Good hearts for bad kidneys?

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Is preoperative renal dysfunction a predictor of worse outcomes after heart transplantation? A new study in the *Journal* by Kolsrud and colleagues,¹ from Gothenburg, Sweden, suggests that it is not. But is there more to this story than meets the eye?

Renal function, or more specifically the glomerular filtration rate (GFR), can be calculated indirectly with estimating equations that adjust the plasma creatinine value against covariates including age, gender, and weight. Commonly used estimating equations include the Modification of Diet in Renal Disease formula, the Cockcroft–Gault formula, and the Chronic Kidney Disease Epidemiology Collaboration. The GFR also can be directly measured on the basis of plasma clearance of substances such as iothexol or ethylenediaminetetraacetic acid. Another recent study by Kolsrud and colleagues² showed poor correlation between the measured GFR and estimated GFR in their center's adult heart transplant population. A second Swedish group also found poor correlation between measured GFR and estimated GFR, particularly in the subset of heart transplant recipients with the most impaired renal function.³

The United Network for Organ Sharing (UNOS) adult heart transplant dataset has been examined by several groups who have reported associations between preoperative renal dysfunction and (1) the need for dialysis in the early postoperative period,⁴ (2) the development of end-stage renal disease,⁵ and (3) worse long-term survival after heart transplantation alone.⁴⁻⁷ Karamlou and colleagues⁴ used the Modification of Diet in Renal Disease formula to estimate GFR in the UNOS heart transplant population from 2000 to 2010 and divided recipients into quintiles based on the estimated GFR. They found that patients undergoing heart transplantation alone in the lowest estimated GFR quintile had significantly decreased survival compared with the other groups and that survival was better in the group with comparable estimated GFR undergoing simultaneous heart-kidney transplantation.

The 2016 International Society for Heart and Lung Transplantation guidelines for heart transplant listing⁸

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Central Message

Is long-term survival after heart transplantation affected by preoperative renal dysfunction? A new study questions this position.

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suggest that an estimated GFR less than 30 mL/min/1.73 m² is a relative contraindication for heart transplantation alone. This is a change from the 2006 guidelines, which used a cutoff of less than 40 mL/min/1.73 m². Many patients with end-stage heart failure have hemodynamically driven renal impairment (cardiorenal syndrome), and renal recovery may occur with restoration of adequate cardiac output. For this reason, a growing area of investigation is the role of bridging therapy with mechanical circulatory support to stabilize renal function before heart transplantation. In practice, predicting which patients are likely to have renal recovery after heart transplantation alone is not straightforward, and most groups rely on a multidisciplinary approach to achieve consensus.

At face value, it may seem that the Gothenburg group's results are contrary to those of large single centers and the UNOS registry, which clearly link worse preoperative renal function with worse long-term survival after heart transplantation.^{4-7,9} The difference is that the Gothenburg study includes not only patients undergoing heart transplantation alone but also those undergoing simultaneous heart-kidney transplantation. Kolsrud and colleagues¹ sell the reader on a management strategy that includes judicious use of simultaneous or delayed kidney transplantation for patients with low GFR. In their study, 40% of the lowest GFR group (measured GFR <30 mL/min/1.73 m²) underwent simultaneous heart-kidney transplantation, and an additional 10% in this group had late kidney transplantation. Heart-kidney transplantation was not frequent in the 30 to 60 mL/min/1.73 m² GFR group, in

which 1.3% received simultaneous heart-kidney transplantation and 2.7% received late kidney transplantation.

Kolsrud and colleagues¹ found that renal function declines after heart transplantation, with a mean decrease in measured GFR of 12% in the first year and a steady decline thereafter. Long-term survival was worse for those who experienced a more exaggerated early decrease (decline in GFR >25% in the first year). The need for early postoperative dialysis, which occurred in 22% of the patients, was associated with worse preoperative GFR and worse long-term survival. However, among the patients who survived this early phase, renal function recovered in most, with only 12% developing end-stage renal disease requiring long-term dialysis.

Kolsrud and colleagues¹ have found a strategy that works for their center, but how to translate this into broader practice is less clear. They argue that measured GFR is a superior method for judging renal function in these patients, yet more investigation is needed to understand the practicality and benefit of this strategy. How to identify patients who will have renal recovery and those who will not, how to determine which patients will benefit from simultaneous heart-kidney transplantation versus sequential, and how to best mitigate against renal deterioration after heart transplantation are vexing questions that remain.

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