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Utilization of Normothermic Machine Perfusion to Rescue Liver Allografts in Unallocated Unstable Donors

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Liver transplantation remains standard of care for end-stage liver disease; a principal barrier to transplantation remains the ongoing organ shortage. Despite persistent efforts to improve utilization, the organ nonuse rate was 17.6% per recovered organ in the United States in 2021 and this has been increasing yearly since 2017.[1] Normothermic machine perfusion (NMP) has been used to expand the donor pool, primarily by increased use of marginal allografts.[1,2]

The degree of autonomic dysfunction in donation after brain death (DBD) and donation after circulatory determination of death (DCD) donors can cause significant donor instability, necessitating urgent recovery. In the United States, donor clinical instability necessitating urgent recovery often can limit the number of organs successfully transplanted owing to rapid allocation and incomplete donor testing results. Serologic testing results for hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV are necessary to limit unintended disease transmission, specific allocation algorithms, and, in cases of HCV, insurance authorization for transplantation given the necessary treatment posttransplant. This often results in kidney only allocation in these donors owing to improved tolerance to cold ischemic times after recovery while awaiting testing results and allocation. We sought to report on using NMP for liver perfusion while awaiting delayed allocation in this unique donor population.

We identified 3 clinically unstable donors at a single organ procurement organization (OPO), Lifesharing, whose test results for HBV, HCV, and HIV were not yet available at the time of recovery. Given the lack of these serologic testing results, organ allocation had not yet occurred. Lifesharing initiated the request for NMP via the TransMedics National Organ Care System Program with the intent for liver allocation on NMP after virologic testing resulted. Donor data were abstracted from the United Network for Organ Sharing and OPO records. Recipient data were collected via medical chart review (IRB#806453).

CASE DESCRIPTION

Case 1

The DBD donor was a 32-y-old man with head trauma and met Public Health Service (PHS) criteria for increased risk of transmission of HBV, HCV, and HIV. The donor was medically unstable because of pulmonary decompensation (Table 1); their timeline is detailed in Figure 1A. Negative testing for HBV, HCV, and HIV resulted 285 min after cross-clamp. Liver allocation occurred 331 min after cross-clamp, was accepted 437 min after cross-clamp, and maintained on NMP for 656 min before transplantation into a 60-y-old woman with alcoholic cirrhosis. Posttransplant, the recipient met the criteria for early allograft dysfunction (EAD), had a Model for Early Allograft Function (MEAF) score of 6.15, and had stage 2 acute kidney injury (AKI; Table 1).[3,4] Extubation occurred 8.6 h after case completion. Intensive care unit (ICU) and hospital length of stay (LOS) were 1 and 5 d, respectively. Three hundred ninety-eight days after transplantation, the recipient has excellent graft function without vascular or biliary complications (Table 2).

Case 2

The DBD donor was a 50-y-old man with head trauma, met PHS increased risk criteria, and was unstable secondary to pulmonary decompensation (Table 1). The donor timeline is detailed in Figure 1B. Liver allocation began 174 min before cross-clamp. HBV and HIV tests were reported as negative 65 min after cross-clamp. Positive HCV antibody, negative

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TABLE 1.

Characteristics of donor and recipient pairs

Donor	1	2	3
Donor type	DBD	DBD	DCD
Age	32	50	32
Cause of death	Trauma	GSW	GSW
Reason for instability	Pulmonary	Pulmonary	Pulmonary
Cold ischemia time, min	117	113	125
Time on pump, min	656	524	830
Cross-clamp to HBV, HIV serologies, min	260	65	295
Cross-clamp to HCV serologies, min	260	277	541
Biopsy results	20% macro Chronic hepatitis	No macro No inflammation	NA
Warm ischemia time, min	NA	NA	17
Recipient	**1**	**2**	**3**
Age	60	61	63
Primary diagnosis	Alcoholic cirrhosis	HCC	HCC
MELD	15	32	32
EAD	Yes	No	Yes
MEAF	6.15	5.62	5.42
AKI	Stage 2	–	Stage 1
ICU LOS, d	1	1	1
Hospital LOS, d	5	4	5
Follow-up time, d	398	420	327

AKI, acute kidney injury (as defined by Kidney Disease Improving Global Outcomes guidelines); DBD, donation after brain death; DCD, donation after circulatory death; EAD, early allograft dysfunction (as defined by Olthoff et al[3]); HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LOS, length of stay; MEAF, Model for Early Allograft Function scoring (as described by Pareja et al[4]); MELD, Model for End-Stage Liver Disease; NA, not available.

TABLE 2.

Recipient allograft function

	Days from Transplant			
Recipient no.	**1**	**10**	**90**	**180**
Recipient 1				
AST	3243	51	9	12
ALT	628	113	6	12
Alkaline phosphatase	49	77	60	52
Total bilirubin	3.89	1.25	0.3	0.5
INR	1.8	–	–	–
Lactate	1.8	–	–	–
Recipient 2				
AST	1176	128	40	25
ALT	554	374	51	24
Alkaline phosphatase	62	192	108	113
Total bilirubin	4.24	1.07	1.07	0.98
INR	1.4	–	–	–
Lactate	0.9	–	–	–
Recipient 3				
AST	2130	26	42	30
ALT	498	74	53	26
Alkaline phosphatase	135	153	82	74
Total bilirubin	5.80	0.85	0.47	0.56
INR	1.6	–	–	–
Lactate	4.1	–	–	–

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio.

nucleic acid testing resulted 277 min after cross-clamp. The liver was accepted 236 min after cross-clamp and was maintained on NMP for 524 min before transplantation into a 61-y-old man with hepatocellular carcinoma. After transplant, the recipient had a MEAF score of 5.62 but no evidence of EAD or AKI (Table 1). The patient was extubated immediately posttransplant; ICU and hospital LOS were 1 and 4 d, respectively. The recipient has excellent graft function 420 d after transplant without vascular or biliary complications (Table 2).

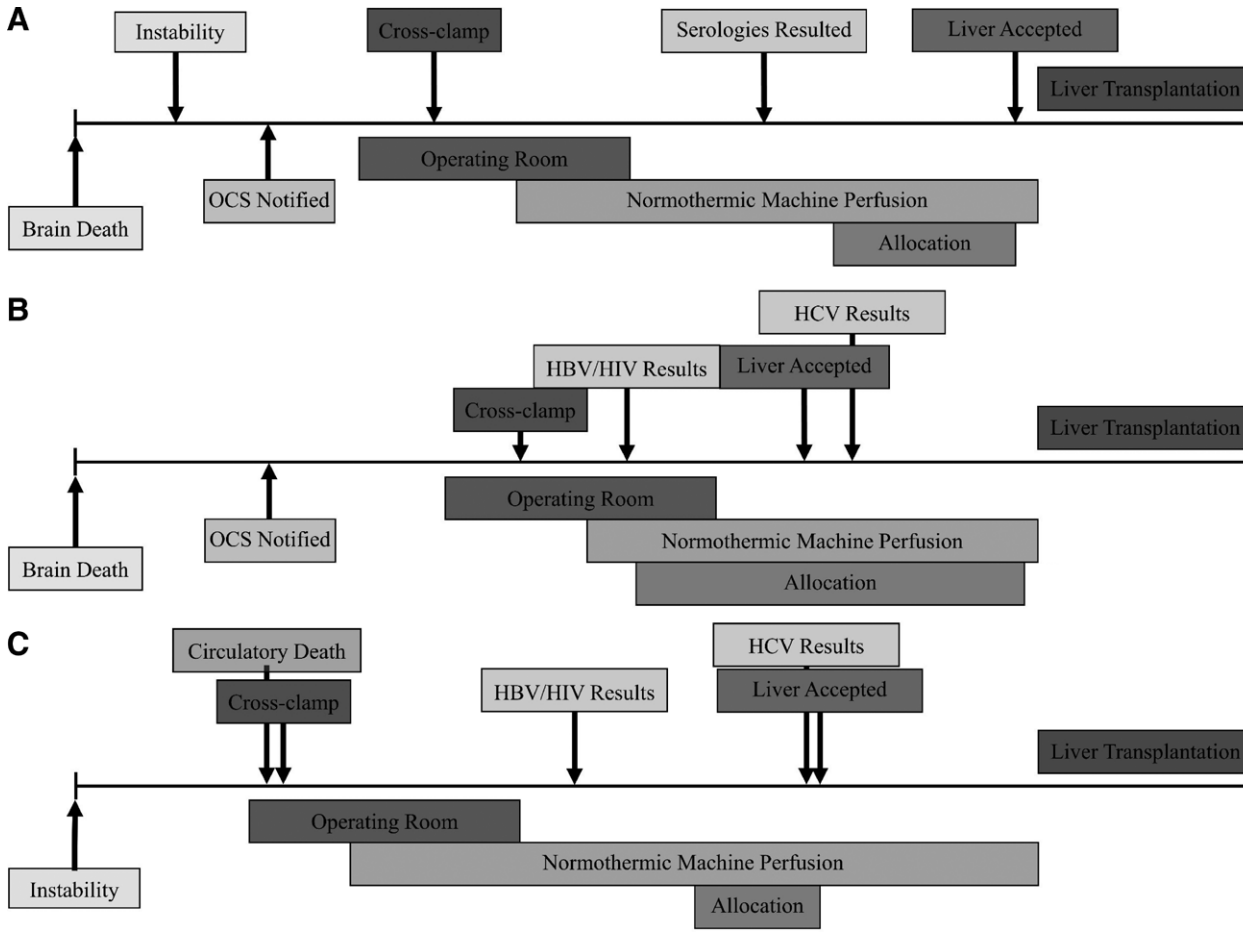

FIGURE 1. Timeline of donor/recipient pairs, not to scale. A, Donor/recipient pair 1. B, Donor/recipient pair 2. C, Donor/recipient pair 3. The donor of donor/recipient pair 2 was intermittently unstable at the time of admission, days before the declaration of brain death.

Case 3

The DCD donor was a 32-y-old man with head trauma and also necessitated urgent recovery owing to pulmonary decompensation (Table 1). Again, serologic testing results were pending and the donor met criteria for PHS increased risk for transmission of HBV, HCV, and HIV. The donor timeline is detailed in Figure 1C. Functional donor warm ischemic time was 17 min. HBV and HIV tests were reported as negative 295 min after cross-clamp. Positive HCV antibody, negative nucleic acid testing resulted 541 min after cross-clamp. Liver allocation began 472 min after cross-clamp, was accepted 547 min after cross-clamp, and perfused on NMP for a total of 830 min before transplantation into a 63-y-old man with hepatocellular carcinoma. Posttransplant, there was evidence of EAD and the MEAF score was 5.42 (Table 1). The recipient was extubated in the operating room and had stage 1 AKI, and ICU and hospital LOS were 1 and 5 d, respectively. At 327 d posttransplant, the recipient had excellent graft function without vascular or biliary complications (Table 2).

DISCUSSION

To our knowledge, this is the first report highlighting the application of NMP to perfuse liver grafts from medically unstable, unallocated donors while awaiting viral test results. In the absence of NMP, these grafts would have likely been discarded because of prolonged cold ischemia time as the serologic testing resulted several hours after cross-clamp in all cases. Although United Network for Organ Sharing guidelines permit allocation without the aforementioned viral test results, in practice, successful allocation occurs infrequently owing to concerns of unintended viral transmission as well as specific allocation algorithms associated with positive test results (ie, the HIV Organ Policy Equity Act for HIV; insurance approval for HCV). Given that all 3 donors met criteria for PHS increased risk for transmission of HIV, HCV, and HBV, the importance of these testing results when discussing and counseling potential recipients of these organs cannot be dismissed. The use of NMP in these cases provided ample time for clinical decision making without the pressure of pending tests or the urgency of cold ischemic limitations.

Liver NMP has been used to expand the organ pool through evaluation and subsequent utilization of marginal organs, including fatty allografts, allografts from septic donors, and DCD donors with historically higher discard rates.[1,5] These cases highlight an alternative way to consider using NMP in scenarios where allocation must or should be delayed. There is a paucity of data on how often donor instability requires urgent recovery before allocation and leads to organ discard, limiting our ability to quantitatively assess the broader benefits of NMP utilization in these scenarios. However, many potential unstable donors may not be considered for a donation or may only be considered for kidney donation, given concerns about the ability to successfully allocate organs postrecovery. The decision to proceed with liver perfusion on NMP was opted for by Lifesharing in a

best-practices effort to maximize the potential of the life-saving gift of transplant. Although the broader impacts on the national or international donation landscape are unclear, it does provide a successful example of using new technology to provide access to transplants in complex donation scenarios.

In other similar circumstances, such as OPO logistic limitations, intraoperative declines, or donor family time constraints, NMP could facilitate successful postrecovery allocation of appropriate grafts that might otherwise lead to the organ being discarded.

It is particularly important to highlight that each graft afforded a patient on the waitlist the chance to receive a life-saving liver transplant. None of these livers would have been allocated if NMP had not been available. Every transplantable graft discarded is a lost opportunity to honor the gift and save a life. The responsibility to honor the gift of life provided by donors and their families and to use all available avenues to safely transplant our recipients is a cornerstone of transplant. Using perfusion technologies in novel ways will allow us to maximize the gift of donation, reduce organ nonuse, and provide life-saving transplants for waitlisted patients.

CONCLUSION

The use of NMP to rescue unallocated liver allografts from unstable donors without appropriate testing offers another novel way to use novel technology to minimize organ nonuse and improve access to liver transplant.

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