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Simultaneous heart-kidney transplant in patients with extracorporeal life support as a bridge to transplantation: *"Non Semper ea sunt quae videntur, argumentum ad ignorantiam"*

Trasplante corazón-riñón simultáneo en pacientes con soporte vital extracorpóreo como puente a trasplante: "Non Semper ea sunt quae videntur, argumentum ad ignorantiam"

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Palabras clave: *trasplante renal, trasplante cardiaco, trasplante de órganos, oxigenación de membrana extracorpórea, oxigenación de membrana extracorpórea venoarterial.*

Abbreviations:
CKD = chronic kidney disease
ECMO = extracorporeal membrane oxygenation
ESRD = early end stage renal disease
LVADs = durable left ventricular assist devices
OPTN = Organ Procurement Transplantation Network
SHK = Simultaneous heart-kidney transplant
tMCS = temporary mechanical circulatory support
UNOS = United Network for Organ Sharing

Combined heart-kidney transplant was initially described in 1978 by Norman et al., who supported a patient experiencing "stone heart syndrome" after valvular surgery using an intracorporeal abdominal left ventricular assist device and dialysis until a suitable donor was identified. The cardiac allograft demonstrated satisfactory function; however, the renal allograft failed to perform adequately, necessitating continued dialysis post-transplant, and ultimately, the patient succumbed to sepsis on postoperative day 15.[1]

End-stage heart failure frequently coincides with renal dysfunction due to the interdependent nature of these organ systems. Simultaneous heart-kidney transplant (SHK) has shown success for select patients. Selection criteria for SHK are complex, highly nuanced, and continually evolving. Challenges persist in distinguishing patients whose renal impairment may be reversible following heart transplant from those with intrinsic advanced kidney disease, for whom SHK offers the most benefit.

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In 2019, a conference held in Boston, Massachusetts, focused on SHK brought together experts to develop candidate evaluation guidelines. The workgroup recommended that a transplant nephrologist assessment should occur when the glomerular filtration rate (GFR) is < 45 ml/min/1.73 m^2, as measured independently at least twice over two weeks. SHK may be considered for patients with GFR < 30 ml/min/1.73 m^2, as well as for those with GFR between 30-44 ml/min/1.73 m^2 accompanied by strong indicators of chronic kidney disease, such as reduced kidney size or persistent proteinuria > 0.5 g/day, assessed individually.[2]

Furthermore, due to variability in SHK listing practices, the United Network for Organ Sharing (UNOS) implemented explicit allocation criteria and a safety net policy in September 2023. This policy seeks to promote equitable distribution of scarce donor organs by defining specific degrees and durations of renal dysfunction required for heart transplant candidates to qualify for SHK listing. It also ensures prioritization for candidates not eligible for simultaneous kidney transplant if severe renal dysfunction persists post-heart transplant. The guidelines stipulate a 90-day evaluation period for chronic kidney disease (CKD) patients and a six-week period for acute kidney injury cases.[3]

In October 2018, Organ Procurement Transplantation Network (OPTN) introduced a modified heart allocation system to better stratify medically urgent candidates and reduce geographic disparities in donor heart access. Recent studies report reduced waitlist times, unchanged waitlist mortality, and comparable survival for recipients under this new system, although heart-kidney candidates were excluded.[4,5]

Over the past decade, the annual number of SHKs performed has increased more than any other multi-organ transplant type.[6] Francke et al.[7] observed an increase in heart-kidney transplants from 181 to 243 during the 19 months surrounding the policy change, and a significant rise in patients who were bridged to heart transplants alone and multiorgan heart transplants using temporary mechanical circulatory support (tMCS) since the policy revision.[8] Although higher rates of acute kidney injury requiring dialysis have been noted among heart transplant-only recipients, no differences were observed in mortality, allograft survival, or rejection within this cohort.[9] Conversely, patients receiving SHK post-policy change exhibited worsened overall survival and kidney allograft outcomes compared to solitary kidney transplant recipients, with an increased risk of death relative to those receiving a kidney after heart transplantation.[7,10]

The first published study in the heart-kidney population reported inferior one-year post-transplant survival for recipients following the allocation policy change.[11] Francke corroborated these results and found that, prior to the allocation change, heart-kidney recipients had similar one-year survival rates to heart-only transplant recipients. After 2018, no added benefit regarding waitlist death/deterioration and heart transplant was detected, despite shorter waitlist times, and one-year post-transplantation survival was worse for heart-kidney recipients under the revised UNOS policy. Changing practice patterns in heart-kidney transplant post-policy era may have resulted in higher-acuity patients undergoing transplantation. While data by Francke et al.[7] indicated similar medical acuity between SHK and heart-only candidates' post-policy change, Clerkin et al.[12] showed that hemodynamic variables did not predict adverse waitlist or transplantation outcomes in status 2 patients. The increased use of tMCS and venoarterial extracorporeal membrane oxygenation (VA-ECMO) in heart-kidney recipients after the policy change likely reflects a sicker patient profile or evolving center strategies to improve the status of patients with advanced renal disease. These factors may contribute to poorer outcomes.

The work of Feng et al.[13] is of particular note. They examined dual transplant outcomes and highlighted challenges for specific patient groups. Their analysis distinguished SHK patients on VA-ECMO (n = 50) from those not on ECMO (n = 724), noting a gradual increase in the use of extracorporeal membrane oxygenation (ECMO) at the time of transplantation, rising from 2% in 2018 to 6% in 2023. Despite higher rates of temporary dialysis perioperatively among ECMO-supported recipients (56 vs 28%), long-term renal function remained similar between groups, as did rates of chronic dialysis and graft failure at two years. However, cardiac outcomes and overall survival were substantially lower among ECMO-supported patients, with discharge survival rates at 76 vs 92.7%, and two-year post-transplant survival at 71.7 vs 83% ($p < 0.001$ and $p = 0.004$, respectively). Cardiac allograft failure was also higher (10 vs 2.7%), and VA-ECMO use was independently associated with increased mortality and cardiac allograft failure.

Limited alternative therapies for critically ill patients with durable left ventricular assist devices (LVADs) compound the clinical complexity, as studies indicate worse survival and elevated post-transplant dialysis utilization in this group.[14] A comprehensive evaluation must look beyond post-transplant outcomes to consider allocation system constraints and registry data limitations. For example, comparable waitlist mortality between ECMO and non-ECMO patients suggests efficient prioritization for the sickest patients, though this does not account for relevant donor or procedural variables.

The challenge of selecting appropriate SHK candidates on VA-ECMO remains substantial, while predicting renal recovery following heart transplant in patients with chronic kidney disease continues to be difficult. Notably, higher creatinine clearance in the ECMO group raises questions about the contributions of irreversible versus reversible

kidney damage. In light of organ shortages and increasing SHK demand, safety net policies may provide opportunities to balance post-HT kidney recovery against risks associated with delayed transplantation in early end stage renal disease (ESRD) patients. SHK in VA-ECMO-supported individuals is particularly demanding and tends to be associated with less favourable outcomes compared to more stable populations.

Looking ahead, the impact of new OPTN regulations on transplantation and outcomes remains to be fully understood. Stricter criteria for SHK may reduce the pool of heart candidates with moderate-to-severe kidney disease if concerns about early mortality prompt caution among transplant centers. Addressing the needs of patients falling into "GFR limbo"–whose eGFR is insufficiently low for heart-kidney listing but at risk of deterioration following immunosuppression–requires careful consideration.

Future research should analyze variables including ECMO configuration, ambulation, nutrition, complications, donor characteristics (donation after circulatory death versus donation after brain death), organ recovery approach, ischemic time, primary graft dysfunction, and postoperative vasoplegia. Despite recent policy changes, evidence regarding elevated mortality among SHK recipients is inconclusive, and it is imperative to recognize that policy impacts often stem more from behavioral adaptation than from the policies themselves. Nonetheless, given that SHK offers lifesaving therapy for patients on VA-ECMO with ESRD and limited alternatives, these findings should not preclude its use among carefully selected candidates.

"Non Semper ea sunt quae videntur, argumentum ad ignorantiam". Things are not always what they seem.

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