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Simultaneous heart, liver and kidney transplantation: A viable option for heart failure patients with multiorgan failure

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Multiorgan dysfunction involving the liver and kidney is not uncommon in patients with end-stage heart failure. Hepatic and renal function abnormalities may be secondary to a systemic disease process that affects the heart, liver and kidney or be a consequence of cardiac failure with venous congestion and arterial hypoperfusion. The presence of advanced liver or kidney disease may increase the likelihood of complications and poor outcomes after heart transplantation if the liver and kidney transplantation are not performed simultaneously. The first simultaneous heart, lung, and kidney (HLK) transplantation in the United States was performed at the University of Pittsburgh in 1989. Unfortunately, the patient died after four months, and the complex nature of the procedure discouraged expanding the use of this operation. The current heart allocation system classifies multiorgan candidates as status 5 and could underestimate the disease severity and urgency of transplantation in these patients. We present our experience with simultaneous HLK transplantation in 6 consecutive patients at our institution. We discuss our patient selection and listing strategy, surgical techniques, and post-transplant course and outcomes.

Six patients received simultaneous HLK transplantation at the University of Chicago Medical Center over a 20-year period (from January 1999 to January 2019). Patient characteristics are shown in Table 1. The age range was 29–65 years. Five recipients (83.3%) were male, and 4 were white (66.7%). The etiology of multiorgan failure was variable. Patient 1 had rheumatic valvular heart disease and liver failure owing to hepatitis C. Patient 2 had an ischemic cardiomyopathy and cryptogenic liver cirrhosis. Patient 3 had Forbes disease, a type III glycogen storage disease associated with progressive cardiomyopathy and liver involvement. Patient 4 had systemic sarcoidosis with heart and liver involvement, while

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patient 5 had sarcoid cardiomyopathy with congestive hepatopathy. Patient 6 had a prior heart transplant for giant cell myocarditis, with allograft failure because of severe tricuspid regurgitation and cirrhosis owing to congestive hepatopathy. In Patients 1–4, kidney disease was due to cardiorenal syndrome, while Patient 5 had diabetic nephropathy, and Patient 6 had renal calcineurin inhibitor toxicity.

Each patient underwent a rigorous pre-transplant workup beginning with a heart transplant evaluation according to our regular listing criteria. Liver and kidney transplant evaluations were subsequently performed with the documentation of a clear rationale for HLK transplantation. The decision regarding liver transplant eligibility was based on the presence of cirrhosis on a liver biopsy. The decision regarding kidney transplant eligibility was based on the patient's glomerular filtration rate and was supplemented by the results of imaging studies or a kidney biopsy. Ultrasound was used to assess renal echogenicity, and a non-contrast abdominal computed tomography scan was used to assess patency and calcification of the iliac vessels. Renal biopsy was pursued when non-invasive modalities provided unclear or conflicting information. Patients were considered acceptable for heart transplant if they were also suitable for liver and kidney transplant. Other transplantrelated parameters are shown in Table 2. Five patients received organs from local donors, and one patient had an out-of-state donor. The donor age range was 25–42 years. All donors had good cardiac, liver and kidney function. Donor to recipient weight matching was performed in all cases except for Patients 1 and 6. Wait times on the transplant list varied significantly (8–565 days).

Orthotopic heart transplant was performed first using a median sternotomy, cardiopulmonary bypass, and the bicaval technique with tricuspid valve repair (DeVega procedure). Following reperfusion of the cardiac allograft, the patients were taken off cardiopulmonary bypass and decannulated, but the chest was left open. Next, orthotopic liver transplant was performed via a midline supraumbilical incision with bisubcostal extension using veno-venous bypass, the cavoplasty technique, and choledocho-choledochostomy. Following completion of the liver transplant, veno-venous bypass was discontinued, and the sternum was closed. The kidney transplant was performed last via a lower abdominal incision (left or right) with the creation of a ureteroneocystostomy. Five of our 6 patients survived the surgery and were successfully discharged home. Within a few hours of the completion of his surgery, Patient 2 developed severe coagulopathy with bleeding into the pericardial space, cardiac tamponade, and circulatory arrest. The pericardium was emergently explored, and an intra-aortic balloon pump was placed, but the patient suffered hypoxic brain damage and was declared brain dead two days later. Another patient had primary graft failure with hemodynamic instability requiring intra-aortic balloon pump placement intraoperatively. A vacuum dressing was applied to the sternal wound, which was closed two days later when he was hemodynamically stable.

Details of the induction therapy could not be retrieved for the first 3 patients. Patient 4 received thymoglobulin, and Patient 5 received basiliximab. Patient 6, a repeat heart transplant patient who was already receiving tacrolimus, did not receive induction. All 5 patients who were discharged were treated with a triple immunosuppression regimen, including tacrolimus, mycophenolate, and corticosteroids to prevent rejection. Prednisone

was tapered according to our weaning protocol. Four of the patients that were discharged home are still alive with a median follow-up of 1,447 days. Patient 1 died 7 years after transplant owing to chronic rejection of the liver allograft. There were no cases of acute rejection of the cardiac or renal allograft. None of the patients developed donor specific antibodies or cardiac allograft dysfunction during follow-up. Patient 3 has Stanford class 4 cardiac allograft vasculopathy.

While dual organ transplant is increasingly performed, simultaneous HLK transplantation remains very rare. Only 17 cases have been performed in the United States, including the 6 cases described in this series. Our experience demonstrates excellent outcomes and highlights the viability of this option in selected patients with multiorgan disease. It may be challenging to find multiple organs of good quality from the same donor.[1] The careful selection of candidates with consideration of the implications on organ allocation is necessary when considering candidates for multiorgan transplantation. The potential advantage for the individual patient must be balanced against the risk of further depleting organs from the donor pool.[2] The allocation of donor organs for multiorgan transplantation is determined by the listing priority of the organ with the most life threatening risk (usually the heart).[3] When a candidate is eligible to receive a heart, the liver and kidney will be allocated to them from the same donor if the donor is located in the same local organ distribution unit where they are registered.[1] If the multiorgan transplant candidate is on a waiting list outside the local organ distribution unit where the donor is located, voluntary sharing of the other organs is required.[1] To ease the burden associated with the scarcity of donor livers, domino liver transplantation techniques should be considered for candidates who qualify for it.[3]

Although there are no published guidelines for candidate selection for multiorgan transplantation,[4] the selection process should be made on an individual basis through a multidisciplinary process involving the heart, liver, and kidney committees. Particular attention should be given to frailty because of the prolonged duration of the surgery and the need to heal multiple incisions post-operatively. To decrease the waitlist time, exceptions can be pursued for candidates when feasible. Multidisciplinary communication is critical in the post-operative phase to ensure comprehensive daily assessments and allow the early recognition of complications. The order of organ transplantation is determined by the tolerance of each graft to cold ischemia.[4] The ischemic time should be shorter than 4 hours for the cardiac allograft.[5] Ideally, ischemic times of 6–10 hours and 24 hours are acceptable for the liver and kidney allograft, respectively. The use of local donors decreases the ischemic times for each organ. In our center, we leave the chest open during the liver transplant to increase surgical access to the liver and reduce the ischemic time for the liver. Adequate cardiac allograft function is ensured off bypass before transplanting the abdominal organs.

Bleeding due to coagulopathy is common during multiorgan transplantation. Maintaining a low threshold for surgical re-exploration is necessary in patients with high transfusion requirements or escalating pressor requirements. Acute graft rejection did not occur in our series, and there was only one case of chronic rejection of the liver. The immuno-protective effect of liver transplantation has previously been demonstrated in heart-liver[4] transplant

recipients, although the precise mechanisms are not understood. A reduction in donor specific antibodies has been shown after liver transplantation in multiorgan recipients.[4] The lack of rejection episodes of the cardiac and kidney allografts suggests that induction therapy may not be necessary in these patients. Similarly, it may be reasonable to reduce the doses of chronic maintenance immunosuppression in HLK transplant recipients. This protective effect may not be present if organs are received from multiple donors.[1]

Simultaneous HLK transplantation is feasible and can be performed in selected patients with good survival. Successful outcomes depend on multidisciplinary input from each organ team throughout the process, including listing, perioperative management, and post-operative follow-up.

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Table 1

Characteristics of Patients Who Received Triple Organ Transplants

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6[a]
Age at transplant, years	63	65	40	55	29	29
Male	Yes	Yes	Yes	Yes	Yes	No
Race	White	White	White	Black	Black	White
Body mass index, kg/m^2	32.5	29.7	23.1	26.3	22.1	18.1
Left ventricular EF, (%)	20	33	20	15	15	38.7
Hypertension	Yes	Yes	Yes	Yes	Yes	No
Diabetes	No	No	No	No	Yes	No
VT, Device type	Yes, ICD	No	No, ICD	Yes, ICD	No, ICD	No, PM
Type of cardiomyopathy	Valvular[b]	Ischemic	GSD 3	Sarcoid	Sarcoid	Valvular[c]
Cause of liver failure	Hepatitis C	Cryptogenic	GSD 3	Sarcoid	Cardiac	Cardiac
Cause of kidney failure	Cardiorenal	Cardiorenal	Cardiorenal	Cardiorenal	Diabetic	CNI toxicity
MCS support pre-transplant	No	No	No	No	No	No
Intra/peri-operative						
Donor ischemic time	X	X	168	144	155	237
Primary graft dysfunction	No	No	No	Yes, RV failure	No	No
Delayed chest closure	No	No	No	Yes, Day 2	No	No
Intra-aortic balloon pump	No	Yes, day 1	No	Yes, day 0	No	No
Induction therapy	-	-	-	Yes, Thymoglobulin	Yes, Basiliximab	No
Post-transplant						
Heart allograft rejection	No	No	No	No	No	No
Liver allograft rejection	Yes, chronic	No	No	No	No	No
Kidney allograft rejection	No	No	No	No	No	No
Reoperation for bleeding	No	Yes, tamponade No	No	No	No	Yes, IAH
Infection	Yes, IHA	NA	No	Yes, CMV	No	No
Elevated DSA	No	NA	No	No	No	No
Time to discharge (days)	19	2	20	16	29	17
Triple immunosuppression[d]	Yes	NA	Yes	Yes	Yes	Yes
CAV, Stanford class	Yes, Class 1	NA	Yes, Class 4	Yes, Class 1	NA	NA
Alive	No	No	Yes	Yes	Yes	Yes
Follow-up time (days)	2763	2	5712	2870	23	21

CAV, Coronary allograft vasculopathy; CMV, cytomegalovirus; CNI, calcineurin inhibitor; CRS, cardiorenal syndrome; DSA; donor specific antibodies; EF, ejection fraction; GSD III, glycogen storage disease type III, Forbes disease; IAH, intraabdominal hematoma; ICD; Intracardiac defibrillator; IHA, intrahepatic abscess; MCS, mechanical circulatory support; NA, not applicable; PM, pacemaker; RV, right ventricular; VT, ventricular tachycardia, X, information not retrievable.

[a] Re-transplant, initial heart transplant for giant cell myocarditis in 2001

[b] Rheumatic valvular disease with replacement of aortic and mitral valve with bio-prostheses

[c] Severe tricuspid valve regurgitation and right heart failure treated initially with tricuspid valve annuloplasty and subsequently with transfemoral tricuspid valve replacement which was complicated by moderate paravalvular regurgitation

[d] Triple immunosuppression regimen included tacrolimus, mycophenolate and methylprednisolone prednisone.

Table 2

Patient Listing Status and Donor Characteristics

	Listing status	List waiting times (Days)	Blood type	Local donor	Sex	Donor age, years	Donor height, inches	Recipient height, inches	Donor to recipient height matching	Donor weight, pounds	Recipient weight, pounds	Donor to recipient weight matching
1	1B	85	AB	Yes	Male	36	5′ 9″	6′ 0″	Yes	150	240	No
2	2	565	0	Yes	Male	42	6′ 4″	5′ 11″	Yes	242	213	Yes
3	1B	198	0	Yes	Male	25	6′0″	5′ 6″	Yes	170	143	Yes
4	1A	94	AB	Yes	Male	30	5′ 9″	5′ 9″	Yes	163	178	Yes
5	2[a]	8	B	Yes	Male	33	5′ 6″	6′ 0″	Yes	142	163	Yes
6	2[a]	58	0	No	Female	34	5′ 5″	5′ 8″	Yes	213	119	No

[a]After the change in the heart allocation criteria, which occurred in October 2018

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