university of groningen

University Medical Center Groningen

University of Groningen

Anesthesia for combined liver-thoracic transplantation

Zeillemaker-Hoekstra, Miriam; Buis, Carlijn I.; Cernak, Vlado; Reyntjens, Koen Mem.

Published in:
Best practice & research. Clinical anaesthesiology

DOI:
10.1016/j.bpa.2020.01.001

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Zeillemaker-Hoekstra, M., Buis, C. I., Cernak, V., & Reyntjens, K. M. (2020). Anesthesia for combined liver-thoracic transplantation. *Best practice & research. Clinical anaesthesiology*, *34*(1), 101-108. https://doi.org/10.1016/j.bpa.2020.01.001

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 05-06-2022

Best Practice & Research Clinical Anaesthesiology 34 (2020) 101–108

Contents lists available at ScienceDirect

Best Practice & Research Clinical Anaesthesiology

journal homepage: www.elsevier.com/locate/bean

9

Anesthesia for combined liver-thoracic transplantation

Miriam Zeillemaker-Hoekstra, MD, PhD, Consultant Anaesthetist [a], Carlijn I. Buis, MD, PhD, Consultant Surgeon [b], Vlado Cernak, MD, Consultant Anaesthetist [a], Koen MEM. Reyntjens, MD, Consultant Anaesthetist [a, *]

[a] *Department of Anesthesiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands*
[b] *Department of Surgery, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands*

Keywords:
Combined liver – thoracic organ transplant
Combined liver – lung transplant
Combined liver – heart transplant

The combined transplantation of a thoracic organ and the liver is performed in patients with dual-organ failure in whom survival is not expected with single-organ transplantation alone. Although uncommonly performed, the number of combined liver-lung and liver-heart transplants is increasing. Anesthetic management of this complex procedure is challenging. Major blood loss, prolonged operation time, difficult weaning of cardiopulmonary bypass and coagulation disturbances are common. Despite the complexity of surgery, the outcome is comparable to single-organ transplant.

© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Transplantation of the liver combined with a thoracic organ (cLiThTx) is a life-saving intervention for patients with dual-organ failure who are unlikely to survive the transplantation of a single organ. This complex procedure is increasingly performed as the number of patients on the waiting list is

* Corresponding author. Department of Anesthesiology, University Medical Center Groningen, University of Goningen, Hanzeplein 1, 9700RB, Groningen, the Netherlands.
E-mail addresses: m.zeillemaker@umcg.nl (M. Zeillemaker-Hoekstra), c.i.buis@umcg.nl (C.I. Buis), v.cernak@umcg.nl (V. Cernak), k.m.e.m.reyntjens@umcg.nl (K.MEM. Reyntjens).

https://doi.org/10.1016/j.bpa.2020.01.001
1521-6896/© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

growing [1]. The anesthetic management of this complex procedure in patients with dual-organ failure is challenging. This review provides an overview of anesthetic management of cLiThTx.

Background

The first successful combined liver-heart transplantation (cLiHTx) was performed in 1984 on a 6-year-old girl with severe heart disease secondary to familial hypercholesterolemia [2,3]. The donated liver and heart were from the same donor and were transplanted on cardiopulmonary bypass (CPB) during a 15-h procedure. They started with the heart, and once function of the new heart was sufficient, the new liver was transplanted with the patient still on CPB. She was discharged from the hospital in good clinical condition 28 days after surgery. Unfortunately, two unsuccessful cases around this time were also reported. Major factor contributing to the fatal outcome of both cases was a size mismatch between donor and recipient [3]. From 1984 to 2000, only 12 cases of cLiHTx are reported [4]. However, over the last decade the number of combined cLiHTx is growing fast. The Organ Procurement and Transplantation Network reports a total number of 312 cLiHTx in the United States since 1992 [5]. For Europe, Eurotransplant report the first cLiHTx in 2010, with a total of 11 cLiHTx up to this date [6]. In the United States, experience with combined liver-lung transplantation (cLiLuTx) is even more limited. Between 1994 and 2016 only 84 cLiLuTx were performed. For Europe, the number of reported cLiLuTx is higher than the number of cLiHTx. Since 2009, Eurotranplant reports 114 cases of cLiLuTx.

Population

Advanced heart disease in liver transplant candidates or severe liver disease in heart transplant candidates are indications for cLiHTx. Likewise, advanced pulmonary disease in liver transplant candidates or severe liver disease in liver transplant candidates are indications for cLiLuTx. In the majority of cases, the cardiac or pulmonary indication for transplantation carries more weight than the liver indication. For instance, in a case with amyloidosis with restrictive cardiomyopathy, the liver is structurally normal but is transplanted to treat the underlying metabolic condition. Therefore, in cLiThTx Model for End-stage Liver Disease (MELD) scores are significantly lower compared to single-organ liver transplant.

The largest cohort of cLiHTx ($n = 97$) is described by Cannon et al. [7]. The most common indications for cardiac transplantation were amyloidosis (27%), congenital cardiac disease (18%), and idiopathic dilated cardiomyopathy (14%). For the liver, the most common indications for transplantation were amyloidosis (28%), cardiac cirrhosis (18%), and chronic hepatitis C (12%). Of the recipients, 70% was male, with a mean ± SD age of 44 ± 16. Cardiac output at registration was 4.5 ± 1.6 L/min, with 25% of the patients on inotropic support and 4% had a ventricular assist device.

Over the last decade, cLiHTx is increasingly performed in patients with severe congenital heart disease (CHD). Improved medical care increased the number of living adults with CHD. Adult patients with a failing Fontan circulation are known to develop advanced liver disease [8]. In CHD, cardiac cirrhosis is the most common hepatic indication for cLiHTx [9]. Compared to patients without CHD, transplanted patients with CHD are significantly younger with a lower Pulmonary Artery (PA) wedge pressure and PA mean pressure [10,9]. MELD scores and other parameters of liver function are comparable [10].

For cLiLuTx pulmonary indications are Cystic Fibrosis and α1-antitrypsin deficiency accompanied by cirrhosis. Indications with end-stage liver disease with pulmonary compromise are portopulmonary hypertension and hypoxia caused by intrapulmonary shunting [11,12]. Cystic Fibrosis is by far the most common indication for cLiLuTx. Around 10% of patients with cystic fibrosis develop cirrhosis, and it is the second cause of death in these patients. For both cLiHTx and cLiLuTx, there are no clear criteria for listing, so guidelines for listing vary by institution.

Preoperative

The decision to perform a combined transplantation results from the fact that the individual organs are too sick to support the effects of a sequential transplantation strategy: the cirrhotic liver does not tolerate a CPB procedure well and patients with end stage liver disease in need of a lung or

heart transplant are too sick to tolerate a liver transplant procedure. Prior to listing, a full preanesthetic evaluation is mandatory. Preoperative evaluation essentially consists of screening of the functional status of the individual organs to be transplanted. A full screening list consists of (but is not limited to):

- Cardiopulmonary exercise testing
- Cancer/malignancy screening
- Evaluation of end organ effects of chronic disease
- Pulmonary function testing
- Hemodynamic evaluation by cardiac catheterization
- Liver biopsy
- INR and metabolic panel to calculate the MELD score
- Thrombocyte count (portal hypertension-related thrombocytopenia)
- Serologic workup for underlying liver diseases (viral or other)
- Abdominal imaging: spleen size, liver nodules or masses, and ascites

A multidisciplinary approach to patients undergoing organ transplantation has proven its benefits over years. In that sense, the pre- per- and postoperative approach of single-organ transplantations has become more or less a routine in transplant centers around the world.

However, it would be unwise to copy paste this approach to combined transplantations. It is our conviction that the preoperative approach should be two folded: at the transplant listing meeting, test results and possible perioperative issues should be discussed (difficulty of resection, ascites, and vascular access). As the team discussing the patient at the listing meeting is possibly not the team actually performing the transplantation procedure, a second meeting, hours in advance of the procedure, with the actual transplantation team, is of inestimable value. The team can discuss the actual status of the patient, vascular access, plan for emergency cannulation, back-up plan, and management of coagulopathy, and estimate the time needed for anesthesia preparation and surgical dissection prior to organ arrivals. The introduction of new machine organ perfusion techniques can help to facilitate this phase of the procedure. Machine perfusion is revolutionizing in the field of liver transplantation and is undergoing rapid clinical implementation [13]. First clinical experiences suggest that machine perfusion results in superior outcome, compared to the transplantation of static cold storage-only preserved human livers [14,15]. *Ex situ* machine perfusion strategies allow among others reconditioning of livers prior to transplantation, rather than standard cold storage alone. Oxygenated machine perfusion could restore mitochondrial function and increase endothelial function and integrity, thereby alleviating the inflammatory response upon reperfusion.

Intraoperative

Surgical considerations

A cLiThTx is performed under the same operative setting. As the acceptable cold ischemic time for lungs and hearts is shorter than for the liver, traditionally the heart or lungs are transplanted prior to the liver. Also, a severely insufficient heart is unlikely to tolerate the hemodynamic changes during transplantation of the liver. In the earliest cLiHTx cases, dissection of the abdomen and chest was performed before arrival of the organs. Both the heart and liver transplants were performed on CPB under full heparinization [2,3]. The liver is done with a piggyback or standard bi-caval technique, with or without veno-venous bypass. For the heart, the bi-caval implantation technique is most often used (70%) [9]. The alternative is the traditional bi-atrial technique. In pediatric cases, the “en-bloc” technique is an alternative in which both the heart and liver are simultaneously implanted on CPB and thereafter simultaneously reperfused [16]. With the growing experience with organ perfusion, the possibility arises to transplant the liver prior in selected patients. The “liver-first” technique was described by Ceulemans et al. who did their first “liver-first” case in a 62-year-old patient with end-stage chronic obstructive pulmonary disease who developed drug-induced acute liver failure during her workup for a bilateral lung transplant [17,18]. The only life-saving therapeutic option was to

combine a lung and liver transplant and she was listed with a high urgency status. Four days later, a liver graft and bilateral lung grafts became available for transplantation. Severe bleeding was anticipated in the recipient because of liver failure-induced severe coagulation disorder, so the decision was made to transplant the liver first while the lungs were on normothermic perfusion and oxygenation [17,18]. Although the liver-first technique is increasingly performed, the standard procedure remains to transplant the lungs prior to the liver. In most cases of cLiLuTx, both lungs are transplanted. The commonly described technique is to transplant the lungs with or without the use of CPB and leaving the chest open prior to liver transplant. An alternative is to close the chest prior to liver transplant to prevent contamination [19]. Some cases describe that the abdominal dissection is performed prior to transplanting the lungs or heart. In case of cLiHTx, this provides the opportunity to perform the abdominal dissection prior to full heparinization for CPB. Abdominal dissection prior to the implantation of the lungs minimized the time that the new lungs are exposed to fluid resuscitations and transfusion of blood products.

Anesthetic management

A liver transplantation with a newly transplanted heart or lung is challenging. The new organ is still recovering from reperfusion. A newly transplanted heart is prone to fluid overload, arrhythmia, and right ventricular failure. Instead of stabilizing at the intensive care unit (ICU), the new heart is subjected to major stressors during subsequent liver transplantation. First, major blood loss and subsequent hypovolemia can accompany the dissection phase. A decrease in preload, as in inferior vena cava clamping is not well tolerated. On the other hand, the volume overload during reperfusion can lead to right ventricular failure. Electrolyte disturbances and acidosis associated with the anhepatic phase and major blood loss can make the heart prone for arrhythmias. In the case of a cLiLuTx, the new lungs are prone to suffer fluid overload if large amounts of fluids are required during liver transplant. This can lead to pulmonary edema and a prolonged time to extubation [20]. Primary graft dysfunction can occur shortly after pulmonary reperfusion. In patients with severe hypoxia inhaled NO is indicated. Extracorporeal life support (ECLS) during liver transplant is indicated in patients with severe hypoxia and/or hypercapnia as severe hypoxia can lead to right ventricular failure and cerebral damage. Moreover, reperfusion of the liver can lead to a sudden increase in cardiac output with high risk of pulmonary shunting, pulmonary hypertension, and pulmonary edema.

The other way around, it is well recognized that patients with severe liver disease are at high risk for morbidity and mortality during cardiac surgery [7,21]. Because of cirrhosis-induced coagulopathy bleeding complications are common and avoiding the use of CPB, if possible, is advised. During cardiac surgery, the physiology of portal hypertension is complicating hemodynamic management and increasing the risk of major bleeding. Patients with end-stage cirrhosis are in a hyperdynamic with a high cardiac output and a low vascular resistance requiring increased vasopressor requirements.

After the first cLiHTx in 1984, several case reports and small series have described surgical management of this complex procedure. The first report focusing on anesthetic management of a cLiHTx was published in 2007, describing the anesthetic considerations of the intraoperative management of a 50-year-old patient with hepatitis C who developed right ventricular failure related to tricuspid valve endocarditis [22]. Since then, reports focusing on the anesthetic management of cLiThTx are still limited. In 2011, Eyraud M et al. describe perioperative management in 3 cLiHTx patients [23]. In those patients, intraoperative hemodynamics were stable, with a mean transfusion need of 12 units of red blood cells. Barbara et al. describe the intraoperative details of 27 cLiHTx patients [24]. Of those, 70% was on inotropic support prior to surgery. Mean $\pm$ SD duration of surgery was 760 $\pm$ 125 min of which 134 $\pm$ 40 min on CPB and 62 $\pm$ 11 min anhepatic. In 2 patients, CPB was used during the liver transplant. Also, in 2 patients inhaled NO was given during liver transplant. Anesthesia was maintained with isoflurane in all cases. Various combinations of inotropic infusions were described, most often involving a positive inotropic and chronotropic agent.

In general, during the induction of anesthesia most patients are on standard noninvasive monitoring. Placing a double-lumen tube is required in case of a cLiLuTx. After induction of 2 arterial lines, a

large peripheral cannula and a central venous catheter (internal jugular vein) are inserted. A PA catheter is useful to monitor cardiac function. Transesophageal echocardiography can be used to monitor filling status, right ventricular function, and the presence of intracardiac thrombi. Continuous monitoring of fluid status is necessary to balance fluid management. As intraoperative coagulopathies are complex, thromboelastography is a valuable tool to guide transfusion management.

There are no recommendations for the general anesthetic management of cLiLuTx, except some reports addressing the mechanical circulatory support. In cLiHTx, performing the entire procedure on CPB offers the advantage of lessening the cardiac stress (hyperkalemia, acidosis, and fluid overload) during hepatic reperfusion. Currently, in most cases CPB is discontinued and anticoagulation is reversed before starting the liver transplant. An alternative is the extended use of CPB with partial flow during liver transplant providing hemodynamic or respiratory support. During CPB, full heparinization is required. After weaning from CPB, heparin is reversed to prevent major blood loss during hepatic dissection and the anhepatic phase. If liver transplant is performed under ECLS, anticoagulants are required, although less than on CPB. For lung transplant, the current standard of care for mechanical circulatory support is ECLS [25]. In 2016, Scheiermann et al. [26] describe the case of a cLiLuTx in which the liver transplantation was successfully performed under ECLS instead of CPB. Venous-arterial extracorporeal life support (vaECLS) with central cannulation was initiated prior to liver transplant because of extensive pulmonary reperfusion edema, pulmonary hypertension, and right heart failure. The patient was successfully weaned from ECLS on the second postoperative day. Despite extensive transfusion requirements and a rethoracotomy, the liver and lungs functioned sufficiently. The decision to use any form of mechanical hemodynamic support during cLiLuTx depends on the clinical status of the patient. In patients with severe pulmonary hypertension, right heart dysfunction, hypoxia, and hemodynamic instability could be indications.

Postoperative

The immediate postoperative care at the ICU is critical in the management of multiorgan transplant patients. Intraoperative hemodynamic monitoring and close monitoring of the function of the two new organs should be continued in the ICU. In the early postoperative period, high levels of inotropic support are often described. Bleeding complications are frequent and a significant number of the described cases require a rethoracotomy. Compared to single-organ liver transplantation, the ICU length of stay is prolonged. Complications associated with liver transplantation are primary graft failure, portal vein thrombosis, and hepatic artery thrombosis. Infectious complications are frequent after lung transplantation. Specific postoperative details of a cohort of 7 CHD (Fontan) patients after cLiHTx were described by D'Souza et al., in 2016 [27]. Median hospital length of stay was 29 days (25–112). Acute kidney injury was the most common postoperative complication (4 out of 7 patients), with 2 patients developing chronic kidney disease without the need for dialysis. Massive postoperative transfusion was required in 3 patients. Three patients had vocal cord dysfunction and 2 patients required a laparotomy because of pneumoperitoneum. In the cohort of 27 cLiHTx patients described by Barbera et al., in 2015, all patients were transferred to the ICU still intubated, ventilated, and sedated. Five of twenty-seven patients required renal replacement therapy and none of the patients required a tracheostomy. There was only a minor transfusion requirement with a median of 2 units of red blood cells during the first 48 h. One patient died within 30 days because of neurological damage and multiorgan failure after surgery complicated by major blood loss after reperfusion and an intracardiac thrombus resulting in right ventricular failure. The immunosuppression protocol is that used for the heart or lung transplant because of the greater tendency of rejection compared to the liver.

Outcome

The largest multicenter cohort uses the UNOS database to describe the outcome after cLiHTx. Between 1987 and 2010, 97 cLiHTx were performed in the United States [28]. Of those 97 transplants, 10 patients received a simultaneous kidney transplant and lungs were simultaneously transplanted in 11 cases. Both liver and heart graft survival were comparable to single-organ transplantation. Patient

survival after 5 years was 72.3% for cLiHTx, 72.4% for liver alone, and 64.8% for heart alone. Although not statistically significant, there was a trend toward a better outcome for patients with amyloidosis. In the largest described cohorts of patients with CHD undergoing cLiHTx, survival rate is comparable to those without CHD and to those who received a single-organ heart transplantation [9,10]. Interestingly, in this relatively large cohort, lower rates of acute cardiac rejection were observed after simultaneous transplantation of the liver. This phenomenon is also observed in a cohort of 40 propensity-matched patients with CHD after cLiHTx compared to heart transplantation alone: acute rejection episodes and treatment for rejection within the first year post transplant were significantly lower [9]. The exact mechanism is unknown; however, the liver seems to play a key role [28]. For cLiLuTx, there is no available evidence comparing combined transplant with lung alone. In comparison with liver alone, cLiLuTx has comparable 1- and 5-year survival [29].

Future

- The number of patients on the waiting list for CLiThTx is increasing.
- Machine organ perfusion in the setting of combined organ liver-thoracic transplantation may optimize the donor organ by preconditioning prior to transplantation, and allows the liver transplant team a superior way of preservation of the liver during the waiting time of the thoracic organ transplantation. Machine organ perfusion of the lungs could make it possible to change the order to liver-first instead of lung-first in specific cases.
- Liver transplantation under mechanical hemodynamic support is indicated when the newly transplanted heart or lungs need extra support. Possible indications are hypoxia, pulmonary edema, pulmonary hypertension, and (right) heart failure.
- Centers performing cLiThTx should report on perioperative management and complications. The currently available reports are limited.

Summary

CLiThTx are increasingly performed, although total numbers are still low. This increase has multiple causes like the improved life expectancy of patients with cystic fibrosis and adults living with CHD who develop dual organ failure. Anesthetic management of cLiHTx and cLiLuTx transplantation is challenging. Patients have (at least) two failing organs and markedly impaired physiological reserve. Prior to surgery, good coordination between all surgical and anesthetic teams is of utmost importance. Major blood loss, prolonged operation time, pulmonary edema, right ventricular failure, and coagulation disturbances are common. Despite the complexity of the procedure, outcome is equivalent to single-organ transplant making it a feasible option for patients with coexisting organ failure. There is a possible immunological advantage by transplanting two organs from the same donor.

Abbreviations

cLiThTx	Combined liver-thoracic transplantation
cLiHTx	Combined liver-heart transplantation
cLiLuTx	Combined liver-lung transplantation
MELD	Model for End-stage Liver Disease
SD	Standard deviation
CPB	cardiopulmonary bypass
ECLS	Extracorporeal life support
vaECLS	venous-arterial extracorporeal life support
ICU	Intensive care unit
CHD	Congenital Heart Disease
ESLD	End-stage liver disease
CHD	Congenital Heart Disease
COPD	Chronic Obstructive Pulmonary Disease

Role of the funding source

No funding.

Declaration of Competing Interest

None declared.

Practice points

- Combined transplantation of the liver and heart and/or lungs are increasingly performed; however, the absolute number is still small.
- The results are comparable to single-organ transplantation.
- There may be a protective effect against pulmonary or cardiac rejection by the simultaneously transplanted liver.
- cLiHTx results in patients with CHD being compared to transplanted patients without congenital disease.

Research agenda

- Collecting and reporting multicenter data on perioperative and ICU management, as the total number per center is limited.

Acknowledgments

None.

References

[1] Wolf jh, Sulewski ME, Cassuto JR, et al. Am J Transpl 2013;13:1806–16.
[2] Startzl T, Bahnson HT, Hardesty RL, et al. Heart-liver transplantation in a patient with familial hypercholesterolaemia. Lancet 1984;23:1382–3.
[3] Shaw Jr BW, Bahnson HT, Hardesty RL, et al. Combined transplantation of the heart and liver. Ann Surg 1985;202(6):667–72.
*[4] Befeler AS, Schiano TD, Lissoos TW, et al. Successful combined liver-heart transplantation in adults: report of three patients and review of literature. Transplantation 1999;689(9):1423–7.
[5] OPTN data, September 10. https://optn.transplant.hrsa.gov; 2019.
[6] Statistics.eurotransplant.org: 2152P_ All ET_heart. 2019.
[7] Park H, Park J, Lee J, et al. Anesthetic management during the first combined heart- liver transplant performed in Korea - a case report-. Kor J Anesthiol 2017;70(5):571–6.
[8] Mori M, Aguirre AJ, Elder RW, et al. Beyond a broken heart: circulatory dysfunction in the failing Fontan. Pediatr Cardiol 2015;35:569–79.
[9] Bryant R, Rizwan R, Zafar F, et al. Contemporary outcomes of combined heart-liver transplant in patients with congenital heart disease. Transplantation 2018;102:e67–73.
[10] Bradley EA, Pinyoluksana K, Moore-Clingenpeel M, et al. Isolated heart transplant and combined heart liver transplant in adult congenital heart disease patients: insights from the united network of organ sharing. Int J Cardiol 2017;228:790–5.
*[11] Brashes NR, Dibardino DJ, McKenzie ED, et al. Combined lung and liver transplantation: the United States experience. Transplantation 2005;80:1161–7.
*[12] Han JL, Beal EW, Mumtaz K, et al. Combined liver-lung transplantation : indications, outcomes, current experience and ethical issues. Transplant Rev 2019;33:99–106.
*[13] de Meijer VE, Fujiyoshi M, Porte RJ. Ex situ machine perfusion strategies in liver transplantation. J Hepatol 2019;70(1):203–5.
*[14] van Rijn R, Karimian N, Matton APM, et al. Dual hypothermic oxygenated machine perfusion in liver transplants donated after circulatory death. Br J Surg 2017;104:907–17.

[15] Dutkowski P, Polak WG, Muiesan P, et al. First comparison of hypothermic oxygenated perfusion versus static cold storage of human donation after cardiac death liver transplants: an international-matched case analysis. Ann Surg 2015;262:764–71.
[16] Hill AL, Maeda K, Bonham CA, et al. Pediatric combined heart-liver transplantation performed en-bloc: a single center experience. Pediatr Transplant 2012;16:392–7.
[17] Ceulemans LJ, Strypstein S, Neyrink A, et al. Combined liver-thoracic transplantation: single –center experience with introduction of the 'liver-first' principle. Transpl Int 2015;29:715–26.
*[18] Ceulemans LJ, Monbaliu D, Verslype C, et al. Combined liver and lung transplantation with extended normothermic lung preservation in a patient with end stage emphysema complicated by drug induced acute liver failure. Am J Transpl 2014;14(10):2412–6.
[19] Couetil JP, Houssin DP, Soubrane O, et al. Combined lung and liver transplantation in patients with cystic fibrosis. J Thorac Cardiovasc Surg 1995;110:1415–22.
[20] McIlroy DR, Pilcher DV, Snell GI. Does anesthetic management affect early outcomes after lung transplant? Br J Anaesth 2009;102(4):506.
[21] Jacob KA, Hjortnaes J, Kranenburg G, et al. Mortality after cardiac surgery in patients with liver cirrhosis classified by the Child-Pugh score. Interact Cardiovasc Thorac Surg 2015;20(4):520–30.
*[22] Diaz GC, Renz JF, Nishanian E, et al. Anesthetic management of combined heart-liver transplantation. J Cardiothorac Vasc Anesth 2007;21:253–6.
*[23] Eyraud D, Ben Menna M, Vaillant JC, et al. Peri-operative management of combined heart-liver transplantation in patients with cirrhosis, renal insufficiency or pulmonary hypertension. Clin Transpl 2011;25:228–34.
*[24] Barbara DW. The peri-operative management of patients undergoing combined heart-liver transplantation. Transplantation 2015;99:139.
[25] Hoechter DJ, von Dossow V, Winter H, et al. The munich lung transplant group: intraoperative extracorporeal circulation in lung transplantation. Thorac Cardiovasc Surg 2015;63(8):706–14.
[26] Scheiermann P, Czerner S, Kaspar M, et al. Combined lung and liver transplantation with extracorporeal membrane oxygenation instead of cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2016;30(2):437–42.
[27] D'Souza BA, Fuller S, Gleason LP, et al. Single-center outcomes of combined heart and liver transplantation in the failing Fontan. Clin Transpl 2017;31:e12892.
*[28] Rana A, Robles S, Russo MJ, et al. The combined organ effect: protection against rejection? Ann Surg 2008;248:871.
[29] Barshes NR, DiBardino DJ, McKenzie ED, et al. Combined lung and liver transplantation: the United States experience. Transplantation 2005;80(9):1161–7.