Author’s response to reviews

Title: A comparative study on the efficacy of a retrograde perfusion technique and an antegrade perfusion technique for donor kidney recovery in transplantation in pigs

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Letter

A point-by-point response to the reviewers’ comments

Reviewer #1:

RESULTS: data on ischemia times are missing and should be included.

Revised: P10, lines 15–17.

DISCUSSION:

- "From an anatomical point of view, RP is clearly a more practical way to perfuse kidneys." This is not true. Perfusing a kidney in a retrograde fashion is as difficult the antegrade perfusion, but the perfusion must be interrupted.

- I think some more comment on the usefulness of RP should be included. The authors fairly state that some kidneys cannot be perfused antegradely because of mechanical reasons. If this kidneys cannot be perfused, will they be useful for transplantation?
Some kidneys cannot be perfused antegrade because of mechanical reasons. If we find the kidneys cannot be perfused using traditional techniques because of intra-operative damage to the renal artery, we immediately perfuse them retrograde. If we find kidneys cannot be perfused because of arterial variation, such as two or three thin arteries, we find the opening of the arteries and perfuse them with a thin irrigation tube. The warm ischemic time was prolonged, and ATN (Acute tubular necrosis) may have increased, but these kidneys were usable for transplantation. In this case, retrograde perfusion was meaningful. For artery variation or damage, before use, we perform angioplasty. One important thing I want to say is the limitation of warm ischemic time is 15 minutes. If the warm ischemic time is more than 15 minutes, the kidney couldn’t be used anyway in our clinical practice.

CONCLUSION:

"Retrograde perfusion is an efficient kidney perfusion method for organ recovery from cadaveric donors." This conclusion can not be obtained from this study. The experiments you have conducted are much more similar to a living donor than a cadaver. The grafts have not been submitted to a long ischemia times as would be in a conventional cadaveric donor. A softer conclusion should be stated.

"Retrograde perfusion could potentially replace AP as a clinical perfusion method." This conclusion is not obtained from the study. Although retrograde perfusion seems to lavage kidneys adequately, this technique does not have enough evidence to replace the gold-standard method, not even "potentially".

Reviewer #2:

1. Good study addressing an interesting question regarding retrograde perfusion.

2. There are a few typos that should be easy to fix.

The whole manuscript was revised by editing company.

3. The warm ischemia time is very short! Typical warm ischemia time for human kidneys is ~ 20 minutes (K Marzouk 2013 and KK Tennankore 2016 - see discussion re: WIT < 10 minutes). The method of calculating WIT should be described and the numbers verified.
A deliberately short primary warm ischemic time was devised in our study. We restricted the warm ischemic time and graft preservation time to as short as possible to evaluate the effects of the RP technique itself on renal graft function after auto-transplantation. Warm ischemic time causes ATN, and greatly affects the transplant result. If ATN occurred, we could not apply hemodialysis in the pig. The pigs may have died of ATN but not of the perfusion technique. In order to avoid ATN, we shortened the warm ischemic time to as short as possible.

4. Ideally the histology would be scored (ATN score, apoptosis score) by a pathologist in a blinded fashion. Also, since needle biopsies of kidney grafts were taken immediately after perfusion, before revascularization, after 24 hours storage, and on day 7 following transplantation, it would be good to show all of the histology with scores in the 2 groups.