Successful adult domino living donor liver transplantation in methylmalonic acidemia: case report

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Background: Liver transplantation (LT) is a therapeutic option in multiple inherited metabolic diseases (IMDs), including methylmalonic acidemia (MMA), as LT reduces the risk of acute metabolic decompensations and long-term complications associated with these diseases. In certain IMDs, such as maple syrup urine disease (MSUD), domino liver transplant (DLT) is an accepted and safe method which expands the donor pool. However, only one adult case of DLT using an MMA donor liver has been reported; outcome and safety are still unknown and questioned.

Case Description: In this case report, we describe our experience with DLT using MMA livers. Two adult MMA patients underwent living donor liver transplant (LDLT); their MMA livers were consecutively transplanted into two patients on the liver transplant waiting list who had limited chance of receiving a liver transplant in the short term due to their low model for end-stage liver disease (MELD) scores. No severe peri- or postoperative complications occurred, however the recipients of the MMA livers biochemically now have mild MMA.

Conclusions: DLT using MMA grafts is a feasible strategy to treat end-stage liver disease and expand the donor organ pool. However, the recipient of the MMA domino liver may develop mild MMA which could affect quality of life, and long-term safety remains unclear. Further long-term of outcomes for domino recipients of MMA livers, focusing on quality of life and any metabolic complications of transplantation are needed to better define the risks and benefits.

Keywords: Methylmalonic acidemia (MMA); living donor liver transplant (LDLT); domino liver transplant (DLT); case report

Introduction

A subset of inherited metabolic diseases (IMDs) which are caused by an enzyme deficiency can be treated with liver transplantation (LT) (1). Domino LT (DLT) using the livers of patients with IMDs was first proposed in 1995 (2). Except for the deficiency of an enzyme which results in the accumulation of certain metabolites, these livers are morphologically normal and fully functional. The enzyme defect is co-transplanted but the donor disease either does not develop in the domino recipient because the recipient has a systemic presence of the deficient enzyme in other tissues, or if the disease does develop, it is expected to be milder and manageable for a long period of time (3).

DLT has been established as a tool that contributes to expansion of the donor organ pool (4). DLTs were first performed using donor livers with familial amyloid polyneuropathy (FAP), familial hypercholesterolemia (FH), and maple syrup urine disease (MSUD) (5-7). Other indications for DLT have included primary hyperoxaluria and acute intermittent porphyria, however the outcome using these livers for DLT was extremely poor (7). *Table 1* has a complete list of indications and outcomes of indications for DLT, while *Tables 2-4* detail the indications and outcomes after DLT in the adult population. Patients with FAP are the most common donors in DLT, however long-term safety is an issue with *de novo* disease reported in 23% of recipients after a median of 7 years (5). In MSUD, long-term safety is excellent with no biochemical abnormalities in the recipient. Consequently, MSUD livers are even used for DLT in pediatric patients (7).

In much of the literature reporting on the long-term outcomes in DLT, the first recipient (or domino donor) was transplanted using a liver from a deceased donor (8). Data on adult living donor DLT (LDDLT) is limited to one case series (9).

Over the last decades, LT has also become a good therapeutic option for patients with methylmalonic acidemia (MMA), but only one case report on DLT using MMA livers has been published (10). MMA is regarded as a more severe metabolic disease and safety for recipients of a DLT using an MMA liver is still questioned (11). The most severe form of MMA is caused by deficiency of the enzyme methylmalonyl-CoA mutase (MUT, OMIM #251000) (12). These patients suffer from recurrent life-threatening acute metabolic decompensations (13). Advances in conventional treatment (dietary restriction of natural protein, while providing enough nutrients, ammonia scavengers, carnitine, and carglumic acid) have greatly improved outcomes (14). Acute decompensations can never be fully prevented, and patients with MMA are still at a high risk of developing long-term complications such complications include kidney insufficiency, neurological complications, vision loss due to optic nerve atrophy and cardiomyopathy (15).

The recent guideline on the treatment of MMA states LT should be considered to increase metabolic stability, or if kidney transplantation (KT) is needed (4,16,17). Even though the risk of acute metabolic decompensation is much lower after LT, as the MUT deficiency remains present in the extra hepatic tissue both decompensation and long-term complications may still occur (12).

In our center, we chose to use the livers of two adult MMA patients for a DLT in two older patients on the waiting list for LT, both of whom had limited chance of receiving a liver transplant from the deceased donor pool in the near future (18). As these recipients have normal enzyme activity in extra hepatic tissues, we expected these patients to biochemically develop mild MMA after transplantation, as previously described in the case report on DLT in MMA (10). As patients with milder forms of MMA have little acute decompensations and less long-term complications, we expected DLT from an MMA patient to be safe. In this single-center case series, we present our experience of consecutive DLT using MMA

Highlight box

Key findings
- Domino liver transplant (DLT) using livers with specific metabolic diseases expands the donor pool for pediatrics as well as adults.
- DLT after living donor liver transplant (LDLT) is safe and feasible, but requires good logistics and planning.

What is known and what is new?
- Livers from patients with metabolic diseases can be used for DLT. Safety and outcomes using methylmalonic academia (MMA) for DLT livers is still questioned.
- MMA livers can be used for DLT after LDLT in adult patients. Our recipients successfully underwent DLT using MMA livers with good outcomes.

What is the implication, and what should change now?
- MMA livers can be successfully used for DLT in the adult population.
- DLT after LDLT should be considered by transplant centers with LDLT capabilities.
- Further long-term of outcomes for domino recipients of MMA livers, focusing on quality of life and any metabolic complications of transplantation are needed to better define the risks and benefits.

Table 1 Indications for DLT

Domino donor disease	Primary defect	Pathological consequences of the defect	*De novo* disease in domino recipient	Accepted indication for DLT
Familial amyloidotic polyneuropathy (5)	Amyloidogenic TTR production	Toxic accumulation of TTR resulting in polyneuropathy and visceral organ damage	Yes, recurrence within 8–9 years	High risk, not recommended in pediatrics
Maple syrup urine disease (6)	Deficiency BCKDH complex	Neurotoxic accumulation of leucine	No	Yes
Methylmalonic acidemia (1)	MCM[†] deficiency	Accumulation of propionyl-CoA resulting in acute metabolic decompensations and mitochondrial dysfunction	Not well reported	Not reported
Propionic acidemia (1)	PCC deficiency	Accumulation of propionyl-CoA resulting in acute metabolic decompensations and mitochondrial dysfunction	Not well reported	Not reported
Primary hyperoxaluria (1)	AGT[†] deficiency	Formation of calcium oxalate monohydrate leasing to progressive renal disease and other organ damage	Yes	No
Acute hepatic porphyria (1)	PBGD[†] deficiency	Accumulation of porphyrin precursors resulting in acute porphyric attacks	Possibly, recurrent acute porphyric attacks in recipient have been reported	No
Familial hypercholesterolemia (5)	LDL receptor deficiency	High circulating cholesterol and subsequent deposits	Yes	High risk, not recommended in pediatrics
Ornithine transcarbamylase deficiency (4)	OTC deficiency	Hyperammonemic decompensations due to dysfunction of the urea cycle	Yes, unless used as an axillary graft	Yes, only when used as an axillary graft

[†], this is the most common cause, but there are also other causative enzyme deficiencies. DLT, domino liver transplant; TTR, transthyretin; BCKDH, branched-chain alpha-ketoacid dehydrogenase; MCM, methylmalonyl-CoA mutase; PCC; propionyl-CoA carboxylase; AGT, peroxisomal alanine:glyoxylate aminotransferase; PBGD, porphobilinogen deaminase; LDL, low density lipoprotein; OTC, ornithine transcarbamylase.

livers. We present this case in accordance with the CARE reporting checklist (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-55/rc).

Case presentation

Case 1: first recipient (domino donor)

A 20-year-old man with MMA (MUT 0, due to two heterozygous pathogenic mutations in the MUT gene: c.654A>C and c.1106G>A), presented to our institution for

LT. Shortly after birth, he had presented with a severe acute metabolic decompensation and was diagnosed with MMA. During childhood and despite a strictly regulated diet and medical management, he had several acute metabolic decompensations resulting in a mild intellectual disability and pyramidal tract syndrome, but he was metabolically stable thereafter. In 2021, he experienced two metabolic decompensations and progressive renal insufficiency (creatinine clearance of 30–35 mL/min). This increase in metabolic decompensations prompted a referral for

Table 2 The metabolic laboratory values of both the MMA patients and the recipients of the MMA livers prior to and after transplantation

| Lab results | Case 1 | | | | Case 2 | | | | Reference |
| | Recipient 1 (MMA patient) | | Recipient 2 (DLT recipient) | | Recipient 1 (MMA patient) | | Recipient 2 (DLT recipient) | | |
	Before LT	Last FU	Before LT	Last FU	Before LT	Last FU	Before LT	Last FU	
Plasma methylmalonic acid (µmol/L)	738.74	315	0.11	86.7	1,420.27	562.07	0.11	635.40	<0.45
Anion gap	22	18	–	18	21	20	–	17	13–17
Ammonia (µmol/L)	27	42	85	18	33	23	24	18	<45
Lactate	–	1.1	1.1	1.4	1.1	1.1	–	1.6	1.3
eGFR creatinine (mL/min)	31	19	>90	65	33	29	>90	32	>90
eGFR cystine (mL/min)	34	17	–	72	–	21	–	19	>90
C3 carnitine	90.47	35.67	–	9.69	44.46	50.37	–	21.88	0.14–0.94
FGF21 (pg/mL)	19,400	548	–	1,250	2,390	216	–	2,570	0–200

MMA, methylmalonic acidemia; DLT, domino liver transplant; LT, liver transplant; FU, follow-up; eGFR, estimated glomerular filtration rate; FGF21, fibroblast growth factor 21.

Table 3 Demographics of adult LDDLT

Reference	Country	No. of patients	Domino donor age (years)	Donor disease	Recipient disease [number of patients]	Domino recipient age (years)	Follow-up
Celik, 2019	USA	17	17.6 (range, 4.8–32.1)	MSUD	PSC [4], CHF [2], A-1 ATD [2], PFIC [2], cystic fibrosis [1], PBC [1], neonatal hepatitis [1], embryonal sarcoma [1], Caroli disease [1], HCC [1], chronic rejection after LT [1]	16.2 (range, 0.6–64.6)	6.4 years
Yamamoto, 2022	Japan	25	36 (range, 25–52)	FAP	HCV [6], HBV [6], ASH [3], Re LTx [4], other [6]	36 (range, 25–52)	68 months
Takeichi, 2005	Japan	1	28	FAP	CAPV [1]	35	10 months
Hashikura, 2005	Japan	7	Unknown	FAP	HCC [6], citrullinemia [1]	–	13–52 months (median, 29 months)
Inomata, 2007	Japan	8	27–50	FAP	HBV [2], HBV/HCC [2], PBC [1], CAPV [1], BA [1], Re LTx [1]	17–58 (median, 40)	8–40 months

LDDLT, living donor domino liver transplantation; MSUD, maple syrup urine disease; PSC, primary sclerosing cholangitis; CHF, congenital hepatic fibrosis; A-1 ATD, alpha 1 antitrypsin deficiency; PFIC, primary familial intrahepatic cholestasis; PBC, primary biliary cirrhosis; HCC, hepatocellular carcinoma; LT, liver transplantation; FAP, familial amyloid polyneuropathy; HCV, hepatitis C virus; HBV, hepatitis B virus; ASH, alcoholic steatohepatitis; Re LTx, re liver transplantation; CAPV, congenital absence of portal vein; BA, biliary atresia.

transplant assessment. During LT screening, the patient was referred to nephrology for assessment for either kidney transplant alone, or combined liver KT (LKT). At our center, MMA patients are only considered for LKT if patients are already on renal replacement therapy. Otherwise, our preference is to perform sequential liver kidney transplants, liver first and kidney transplant in a later stage if still necessary. At the conclusion of transplant assessment, a multidisciplinary discussion took place which decided the patient would undergo LT first—this was

Table 4 Graft and patient survival

Reference	Graft failure, n	1-year patient survival (%)	5-year patient survival (%)	Re-transplantation of domino liver, n
Celik, 2019	0	100	100	0
Yamamoto, 2022	0	84	67.3	0
Takeichi, 2005	0	–	–	0
Hashikura, 2005	0	100	–	0
Inomata, 2007	0	100	–	0

indicated to prevent further acute metabolic complications, followed by KT if needed in the future. It was hoped that the LT would stabilize his kidney insufficiency or even improve renal function, avoiding the need for KT at all.

To prevent high risk of acute metabolic decompensation, the MMA recipient was given 3 L of glucose 10% while he was fasting to prevent catabolism. Carnitine was given, and each hour we checked plasma ammonia, lactate, PH, bicarbonate, glucose, and the anion gap and ketones in urine. Bicarbonate was given to correct acidosis peri-operatively when needed. Sodium benzoate and carglumic acid was available in the operation room so it could be started in case ammonia levels would rise >80 µmol/L. Propofol was not used (19).

The sister of the patient was screened for living liver donation. Her preoperative evaluation revealed no medical history or abnormal laboratory/imaging findings. Genetic testing excluded carrier status for MMA. She donated her right liver lobe with single arterial, portal venous, hepatic venous, and biliary anatomy, with a graft-to-recipient weight ratio (GRWR) of 0.67. Her surgery and recovery were uneventful.

The LDLT was surgically uneventful and without any acute metabolic dysregulation. The anastomotic time was 30 minutes and cold ischemia time was 2 hours and 6 minutes. The estimated blood loss was 500 mL. During the end of the hepatectomy phase, a careful decision was made in which place the vessels could be cut, so this liver could be used for domino donor liver implantation. After the successful LDLT, the first recipient was transferred to the intensive care unit (ICU) and discharged after 3 days to the general liver transplant ward. During days 4–8, the patient developed a metabolic decompensation which was probably triggered by catabolism. Ammonia levels rose to a maximum of 170 µmol. This was successfully treated with a restriction of natural protein to 0.75 g/kg/day, sodiumbenzoat and carglumic acid.

This patient was discharged 14 days postoperatively. The immunosuppression regimen consisted of prednisone, tacrolimus, and mycophenolate mofetil with basiliximab as an induction therapy, but levels of tacrolimus were kept as low as possible to prevent calcineurin induced neurotoxicity to which patients with MMA may be more at risk (20). A new tremor was seen on the outpatient clinic, possibly because of mild tacrolimus toxicity. Since discharge he has been metabolically stable, with improved methylmalonic acid, C3 carnitine, and fibroblast growth factor 21 (FGF21) values (*Table 2*). Unfortunately, his kidney function has deteriorated and he is currently undergoing screening for living related kidney transplant.

Case 1: second recipient (domino recipient)

The domino recipient was a 55-year-old man, who was diagnosed with liver cirrhosis due to hepatitis B and hepatocellular carcinoma (HCC). His HCC was under control with no recurrence at the time of transplant, however the patient was sarcopenic with severe refractory ascites, portal hypertension, and hepatic encephalopathy. He had a Child-Pugh score of C. He had no living liver donor and with a low model for end-stage liver disease (MELD) score of 11, a liver transplant from the deceased donor pool was unlikely in the short term. After counseling from our metabolic team, hepatology and liver transplant surgeons, the patient provided informed consent to undergo DLT with a liver graft from an MMA patient.

The liver was removed with caval-sparing technique. During implantation, we had to deal with shorter vessels than normal by partially clamping the caval vein and conserving as much of the hepatic veins, portal vein, and hepatic artery as possible. Caval vein anastomosis was performed using a 180° rotated, adequately trimmed, free iliaco-caval venous graft, creating an inverted venous Y-graft, allowing for transplantation of the domino allograft

into the DLT recipient by a conventional end-to-side piggyback technique (21,22). Hepatic arterial anastomosis was performed between donor proper hepatic artery and recipient right hepatic artery. A duct-to-duct anastomosis was performed to reconstruct the biliary system. The estimated blood loss was 5,500 mL. The patient was transferred to the ICU and was moved to the general liver transplant ward on day 3 postoperatively. The postoperative course was complicated by infection, requiring antibiotic treatment.

Four weeks after transplantation he was discharged home. In the postoperative period, the patient has developed biochemical signs of mild MMA (*Table 2*), but there were no clinical signs of metabolic dysregulation due to MMA. His immunosuppressive regimen consisted of prednisone, tacrolimus with basiliximab as an induction therapy. He has developed mild kidney insufficiency, and his postoperative course was complicated by cytomegalovirus (CMV) reactivation and recurrent scabies infections. Nineteen months after DLT his liver function remains normal, he has no signs of HCC recurrence, and his quality of life is satisfactory.

Case 2: *first recipient (domino donor)*

A 38-year-old female with MMA (MUT 0 phenotype due to 2 heterozygous pathogenic mutations in the MUT gene c.654A>C and c.1677-1G>C) presented for LDLT and as a liver donor for DLT. Her medical history consisted of hypertension, bilateral optic nerve atrophy, pancreatitis and hyperparathyroidism requiring parathyroidectomy. She had several metabolic decompensations during her childhood but had been relatively stable in adulthood, due to a strict medication regimen and diet. She developed progressive renal insufficiency (creatinine clearance of 35 mL/min) and was therefore referred to our institution for a liver transplant and hopefully stabilize kidney function. In line with our protocol, the patient underwent evaluation for LKT by nephrologists during the LT screening. Due to her stable creatinine glomerular filtration rate (GFR) of 35 mL/min, during our multidisciplinary team meeting she was listed for LT to prevent further long-term complications of MMA, prevent metabolic decompensations, and hopefully preserve her current renal function. If a KT was needed, this could be performed safely after the LT. Her MELD score was 16.

The recipient had a family friend, who screened for living liver donation. She could donate her right liver lobe with one right hepatic artery, right portal vein, one right hepatic vein, one segment 6 vein, and two bile ducts. The GRWR was 0.82. Her liver donation surgery was uneventful, and her recovery was uncomplicated.

The LDLT was uneventful without any acute metabolic dysregulation. The anastomotic time was 49 minutes and cold ischemia time was 2 hours and 27 minutes. The estimated blood loss was 2,000 mL. We used the same method to take out the donor liver as mentioned in the previous case. The patient was transferred to the ICU postoperatively. Two days after the LDLT, a routine ultrasound of the liver showed no hepatic artery signal. We performed immediate laparotomy with thrombectomy. All consecutive Doppler ultrasounds confirmed patency of the hepatic artery.

The immunosuppressive regimen consisted of prednisone, tacrolimus, and mycophenolate mofetil with basiliximab as an induction therapy. Postoperatively there was no metabolic decompensation. She was discharged home after 5 weeks. Since discharge she has been metabolically stable, with improved methyl malonic acid, C3 carnitine, and FGF21 values (*Table 2*). Her kidney function had initially improved after LT, and stabilized with an estimated GFR (eGFR) of 55 mL/min. Unfortunately, she was diagnosed with endocarditis 7 months after LDLT and underwent an aortic valve replacement. During this period, she developed acute kidney insufficiency. Her eGFR has now stabilized at 29 mL/min, and she has regular follow-up appointments with a nephrologist at our institution.

Case 2: *second recipient (domino recipient)*

The domino recipient was a 70-year-old man who was on the LT waiting list due to HCC and hepatitis B. He had been on the waiting list for more than 6 months without a liver offer and had repeated recurrence of his HCC but was still within Milan criteria. Aside from the recurrent HCC, the patient was in good physical condition. He had a Child-Pugh score of A. He had no available living donor, and a low MELD score of 8. After counseling, he provided informed consent and agreed to undergo DLT with a liver graft from an MMA patient.

The liver of the domino recipient was removed with a standard cava sparing technique and the domino allograft was implanted with the same method described in the first case. The estimated blood loss was 3,600 mL. The patient was transferred to the ICU. He was moved to the general liver transplant ward on day 3 after liver transplant. The postoperative course was complicated by an arterial

bleeding from the falciform ligament which was successfully controlled.

Eleven days after DLT he was discharged home. The patient was admitted twice with high potassium, metabolic acidosis, and acute kidney injury due to dehydration. Postoperatively, there were signs of metabolic dysregulation. His immunosuppressive regimen consisted of prednisone, tacrolimus with basiliximab as an induction therapy. Unfortunately, the patient developed a kidney insufficiency in the postoperative phase, due to calcineurin induced toxicity in combination with acute tubular necrosis. His postoperative course was further complicated by diabetes mellitus, and CMV reactivation. He also developed a cavernous lung lesion 8 months after transplantation which is infectious in origin (aspergilloma). There was recently also a suspected outflow obstruction, which required stenting. The plasma MMA value has increased to 635 µmol/L at last follow-up (*Table 2*). Because of these complications, 17 months after DLT he remains tired, and his quality of life is lower than expected.

Ethical statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients or their legal guardians for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

This is one of the first case report of adult LDDLTs with MMA donor livers with 2 years of follow-up. Although DLT from deceased donors has been performed in at least 50 documented cases since 1995, there are limited reported cases of DLT following LDLT (23,24). One possible explanation for this is the increased level of surgical complexity—the short length of vasculature in both living donor and domino grafts make these surgeries technically more difficult (23,24). However, domino liver grafts have less ischemia-reperfusion time than organs obtained from both brain death and cardiac death deceased donors, and the domino donors are often younger; DLT results therefore are not markedly different than results gained from DDLT within the first 5 years (24,25). DLT results 5 years or more

after transplant are scarce (*Table 3*).

The main unresolved question regarding DLT is which metabolic diseases are an acceptable source of domino liver grafts. This risk is often difficult to evaluate; the inability of clinicians to provide fair and accurate information to future DLT recipients remains a barrier to the wider implementation of DLT.

To reduce some of these barriers, the Domino Liver Transplant Registry was established to collect information on the frequency of DLT and the metabolic diseases of the domino donors. This registry also includes DLT using MMA livers. However, it is unclear how many of the total number are domino transplants using MMA livers.

Selection of the domino recipient plays a critical role. Our DLT recipients benefited from a shorter waiting time when compared to the deceased donor transplant list, an organ from a younger donor and an organ with lower chance of preservation injury. Both our selected DLT recipients faced a lengthy wait for a LT from the deceased donor pool, and could have been delisted for LT entirely if their HCC had progressed beyond transplant criteria (22,25-27).

Although no clear framework or protocol exists for identifying potential DLT recipients, we offered DLT as an option to recipients who were actively listed for LT, with low MELD scores and no live donor available (23,24,28). DLT recipients were counseled by experts in hepatology, transplant surgery and metabolic diseases, and offered a conversation with a Domino Donor Advocate—based on the independent living donor advocate concept—to assist with decision making and ensure truly voluntary consent was given (27,28). Both DLT recipients were given adequate time to think about the option of DLT and ask questions before providing written consent to the procedure (28,29).

Most cases of DLT have utilized liver grafts from patients with FAP (24,25). The liver produces 95% of the insoluble transthyretin (TTR) which is responsible for the disease progression, meaning a liver transplant for FAP patients is curative (29-31). Initially, it was thought that the transmission of the FAP disease to a DLT recipient would take 20–30 years, however we now know that recurrence may occur earlier and in a more severe form than anticipated (30,32). A 23% rate of recurrence has been reported in recipients who received a DLT using a FAP liver graft, after a median follow-up of 7 years (24,25). The use of FAP livers as DLT grafts varies greatly from the use of MMA for DLT; FAP livers produce the majority of the TTR which causes the symptoms and disease progression,

so it is likely that FAP DLT recipients have a higher recurrence rate. While MMA DLT recipients are likely to have elevated methylmalonate in blood and urine after transplant—while consuming an unrestricted diet—no classical MMA symptoms or metabolic decompensations are expected to occur as the DLT recipient has no mutase deficiency in extra hepatic tissues (10).

There is limited experience with the use of domino MMA liver grafts, however the literature suggests that in MMA patients themselves the rate of metabolic decompensation can be reduced by 85% after LT (10). We predicted that the use of an MMA-affected liver for DLT would inevitably cause higher than normal MMA levels in the domino recipient (10). We believed that the wait list mortality for the domino recipients exceeded the morbidity associated with their post-transplant outcomes using an MMA domino liver (*Table 4*).

The first DLT recipient has a good quality of life after DLT, despite higher levels of both FGF21 and plasma MMA after DLT (*Table 2*). The second DLT recipient however has had a very complicated postoperative course. Both plasma MMA and FGF21 remain significantly elevated (*Table 2*). FGF21 correlates closely in MMA patients (and perhaps then DLT recipients of MMA livers) with mitochondrial dysfunction and metabolic stress (31). The reduced renal function in this patient could be caused by the significantly high plasma MMA levels, likely the high FGF21 levels reveal that this liver is most likely severely affected by the mitochondriopathy of MMA (32).

While short-term outcomes are good, studies that report on the long-term outcome of DLT recipients are needed to determine the long-term viability of DLT using MMA livers (*Table 4*) (32,33). Our experience shows that both patients have had complex post-transplant courses, wherein the role of the domino MMA liver is not entirely clear (34).

Conclusions

In this case study, we present our experience with DLT using two MMA livers from recipients who underwent adult-to-adult LDLT. DLT using grafts with specific metabolic disorders such as MMA expands the donor pool not only in the pediatric population, but also for adult recipients. Ongoing studies of long-term outcomes for domino recipients of MMA liver, including quality of life and long-term complications of transplantation with a mutase-deficient graft, are important to better define the risks and benefits of such a procedure.

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