MARS therapy, the bridging to liver retransplantation – Three cases from the Hungarian liver transplant program

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Abstract: Besides orthotopic liver transplantation (OLT) there is no long-term and effective replacement therapy for severe liver failure. Artificial extracorporeal liver supply devices are able to reduce blood toxin levels, but do not replace any synthetic function of the liver. Molecular adsorbent recirculating system (MARS) is one of the methods that can be used to treat fulminant acute liver failure (ALF) or acute on chronic liver failure (AoCLF). The primary non-function (PNF) of the newly transplanted liver manifests in the clinical settings exactly like acute liver failure. MARS treatment can reduce the severity of complications by eliminating blood toxins, so that it can help hepatic encephalopathy (HE), hepatorenal syndrome (HRS), and the high rate mortality of cerebral herniation. This might serve as a bridging therapy before orthotopic liver retransplantation (reOLT). Three patients after a first liver transplantation became candidate for urgent MARS treatment as a bridging solution prior to reOLT in our center. Authors report these three cases, focusing on indications, MARS sessions, clinical courses, and final outcomes.

Keywords: liver failure, MARS therapy, retransplantation

Introduction

Severe liver failure is a life threatening disorder with high mortality rate. Multiple causes with various pathologies can lead to irreversible liver insufficiency. Despite intensive care treatment patient survival rate is at the low level of 20–60% without orthotopic liver transplantation (OLT), which is the only definite solution for acute liver failure (ALF). The availability of OLT is limited due to the well-known donor organ shortage that enforces clinicians to adjust alternative medication to gain time until a suitable donor organ becomes available. Despite adequate intensive therapy ALF and acute on chronic liver failure (AoCLF) can lead to multiorgan failure (MOF). Besides usual intensive therapy, extracorporeal assist devices can be effective help as a complement medical treatment option.

Liver failure causes hepatorenal syndrome (HRS) with acute renal failure, hepatopulmonary syndrome (HPS) with respiratory failure, severe disseminated coagulopathy, acute encephalopathy, hemodynamic aberration, and severe sepsis [1]. Considering the common pathway of liver failure, it can be divided into the following categories: acute liver failure (ALF), acute on chronic liver failure (AoCLF), and end stage liver disease. The etiology of ALF can be primary, such as toxin- or drug-induced insults, fulminant hepatotropic viral infections, and metabolic disorders (like Wilson's disease), and also can be secondary ALF that can arise from cardiovascular reasons such as cardiogenic shock or severe sepsis. AoCLF occurs when a sudden event (gastrointestinal bleeding, alcohol abuse, or infection) leads to the acute deterioration of liver function in patients with pre-existing compensated chronic liver disease or cirrhosis [2].

Since 1970s, plasmapheresis was clinically endeavored for treatment of fulminant liver insufficiency with moderate results, reaching 40% of survival rate compared to 20–25% with supportive therapy [3]. Bioartificial methods are capable to replace both synthetic and detoxicating function of the liver, but are still in experimental phase and still awaiting widespread human clinical application. Artificial liver supply methods are

already available since 1999, as costly but highly effective choices for temporary treatment of liver failure. These devices are intended to remove both protein-bound and water-soluble toxins, although provide no supplement the synthetic function of the liver. Three systems spread in Europe, each using albumin dialysis. Single pass albumin dialysis (SPAD) uses a continuous veno-venosous hemodiafiltration (CVVH) that contains a standard dialysis solution with additional 4.4% albumin. Molecular adsorbent recirculating system (MARS) uses two dialyzing circuits, an albumin (20%), and a renal circuit. The albumin dialysate is subsequently cleaned by a charcoal and an ion exchanging column. By eliminating bilirubin, ammonia, lactate, aromatic amino acids, and free fatty acids from plasma, detoxication can prevent the patient from the fatal complication of hepatic encephalopathy (HE) and reduce the high mortality rate of brain edema and cerebral herniation. Fractionated plasma separation and adsorption (FPSA) system is different: the patient's albumin is separated across a membrane and then dialyzed through adsorptive columns. This method is used in Prometheus device that combines FPSA method with high-flux hemodialysis [3, 4]. Several publications have arisen in the past decade proving the clinical benefits of each system, but no such a complete and long-term treatment is assured by any of these methods as it is by hemodialysis for end stage renal failure patients.

As formerly mentioned OLT is the best solution for liver failure, but what is to be done when a post-transplant patient is suffering from acute or acute on chronic liver failure? A special category of parenchymal causes for ALF could be the insufficiency of a newly transplanted liver in form of a primary non-function (PNF). PNF occurs in 3–6% after OLT and is a feared complication that can evolve due to organ preservation injury, prolonged cold ischemic time (CIT) or warm ischemic time (WIT), fatty transplanted liver, organ retrieved from extended criteria donor (age, hypernatremia, grafts from donation after cardiac death), and OLT for a very high MELD score recipient. PNF shows the symptoms and signs of ALF with elevated liver transaminase level, jaundice, encephalopathy, coagulopathy, and, in severe cases, renal and respiratory complications [5]. After a successful OLT, long-term survival is greatly influenced by the recurrence of original liver disease. Alcoholism, viral infection, bilio-congestive, and autoimmune disorders can reoccur and lead to the slow deterioration of transplanted liver [6]. Fulminant relapses of these chronic diseases can also appear as AoCLF in transplanted patients as well as in non-transplant patients.

Case Reports

Five hundred and twelve liver transplantations have been performed between 1995 and 2012 in our department. Among these transplantations, 34 were orthotopic liver retransplantation (reOLT), 33 secondary, and 1 tertiary. Among the 34 reOLT cases, the original indication for transplantation was mainly hepatitis C virus (HCV), autoimmune hepatitis, ALF [7], cryptogen cirrhosis, primary sclerosing cholangitis (PSC), and other cholestatic disorders. Seventeen of the reOLTs were done in the early postoperative course (within 3 months) and 17 in the late postoperative period. More than half (60%) of the early retransplantations were needed because of

Table I Data on the presented cases show that subsequent MARS treatments could not stop the progression of liver failure in case 2 and case 3. An increase in MELD score was detected. Regression of MELD score in case 1 could be explained by the short period of time between operations

	Case 1	Case 2	Case 3
Age (by the time of reOLT)	54	65	30
Gender	Male	Female	Female
Primary indication	HCV + alcohol	PBC	PSC
MELD before OLT	12	12	n/a
CIT for OLT	10 h 58 min	6 h 2 min	7 h 44 min
Length of operation	10 h 25 min	5 h 10 min	5 h 25 min
OLT blood transfusion	3200 mL	800 ml	1000 mL
OLT complication	VC anastomosis 2× resuturing	VC anastomosis resuturing, fatty donor liver	None
Inter OLT period	4 days	11 days	7 years
Secondary indication	PNF – ALF	PNF – ALF	PSC – AoCLF
MELD before MARS session	32.50	27.20	29.50
MELD before reOLT	31.10	32.60	32.60
No. of MARS treatments	2	5	4
Renal replacement therapy	Yes	No	Yes
Survival	>14 months	>21 months	26 months

Table II Timing and length of individual MARS treatments for each patient reflect the fulmination of liver failure. In case 1 and case 2, MARS was on subsequent days and less frequent in case 3. In case 1 and case 3, a shorter treatment was given immediately prior to reOLT

	MARS	Preoperative timing (day)	Length (h)
Case 1	MARS I	T-1	8
	MARS II	T	5
Case 2	MARS I	T-7	9
	MARS II	T-6	8
	MARS III	T-5	8
	MARS IV	T-3	7
	MARS V	T-1	8
Case 3	MARS I	T-13	8
	MARS II	T-11	8
	MARS III	T-6	8
	MARS IV	T	5

hepatic artery thrombosis (HAT) [8] and 20–20% for PNF and venous outflow disturbance. Only three of these patients had received extracorporeal liver replacement therapy before reOLT. MARS device was used in a various sequence depending on the clinical status of patients, and also, the duration for application usage also varied. Highlighted data and information are presented in *Table I*, and the timing and length of individual MARS treatments are shown in *Table II*.

Case 1

The first presented patient is a 54-year-old male, who had alcohol-induced chronic liver failure turned to cirrhosis, but also had formerly received interferon therapy as HCV treatment with no response. His clinical status proceeded, while parenchymal and vascular decompensation evolved. Preoperative examinations had proved grade II esophageal varices, type 2 diabetes mellitus, and a recurring hospitalization due to severe hepatic encephalopathy. OLT was performed using cross-clamp method. This is to be mentioned that the upper anastomosis of the vena cava (VC) needed to be resutured twice, with the opening of the pericardium, which led to an extended WIT. During transplantation, excessive amount of blood transfusion was necessary. In the immediate postoperative course, further blood, plasma, and thrombocyte transfusions were needed. After the exclusion of other possible causes, and according to relevant laboratory results, PNF was diagnosed. Urgent MARS treatments were carried out in two sessions, first 3 days after OLT (8-h session) and second on the day of retransplantation, right before the procedure (5-h treatment). ReOLT was performed on the fourth day after primary transplantation requiring further blood transfusion and thrombocyte supplement. During reOLT, the abdominal wall could only be reconstructed with the implantation of dual layer mesh to avoid compression on the liver graft. As the edema of the liver decreased, the mesh was explanted, after a few days. Extended postoperative course included temporary CVVH, hemodiafiltration, and hemodialysis by reason of renal insufficiency, but finally, kidney function became settled. Both synthetic and detoxicating function of the liver improved rapidly after reOLT. The patient was treated for lobar pneumonia and later dismissed in a good status. He does well so far.

Case 2

A 65-year-old woman suffered from primary biliary cirrhosis (PBC) and had been referred to our department. Several endoscopic sclerotherapies were carried out previously, and a splenorenal shunt operation was executed because of portal hypertension and repeated variceal bleeding. The patient underwent OLT in 2011, when a 22-year-old brain-dead donor was offered with a moderate fatty donor liver. OLT was performed with cross-clamp technique. The preexisting splenorenal shunt was not ligated during the operation. This decision later turned out to be a mistake. During the suturing of the upper VC anastomosis, some technical difficulties had arisen for what the resuturing became necessary with a prolonged WIT. During the next days, initial poor function (IPF) of the transplanted liver was detected, with permanently increased serum bilirubin and INR, and a concomitant diminished portal flow. This was due to the formerly processed and still working splenorenal shunt. Radiological interventions were used to reduce the circulation of the shunt and strengthen portal flow, with a moderate success. MARS treatment was five times subsequently performed to reduce toxic substance levels and consequent encephalopathy. By this time, the outflow from the liver graft via the re-sutured VC anastomosis became normal.

After several days of deteriorating state in spite of all efforts, urgent need for retransplantation was declared with the indication of PNF and compromised portal inflow. By the usage of MARS, the patient had survived until the 11th postoperative day when a suitable donor was reported, and the reOLT was performed, with AB0 identical and CMV +/+ full sized graft, and cross-clamp technique. The postoperative ultrasonography showed an extended subcapsular hematoma in the right lobe, which needed no surgical intervention and dissolved after time. The function of the transplanted liver improved stepwise. Eighteen days after reOLT, suddenly the symptoms of peritonitis appeared; thus, a further urgent reoperation was done. During the operation, the perforation

Table III Serum parameters in effect of MARS treatments. Albumin and INR results are also influenced by exogenous supplement. Decrease in the level of cholinesterase, and the slight increase of ammonia level shows that MARS therapy could not entirely keep up with the progression of liver failure

Parameter	Unit	Before MARS	After MARS	Percent change	*p* Value
Carbamide	mmol/L	20.5 ± 12.0	13.7 ± 6.7	–0.3318	0.0488
Creatinine	μmol/L	213.6 ± 85.7	151.8 ± 51.7	–0.2891	0.0155
Bilirubin, total	μmol/L	411.4 ± 250.0	325.6 ± 156.0	–0.2085	0.0126
Bilirubin, conj.	μmol/L	318.8 ± 237.0	224.0 ± 147.5	–0.2972	0.0077
ALP	U/L	272.7 ± 115.8	234.6 ± 89.5	–0.1397	0.0607
SGOT	U/L	535.5 ± 746.7	375.9 ± 379.7	–0.2981	0.0856
SGPT	U/L	420.2 ± 450.9	368.4 ± 353.7	–0.1232	0.0152
GGT	U/L	108.9 ± 65.0	92.9 ± 54.5	–0.147	0.0210
LDH	U/L	702.0 ± 382.3	462.9 ± 272.4	–0.3406	0.1122
Lactate	mmol/L	7.2 ± 1.5	4.7 ± 1.8	–0.3431	N/A
Cholinesterase	U/L	5897.9 ± 1514.2	5198.5 ± 1348.2	–0.1186	0.0876
Ammonia	μmol/L	73.6 ± 56.4	75.0 ± 49.8	0.019	0.2995
Albumin	g/L	37.3 ± 5.67	43.6 ± 10.33	0.1693	0.0247
INR		1.8 ± 0.6	1.9 ± 0.5	0.0875	0.2443
MELD		32.1 ± 4.5	28.4 ± 4.2	–0.1144	0.028

of the transverse colon was diagnosed and a biluminar transversostomy was created. The patient was then treated extensively in our intensive care unit, due to critical illness neuropathy, that occurred with the paresis of the lower limbs, besides deep vein thrombosis and Herpes zoster infection. Finally, the patient was dismissed with minor remnant complaints. Long-term follow-up recorded full recovery.

Case 3

Young female patient suffering from primary sclerosing cholangitis (PSC) had received a full sized AB0 compatible cadaver liver graft OLT at the age of 23. Three years later, the possible relapse of PSC and the obstruction of common bile duct were justified; thus, a choledochojejunostomy was performed. Since then, a more frequent hospitalization was necessary due to recurrent ascending cholangitis. Seven years after the primary OLT, the patient's status has gradually deteriorated. After admission for symptoms of cholangitis, a rapidly worsening hepatic function was observed, and despite proper intensive care, ALF with encephalopathy had evolved. ReOLT was decided due to the possible relapse of PSC, and the vanished bile ducts syndrome, with jaundice, and the signs of AoCLF. Four sessions of consecutive MARS treatment were necessary until a proper donor has been reported, and the urgent reOLT was performed. The operation was carried out with the cross-clamp technique, and the bile ducts were reconstructed via hepatico-jejunostomy using the formerly created jejunum limb. In the early postoperative period, a reoperation was done to evacuate an intraabdominal hematoma. Further, a histologically verified, mild (1/9 grade) acute rejection was treated with steroid bolus (3 times 1000 mg Solu Medrol), and due to kidney impairment, hemodialysis was necessary twice. The patient left our departments with no complaints.

One year after reOLT, the formerly known, but remittent ulcerative colitis relapsed. The adequate drug therapy was administered. Two years after reOLT, the patient was admitted to our hospital for manifest ascending cholangitis and bile duct obstruction had developed. The conclusion was the diagnosis of repeated relapse of PSC. The percutaneous transhepatic drainage of biliary system was done, but besides adequate therapy (hemodialysis, plasma pheresis, and steroid treatment), a progressive AoCLF, septic status, and consecutive HRS and HE evolved. Hemodialysis, plasmapheresis, and steroid treatment were induced. Due to severe gastrointestinal bleeding from the colon, an urgent subtotal colectomy was done, and also an almost immediate reoperation afterwards due to bleeding complication. The histology has proved the severe (Mayo score: 3) relapse of ulcerative colitis of the entire colon. In spite of the further intensive care, the patient's status deteriorated, and MOF evolved. Contraindication for tertiary liver transplantation was declared with the reason of septicemia, expected prognosis, and surgical technical considerations together. The patient shortly passed away.

Laboratory tests were made before and after each MARS treatment, in case of all patients and cases. Data are summarized in *Table III*. Serum levels, of renal function parameters, liver enzymes, bilirubin, and lactate dehydrogenase (LDH), and lactate levels all decreased after

MARS treatment. Decrease was significant ($p < 0.05$) for carbamide, creatinine, total and conjugated bilirubin, SGPT and GGT compared to the initial blood level. On the other hand, it is to be noticed, that serum ammonia levels did not show decrease, but a slight, non-significant (from 73.6 ± 56.4 μmol/L to 75.0 ± 49.8 μmol/L, $p = 0.2995$) increase was observed, showing that MARS treatment could not keep up with the progression of ALF. INR showed a negligible (8.75%, $p = 0.2443$) increase after MARS. MARS therapy did not substitute the synthetic function of the liver, and the decrease of cholinesterase level (from 5897.9 ± 1514.2 U/L to 5198.5 ± 1348.2 U/L, $p = 0.0876$) reflects a perishing change in liver's synthetic function. The considerable ($p = 0.0247$) elevation of albumin levels could not be effected by MARS, but rather by the simultaneous supplement therapy. According to the results, the calculated MELD score before and after MARS treatments showed a minimal, but significant decrease (32.1 ± 4.5 to 28.4 ± 4.2, $p = 0.0287$). It is obvious that the separate MARS treatments' detoxicating effect together with supplemental therapy slows down the course of liver failure. Comparison of *Table I* and *Table III* draws to attention, that the individual MARS treatments were effective in diminishing the blood level of toxic substances; therefore, a decrease in average calculated MELD score was also observed. In spite of this fact, the complete sequence of MARS therapy could not reverse the progression of the liver failure. Thus, the reOLT was performed besides an increased MELD score compared to the one before MARS therapy. For case 2 and case 3, it is to be mentioned, that more time had passed in the state of a liver failure, proving that the natural process of liver insufficiency irreversibly deteriorates along with the applied MARS therapy.

Discussion

Several publications refer on the efficacy and effect of extracorporeal liver supplementary device therapy. Indication for application of such devices is ALF, AoCLF, HE, HRS, and less likely drug intoxication. Also, a possible application is a temporary treatment after extended hepatic resections until the regeneration of the liver. It is already proven that water-soluble and albumin-conjugated toxin elimination in liver failure patients are all performed by SPAD, MARS, and Prometheus as well [9, 10]. Although slight differences are also shown, according to published studies, Prometheus system seems to be more effective in eliminating albumin bound toxin levels (ammonia, direct bilirubin, and urea) than MARS [2, 9, 11]. In the three cases of our study, we found that both direct and indirect bilirubin, lactate, and both creatinine and urea levels significantly decreased; however, the serum ammonia level slightly increased.

Hepatic encephalopathy evolves in the basis of high toxin levels in the serum that leads to cerebral edema. Wang et al. presented a summary of 252 cases of acute liver failure patients treated with MARS and proved the decrease of hepatic encephalopathy [12]. Kantola et al. [17] had come to the same conclusion regarding the effect of MARS on HE. On the other hand, it turned out that HE is the second, the most important prognostic factor in the survival of LF, besides the etiology itself. They also declared that MARS treatment is ineffective in case of AoCLF, unless a coming OLT is in sight [13]. Publications are controversial about the effect of MARS on HRS by eliminating vasodilatating substances. While Wang et al. [12] found MARS to have a beneficial effect on HRS, Wong et al. [14] observed six patients with refractory ascites and cirrhosis, and although he found decrease in the serum nitrogen-oxide levels, no significant difference was observed in the neurohormone and cytokine levels; thus, no effect on HRS could be proved clearly [14]. Several studies refer to cytokine (IL-1, IL-6 IL-10, and TNF-α) levels decreased by MARS [14, 15].

In terms of survival, Hessel et al. reported an analysis of 149 patients with AoCLF of which 67 had received MARS therapy. A gain of 0.66 life years was calculated in favor to the MARS-treated patients compared to those who were only treated with standard medication. This report also showed the acceptable cost effectiveness of MARS [16]. Kantola et al. summarized a 10-year experience and referred to a 6-month improvement of patient survival, both with or without OLT [17]. Several analyses refer to the suitability of MARS for patients suffering from AoCLF for any reasons and ALF due to graft failure of a transplanted liver or for other reasons. As we found in our cases, these publications also show that, in terms of survival, the use of MARS alone is not effective enough due to MOF, but the application of MARS followed by a OLT/reOLT procedure is highly successful [13, 17, 18].

More and more centers report on successful treatments with MARS as a bridging therapy prior to OLT. Liu et al. reported two cases of liver transplant patients who suffered PNF after transplantation possible due to extended cold ischemic time. They used MARS as a bridging therapy to reOLT [19]. Ding et al. reported 8 cases with AoCLF who were treated with MARS, and then successful OLT was performed [20]. Novelli et al. reported a series of 18 patients after OLT, suffering from PNF and getting continuous MARS treatment. In this study, 11 patients survived, 6 with retransplantation and 5 without it. Of the 7 patients who died, 4 had passed after and 3 before reOLT [21]. We presented two cases of post-transplant patients who underwent OLT and acute liver failure by PNF, possibly evolved due to the combination of prolonged warm ischemic time, usage of an extended criteria donor organ, and surgical complications. Both patients were treated with MARS, multiple

times for ALF as a bridging therapy to successful reOLT, which was performed within a few days. Both of them has fully recovered and still alive to date.

The third introduced case was a young female who were 7 years after the primary liver transplantation. The possible recurring chronic liver disease (PSC) turned into a fulminated clinical setting because of the repeated cholangitis and this deterioration led to an AoCLF. A series of MARS treatment was performed to gain time before liver retransplantation could be performed. Twenty-five months of disease free survival was recorded after reOLT when the recurring PSC, and cholangitis finally developed fatal MOF. All three patients were effectively treated with MARS and obviously showed us that, together with conventional renal replacement therapy and good conventional intensive care, MARS is a suitable bridging therapy before liver retransplantation for graft failure ALF or AoCLF patients.

Abbreviations

ALF: acute liver failure; AoCLF: acute on chronic liver failure, CIT: cold ischemic time; CVVH: continuous veno-venosous hemodiafiltration; FPSA: fractionated plasma separation and adsorption; HE: hepatic encephalopathy; HPS: hepatopulmonary syndrome; MARS: molecular absorbent recirculating system; HRS: hepatorenal syndrome; MOF: multiorgan failure; OLT: orthotopic liver transplantation; PNF: primary non-function; reOLT: orthotopic liver retransplantation; SPAD: single pass albumin dialysis; VC: vena cava, WIT: warm ischemic time

References

1. Tan HK: Molecular Absorbent Recirculating System (MARS). Ann Acad Med Singapore 33, 329–335 (2004)
2. Rademacher S, Oppert M, Jörres A: Artificial extracorporeal liver support therapy in patients with severe liver failure. Expert Rev Gastroenterol Hepatol 5(5), 591–599 (2011)
3. Schuller J: Szupportív májpótló eljárások a fulmináns májelégtelenség kezelésében. LAM 20(2), 137–142 (2010)
4. Karvellas CJ, Gibney N, Kutsogiannis D, Wendon J, Bain VG: Bench-to-bedside review: Current evidence for extracorporeal albumin dialysis systems in liver failure. Crit Care 11(3), 215 (2007)
5. Schiff ER, Maddrey WC, Sorrell MF (2012): Schiff's Diseases of the Liver, Eleventh Edition. Wiley-Blackwell, John Wiley & Sons Ltd., Cvicester, West Sussex, UK
6. Nemes B, Sótonyi P, Lotz G, Heratizadeh A, Gelley F, Doege C, Hubay M, Schaff Zs, Nashan B: Localization of apoptosis proteins and lymphocyte subsets in chronic rejection of human liver allograft. IMAS 2(2), 77–84 (2010)
7. Nemes B, Zádori G, Görög D, Fehérvári I, Kóbori L, Langer RM: Liver transplantation for acute liver failure: The Hungarian experience. Transplant Proc 43(4), 1278–1280 (2011)
8. Doros A, Nemes B, Máthé Z, Németh A, Hartmann E, Deák PÁ, Lénárd ZsF, Görög D, Fehérvári I, Gerlei Zs, Fazakas J, Tóth Sz, Kóbori L: Treatment of early hepatic artery complications after adult liver transplantation: A single center experience. IMAS 2(4), 159–164 (2010)
9. Rifai K, Manns MP: Review article: Clinical experience with Prometheus. Ther Apheresis Dial 10(2), 132–137 (2006)
10. Evenepoel P, Laleman W, Wilmer A, Claes K, Maes B, Kuypers D, Bammens B, Nevens F, Vanrenterghem Y: Detoxifying capacity and kinetics of prometheus – A new extracorporeal system for the treatment of liver failure. Blood Purif 23(5), 349–358 (2005)
11. Bacher A, Zimpfer M: Hot topics in liver intensive care. Transplant Proc 40, 1179–1182 (2008)
12. Wang MM, Chen SJ, Ye QF, Yang YJ, Chen SB, Zhou XM, Guo LM, Zhang YX, Ding XQ, Hu XB, Luo HT, Liu YH, Wang WY: Liver support therapy with molecular adsorbents recirculating system in liver failure: A summary of 252 cases from 14 centers in China. Chin Med J 121(21), 2197–2201 (2008)
13. Kantola T, Koivusalo AM, Parmanen S, Höckerstedt K, Isoniemi H: Survival predictors in patients treated with a molecular adsorbent recirculating system. World J Gastroenterol 15(24), 3015–3024 (2009)
14. Wong F, Raina N, Richardson R: Molecular adsorbent recirculating system is ineffective in the management of type 1 hepatorenal syndrome in patients with cirrhosis with ascites who have failed vasoconstrictor treatment. Gut 59(3), 381–386 (2010)
15. Novelli G, Annesini MC, Morabito V, Cinti P, Pugliese F, Novelli S, Piemonte V, Turchetti L, Rossi M, Berloco PB: Cytokine level modifications: Molecular adsorbent recirculating system versus standard medical therapy. Transplant Proc 41, 1243–1248 (2009)
16. Hessel FP, Bramlage P, Wasem J, Mitzner SR: Cost-effectiveness of the artificial liver support system MARS in patients with acute-on-chronic liver failure. Eur J Gastroenterol Hepatol 22(2), 213–220 (2010)
17. Kantola T, Ilmakunnas M, Koivusalo AM, Isoniemi H: Bridging therapies and liver transplantation in acute liver failure 10 years of MARS experience from Finland. Scand J Surg 100(1), 8–13 (2011)
18. Gaspari R, Cavaliere F, Sollazzi L, Perilli V, Melchionda I, Agnes S, Gasbarrini A, Avolio AW: Molecular Adsorbent Recirculating System (MARS) in patients with primary nonfunction and other causes of graft dysfunction after liver transplantation in the era of extended donor criteria. Transplant Proc 41, 253–258 (2009)
19. Liu YH, Wang Y, Yu LX, Sun LY, Feng BL, Shen ZY, Wang MM: Artificial liver support molecular adsorbents recirculating system therapy as a bridge to re-transplantation in two cases of long anhepatic duration. Hepatobiliary Pancreat Dis Int 3(2), 316–317 (2004)
20. Ding YT, Xu QX, Qiu YD, Yang YJ: Molecular adsorbent recycling system in treating patients with acute liver failure: a bridge to liver transplantation. Hepatobiliary Pancreat Dis Int 3(4), 508–510 (2004)
21. Novelli G, Rossi M, Poli L, Morabito V, Bussotti A, Pugliese F, Ruberto F, Novelli S, Mennini G, Berloco PB: Primary nonfunction: timing retransplantation versus hemodynamic parameters and kidney function. Transplant Proc 40, 1854–1857 (2006)