LETTER TO THE EDITORS

Reply to Sharif et al.

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Dear Editor,

We sincerely appreciate your professional comments, and we are not surprised that you have concerns about the organ resources. That is because using organs procured from executed prisoners is considered unethical, and the articles suspected involving relevant data are often rejected by many academic journals. But I want to say that from January 1, 2015, no organ from executed prisoners is used any more in China.

On December 7, 2019, conference on the development of organ donation and transplantation of China was successfully held in Kunming. Over 100 experts from more than 30 countries attended the meeting and made speeches against politicizing organ transplantation. The participants included members of the task force on organ transplantation of the World Health Organization, The Transplantation Society, and other international transplant societies. In response to some so-called "academic papers," which slandered China still using organs from executed prisoners, especially an article published by *BMJ* on November 14, 2019 (Rogers *et al.*), Chinese and international experts criticized the unreliable rumors. Jiefu Huang, director of the China National Organ Donation and Transplantation Committee, reaffirmed that in May 2007, the state council promulgated the Human Organ Transplantation Regulations. In 2011, the Amendment (VIII) of the Criminal Law of the People's Republic of China made it clear that the organ trafficking was a serious criminal crime, providing legal guarantee for cracking down relevant illegal and criminal acts. Definitely, since 2015, voluntary donations by Chinese citizens have been the only legal source of organ transplants. From 2015 to 2018, the number of organ donations completed in China each year was 2766, 4080, 5146, and 6302, with a rapid growth, and the number of organ donations in 2018 ranked second in the world. Jose Nunez, a World Health Organization (WHO) officer who oversees global organ transplantation, said during the conference that the development of China's organ donation and transplantation is on the right path and in line with the guiding principles of the WHO. Much more details of the news reporting can be seen from https://baijiahao.baidu.com/s?id=1652448751772751083&wfr=spider&for=pc or http://www.xinhuanet.com/english/2019-12/08/c_138615720.htm.

Taken together, we are able to give you an absolute guarantee that there are no data sourced from executed prisoners' donation in this study, which included deceased donor transplants between 2015 and 2016.

However, we think our paper still has some small defects, which could mislead the audiences. After checking the data in the tables, we are very sorry for our carelessness in some errors of warm ischemia time and inadequate explanations, which were described as follows.

Can the authors explain why the mean age of their donor pool is so low by international standards, provide a further breakdown of donor characteristics, and indicate causes of death?

Answer: Thank you for your careful comments. Our analysis showed that large variance existed in the donor age as the standard deviations was above 15 years, suggesting that some very younger donors were included in. Nowadays, kidney graft from pediatric donor to adult recipient has been an important strategy to expand the donor pool, especially in China, which organ is badly lack. Zhu *et al.* [1] reported that single-kidney transplantation from pediatric donors aged 8–36 months to selected adult recipients produced excellent intermediate-term outcomes, comparable with those when older pediatric donors (aged >3 years) were used. Jiang *et al.* [2] reported that single-kidney transplantation from pediatric deceased donors to adult recipients is effective and safe with acceptable outcomes, and it will be a promising expansion to the donor pool. In the present database analyzed, there were 180 adult

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DCD and DBCD kidney transplantation from pediatric donors (aged <18 years), which might be a major reason of younger mean age of donors. Moreover, trauma is a major cause of donor death in China, which involving many young people. Based on these Chinese characteristics, we believe that "international standards" could not be the only criterion for the judgement on paper's objectivity.

Can the authors explain how they are defining and measuring WIT, and why it is short by international standards?

Answer: I express the depth of my gratitude to you for your agile observation about the WIT. The explanation for it is as follows:

Firstly, there is no standard definition for donor warm ischemia time (DWIT) in deceased donor and multiple criteria for DWIT are used currently. For example, Monbaliu *et al.* [3] defined DWIT as the period between stopping ventilatory support until the start of cold flush out the abdominal organs. Kalisvaart *et al.* [4] divided DWIT into two periods: the agonal phase (from withdrawal of treatment until circulatory arrest) and the asystolic phase (circulatory arrest until cold perfusion). In Australia, the WIT is defined as the time from irreversible cessation of circulation until commencement of preservation solution for organ procurement [5], but it remains unclear whether it includes the "no-touch" time. So it can bring different understanding about it. And as to controlled DCD and uncontrolled DCD, two different organ types, both the definitions of the DWIT are not same [6]. Some countries also recommend the concept of functional warm ischemia time [7]. Even there is definition according to the donor blood pressure or oxygen saturation (SaO_2), moreover, the threshold of the blood pressure (e.g., SBP <80 mmHg or 50 mmHg) is not standardized, and different centers proposed different donor hemodynamic values to define the start of function warm ischemia time [8,9]. As a result of these different definitions and criterions, great confusion definitely exists and the limit of WIT presents great difference between transplant centers.

As for this study, warm ischemia time was recorded as the period from the irreversible cession of circulation to the hypothermic perfusion by most of Chinese organ transplant centers, which might shorten the WIT compared to the time from the termination of life support to the hypothermic perfusion or cold preservation.

Secondly, given inferior donor organ quality, "uncontrolled cardiac arrests"(classification of Maastricht I and II) are next to impossible in China that means most of the DCD and all the DBCD could be classified to "controlled cardiac arrests" (Maastricht III, IV). Moreover, donated kidney with WIT >30 min is used very cautiously driven by the concerns of inferior outcomes, long-term tension in the doctor–patient relationship and economic reasons. Nowadays, a series of kidney transplant quality control specification are under revision in China, recommending that DWIT should be calculated from the time of cardiac arrest to the start of cold perfusion. This definition of DWIT is clear and easy to compare among different transplant centers, and many experts believed that no more than 10 min are feasible. So we believe that data quality of WIT reported by different organ transplant centers in China will be much improved in the future.

Thirdly, we had checked the original data of WIT and awkwardly found some significantly abnormal (≤3 min) data. We have to admit that Chinese national transplant recipient registry is still in its infancy, and we also mentioned that in the manuscript, all the data included in this study were manually reported. Therefore, it could inevitably result in some data missing and reporting errors, especially in the context of unclear definition of WIT. We neglected it before and should delete the extremely abnormal minimum data when the initial analysis was made.

So, thanks for your kindly reminder, we design a threshold value (>3 min) for WIT. After we deleted the abnormal WIT(≤3 min) data, the WIT in the DCD, DBCD, and DD group should be 7.1 ± 6.0, 9.4 ± 8.1 min, and 8.5 ± 7.4 min, respectively, in the Table 1. Accordingly, the WIT of DD in the supplementary Table 1 should also be corrected as 8.5 ± 7.4 min. The result is consistent with the report by Sun *et al.* [10] which showed that 57.8% of DBCD donors had warm ischemia time 10–20 min. These errors attributed to our carelessness about dealing with significantly abnormal data.

Again, we sincerely apologize for our carelessness in calculating the DWIT and wish to have a chance to correct them in the final publication.

REFERENCES

1. Zhu L, Fu C, Chen S, *et al.* Successful single-kidney transplantation in adult recipients using pediatric donors aged 8 to 36 months: comparable outcomes with those using pediatric donors aged >3 years. *Transplantation* 2019; **103**: 2388.

2. Jiang Y, Song T, Qiu Y, *et al*. Outcomes of single kidney transplantation from pediatric donors: a single-center experience. *Pediatr Transplant* 2018; **22**: e13196.
3. Monbaliu D, Van Gelder F, Troisi R, *et al*. Liver transplantation using non-heart-beating donors: Belgian experience. *Transplant Proc* 2007; **39**: 1481.
4. Kalisvaart M, de Haan JE, Polak WG, *et al*. Onset of donor warm ischemia time in donation after circulatory death liver transplantation: hypotension or hypoxia? *Liver Transpl* 2018; **24**: 1001.
5. Organ And Tissue Donation After Death For Transplantation Guidelines. For Ethical Practice, For Health Professionals. https://www.nhmrc.gov.au/research-policy/ethics/ethical-guidelines-organ-and-tissue-donation-and-transplantation.
6. Shemie SD, Baker AJ, Knoll G, *et al*. National recommendations for donation after cardiocirculatory death in Canada. *CMAJ* 2006; **175**: S1.
7. Antoine C, Mourey F, Prada-Bordenave E, *et al*. How France launched its donation after cardiac death program. *Ann Fr Anesth Reanim* 2014; **33**: 138.
8. NHS Blood and Transplant National Standards for Organ. Retrieval from Deceased Donors. 2012. https://www.bts.org.uk/Documents/9.1.13%20Retrieval%20Standards%20Document%20v2%206%20effective%20010113.pdf.
9. Organ Procurement and Transplant Network. Glossary. https://optn.transplant.hrsa.gov/resources/glossary. Accessed September 12, 2018.
10. Sun Q, Zhou H, Cao R, *et al*. Donation after brain death followed by circulatory death, a novel donation pattern, confers comparable renal allograft outcomes with donation after brain death. *BMC Nephrol* 2018; **19**: 164.