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INVITED COMMENTARY

The rising scourge of acute renal injury after heart transplantation

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Over half a century, heart transplantation has evolved as the optimal therapy for the treatment of end-stage heart disease. Despite significant progress in the field with improved immunosuppression leading to decreased rejection and infection rates, post-transplant outcomes remain dependent on several factors including preserved function of extra-cardiac organs. Of particular importance, renal function after heart transplantation has been an important determinant of survival. Combined heart-kidney transplantation has been increasingly performed and associated with improved outcomes in patients with decreased renal function requiring heart transplantation [1]. Chronic renal injury after heart transplant is well recognised with 25% of recipients developing severe renal failure at 10 years [2]. This has been attributed to a variety of risk factors including hypertension and diabetes mellitus common after transplant and prominently, long-term use of calcineurin inhibitors. The effects of acute renal failure at the time of transplant however are less well studied. The cardio-renal axis is paramount with advancing heart failure and complex pathophysiological processes contribute to mutual dysfunction. These include neurohormonal activation, endothelial dysfunction and hemodynamic factors, namely reduced cardiac output, arterial hypoperfusion and venous congestion [3]. Renal function may be further compromised at the time of transplant due to perturbations from cardio-pulmonary bypass, blood loss, post-transplant graft dysfunction and need for vasopressors or mechanical support. Efforts to improve our understanding of this complex interplay are much needed.

In a retrospective registry analysis, Wang *et al.* [4] assess the impact of severe acute kidney injury requiring renal replacement therapy on survival and renal function of heart transplant recipients. The data are derived from a large cohort from the UK Transplant Registry. The study evaluated risk factors for severe acute kidney injury requiring renal replacement therapy (RRT) early after transplant. A regression model was used to identify predicting factors of mortality and end-stage renal disease (ESRD). RRT was associated with lower survival at all timepoints but especially in the immediate post-transplant period. Interestingly, conditional on 3-month survival, RRT did not impact long-term mortality, although the need for RRT after transplant was associated with an increased risk for the development of ESRD in the long term.

The interpretation of this data should be considered in the context of some unique features of the cohort. The use of RRT after transplant was high with more than a quarter of the patients requiring RRT in the entire study but almost half the patients needing RRT in the most recent era. There appeared to be a

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variability between centres in the use of RRT. The increase in RRT usage over time was accompanied by greater acuity of recipients as reflected by urgency status, and need for inotropic or mechanical support. Significantly, risk of RRT was not only associated with donor age but also with severe primary graft dysfunction (PGD; OR 7.7). Notably, severe PGD rates increased 5-fold from the earliest era (3.6%; 1995–2000) to the most recent era (20.7%; 2011–2017) and this appears to have been the main driver for RRT need and early mortality (54.8% at 90 days). This may explain the lack of impact of RRT on 3-month conditional survival as PGD by definition occurs early and when severe frequently compromises vital organs, resulting in high early mortality rates [5].

With respect to the long-term hazard for developing ESRD, recipients not requiring RRT had a decreased risk with each successive era. In contrast, the need for RRT post-transplant was associated with increased hazard for ESRD and this hazard increased with each successive era paralleling recipient acuity and PGD rates.

As a registry study spanning more than two decades, there are significant limitations which constrain the interpretation of the data. Details on renal function prior to transplant including proteinuria was not available. Data on immunosuppression would have been informative. Induction therapy is often used to delay initiation of calcineurin inhibitor therapy to allow renal recovery and has been adapted from renal transplantation but without much data for its efficacy in heart transplantation. Long-term renal function may be modulated by changes in immunosuppression, particularly with adoption of a calcineurin-free regimen. Duration of RRT was not documented and therefore values of serum creatinine stated need to be interpreted with some caution. Hemodynamic data pre-transplant was lacking in a third of the cohort.

The authors are to be lauded for bringing the subject of RRT after heart transplantation to the foreground given the increasing use documented. The study emphasises the need to optimise renal function at transplant to minimise risk of RRT through judicious hemodynamic management and renal protection. More research is needed on the complex mechanisms leading to cardio-renal syndrome, and there is an urgency to develop techniques which can more accurately predict post-transplant renal function. These data contribute to a timely discussion on stratifying patients for the need for combined heart-kidney transplant in an era when both organs are in increasing demand.

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REFERENCES

1. Karamlou T, Welke KF, McMullan DM, *et al*. Combined heart-kidney transplant improves post-transplant survival compared with isolated heart transplant in recipients with reduced glomerular filtration rate: analysis of 593 combined heart-kidney transplants from the United Network Organ Sharing Database. *J Thorac Cardiovasc Surg* 2014; **147**: 456.e1.
2. Khush KK, Cherikh WS, Chambers DC, *et al*. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-sixth adult heart transplantation report – 2019; focus theme: donor and recipient size match [published correction appears in J Heart Lung Transplant. 2020 Jan;39 (1):91]. *J Heart Lung Transplant* 2019; **38**: 1056.
3. Liu S. Heart-kidney interactions: mechanistic insights from animal models. *Am J Physiol Renal Physiol* 2019; **316**: F974.
4. Wang L, Wang T, Rushton SN, Parry G, Dark JH, Sheerin NS. The impact of severe acute kidney injury requiring renal replacement therapy on survival and renal function of heart transplant recipients – a UK cohort study. *Transpl Int* 2020. https://doi.org/10.1111/tri.13675
5. Kobashigawa J, Zuckermann A, Macdonald P, *et al*. Report from a consensus conference on primary graft dysfunction after cardiac transplantation. *J Heart Lung Transplant* 2014; **33**: 327.