

Effect of Mechanical Perfusion on Ischemia-reperfusion Injury after Liver Transplantation

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How to cite this paper: Ruichao Wu, Wang Li, Jianghua Ran. (2022) Effect of Mechanical Perfusion on Ischemia-reperfusion Injury after Liver Transplantation. *International Journal of Clinical and Experimental Medicine Research*, 6(4), 408-412.
DOI: 10.26855/ijcemr.2022.10.014

Received: September 22, 2022

Accepted: October 17, 2022

Published: November 15, 2022

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Abstract

Ischemia-reperfusion injury is one of the main factors of organ loss after liver transplantation. The occurrence of this complication is affected by acidosis, oxygen free radical explosion, inflammatory changes and other factors, and this complication is also the focus of research in the field of organ transplantation. The most ancient method of donor liver preservation is static cold preservation, but this method can not effectively meet the needs of the development of organ transplantation. With the development of mechanical perfusion technology, its research in donor liver preservation has gradually increased and matured, which is expected to become the main technology for donor liver repair and preservation in the future. Combined with existing animal studies, mechanical perfusion has a prominent effect on saving marginal donor liver, which is helpful to control ischemia-reperfusion injury after liver transplantation and promote the improvement of postoperative liver function. In recent years, some developed countries have applied mechanical perfusion technology in clinical diagnosis and treatment, and achieved certain results, but there are relatively few clinical data at the present stage. Based on the development background of mechanical perfusion technology and the principle of mechanical perfusion technology, this paper analyzed the influence of mechanical perfusion on ischemia-reperfusion injury after liver transplantation based on the relevant literature in recent years.

Keywords

Mechanical perfusion, Liver transplantation, Ischemia-reperfusion injury

Introduction

Liver transplantation is the most effective way to treat end-stage liver disease in the medical field at present. Liver ischemia-reperfusion injury is a common postoperative complication in such patients, which mainly includes liver ischemia-reperfusion injury, reperfusion injury after hepatic blood recanalization and other types [1]. The complications of the mechanism is relatively complex, is generally believed that it is associated with liver ischemia hypoxia, after the occurrence of liver ischemia-reperfusion injury will occur a series of pathological changes, such as the abnormal mitochondrial function damage, reactive oxygen species generation and so on, causes the body to produce inflammatory change, oxidative stress and DNA damage such as [2, 3]. Severe cases will lead to autophagy and necrosis of local cells, which will affect the prognosis of liver transplantation patients. At present, there is still a lack of specific means for the prevention of ischemia-reperfusion injury after liver transplantation, and the prevention is generally carried out from anti-inflammatory and antioxidant aspects [4], [5].

Always, medicine for the preservation of donor livers with static cold storage is given priority to, simple technology and low price, and along with the development of organ transplant technology, liver preservation technology is also in constant improvement, machine perfusion is one of the new direction, machinery perfusion for liver preservation, by nutrients and oxygen supplementation can effectively relieve liver loss of ATP, The donor liver ischemia-reperfusion injury was controlled [6]. This paper analyzes the effect of mechanical perfusion on post-operative ischemia-reperfusion injury based on the relevant research data of mechanical perfusion in the field of liver transplantation.

1. Brief introduction of the development background of mechanical perfusion technology

After decades of development, organ transplantation has now entered a more mature stage. At present, there are more than 50 institutions with the conditions and techniques for liver transplantation in China, and Chinese doctors have accumulated relatively rich practical experience in liver transplantation in recent decades. The effect and quality of liver transplantation are affected by many factors, such as the diagnosis and treatment level of the medical team, clinical experience, donor liver preservation conditions, and rejection of transplantation after transplantation [7, 8]. The donor liver used in liver transplantation in China mainly comes from dead donors, and the actual distance between recipient and donor is not controllable, which puts forward higher requirements for donor liver preservation technology. In liver transplantation for over forty years, static cold preservation of donor livers preserved has always been the preferred way, namely the liver from a donor immediately after cooling below 10 °C, the donor liver into after about 1 ~ 4 °C temperature change until the transfer in the preservation of the fluid, static cold storage can effectively retain for liver mitochondrial function and energy metabolism after liver transplantation. Mechanical perfusion preservation technology is also one of the organ transplantation preservation technologies, which was applied to kidney transplantation surgery in the 1990s, and relevant studies have confirmed that the application effect of this technology is better than static cold preservation [9], [10]. However, the application period of mechanical perfusion preservation technology in liver transplantation is relatively short. Relevant studies have found that mechanical perfusion of experimental dog liver can preserve the isolated liver for more than 72 hours [11, 12].

2. Principle analysis of mechanical perfusion technique

Static cold preservation is still the gold standard of organ preservation. The low temperature and preservation solution in this technology can control the metabolism level of organ tissues and alleviate the cell level. However, low temperature can only reduce tissue metabolism, and the rate of metabolic reduction is limited, and the accumulation of metabolites will still occur in the process of organ preservation and transportation [13, 14]. ATP needs to be consumed in the process of tissue metabolism, which will lead to calcium influx in the cells of organs, electrolyte imbalance inside and outside the cells, and then lead to organ edema and increase the risk of ischemia-reperfusion injury after organ transplantation [15, 16]. The temperature can be adjusted in combination with specific conditions in mechanical perfusion. Compared with static cold preservation, the mechanical perfusion system can realize the supply of nutrients and the removal of metabolic wastes in the process of organ transfer and transportation, and play a role in maintaining the vitality of organ tissues and cells and controlling ischemia-reperfusion injury [17]. Animal studies have shown that mechanical perfusion preservation technology is helpful to maintain the hemodynamic level of organ vasculature and maintain organ vitality. However, the implementation of mechanical perfusion preservation technology depends on the mechanical perfusion system, which will cause certain mechanical stress damage to organs, which is the main limitation of the current clinical application of this technology. At present, mechanical perfusion preservation technology applied in organ transplantation research will be differentiated according to specific conditions and actual needs, such as oxygen-carrying and non-oxygen-carrying mechanical perfusion, normal temperature or low temperature mechanical perfusion, etc., which can better meet different organ transplantation situations [18, 19].

3. Effect of mechanical perfusion on ischemia-reperfusion injury after liver transplantation

Mechanical perfusion covers the whole process of liver transplantation from the body to the body. This technology realizes the injury control of liver transplantation from the body to the body by simulating liver perfusion under physiological state. Ischemia-reperfusion injury after liver transplantation occurred cannot avoid completely, and the complications after liver transplantation is secondary to the primary nonfunction primary factor, the current medical experts in this field is generally believed that the occurrence of ischemia-reperfusion injury after liver

transplantation is the result of comprehensive shaping of many factors [20], oxygen free radical and inflammatory factor is a hotspot of research in recent years. Mechanical perfusion can effectively control the level of inflammatory factors in the early stage after liver transplantation, so as to alleviate the degree of ischemia-reperfusion injury caused by it. Static cold preserved by low temperature control after the donor liver in vitro tissue metabolism and nutrient consumption, but not to inhibit [21] of this process, therefore in the process of save for metabolism of liver is still in a constant state, and the state of ischemia hypoxia increases based energy metabolism level, restore perfusion after liver transplantation the metabolic situation exacerbate. As a result, the balance of oxygen free radicals is broken and a large number of free radicals are generated, thereby aggravating inflammatory changes and affecting the effect of liver transplantation. The mechanical perfusion preservation technology can provide continuous perfusion preservation to the donor liver through centrifugal pump, circulating flow, temperature and pressure control and other technologies. Among them, the most widely used cryogenic mechanical perfusion can be used to preserve the donor liver under the condition of 4-8 °C, and the low temperature can control the oxygen demand of the donor liver. At the same time temperature conditions can also reduce the liver tissue metabolism, mechanical perfusion of low perfusion can be in a state of liver in vitro of cold ischemia after missing component cell metabolism, regulation, to control the metabolism of the liver and dissimilation, ease the metabolism of nutrients loss caused by ischemia-reperfusion injury after liver transplantation [22]. During the metabolism of liver in vitro, ATP metabolites accumulate, while mechanical perfusion can realize the continuous circulation of metabolites, and release metabolic wastes through endothelium-parenchyma contact, thus avoiding liver damage caused by ATP metabolites accumulation [23]. Machine perfusion technology can also improve liver microcirculation, replenish oxygen, energy and remove metabolic wastes through perfusion, create favorable conditions for functional recovery after liver transplantation and reduce the risk of adverse events such as ischemia-reperfusion injury and delayed graft failure after liver transplantation [24]. In recent years, conventional mechanical perfusion technology is also under constant research. This technology keeps the donor liver temperature at about 37°C and ensures the aerobic metabolism of the donor liver tissue through oxygen supply. An animal study [25] is pure refrigeration technology and mechanical perfusion technique is applied to donor livers preserved in low temperature, the impact on inflammatory factor and so on after liver transplantation were analyzed, the study included 90 male dogs, conduct research, each 30 was divided into three groups, respectively for low temperature mechanical perfusion preservation group, the donor group and simple cryopreservation groups. During liver transplantation, a certain number of experimental dogs were selected from each group to carry out the study. The inflammatory cytokines and apoptotic factors of experimental dogs receiving liver transplantation were detected before liver transplantation, before liver transplantation and 60min after liver transplantation. The results showed that 60 min after liver transplantation cryogenic mechanical perfusion preservation group 1 beta dog interleukins, tumor necrosis factor alpha and interleukin - 8, macrophage inflammatory protein alpha, macrophage inflammatory protein 1 beta levels are lower than pure cryopreservation groups, the study found that low temperature mechanical perfusion to upstream from the inflammatory reaction in the body's inflammatory condition control, So as to alleviate the inflammatory cell infiltration in the liver after liver transplantation. The donor liver preserved by mechanical perfusion can obtain relatively sufficient energy for metabolism and maintain the physiological function of the donor liver.

4. Summary

Mechanical perfusion preservation technology, mechanical perfusion system of blood vessels and organs, mechanical perfusion preservation technology implementation process, the need to be transplanted organ preservation solution of continuous pumping, pumping process continue to transplant organs from body to transplant the whole, compared with the static cold storage technology, this technology can physiological state of the simulation of the continuous perfusion in vitro organ, so as to control the organ injury after in vitro, some experiments have confirmed that mechanical perfusion preservation technology can control the degree of postoperative ischemia-reperfusion injury by controlling the early inflammatory reaction, oxygen free radical explosion, acid-base disorder and so on after liver transplantation. In recent years, organ donation has been developing and maturing in China, and the marginal donor base has increased, which puts forward higher requirements for organ preservation technology. Mechanical perfusion preservation technology is expected to repair and evaluate the donor liver, so as to benefit more patients in need of liver transplantation.

The project:

(1) Subject name: Yunnan Provincial Organ Transplant Clinical Medical Center open topic: The Mechanism of Ca²⁺-CaM-CaMK II γ Signal Pathway Regulating Apoptosis after DCD Liver Transplantation in Rats (project number: 2020SYZ-Z-003).

(2) Subject name: Yunnan Provincial Organ Transplant Clinical Medical Center open topic: The effect of inhibiting CaMKII γ signal pathway on apoptosis after DCD liver transplantation in rats (project number: 2020SYZ-Z-029).

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