) to regulate digestive function and balance Qi; *danzhong* (CV17) was used for regulating Qi and "blood". When using needles, infrared treatment to warm the *shenque* (RN8) acupoints amplified the effects of acupuncture. After synergistic treatment with acupuncture, the hemodynamics of both patients were significantly improved. Basic studies have shown that acupuncture can regulate blood pressure in hypotensive model rats [11,12]. Of course, further exploration of the mechanism of TCH combined with acupuncture on CS blood pressure regulation still needs to be explored further. In terms of safety, *radix aconiti carmichaeli* is an important traditional Chinese herb used in CS treatment, which strengthens heart and addresses arrhythmia [13]. In the 2015 edition of the Chinese Pharmacopoeia, the dosage of *radix aconiti carmichaeli* is recommended to be 3 g/d to 15 g/d [14], but in classic ancient books of TCM, the dosage of *radix aconiti carmichaeli* in the treatment of CS is often large. As one of the main components of *radix aconiti carmichaeli*, aconite alkaloid has a certain toxicity and its toxicity may increase with the increase of the dosage of aconite. In view of the potential toxicity of *radix aconiti carmichaeli*, ancient books of TCM put forward some detoxification methods. For example, the toxicity of *radix aconiti carmichaeli* can be reduced by adding licorice root and peony into the prescription containing aconite. Modern studies show that glycyrrhizic acid and flavonoids in licorice can reduce aconitine and the content of toxic substances in *radix aconiti carmichaeli* [15]. In addition, long-term decocting of *radix aconiti carmichaeli* can also destroy the components of aconitine and reduce drug toxicity. The dose of *radix aconiti carmichaeli* applied to the two patients in these case reports exceeded the recommended dose in the Chinese Pharmacopoeia, but after a long time of separate decocting and the "detoxification" method combined with licorice root and peony, neither of the two patients showed clinical manifestations of aconite poisoning. Of course, there is still much room for further exploration and research on the safety of *radix aconiti carmichaeli*.

Summary

With the usage of TCH combined with acupuncture, the two patients with refractory CS improved significantly either in terms of their shock state or long-term clinical prognosis, especially in the context of the poor results of standardized Western medicine treatment. Given the high fatality rate of CS, TCH combined with acupuncture may offer new opportunities. However, due to the limitations of case reports, the efficacy and safety of our therapy need to be evaluated in studies with more patients.

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