Is Warm Ischemia Not a Risk Factor for Delayed Graft Function in a Living-Donor Kidney Transplant?

Taqi T. Khan,1 Faheem Akhtar,2 Basem Koshaji1

Abstract

The association between prolonged donor warm ischemia time and poor early graft function has been challenged, but with little evidence. We intend to remove ambiguities and present evidence from the current literature. All donor surgeons must strive to limit warm ischemia to reduce poor early graft function and improve long-term outcomes.

We read with interest the paper comparing long-term graft function in laparoscopically recovered kidneys versus open nephrectomy.1 The indirect message delivered by the authors that prolonged donor warm ischemia (WIT) is not associated with delayed graft function (DGF) is misleading and dangerous and raises several questions about this study. The statement that DGF and not prolonged WIT negatively affect long-term graft outcomes implies that prolonged WIT is not a risk factor for DGF. We will attempt to clarify some of these issues and present some evidence that we feel central to understanding poor early graft function (DGF and slow graft function).

In their study, the inherent and significant difference in WIT between laparoscopic donor nephrectomy and open donor nephrectomy (8.7 ± 2.7 min vs 1.8 ± 0.92 min) is not surprising and is similar to other studies.2-4 What is surprising is that this did not translate into an increased incidence of DGF, a donor with a WIT of 10 to 17 minutes should, by itself, be expected to guarantee enough acute kidney injury to cause poor early graft function. But when combined with the effects of pneumoperitoneum, the expectations of immediate graft function should decrease even further. This is corroborated by zero time histologic evidence of widespread cortical and capsular injury in the kidneys recovered by laparoscopic donor nephrectomy that was not seen in those recovered by open donor nephrectomy.5 However, in the authors study, despite severely prolonged WIT, there was no significant difference in the rate of DGF in laparoscopic donor nephrectomy and open donor nephrectomy. In contrast, strong rationale for donor surgeons to limit WIT is provided in the study by Noguiera and associates, because of its association with poor early graft function (EGF) and long-term outcomes.3

There is a large body of evidence in the recent literature linking donor warm ischemia to poor EGF and impaired long-term outcomes in live-donor kidney transplant.2,3,6 Additionally, poor EGF also is an independent risk factor for acute rejection and negatively affects long-term outcomes.2,3

It is difficult to understand how the authors managed to avoid poor EGF with such prolonged WIT? Recent studies have shown that kidneys recovered by laparoscopic donor nephrectomy have higher poor EGF and consequently, poorer outcomes.3,6 Many other relevant data that can influence EGF are also not available in the study, such as the recipient WIT or anastomosis time, cold ischemia time (a one-man team doing both the donor and recipient can have longer CIT), and the type of preservation solution. The recipe used by the authors has given unexpectedly good results considering the number of graft unfriendly factors involved. Antithymocyte antibody induction is used by the authors only when indicated, but it is unclear what these indications are, and the early use of cyclosporine can hardly be expected to facilitate graft function. The mean WIT in recipients with DGF was 6.2 minutes.
and 5.2 minutes in those without DGF, but how does this explain more DGF in kidneys recovered by open donor nephrectomy (11 vs 8) when the mean WIT in open donor nephrectomy was only 2 minutes? Logically, this would mean that most of the DGF would be expected in kidneys recovered by laparoscopic donor nephrectomy, not open donor nephrectomy.

Other known risk factors for poor outcomes in live-donor kidney transplant have not been mentioned by the authors. The presence of diabetes\(^2,7\) and acute rejection\(^2,3,4\) are known to have a significant negative effect on EGF and long-term outcomes, and it would be interesting to know what percentage of the authors recipients developed acute rejection and how many had diabetes?

The authors claim that a WIT less than 35 minutes does not impair graft function in deceased donor transplant, they seem to have overlooked the fact that this 35 minutes WIT is recipient WIT or anastomosis time and not donor WIT, making any comparison inappropriate. Donor WIT in deceased-donor transplant is close to zero, because cross-clamping and cold perfusion are simultaneous.

Importantly, the authors have not hypothesized as to what actually caused DGF in their live-donor kidney transplant cohort where donor WIT was not a real concern. There is contradiction in their conclusion that every effort must be made to avoid poor EGF to improve graft outcomes in live-donor kidney transplant but paradoxically, do not insist on increasing efforts to reduce donor WIT.

References