

課題番号 (Project number) : 49

Strategies of donor lung preservation after cessation of circulation

[1] 組織 (Research group)

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研究費(Expenditure report of research funds) :

物件費 400,000 YEN

[2] 研究経過 (Research setup)

Lung transplantation (LTx) is a lifesaving therapy for patients with end-stage lung diseases. However, the number of patients waiting for LTx greatly exceeds the number of donors available. In order to overcome the shortage of lungs, many lung transplant programs are interested in using organs from donors after circulatory death (DCD). However, about 40-50% of potential cDCD are declined because death does not occur in a suitable time frame currently accepted of 120 min from withdrawal of life support therapies (WLST) and cardiac arrest (Machuca TN, Cypel M, et al. Am J Transplant. 2015;15:993-1002, Figure 1). Therefore, improved strategies to preserve lungs after death may enable teams to recover lungs from more cDCDs, even if few hours of no circulation, that is warm ischemia time (WIT), occurs until recovery teams can arrive to donor hospitals.

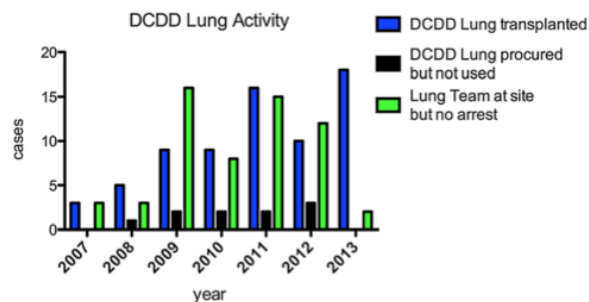


Figure. 1

Carbon monoxide (CO) is a lipid-soluble, endogenously produced gaseous messenger molecule, collectively known as a gasotransmitter, which has been shown to exert anti-inflammatory, anti-apoptotic, anti-proliferative, and vasodilative properties in multiple organs following ischemic injury, including the lung. In the ex vivo lung perfusion (EVLV) system, lungs can be ventilated and perfused in a highly controlled environment, providing an ideal platform to assess the effects of CO on ischemia-reperfusion injury in both animal and human tissue. The first purpose of this study was to verify whether CO administration during warm ischemia time and/or EVLP may exert beneficial effects in lung utilization.

In addition, prone positioning in acute respiratory distress syndrome (ARDS) has been shown to provide a more homogeneous distribution of alveolar distending pressure, to reduce lung injury, and to improve outcomes. However, there have been no reports about prone positioning for management of organ donors. We hypothesized prone positioning during WIT after cardiac death could decrease atelectasis and homogeneously distribute alveolar inflation (a critical feature of lung preservation) leading to improved lung function during ex vivo lung perfusion (EVLV). The second purpose of this study was to determine the effect of donor positioning on the quality of lung preservation after cardiac arrest.

[3] 成果 (Research outcomes)

(3-1) 研究成果 (Results)

The established pig cDCD model closely simulated clinical cDCD scenario with average time from WLST to arrest of 27 minutes. CO during both WIT and EVLP was able to extend the acceptable WIT to 3 hours, have a significant impact in increasing lung utilization in cDCDs. However, a limitation of this strategy was that CO gas was not able to be distributed if there were atelectatic area in the lungs.

Second step of this study was performed to overcome this limitation. In the same experimental model of cDCD, prone positioning provided better alveolar air redistribution and prevented the development of lung atelectasis (Figure 2) and cell death during WIT, with a consequent dramatic improvement of lung function during the assessment phase in the EVLP platform. The more homogeneous distribution of alveolar distending pressure in prone compared to supine position may be crucial to maintain alveolar recruitment in lung donors, thereby improving lung preservation and function.

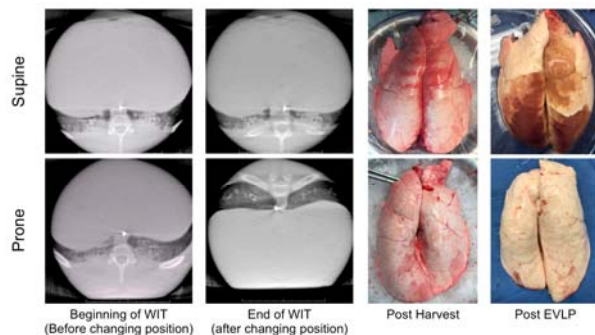


Figure. 2

(3-2) 波及効果と発展性など (Future perspectives)

CO application and prone positioning of DCD donors may increase the number of organs suitable for lung transplantation and recipient outcomes. In this study, there were dramatic improvements of lung function during EVLP even if only prone positioning of DCD donors. However, there have been no reports about prone positioning for management of organ donors even though it is simple strategy and available in all donor hospitals. The results would help many donor management teams to try the prone positioning in several settings.

[4] 成果資料 (List of Papers)

(1) Watanabe Y, Galasso M, Watanabe T, Ali A, Chan HHL, Qaqish R, Summers C, Ramadan K, Pinto Ribeiro RV, Zhang Y, Gazzalle A, Waddell TK, Liu M, Keshavjee S, Del Sorbo L, Cypel M. Prone Positioning Attenuates Lung Injury During Warm Ischemia in a Large Animal Controlled Donation after Cardiac Death Model. The International Society for Heart and Lung Transplantation 38th Annual Meeting and Scientific Sessions. Nice, France. April 11-14, 2018.

(2) Watanabe Y, Galasso M, Watanabe T, Ali A, Chan HHL, Ramadan K, Pinto Ribeiro RV, Zhang Y, Gazzalle A, Liu M, Keshavjee S, Del Sorbo L, Cypel M. Prone positioning attenuates lung injuries during warm ischemia time in a swine donation after cardiac death model. Medicine by Design 2nd Annual symposium. Toronto, Canada. December 5, 2017.

(3) Watanabe Y, Galasso M, Watanabe T, Ali A, Chan HHL, Ramadan K, Pinto Ribeiro RV, Zhang Y, Gazzalle A, Liu M, Keshavjee S, Del Sorbo L, Cypel M. Prone positioning attenuates lung injuries during warm ischemia time in a swine donation after cardiac death model. TGRI Research day 2017. Toronto, Canada. October 11, 2017.

(4) Watanabe Y, Nakajima D, Taniguchi Y, Pipkin M, Chen M, Ohsumi A, Takahashi M, Watanabe T, Qaqish R, Caldarone L, Summers C, Waddell TK, Liu M, Keshavjee S, Okada Y, Cypel M. Strategies of Lung Preservation after Absence of Circulation. International session of the 117th Annual Congress of the Japan Surgical Society. Tokyo, Japan. April 27-29, 2017.

(5) Watanabe Y, Nakajima D, Taniguchi Y, Pipkin M, Chen M, Qaqish R, Caldarone L, Watanabe T, Ohsumi A, Kanou T, Takahashi M, Gazzalle A, Galasso M, Ali A, Summers C, Waddell TK, Liu M, Keshavjee S, Cypel M. Carbon Monoxide Can Rescue Lungs from Controlled Donors after Cardiac Death and Prolonged Warm Ischemia. The International Society for Heart and Lung Transplantation 37th Annual Meeting and Scientific Sessions. San Diego, CA, USA. April 5-8, 2017.