Hindawi
Stem Cells International
Volume 2022, Article ID 8513812, 12 pages
https://doi.org/10.1155/2022/8513812

Research Article

Normothermic *Ex Vivo* Heart Perfusion with Mesenchymal Stem Cell-Derived Conditioned Medium Improves Myocardial Tissue Protection in Rat Donation after Circulatory Death Hearts

Zifeng Zeng,[1] Liwei Xu,[1] Yu Xu,[1] Yongsheng Ruan,[2] Deshen Liu,[1] Jiale Li,[1] Chuanjie Niu,[1] Shaoyi Zheng,[1] Pengyu Zhou,[1] and Zezhou Xiao[1]

[1]*Department of Cardiovascular Surgery, Nanfang Hospital, Southern Medical University, Guangzhou 510000, China*
[2]*Department of Pediatrics, Nanfang Hospital, Southern Medical University, Guangzhou 510000, China*

Correspondence should be addressed to Shaoyi Zheng; zhsy@smu.edu.cn, Pengyu Zhou; pyzhou@smu.edu.cn, and Zezhou Xiao; 07zzxiao@smu.edu.cn

Received 16 August 2022; Revised 12 October 2022; Accepted 21 October 2022; Published 17 November 2022

Academic Editor: Liren Qian

Objective. Adopting hearts from donation after circulatory death (DCD) is a promising approach to enlarge the donor pool. Nevertheless, DCD hearts experience severe warm ischemia/reperfusion (I/R) injury. Recent studies have demonstrated that conditioned medium (CM) derived from bone marrow mesenchymal stem cells (BMSCs) has the potential of reducing organ I/R injury. Therefore, we investigated whether DCD heart preservation with normothermic *ex vivo* heart perfusion (EVHP) and BMSCs-CM treatment could alleviate myocardial warm I/R injury in the DCD hearts. *Methods*. We randomly divided donor rats into two groups: (1) DCD-Control group and (2) DCD-CM group. Before DCD heart preservation with the normothermic EVHP system for 105 minutes, rats suffered from a 25-minute warm ischemia injury in the DCD procedure. Vehicle or CM (300 μl) was added to the perfusate at the beginning of the perfusion process. The cardiac function of DCD hearts in the DCD-Control and DCD-CM groups was measured every 30 minutes. Besides, non-DCD hearts were harvested from the beating-heart rats. *Results*. The antibody array demonstrated that the CM contained 14 bioactive factors involved in apoptosis, inflammation, and oxidative stress. Warm ischemia injury resulted in a significant increase in the level of oxidative stress, inflammation, and apoptosis in the DCD hearts of DCD-Control group. Furthermore, compared with the DCD-Control group, CM treatment increased the developed pressure, dP/dt_{max} and dP/dt_{min} of the left ventricular in the DCD hearts during a 90-minute EVHP. Moreover, the administration of CM attenuated the level of oxidative stress, inflammation, and apoptosis in the DCD hearts of the DCD-CM group. *Conclusions*. Normothermic EVHP combined with CM treatment can alleviate warm I/R injury in the DCD hearts by decreasing the level of oxidative stress, inflammatory response, and apoptosis, which might alleviate the shortage of donor hearts by adopting DCD hearts.

1. Introduction

Heart transplantation remains the most appropriate therapy for end-stage heart failure [1]. Unfortunately, despite the increasing number of heart failure patients, the shortage of suitable donor hearts has limited the development of heart transplantation [2]. Recent studies have shown that adopting hearts from donation after circulatory death (DCD) can significantly expand the donor pool [3]. In the United Kingdom, it is predicted that adopting strict DCD donor selection criteria will result in a 56% increase in the number of heart transplantation [4], which will significantly reduce waiting-list mortality. Furthermore, compared with conventional brain-dead (BD) heart transplantation, DCD heart transplantation provided a similar 30-day or 1-year postoperative survival rate [5, 6]. However, due to inevitable warm ischemia time, DCD hearts undergo more severe myocardial ischemia/reperfusion (I/R) injury [7].

Mesenchymal stem cells (MSCs) are pluripotent, self-renewing cells [8]. The administration of MSCs is