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Case Report

Heart-liver-kidney transplantation for AL amyloidosis using normothermic recovery and storage from a donor following circulatory death: Short-term outcome in a first-in-world experience

Aleah L. Brubaker [1,*,†], Marcus A. Urey [2,†], Raeda Taj [1], Justin R. Parekh [1], Jennifer Berumen [1], Mark Kearns [3], Mita Shah [4], Adnan Khan [4], Yuko Kono [5], Veeral Ajmera [5], Pranab Barman [5], Hao Tran [2], Eric D. Adler [2], Jorge Silva Enciso [2], Fotis Asimakopoulos [6], Caitlin Costello [6], Richard Bower [7], Ramon Sanchez [8], Victor Pretorius [3], Gabriel T. Schnickel [1]

[1] *Department of Surgery, Division of Transplant and Hepatobiliary Surgery, University of California San Diego, San Diego, California, USA*
[2] *Department of Medicine, Division of Cardiology, University of California San Diego, San Diego, California, USA*
[3] *Department of Surgery, Division of Cardiothoracic Surgery, University of California San Diego, San Diego, California, USA*
[4] *Department of Medicine, Division of Nephrology, University of California San Diego, San Diego, California, USA*
[5] *Department of Medicine, Division of Hepatology, University of California San Diego, San Diego, California, USA*
[6] *Department of Medicine, Division of Bone Marrow Transplant, University of California San Diego, San Diego, California, USA*
[7] *Department of Gastroenterology, Naval Medical Center San Diego, California, USA*
[8] *Department of Anesthesia, University of California San Diego, San Diego, California, USA*

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ABSTRACT

AL amyloidosis is a rare condition characterized by the overproduction of an unstable free light chain, protein misfolding and aggregation, and extracellular deposition that can progress to multiorgan involvement and failure. To our knowledge, this is the first worldwide report to describe triple organ transplantation for AL amyloidosis and triple organ transplantation using thoracoabdominal normothermic regional perfusion recovery with a donation from a circulatory death (DCD) donor. The recipient was a 40-year-old man with multiorgan AL amyloidosis with a terminal prognosis without multiorgan transplantation. An appropriate DCD donor was selected for sequential heart, liver, and kidney transplants via our center's thoracoabdominal normothermic regional perfusion pathway. The liver was additionally placed on an ex vivo normothermic machine perfusion, and the kidney was maintained on hypothermic machine perfusion while awaiting implantation. The heart transplant was completed first (cold ischemic time [CIT]: 131 minutes), followed by the liver transplant (CIT: 87 minutes, normothermic machine perfusion: 301 minutes). Kidney transplantation was performed the following day (CIT: 1833 minutes). He is 8 months posttransplant without evidence of heart, liver, or kidney graft dysfunction or rejection. This case highlights the feasibility of normothermic recovery and storage modalities for DCD donors, which can expand transplant opportunities for allografts previously not considered for multiorgan transplantations.

A 40-year-old man presented to the emergency room with a chief complaint of 2 months of worsening lower extremity edema. Months earlier, he was diagnosed with recurrent pneumonia attributed to hypogammaglobinemia. His history was also notable for ascites, dyspnea on exertion, and foamy urine. Work-up revealed nephrotic-range proteinuria (9 g protein) on 24-hour urine collection. He had an elevated kappa-to-lambda free light chain ratio of 9, and kidney biopsy demonstrated amyloid deposition. Liver biopsy revealed amyloid deposition

Abbreviations: CIT, cold ischemic time; DCD, donation after circulatory death; NMP, normothermic machine perfusion; OCS, organ care system; TA-NRP, thoracoabdominal normothermic regional perfusion; WIT, warm ischemic time.

* Corresponding author. 9300 Executive Drive, MC 7745, La Jolla, CA 92037-7745, USA.
E-mail address: abrubaker@health.ucsd.edu (A.L. Brubaker).
† These authors contributed equally: Aleah L. Brubaker and Marcus A. Urey.

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with hepatocyte compression; his hepatic venous pressure gradient was 12 mm Hg, confirming sinusoidal portal hypertension. Liquid chromatography with tandem mass spectrometry confirmed AL amyloidosis with kappa restriction. Comprehensive evaluation demonstrated heart, liver, kidney, and gastrointestinal tract involvement; laboratory evaluation was consistent with revised Mayo stage III (troponin: 183 ng/L; N-terminal pro-brain natriuretic peptide (NT-proBNP): 4208 pg/mL).

The ANDROMEDA protocol was started with cyclophosphamide, bortezomib, dexamethasone, and daratumumab.[1] He achieved a hematologic complete response but developed progressive multiorgan deterioration with worsening restrictive cardiomyopathy, oliguric renal failure necessitating dialysis, and twice-weekly paracenteses for refractory ascites. The consensus was that he had a terminal prognosis without urgent multiorgan transplantation and was approved for listing by a multidisciplinary transplant team. The utilization of donation after circulatory death (DCD) donors via our center's thoracoabdominal normothermic regional perfusion (TA-NRP) pathway was approved by the surgical teams. For heart transplantation, a status 2 exception was approved by the United Network for Organ Sharing regional review board. He was listed as per the United Network for Organ Sharing criteria for liver (allocation Model of End-Stage Liver Disease score: 29) and kidney transplantation and remained hospitalized, awaiting transplantation. He received an acceptable DCD multiorgan offer 145 days after beginning treatment for AL amyloidosis and 56 days after the transplant listing.

Donor operative planning included the use of TA-NRP for organ recovery with subsequent ex vivo normothermic machine perfusion (NMP) for the liver and hypothermic machine perfusion for the kidney (Fig. 1). The TA-NRP team is a 2-surgeon team with a third assistant working together to initiate bypass after the mandatory hands-off period; there is no concomitant attempt to prepare for abdominal cannulation in the event of failed TA-NRP. The ability to initiate bypass swiftly is aided by optimal preoperative communication between all teams and limiting the scope to ensure bypass initiation rather than having 2 recovery teams working in concert.

The donor was a 19-year-old man who had head trauma. Functional warm ischemic time (WIT), defined as sustained systolic blood pressure of <80 mm Hg or oxygen saturation of <80% until the initiation of TA-NRP, was 20 minutes (total WIT from extubation to the initiation of TA-NRP was 21 minutes). For TA-NRP DCD allografts for combined heart-liver-kidney recipients, the limitation on functional WIT is driven by the liver team; the liver team limits the functional WIT to 35 minutes from the definition above, whereas the cardiac team will wait up to 2 hours from an oxygen saturation of $\underline{\leq}$70% or mean arterial pressure of $\underline{\leq}$50 mm Hg. The time to initiate TA-NRP from the incision was 3 minutes. The total bypass time was 96 minutes, with a wean at 43 minutes to assess independent cardiac function; the bypass was then resumed for the duration of the procurement. The starting lactate level after the bypass was 8.7 mmol/L, with a base deficit of −7; the final lactate level before cross-clamp was 6.1, with a base excess of 4. The intraoperative assessment deemed all organs suitable for transplant. For TA-NRP DCD cardiac allografts, the intraoperative assessment is based on visual inspection and the ability to generate adequate blood pressure off bypass. If there are any allograft concerns, mixed venous oxygen saturation is used to assess cardiac output; an intraoperative echocardiogram is not utilized. Liver allograft acceptance on TA-NRP is based on visual inspection, lactate clearance, and biopsy, as indicated by the recovering surgeon. Bile production can be visualized after the division of the bile duct. After recovery, the heart was placed in static cold storage; the liver was placed on an ex vivo NMP device (TransMedics Portable Organ Care System (OCS)), and the kidney was placed on hypothermic machine perfusion until implantation. The placement of the liver on NMP-OCS following TA-NRP allowed for ongoing allograft recovery, minimization of cold ischemic time (CIT), and mitigation of reperfusion syndrome.

The multiorgan transplant was completed sequentially. The heart transplant was completed first (CIT: 131 minutes), and the recipient was weaned off bypass with good allograft function. The liver transplant was performed in the standard piggyback fashion without venovenous bypass (CIT: 87 minutes; NMP-OCS perfusion time: 301 minutes). The impact of liver reperfusion on the transplanted heart was minimal; there were no major hemodynamic or rhythm changes. Minimal cardiac perturbations were seen on intraoperative transesophageal echocardiogram. After liver transplantation, the chest was left open because of coagulopathy, and the patient was taken to the intensive care unit. Kidney transplantation was performed the next day (CIT: 1833 minutes), followed by chest closure (Fig. 1).

Given the pretransplantation use of daratumumab,[2-4] a modified noninduction immunosuppression protocol was used, consisting of high-dose intravenous methylprednisolone followed by a prednisone taper, tacrolimus, and mycophenolate mofetil. There was no evidence of early allograft dysfunction of the heart or liver (Table 1). Renal replacement therapy was required for 3 days posttransplant. Notable postoperative complications that resolved before discharge included respiratory failure requiring tracheostomy with eventual decannulation, altered mental status, severe malnutrition, urinary tract infection, BK viremia, and ileus because of gastrointestinal amyloid involvement. The patient was discharged on postoperative day 45. At the time of submission of this article, the patient was 8 months posttransplant and did well without evidence of any allograft dysfunction or rejection (Table 1). Surveillance right heart catheterizations and endomyocardial biopsies were free of graft dysfunction or rejection. There were no biliary complications, and he had normal gastrointestinal function. His current glomerular filtration rate is >60 mL/min/1.73m^2, with a creatinine level

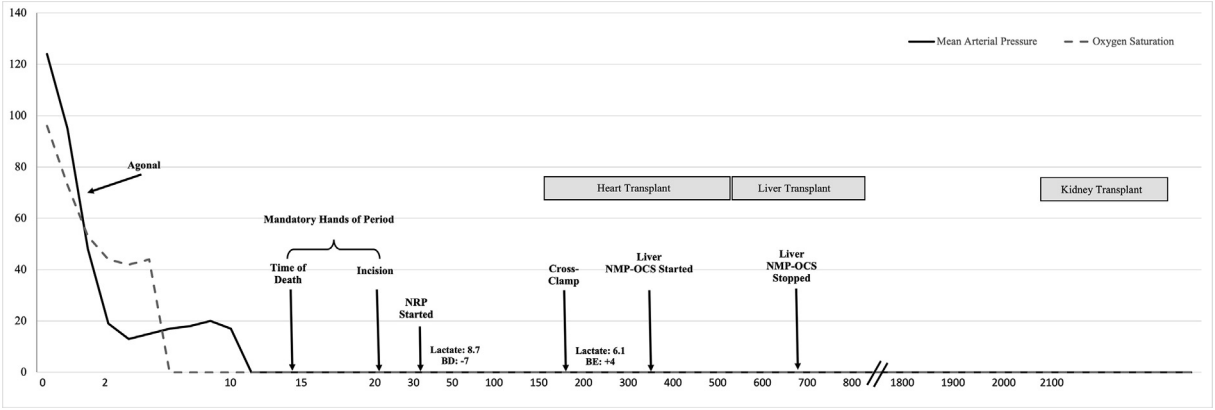

Fig. 1. Procurement and transplant timeline. BD, base deficit; BE, base excess; NMP, normothermic machine perfusion; NRP, normothermic regional perfusion; OCS, organ care system.

Table 1
Measures of organ specific function post-transplant.

	CO	LVEF %	RVSP	AST	ALT	TB	AP	Cr	GFR
6 h	5.6	N/A	N/A	201	154	1.53	76	2.33 (CRRT)	N/A
24 h	5.6	N/A	N/A	128	118	1.73	71	1.71 (CRRT)	N/A
72 h	5.5	N/A	N/A	99	116	1.12	139	1.29 (CRRT)	N/A
7 d	N/A	80%	29	31	57	0.75	106	2.87	25
30 d	6.3	70%	31	26	52	0.55	197	1.64	47
6 months	N/A	N/A	N/A	17	24	0.33	157	1.57	57
8 months	N/A	59%	28	20	20	0.34	182	1.49	>60

CO, cardiac output (L/min); LVEF%, left ventricular ejection fraction (%); RVSP, right ventricular systolic pressure (mmHg); AST, aspartate aminotransferase (U/L); ALT, alanine transaminase (U/L); TB, total bilirubin (mg/dL); AP, alkaline phosphatase (U/L); Cr, creatinine (mg/dL); CRRT, continous renal replacement therapy; GFR, glomerular filtration rate (mL/min/1.73m2); h, hour; d, day.

of 1.49 mg/dL and minimal proteinuria. He sustained a hematologic complete response to his AL amyloidosis. To our knowledge, this represents the first case of triple organ transplantation for AL amyloidosis using TA-NRP recovery from a DCD donor.

AL amyloidosis is a rare condition originating from the expansion of a plasma cell clone that is characterized by the overproduction of an unstable free light chain, protein misfolding and aggregation, and extracellular deposition leading to organ dysfunction.[5] Approximately 50% of patients have cardiac involvement, and nephrotic-range proteinuria or end-stage renal disease occurs in two-thirds of patients.[5,6] The liver is the third most common organ involved.[7] For patients with multiorgan AL amyloidosis, the pathway to transplantation can be limited by a severe systemic disease that is underestimated by current allocation policies. Specific to this case, our surgical teams opted to evaluate organs via our center's DCD TA-NRP pathway to expedite transplantation given the concern for significant clinical deterioration while on the waitlist that would eventually preclude transplantation.

Our center has been conducting TA-NRP recovery for DCD donors since May 2020. Our clinical experience in cardiac and liver transplantations from these donors has been markedly positive and supported our clinical decision to proceed with multiorgan DCD transplantations. Additional liver support with NMP offered a secondary means for ongoing liver allograft recovery during heart transplantation, limiting CIT and minimizing reperfusion syndrome.[9] The use of normothermic recovery and storage modalities for DCD donors can expand transplantation opportunities for allografts previously not considered or underutilized for multiorgan transplantations into appropriate recipients, particularly for those with narrow pathways to transplantation.

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Data availability statement

The data that support the findings of this report are available from the corresponding author, ALB, upon reasonable request.

Disclosure

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ORCiD

Aleah L. Brubaker https://orcid.org/0000-0003-4795-2562
Marcus A. Urey https://orcid.org/0000-0001-8311-5003
Raeda Taj https://orcid.org/0000-0003-0602-8015
Justin R. Parekh https://orcid.org/0000-0002-1725-6155
Jennifer Berumen https://orcid.org/0000-0001-8032-888X
Mark Kearns https://orcid.org/0000-0002-7639-6182
Mita Shah https://orcid.org/0000-0003-0003-9899
Adnan Khan https://orcid.org/0000-0001-6622-702X
Yuko Kono https://orcid.org/0000-0002-9357-4104
Veeral Ajmera https://orcid.org/0000-0001-5626-0942
Pranab Barman https://orcid.org/0000-0003-3854-3417
Hao Tran https://orcid.org/0000-0001-6118-303X
Eric D. Adler https://orcid.org/0000-0002-4765-0188
Jorge Silva Enciso https://orcid.org/0000-0002-9493-0932
Fotis Asimakopoulos https://orcid.org/0000-0002-5099-1696
Caitlin Costello https://orcid.org/0000-0002-3405-5937
Richard Bower https://orcid.org/0000-0002-7024-5834
Ramon Sanchez https://orcid.org/0000-0001-6628-7591
Victor Pretorius https://orcid.org/0000-0001-6360-4002
Gabriel T. Schnickel https://orcid.org/0000-0003-4392-2200

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