OBSERVATIONAL STUDY

OPEN

Molecular Adsorbent Recirculating System for Acute Liver Failure in a New Pediatric-Based Extracorporeal Liver Support Program

David R. Baker, MD[1]
Helen Mac, MD[2]
Benjamin Steinman, MD[3]
Sara H. Soshnick, DO, MS[1]
Shalom Z. Frager, MD[4]
Beatrice Goilav, MD[3]
Debora Kogan-Liberman, MD[5]
Nadia Ovchinsky, MD, MBA[5]
Mark Shlomovich, MD[1]

IMPORTANCE: Acute liver failure (ALF) carries significant morbidity and mortality, for both pediatric and adult patients. Albumin dialysis via the molecular adsorbent recirculating system (MARS) is a form of extracorporeal liver support (ELS) that can reduce hepatic encephalopathy (HE), a main driver of mortality in ALF. However, data on MARS and its benefit on mortality have been inconsistent.

OBJECTIVES: We sought to report our experiences and patient outcomes from the first 2 years of operation of a new ELS program, within an established pediatric liver transplantation center.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective review of outcomes in pediatric and adult patients treated with MARS therapy for ALF, from 2021 to 2022.

MAIN OUTCOMES AND MEASURES: Outcomes included reduction in HE and biochemical markers of ALF after MARS therapy, survival, and transplant-free survival. Comparisons were made via Wilcoxon signed-rank test.

RESULTS: Five pediatric and two adult patients underwent MARS for ALF. Ages ranged from 2 to 29 years. Overall, 21 MARS runs were performed (median 3 runs per patient, 12.4 hr per run [interquartile range, IQR 10.1–17]). Overall survival was 85.7%, and transplant-free survival was 71.4%. There was a statistically significant reduction in HE score with MARS therapy (median 3 [IQR 3–4] to 1 [IQR 0–1], $p = 0.03$), and in ALF biomarkers including ammonia (256 μL/dL [195–265] to 75 μL/dL [58–101], $p = 0.02$), aspartate aminotransferase (6,362 U/L [920–8,305] to 212 U/L [72–431], $p = 0.02$), alanine aminotransferase (8,362 U/L [3,866–9,189] to 953 U/L [437–1,351], $p = 0.02$), and international normalized ratio (4.5 [3.3–6.7] to 1.3 [1.2–1.4], $p = 0.02$).

CONCLUSIONS AND RELEVANCE: MARS therapy for ALF was well tolerated by both pediatric and adult patients, and resulted in significant improvement in clinical and biochemical parameters. We demonstrated encouraging overall and transplant-free survival, suggesting that early initiation of MARS with relatively long and frequent cycle times may be of significant benefit to ALF patients, and is worthy of additional study in larger cohorts.

KEY WORDS: adult; extracorporeal circulation; hepatic encephalopathy; liver failure; liver transplantation; pediatric

Acute liver failure (ALF) leads to significant morbidity, mortality, and the potential need for liver transplantation (LT). Even in the transplantation era, mortality in ALF can approach 20% in pediatrics and 30% in adult patients (1, 2). Transplant-free survival is in the range of 50% in adult patients, and 55% in pediatric patients (2, 3). Complications include hepatic encephalopathy (HE), coagulopathy, severe hyperbilirubinemia, and altered hemodynamics (1). Extracorporeal liver support (ELS) modalities have been available for several decades and aim to eliminate toxins from the blood that

DOI: 10.1097/CCE.0000000000001002

KEY POINTS

Question: Is molecular adsorbent recirculating system (MARS) therapy of benefit in acute liver failure (ALF)?

Findings: We reported patient outcomes within the first 2 years of a new pediatric MARS program. Overall transplant-free survival was good, and MARS therapy improved hepatic encephalopathy and biomarkers of ALF. Longer, more frequent MARS cycles may have contributed to favorable outcomes.

Meaning: MARS therapy appears to be beneficial in pediatric and adult patients with ALF, as a bridge to LT or recovery of native function. Our experience in initiating a MARS program was encouraging and suggests larger investigations into a potential survival benefit are warranted.

are unable to be cleared by a failing native liver. ELS also may promote an environment for the regeneration of native hepatocytes (4, 5). There are two categories of ELS devices—albumin dialysis and bioartificial liver support systems. The molecular adsorbent recirculating system (MARS) is the most widely used and best-studied form of albumin dialysis and is currently approved by the U.S. Food and Drug Administration (FDA) for the management of hepatotoxic ingestions. It uses an albumin-enriched dialysate fluid to filter a patient's blood of both protein-bound and water-soluble toxins. The toxin-laden albumin dialysate then passes through a conventional continuous renal replacement therapy (CRRT) machine and is dialyzed against conventional dialysate solutions for the removal of water-soluble toxins. At this point, the functions of conventional CRRT can be performed, including fluid removal and balancing of electrolytes and acid–base status. The albumin dialysate then passes through a pair of special MARS adsorption columns—an activated charcoal filter, which removes protein-bound substances, and an ion-exchange resin that removes anionic substances. The albumin dialysate finally recirculates back to the blood circuit for further detoxification of patient's blood (5, 6). Initially, target therapy times of 8 hours were described, but longer runs were also reported (7).

MARS has been found to improve HE, which is associated with significant morbidity, in both pediatric and adult ALF patients (1). Although there is some suggestion that MARS conveys a reduction in mortality in ALF, to date, large, randomized trials in adult patients have not reliably and reproducibly demonstrated a mortality benefit (5, 7–11). Several pediatric centers have published retrospective studies demonstrating tolerance of MARS in children with ALF and its use in other indications, including specific hepatotoxic ingestions and cholestatic pruritis (1, 4–16). Most importantly, some groups have reported promising results regarding improvement in HE, hemodynamics, and biochemical markers in ALF patients (17–20).

These reported benefits have resulted in the inclusion of MARS in what has been described as hybrid extracorporeal therapy for ALF. This strategy for ALF management deploys multiple known extracorporeal modalities to treat the various complications of ALF: significant hyperammonemia can be treated with CRRT, life-threatening coagulopathy with plasma exchange, and severe HE with MARS (17). With this approach in mind, we initiated an ELS program in 2021 at the Children's Hospital at Montefiore, an urban pediatric quaternary care center within a larger medical system, with a robust pediatric liver referral center and transplantation program. Here, we aim to describe our approach to ELS and outline our clinical outcomes in our first 2 years of operation.

MATERIALS AND METHODS

We performed a retrospective review of seven patients who underwent MARS therapy from 2021 to 2022 for ALF at the Children's Hospital at Montefiore in the Bronx, New York. Of these seven patients, five were children and two were adults from our connected adult hospital, which has a robust adult liver service but not MARS capability. The Montefiore Medical Center/Albert Einstein College of Medicine Institutional Review Board (IRB) approved this project and waived informed consent due to the retrospective nature of the study and low risk to subjects (approved February 14, 2023 as "Retrospective Review of outcomes related to the use of the molecular adsorbent recirculating system [MARS] in patients with liver failure and/or severe hyperbilirubinemia," IRB number 2022-14505). All procedures were performed in accordance with

the ethical standards of the aforementioned IRB and with the Helsinki Declaration of 1975. Retrospective and follow-up data from patients who received MARS therapy at our institution were gathered through electronic health record review. HE was defined as grade I (least severe) through IV (most severe) by West Haven criteria (1, 21). All patients demonstrated coagulopathy with an international normalized ratio (INR) greater than 2 after correction with vitamin K.

ELS Protocol

Patients qualified for MARS therapy as per our institutional ELS protocol (**Supplemental Fig. 1**, http://links.lww.com/CCX/B268). Patients were considered for ELS as a bridge to transplantation in the setting of ALF, post-LT graft failure, hepatotoxic ingestion, or other etiologies agreed upon by a multidisciplinary team. CRRT alone was indicated if oliguric acute kidney injury, fluid overload greater than 15% of dry weight, or hyperammonemia greater than 100 mmol/L. Therapeutic plasma exchange was indicated in the presence of life-threatening bleeding or refractory coagulopathy. MARS was indicated in the presence of grade 3 HE or higher, grade 2 HE or higher with at least one additional failing organ system, hepatotoxic intoxication, or post-liver transplant with either graft primary nonfunction, delayed function, or failure. MARS sessions were planned for a minimum of 8 hours and a maximum of 24 hours. Therapy was to be discontinued upon departure from the unit for LT, resolution of HE with improvement in synthetic function, or if no improvement after three MARS cycles of adequate duration (at least 8 hr each). MARS is currently FDA-approved in the United States for hepatotoxic ingestions; off-label use for HE associated with ALF (as a bridge to transplantation or recovery) was discussed as a part of the consent process.

Intervention

MARS therapy was delivered via the X-MARS kit with the PrismaFlex CRRT machine (Baxter, Deerfield, IL) as per the manufacturer's recommendation. PrismaFlex was set to continuous venovenous hemodiafiltration (CVVHDF) mode. Albumin dialysate of 16.7% was prepared by our pharmacy for use on the X-MARS circuit. The albumin flow rates ranged from 3 mL/kg/min in young children to a maximum of 250 mL/min in older children and adults. Clearance rates ranged from 2,700 mL/hr/1.73 m^2 to 8,000 mL/hr/1.73 m^2, clinically determined by the need for ammonia clearance. All patients who were prescribed circuit anticoagulation received heparin as per our institutional CRRT protocol.

Statistical Analysis

Categorical data were expressed as percentages, and continuous data as medians with interquartile ranges (IQRs). Wilcoxon signed-rank tests were used to determine statistical significance, with an alpha (α) equal to 0.05 (two-sided).

RESULTS

During the study period, five pediatric and two adult patients underwent MARS therapy for the indication of ALF. There were three male patients (43%) and four female patients (57%), with ages ranging from 2 to 39 years. A total of 21 MARS runs were performed, with an average of 3 runs per patient. Average MARS run time per patient ranged from 8 to 19 hours (median 12.4 hr per run [IQR 10.1–17]). Only 1 of the 21 MARS runs (4.8%) required early termination due to intolerance (hemodynamic instability). The cause of ALF was indeterminate in five of the seven cases, with one case of viral ALF driven by varicella infection and one case of acetaminophen toxicity. Both mechanical ventilation and inotropic support were required in three of the seven patients (43%). Overall survival was 85.7%, and transplant-free survival was 71.4%. At the time of article preparation (24 mo from the first case and 10 mo from the seventh case), five of the seven had recovered native liver function, one was transplanted successfully, and one died of irreversible neurologic injuries related to ALF and multiple organ dysfunction. Four patients received at least 1 day of CVVHDF alone in addition to CRRT use in conjunction with MARS (indications were hyperammonemia and transient anuria in one patient). One patient received plasmapheresis twice at an outside institution before being transferred to our facility for MARS evaluation (**Tables 1** and **2**).

MARS therapy was associated with a reduction in almost all clinical and biochemical parameters collected. There was a statistically significant improvement in HE score (median 3 pre-MARS [IQR 3–4] to 1 post-MARS [IQR 0–1], $p = 0.03$), ammonia (256 μL/dL [195–265]

TABLE 1.
Patient Characteristics

Patient	Age, Sex	Weight (kg)	Medical History	Etiology	Pediatric End-Stage Liver Disease Score/ Model for End-Stage Liver Disease Score	Listed for Liver Transplant?	Outcome
1	17 yr, male	92	Non-alcoholic fatty liver disease	Indeterminant	31	Yes	Recovered
2	4 yr, female	32	Methicillin-sensitive *Staphylococcus aureus* osteomyelitis with recent washout	Indeterminant, suspected inhaled anesthetic-induced.	8	Yes	Recovered
3	14 yr, female	75.8	None	Indeterminant	39	Yes	Recovered
4	8 yr, male	25	Focal segmental glomerulosclerosis, chronic immunosuppression, idiopathic intracranial hypertension, prothrombin mutation.	Varicella-induced viral acute liver failure	25	Not a candidate: severe viral infection and multiple organ failure	Recovered
5	2 yr, male	13.6	*UDP-glucose 6-dehydrogenase* gene mutation, cortical dysplasia, seizures, and global delay	Indeterminant, possibly enterovirus-induced	32	Not a candidate: severe neurologic disorder	Death–irreversible neurologic injury
6	26 yr, female	85.5	Recently postpartum. concurrent HELLP syndrome; acute fatty liver of pregnancy	Indeterminant	41	Not a candidate: multisystem organ failure due to HELLP	Recovered
7	39 yr, female	68	None	Acetaminophen toxicity	33	Yes	Transplanted successfully

HELLP = Hemolysis, Elevated Liver enzymes, and Low Platelets.
Pediatric End-Stage Liver Disease Score/Model for End-Stage Liver Disease Score are calculated at the time of listing for liver transplantation, or molecular adsorbent recirculating system evaluation if not listed for transplant.

TABLE 2.
Molecular Adsorbent Recirculating System Parameters

Patient	Molecular Adsorbent Recirculating System Cycles	Average Cycle Time (hr)	Dialysate Flow Rate (mL/hr)	Total Clearance (mL/hr/1.73 m^2)	Average Blood Flow Rate (mL/min)	Additional Extracorporeal Therapies	Heparin Dosing
1	3	19	3,000 to 5,000	3,700 to 5,354	180	1 d of CVVHDF for hyperammonemia pre-MARS	500 units bolus, 600 units/hr maintenance
2	3	10.2	600	2,096	240	None	8–15 units/kg bolus, 3–10 units/kg/hr maintenance
3	3	10	1,500	2,850	180	Required CVVHDF for transient anuria post-MARS	400 units bolus, 200–500 units/hr maintenance
4	5	12.4	1,000 to > 2,000	3,233 to > 4,850	250	Plasmapheresis ×2 at outside institution; CVVHDF for temporary anuria post-MARS	10 units/kg bolus, 5 units/hr maintenance
5	3	17	500 to 850	3,200 to 8,000	150	CVVHDF initiated pre-MARS	10–20 units/kg bolus, 10 units/kg/hr maintenance
6	3	17	2,500	4,140	250	None	500 units/kg bolus, 100 units hr maintenance
7	1	8	1,000 to 7,000	2,000 to 8,000	250	Continuous venovenous hemodialysis	None

CVVHDF = continuous venovenous hemodiafiltration, MARS = molecular adsorbent recirculating system.

to 75 µL/dL [58–101], $p = 0.02$), aspartate aminotransferase (6,362 U/L [920–8,305] to 212 U/L [72–431], $p = 0.02$), alanine aminotransferase (8,362 U/L [3,866–9,189] to 953 U/L [437–1,351], $p = 0.02$), and INR (4.5 [3.3–6.7] to 1.3 [1.2–1.4], $p = 0.02$). Although there was an overall reduction in total bilirubin (5.8 mg/dL [4–6.8] to 2.9 mg/dL [1.9–6.6], $p = 0.47$) and direct bilirubin (2.9 mg/dL [2.4–3.1] to 1.9 mg/dL [1.22–4.2], $p = 0.5$), these changes did not reach statistical significance (**Table 3**, **Figs 1** and **2**).

TABLE 3.
Change in Biomarkers/Clinical Parameters

Biomarker	Pre-MARS	Post-MARS	*p*
Grade hepatic encephalopathy	3 (3–4)	1 (0–1)	0.03
Ammonia	256 (195–265)	75 (58–101)	0.02
International normalized ratio	4.5 (3.3–6.7)	1.3 (1.2–1.4)	0.02
Aspartate aminotransferase	6,362 (920–8,305)	212 (72–431)	0.02
Alanine aminotransferase	8,362 (3,866–9,189)	953 (437–1,351)	0.02
Total bilirubin	5.8 (4–6.8)	2.9 (1.9–6.6)	0.47
Direct bilirubin	2.9 (2.4–3.1)	1.9 (1.2–4.2)	0.5

MARS = molecular adsorbent recirculating system.
Data expressed as medians (interquartile range).

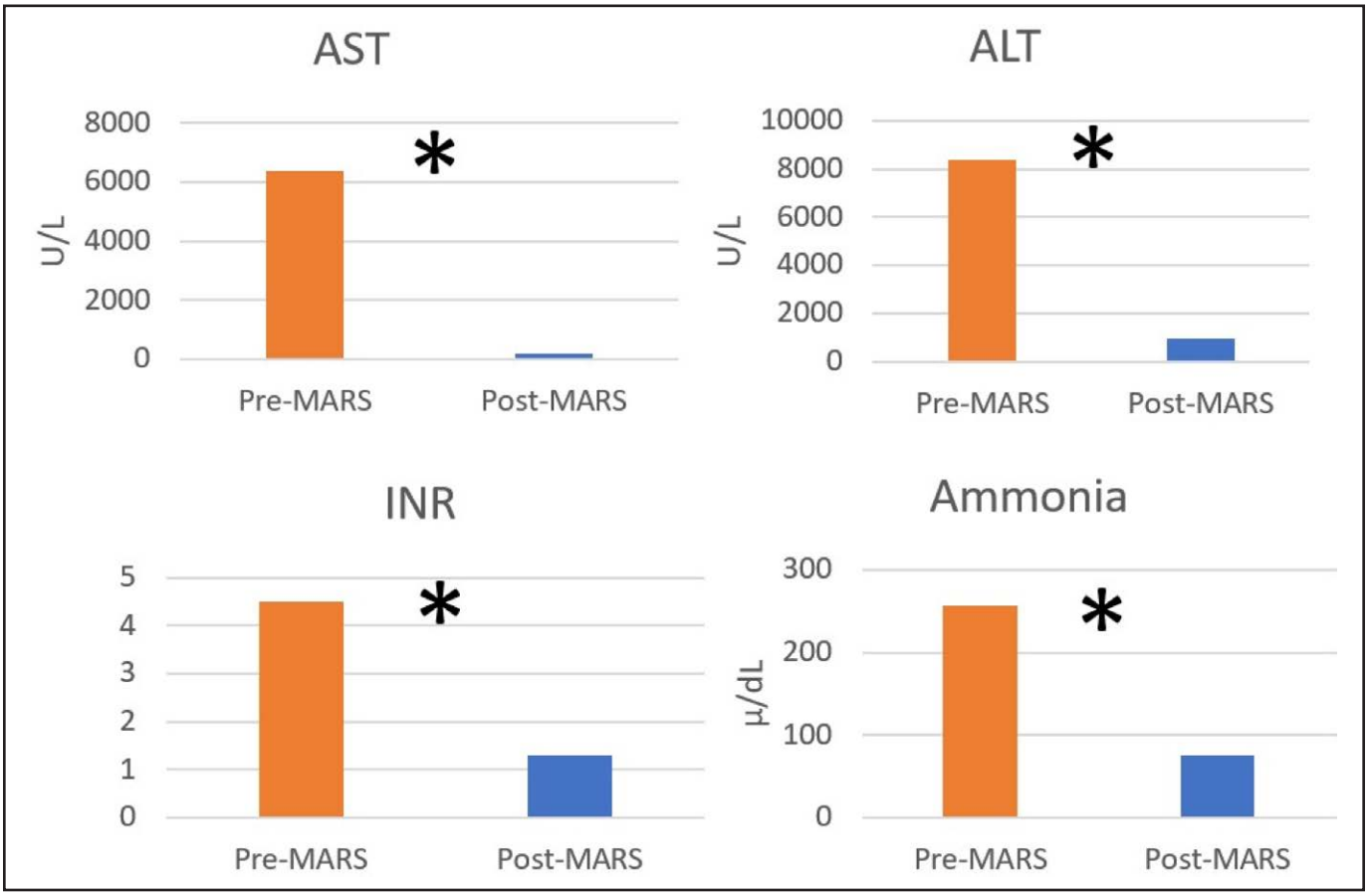

Figure 1. Change in biochemical and clinical parameters (group medians). *Asterisks* denote statistical significance. AST = aspartate aminotransferase, ALT = alanine aminotransferase, INR = international normalized ratio, MARS = molecular adsorbent recirculating system.

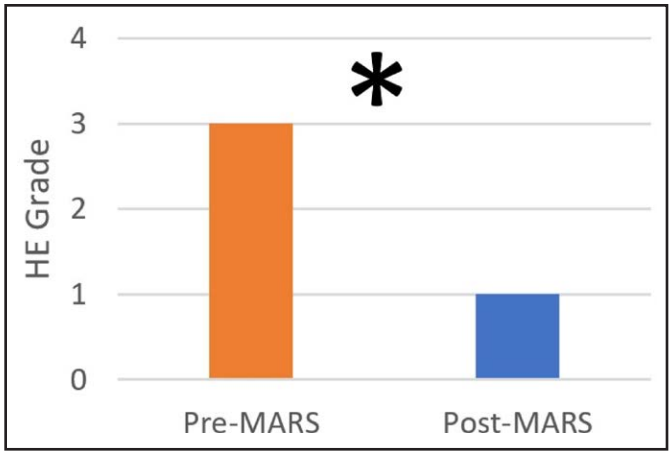

Figure 2. Change in hepatic encephalopathy (HE) (group median). *Asterisk* denotes statistical significance. MARS = molecular adsorbent recirculating system.

DISCUSSION

We initiated a pediatric-based ELS program to manage the severe complications of ALF with a protocolized approach to extracorporeal therapy. As such, we used MARS therapy for the treatment of severe HE, as a bridge to LT or recovery in severely ill ALF patients, and as a bridge to recovery in those not considered candidates for LT. In the first 2 years of our ELS program, we treated five pediatric and two adult ALF patients with MARS therapy, with promising results. We had encouraging overall survival for such a severe disease process and showed improvement in all measured biomarkers excluding bilirubin. Importantly, we demonstrated a significant improvement in neurologic status as measured by HE score. MARS therapy was well-tolerated, with no identified episodes of bleeding or thrombosis, and only one episode of transient hypotension upon initiation of the extracorporeal therapy. Five of our patients recovered native liver function, one was transplanted successfully, and one died of irreversible neurologic injury related to ALF.

Overall mortality in ALF patients of all ages receiving MARS therapy varies from 10 to 55%; risk factors for higher mortality on MARS include lack of improvement in the degree of HE as well as indeterminate etiology of ALF (2, 3, 17, 22). The single mortality in our cohort occurred in a 2-year-old male child with an underlying genetic syndrome, which precluded his qualification for LT. Therefore, he was referred to our center relatively late in the course of his illness, and exclusively for the possibility of MARS therapy in hopes of reversing his neurologic deterioration. Before initiation of MARS, he had progressed to stage 4 HE with loss of the majority of his brainstem reflexes and had significant hemodynamic instability. It is unclear whether earlier initiation of MARS may have allowed for a more favorable outcome.

The single patient in our cohort who underwent LT was an adult with acetaminophen-induced ALF. Given the severity of her illness at presentation, she received a planned single 8-hour session as a suitable graft had been identified for her. Within 2 hours of initiation of therapy, her neurologic status was improving with redevelopment of pupillary and cough reflexes as well as facial grimace. Despite this improvement, the severity of her HE and the availability of a suitable graft led us to proceed with the decision to transplant. Given that six of seven patients in our cohort survived, and five of seven had full recovery of their native liver function following 3–5 cycles of MARS therapy, we believe that our outcomes compare favorably to those reported in ALF, and ALF treated with MARS. Given the size of our cohort, we are unable to comment on a potential relationship between patient age and the effective duration of MARS.

One factor that may have contributed to our promising results is that our approach called for early deployment of MARS, as soon as initiation criteria were met. In addition, we targeted multiple cycles with longer cycle times, with a goal of up to 24 hours each. Although this approach is in line with what some other groups have reported, it is important to mention that some of the largest randomized trials which failed to show survival benefits used much shorter average MARS cycles (5). The two largest early trials that failed to show survival benefit after MARS therapy used very short and infrequent MARS cycles. In one such trial, there was a very rapid progression from ALF diagnosis to transplantation in both the treatment and control group, possibly leading to a failure to capture the therapeutic window for MARS therapy (7, 9, 23, 24). More recent work, notably studies that incorporate longer exposure to MARS therapy, has been more promising. A recent large propensity score-matched retrospective cohort analysis of adult patients receiving MARS suggests an increase in 21-day transplant-free survival with MARS therapy (11). A 2022 international

consensus statement suggests that the potential benefits of MARS are sufficiently well-documented to support the use of MARS therapy in carefully selected patients within experienced liver centers (5). Further prospective, randomized trials incorporating longer, and more frequent MARS use are needed to truly determine the full potential benefits of MARS therapy. Unfortunately, Baxter recently issued an end-of-life notification for the MARS 1TC monitor. It is our hope that an updated version of the technology will be made available to allow for further research into the potential benefits of albumin dialysis in this high-risk patient population.

Despite largely favorable outcomes, our study had several limitations. First, our work is retrospective, and derived from a small cohort treated at a single center. We also do not have granular data on hemodynamics during or after MARS therapy, but in our sample, only one single MARS run was aborted due to hemodynamic intolerance. Additionally, our patients were treated with a combined extracorporeal approach, with the majority of our patients receiving additional CRRT outside of MARS therapy, and one patient underwent plasma exchange before transfer to our institution and initiation of MARS. There is some suggestion that the combination of CRRT and plasma exchange may convey some of the benefits ascribed to MARS (25). Although it is unlikely that the use of additional CRRT (and plasma exchange in one patient) within our cohort significantly confounded our results, a large, direct comparison of the different extracorporeal modalities used in liver failure may ultimately be needed.

CONCLUSIONS

We found that the use of MARS is both feasible at an experienced pediatric liver center, and well-tolerated by pediatric and adult ALF patients. In our first 2 years as a MARS center, our patients who received MARS therapy demonstrated improvement in biochemical and clinical parameters as well as excellent overall and transplant-free survival compared with published values (1–3). However, additional larger trials are required to definitively establish MARS as a treatment modality for pediatric ALF. Future studies, whether prospective or retrospective, pediatric or adult, should incorporate early use of MARS with longer cycle times, to best determine if MARS therapy truly conveys a survival or transplant-free survival benefit in ALF.

1 *Division of Pediatric Critical Care, The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.*

2 *Division of Pediatric Gastroenterology, Hepatology, and Nutrition, The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.*

3 *Division of Pediatric Nephrology, The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY.*

4 *Division of Hepatology, Department of Medicine, Montefiore Medical Center, Bronx, NY.*

5 *Division of Pediatric Gastroenterology and Hepatology, Hassenfeld Children's Hospital, NYU Grossman School of Medicine, New York, NY.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Dr. Ovchinsky receives research support from Albireo, Mirum, and Travere, and is a consultant for Albireo. The remaining authors have disclosed that they do not have any potential conflict of interest.

For information regarding this article, E-mail: mshlomov@montefiore.org

REFERENCES

1. Lutfi R, Abulebda K, Nitu, Mara E, et al: Intensive care management of pediatric acute liver failure. *J Pediatr Gastroenterol Nutr* 2017; 64:660–670
2. Reuben A, Tillman H, Fontana RJ, et al: Outcomes in adults with acute liver failure between 1998 and 2013: An observational cohort study. *Ann Intern Med* 2016; 164:724–732
3. Ng VL, Li R, Loomes KM, et al; Pediatric Acute Liver Failure Study Group (PALFSG): Outcomes of children with and without hepatic encephalopathy from the pediatric acute liver failure study group. *J Pediatr Gastroenterol Nutr* 2016; 63:357–364
4. García Martínez JJ, Bendjelid K: Artificial liver support systems: What is new over the last decade? *Ann. Intensive Care* 2018; 8:109
5. Saliba F, Bañares R, Larsen FS, et al: Artificial liver support in patients with liver failure: A modified DELPHI consensus of international experts. *Intensive Care Med* 2022; 48:1352–1367
6. Baxter International: Liver detoxification; Acute Therapies Products. Available at https://usrenalacute.baxter.com/therapies/mars. Accessed December 9, 2022
7. Alshamsi F, Alshammari K, Belley-Cote E, et al; GUIDE Group: Extracorporeal liver support in patients with liver failure: A systematic review and meta-analysis of randomized trials. *Intensive Care Med* 2020; 46:1–16
8. Stadlbauer V, Wright GAK, Jalan R: Role of artificial liver support in hepatic encephalopathy. *Metab Brain Dis* 2009; 24:15–26

9. Vaid A, Chweich H, Balk EM, et al: Molecular adsorbent recirculating system as artificial support therapy for liver failure: A meta-analysis. *ASAIO J* 2012; 58:51–59
10. Bañares R, Nevens F, Larsen FS, et al; RELIEF study group: Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: The RELIEF trial. *Hepatology* 2013; 57:1153–1162
11. MacDonald AJ, Subramanian RM, Olson JC, et al; U.S. Acute Liver Failure Study Group: Use of the molecular adsorbent recirculating system in acute liver failure: Results of a multicenter propensity score-matched study. *Crit Care Med* 2022; 50:286–295
12. Niu H, Atallah E, Alvarez-Alvarez I, et al: Therapeutic management of idiosyncratic drug-induced liver injury and acetaminophen hepatotoxicity in the paediatric population: A systematic review. *Drug Saf* 2022; 45:1329–1348
13. Wittebole X, Hantson P: Use of the molecular adsorbent recirculating system (MARS™) for the management of acute poisoning with or without liver failure. *Clin Toxicol (Phila).* 2011; 49:782–793
14. Pinto VL, Wenderfer SE, Morris J, et al: Treatment of severe amlodipine toxicity with molecular adsorbent recirculating system. *Kidney Int Rep* 2018; 4:346–349
15. Cheungpasitporn W, Thongprayoon C, Zoghby ZM, et al: MARS: Should I use It? *Adv Chronic Kidney Dis* 2021; 28:47–58
16. Schaefer B, Schaefer F, Wittmer D, et al: Molecular Adsorbents Recirculating System dialysis in children with cholestatic pruritus. *Pediatr Nephrol* 2012; 27:829–834
17. Akcan Arikan A, Srivaths P, Himes RW, et al: Hybrid extracorporeal therapies as a bridge to pediatric liver transplantation. *Pediatr Crit Care Med* 2018; 19:e342–e349
18. Lexmond WS, Van Dael CM, Scheenstra R, et al: Experience with molecular adsorbent recirculating system treatment in 20 children listed for high-urgency liver transplantation. *Liver Transpl* 2015; 21:369–380
19. Novelli G, Rossi M, Morabito V, et al: Pediatric acute liver failure with molecular adsorbent recirculating system treatment. *Transplant Proc* 2008; 40:1921–1924
20. Bourgoin P, Merouani A, Phan V, et al: Molecular Absorbent Recirculating System therapy (MARS®) in pediatric acute liver failure: A single center experience. *Pediatr Nephrol* 2014; 29:901–908
21. Dharel N, Bajaj JS: Definition and nomenclature of hepatic encephalopathy. *J Clin Exp Hepatol* 2015; 5:S37–S41
22. Kantola T, Koivusalo AM, Parmanen S, et al: Survival predictors in patients treated with a molecular adsorbent recirculating system. *World J Gastroenterol* 2009; 15:3015–3024
23. Gerth HU, Pohlen M, Thölking G, et al: molecular adsorbent recirculating system (MARS) in acute liver injury and graft dysfunction: Results from a case-control study. *PLoS One* 2017; 12:e0175529
24. Saliba F, Camus C, Durand F, et al: Albumin dialysis with a noncell artificial liver support device in patients with acute liver failure: A randomized, controlled trial. *Ann Intern Med* 2013; 159:522–531
25. Schaefer B, Schaefer F, Engelmann G, et al: Comparison of Molecular Adsorbents Recirculating System (MARS) dialysis with combined plasma exchange and haemodialysis in children with acute liver failure. *Nephrol Dial Transplant* 2011; 26:3633–3639