DOI: 10.4149/BLL_2020_081

Bratisl Med J 2020; 121 (7)
493 – 498

CLINICAL STUDY

Impact of the venting via vena cava inferior on the outcome of liver transplantation

Janek J[1], Laca L[2], Kminiak R[1], Necpal R[1], Slobodnik I[3], Hampl F[3], Valky J[4], Skladany L[5], Blazej S[6], Dedinska I[2]

Department of Vascular Surgery, F.D. Roosevelt's Faculty Hospital, Banská Bystrica, Slovakia.
idedinska@yahoo.co.uk

ABSTRACT
BACKGROUND: The liver transplantation is a standard treatment method for the indicated group of patients with a final hepatic failure. The aim of this paper was to compare two reperfusion methods of implanted liver, non-venting and venting vena cava, and to evaluate the impact of both techniques on the post reperfusion syndrome.
METHODS: We compared two groups of patients: non-venting (n = 42) and venting (n = 41). We monitored bilirubin, liver enzymes and hemodynamic changes after reperfusion. We recorded monitored parameters immediately prior to the transplantation, during and after the reperfusion and on the 1st postoperative day. All liver grafts were used from the donors after a brain death.
RESULTS: We did not find a statistically significant difference in input monitored parameters. We detected significant changes of pH after reperfusion in both monitored groups. We determined a significantly better saturation in the non-venting group, bigger consumption of fresh frozen plasma and thrombo-concentrate in the non-venting group, a significantly higher value of total bilirubin and a lower value of Quick's time in the non-venting group.
CONCLUSION: Venting via vena cava inferior did not impact the perioperative and early postoperative course of liver transplantation in our group of patients. However, further analyses are required *(Tab. 2, Fig. 3, Ref. 20)*. Text in PDF *www.elis.sk*
KEY WORDS: liver transplantation, venting via vena cava, post reperfusion syndrome.

List of abbreviations: ESLD – End Stage Liver Diseases, UW – University of Wisconsin, HTK – Histidine Tryptophan Ketoglutarate, PRS – post reperfusion syndrome, CTP – Child Turcotte Pugh, MELD – Model of End Stage Liver Diseases, BP – blood pressure

Introduction

Liver transplantation is today considered a life-saving treatment for patients with terminal acute or chronic failure of the liver – ESLD (End Stage Liver Diseases) or for a certain group of patients with tumour diseases (1). The preservation of the liver is a substantial part of the whole transplantation process, because it provides time for the preparation of the recipient and the participating team.

The basic aim of the liver preservation is an immediate onset of its function after implantation in the body of the recipient. A failure of liver after transplantation is divided into three categories: 1. primary graft afunction, which means an irreversible failure of the liver after its transplantation, 2. primary graft dysfunction, which means a partial failure of liver functions, 3. later onset of graft functions, which means the liver starts functioning only after a certain time. The basic strategy for liver preservation today is hypothermia and pharmacological inhibition to slow down metabolic processes during anoxia (2). There are four phases, during which the liver damage occurs, namely:

1. Pre-preservation damage. This phase takes place in the body of the donor. It includes conditions of donor's resuscitation, hypotension and hemodynamic instability.
2. Phase of the preservation during a cold ischemia.
3. Rewarming of the graft during implantation, so-called rewarming injury. This is the phase of implantation (construction of vascular anastomoses) and manipulation with the liver in the body of the recipient, but without connection to circulation of the recipient.
4. This phase is the damage of the liver by the reperfusion – the reperfusion syndrome (3).

[1]Department of Vascular Surgery, F.D. Roosevelt's Faculty Hospital, Banská Bystrica, Slovakia, [2]Department of Surgery and Transplantation Center, University Hospital Martin and Jessenius Medical Faculty of Comenius University, Slovakia, [3]Department of Surgery, F.D. Roosevelt's Faculty Hospital, Banská Bystrica, Slovakia, [4]Department of Anesthesiology and Intensive Medicine, F.D. Roosevelt's Faculty Hospital, Banská Bystrica, Slovakia, [5]Internal Department, F.D. Roosevelt's Faculty Hospital, Banská Bystrica, Slovakia, and [6]Colorectal Surgery Unit, Derriford Hospital, Plymouth

Address for correspondence: Ivana Dedinska, MD, PhD, Department of Surgery and Transplantation Center, University Hospital Martin, Kollarova 2, SK-036 01 Martin, Slovakia.
Phone: +421.43.4203920

Since the UW (University of Wisconsin) solution introduction to the clinical practice, the liver transplantation has become a routine treatment method in the world. Several clinical studies state the primary graft afunction occurs only in the range 4–7.5 %, when using the UW solution with a cold ischemia less than 16 hours (4). The liver can be rinsed after implantation of liver into the body of the recipient immediately prior to the reperfusion with special solutions, such as Carolina rinse solution. It prevents the influx of cold solution rich in potassium from the implanted liver directly into the heart of the recipient. Rinse solutions contain also other components improving the transplantation result, such as: antioxidants, hydroxyethyl starch, adenosine and others (5, 6). After the initial enthusiasm, however, only a small effect on the post-transplant function of the liver was determined (lower levels of transaminases and bilirubin), and therefore their application is currently gradually abandoned and the majority of workplaces rinses the implant with the recipient's blood through infrahepatic anastomosis (7).

The aim of the liver reperfusion (antegrade or retrograde) is to renew the blood flow in the implanted organ. In case of the antegrade reperfusion, the preservation solution is either discharged into the system circulation with the risk of PRS occurrence or is discharged outside the circulation – venting via vena cava. In the first case we talk about a system reperfusion and in the latter about non-system reperfusion (8). The most often used technique is the method of sequential antegrade reperfusion with an initial portal revascularization. The reason for this order is to renew the blood flow in the implant through vena portae as quickly as possible, because its construction is technically less difficult and can be performed quickly. The rewarming time/injury is thus minimized, because the inserted liver graft is warmed from the recipient's body. Another advantage of this procedure is a quick release of an acute portal hypertension caused by the clamp applied to vena portae (9).

We have been using the technique of sequential antegrade reperfusion with the initial portal revascularization at our workplace since the start of liver transplantation program; during the first period with a system reperfusion and later we moved to a non-system reperfusion – venting via vena cava inferior.

The aim of this paper was to compare two methods of implanted liver reperfusion during the transplantation with the evaluation of the impact of both techniques on the post reperfusion syndrome (PRS) during the operation and the evaluation of the impact on the early postoperative development. We have compared the system and non-system reperfusion with the assumption that the second reperfusion method would be more beneficial for the perioperative and postoperative development, as the cold preservation solution with accumulated toxic substances did not get directly in the recipient's heart.

Methods

It was a prospective study on patients, who underwent liver transplantation from the donors after brain death in the F.D. Roosevelt's Faculty Hospital in Banská Bystrica. We determined input data for each patient consisting of age, MELD score (Model of End Stage Liver Diseases), CTP (Child Turcotte Pugh) score, percentage of donor hepatic steatosis and age of donor. The group of patients was divided to two groups according to the type of reperfusion – non-venting and venting.

In the non-venting group, we released vascular clamps after sewing of the cavo-caval anastomosis and porto-portal anastomosis with a subsequent discharge of the cold preservation solution with accumulated metabolites of the anaerobic cold ischemia directly into the recipient's circulation. In the venting group, we performed the reperfusion by the second method, i.e. after a partial sewing of the cavo-caval anastomosis, we left it partially open on the vascular Satinský clamp on the vena cava. We subsequently performed the reperfusion of the implanted liver through the constructed porto-portal anastomosis. We discharged the preservation solution through the partially open cavo-caval anastomosis outside the patient's circulation. We sampled the discharged effluent for a laboratory examination. Afterwards, we completed the sewing of the cavo-caval anastomosis, released Satinský clamp and thus completely renewed the circulation in the transplanted liver. In this way, the cold preservation solution with accumulated metabolites of anaerobic ischemia did not get into the patient's circulation.

We monitored the same clinical and laboratory parameters in both groups, which we mutually compared. We monitored: Model of End Stage Liver Diseases – MELD, CTP – Child Turcotte Pugh, plasmatic concentrations of Na, K, Cl, Ph, blood pressure, pulse, Mean Arterial Pressure – MAP, central venous pressure – CVT, presence of cardiac rhythm disorder, necessity of resuscitation and duration of cold ischemia.

We recorded the monitored parameters immediately prior to the transplantation, during and after the reperfusion and on the 1st postoperative day.

All patients were treated by one surgeon.

We performed a mathematical modelling, estimated the parameters as well as did the graphic visualization of analysis in the user interface of the R program, version 3.22 (R Core Team, 2017), using basic libraries. Comparisons of continuous variables between the groups were carried out using parametric (t-test) or nonparametric (Mann-Whitney) tests; associations between categorical variables were analysed using the $\chi 2$ test and Fisher's exact test, as appropriate; we considered the value $p < 0.05$ statistically significant.

The study was approved by the institutional review board (No: EK 1645/2015).

Results

The non-venting group included 42 patients; the venting group 41 patients. Characteristics of the groups are shown in Table 1.

Tab. 1. Characteristics of the group.

	non-venting	venting	p
recipient's age (years)	50.26±10.34	51.54±10.3	0.575
MELD	17.26±6	16.41±5.77	0.514
CTP	6.62±2.94	6±2.98	0.952
graft steatosis (%)	11.31±14.1	6.71±9.98	0.090
donor's age (years)	40.33±14.92	42.17±16.91	0.601

MELD – Model of End Stage Liver Diseases, CTP – Child Turcotte Pugh

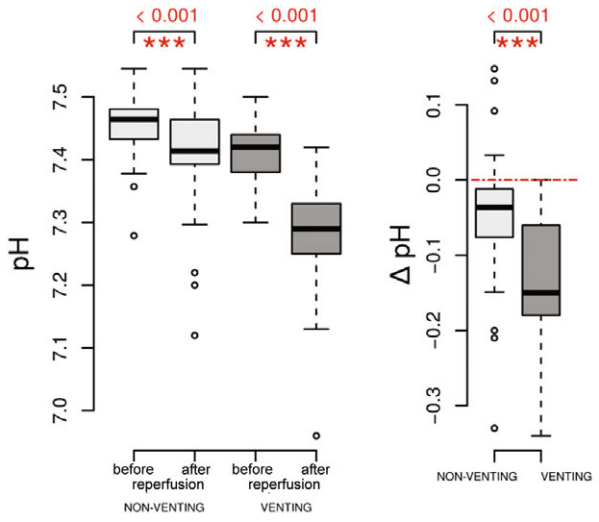

Fig. 1. Comparison of pH value before and after reperfusion and mutual comparison of changes between non-venting and venting groups

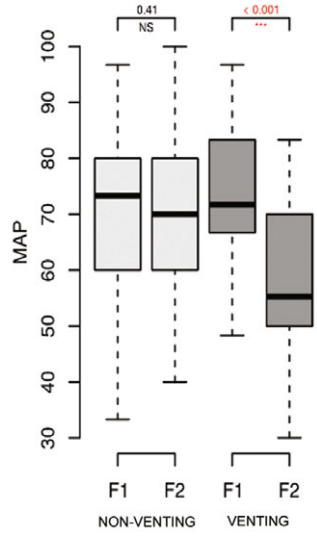

Fig. 3. Comparison of mean arterial pressure (MAP) before and after reperfusion and mutual comparison of changes between non-venting and venting groups

We did not find any statistically significant difference in the input monitored parameters. The cold ischemia period was in the non-venting group 430 minutes and in the venting group 426 minutes (p = NS), which confirmed that groups were homogeneous with regards to the recipient and the donor.

We did not find any statistically significant difference between the non-venting and venting group in the comparison of the consumption of erythrocyte concentrate during the transplantation and on the 1st postoperative day. The average consumption of erythrocyte concentrate units was 6.17 units in the non-venting group and 5.46 units in the venting group.

A statistically significant difference was not confirmed in the comparison of potassium before and after reperfusion in the monitored groups; the change of the potassium value was also without any statistically significant difference. On the other hand, we found significant changes of pH after reperfusion in both monitored groups (Fig. 1).

By analysing the values of systolic and diastolic blood pressure (BP) in 3 phases: (F1 – before reperfusion, F2 – after reperfusion, F3 – the first postoperative day) we identified a significant increase of both the systolic and diastolic BP after reperfusion in both monitored groups. By comparing the non-venting and venting groups, we found a significant decrease of both the systolic and diastolic BP (phase 1-2) and a significant increase of systolic BP in phase 2-3 in the venting group (Fig. 2).

We recorded a significant decrease of the mean arterial pressure after reperfusion in the venting group (Fig. 3).

Table 2 shows clinical parameters. We found a significantly better saturation in the non-venting group; a larger consumption of fresh frozen plasma and thrombo-concentrate in the non-venting group; a significantly higher value of total bilirubin and lower value of Quick's time in the non-venting group.

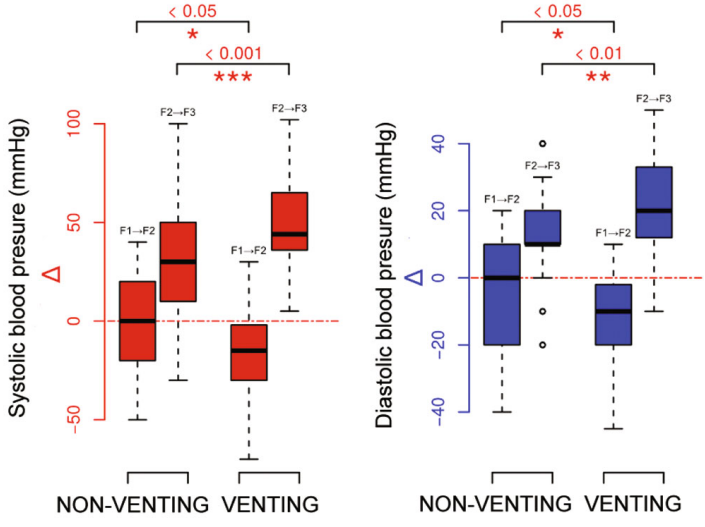

Fig. 2. Comparison of values of systolic and diastolic blood pressure between transplantation phases (F1 – before reperfusion, F2 – after reperfusion, F3 – the first postoperative day) and between non-venting and venting groups (red – systolic, blue – diastolic)

Discussion

In our analysis, we included 42 patients after liver transplantation in the non-venting group and 41 patients after liver transplantation in the venting group. After comparison of input monitored parameters, we did not find any statistically significant differences. The risk factors for post reperfusion

Tab. 2. Average values of clinical parameters.

	non-venting	venting	p
CIT (min)	429.29±137.59	426.83±122.66	0.931
saturation (%)	98.1±2.01	96.71±1.82	<0.0001
diuresis (ml/hour)	90.41±44.07	81.59±53.62	0.417
erythrocyte concentrate (unit)	6.17±5.09	5.46±3.69	0.474
ČMP (unit)	27.29±10.37	12.8±6.4	<0.0001
thrombo-concentrate (unit)	1.5±1.63	0.68±1.01	<0.01
total bilirubin (μmol/l)	103.55±79.64	70.82±54.96	<0.05
Quick's time	54.44±11	63.84±12.46	<0.001
Hemoglobin (g/l)	83.19±16.49	88.85±12.42	0.081
AST (μkat/l)	14.73±22.42	16.08±26.33	0.801
ALT (μkat/l)	8.31±13.03	10.01±12.8	0.550
ALP (μkat/l)	1.74±0.65	1.72±0.97	0.924
GMT (μkat/l)	1.21±0.87	1.58±1.16	0.104

CIT – cold ischemia time, ČMP – fresh frozen plasma, AST – aspartate aminotransferase, ALT – alanine aminotransferase, ALP – alkaline phosphatise, GMT – gamma glutamyl transferase

syndrome from the perspective of the donor are: age of the donor, cold ischemia time, donor risk index, presence of macrovesicular steatosis and large grafts as converted to the general size of the recipient's body (10, 11, 12, 13). The risk factors from the perspective of the recipient are: age of the recipient, MELD score, hemodynamic response to clamping of the vena cava inferior and warm ischemia in graft implantation (14, 15, 16). The development of post reperfusion syndrome is attributed also to the type of preservation solution. Only the HTK solution was used in our analysis in both groups, so both non-venting and venting groups were equal also in this regard.

There were changes in K+ levels after the reperfusion with a minimum decrease in serum levels and minimum difference between the non-venting and venting groups. We found that the venting technique only minimally affected serum levels of potassium in samples taken from patient's peripheral artery 5 minutes after a reperfusion. We assumed that accumulated K+ in the preservation solution in the liver would cause in the non-venting group increase of potassium serum levels, but this assumption was not confirmed. We explain it by already diluted level of K+ serum concentration, because samples were taken 5 minutes after the reperfusion. It is rather the bolus increase of K+ concentration with an immediate and direct impact on the myocardium that affects the pathophysiology of the post reperfusion syndrome. Literature states the causes of hyperkalaemia in early post reperfusion period a metabolic acidosis in anhepatic phase, exogenous intake of K+ in case of excessive transfusions of erythrocyte concentrates due to large losses during explantation of the liver or usage of preservation solution UW – University of Wisconsin, which is hyperkaliaemic. A significant hyperkalaemia was referred especially in case of livers taken from donors with non-beating heart, so-called DCD - Donor Circulatory Death (17).

In monitoring the dynamics of pH change we recorded a decrease of pH in both groups after reperfusion. We found that venting via vena cava did not affect the pH level in the serum 5 minutes after the reperfusion. Total pH of the patient was more affected by the surgery stress, hypothermia or also a loss of blood.

We found in our measurements a paradoxically higher decrease of pH in the venting group. Our assumption that by discharging acidic effluent the pH in the patient's serum will increase was not confirmed. However, to accurately assess the pH effect in the non-venting group it would be necessary to take blood samples during reperfusion directly from the right atrium.

The analysis of changes of systolic and diastolic pressures in individual transplantation phases (F1 – before reperfusion, F2 – after reperfusion, F3 – the first postoperative day) showed a statistically significant decrease of the systolic and diastolic pressure in the venting group after a reperfusion (comparison F1 – F2) by 17.8/12.6 mm Hg. These values attested a statistically largest pressure decrease in the venting group after reperfusion, which we did not expect. We explained this decrease by a bolus discharge of the preservation solution and portal blood during reperfusion. We discharged the volume 400 ml into surgical extractor. We explained the short-term decrease of pressure in the venting group by a sudden discharge of effluent in the said volume, what was not critically manifested in the patient in the general context of haemodynamics of reperfusion.

By analysing the mean arterial pressure, we found that there was a statistically significant average decrease of MAP present in the venting group as compared to the non-venting group during reperfusion. We recorded the MAP decrease by 30 % and more compared to the input value in the non-venting group in 6 patients and in the venting group in 10 patients. We explained this as the consequence of a sudden discharge of effluent in the said volume, which induced the decrease of pressure by more than 30 %. However, we did not observe rhythm disorders or resuscitation event in these patients, which are typical for developed post reperfusion syndrome. Ryu et al found in their study that after the administration of phenyleprine or Epinephrine there was a significant reduction of occurrence of the post reperfusion syndrome and reduction of the need of vasoactive substances during neohepatic (after reperfusion) phase of transplantation (18). Fukuzawa et al analysed in their study of 715 patients the occurrence and course of the post reperfusion syndrome. They found more significant decrease of MAP in the group with post reperfusion syndrome. They stated that a gradual hemodynamic recovery of the patient started not already after the portal, but only after the arterial revascularization of the transplanted liver. They explained it by the fact that the rinse of the preservation solution only with portal blood was insufficient and a complete discharge of vasoactive and inflammatory mediators happened only after the revascularization of the arteria hepatica of the graft (10). This theory suggests that venting only via the portal blood, as we did in our study, might not be sufficient as a prevention of the post reperfusion syndrome.

After we compared the consumption of erythrocyte concentrate (but also thrombo-concentrate) during the transplantation and on the 1st postoperative day we found that there was no statistically significant difference between the non-venting and venting groups. This is an important finding, because we discharged 400 ml of the preservation solution together with the portal blood from the patient's body in the venting group and this volume was

not immediately substituted. Despite that this blood loss did not manifest in any significant way in the increased consumption of erythrocyte concentrate units. We assumed that we should have a reduced consumption of erythrocyte concentrate units in the venting group by prevention of the post reperfusion syndrome, but this assumption was not confirmed. We think that routine use of cell saver also contributes to even consumption of erythrocyte concentrate units in both groups. Based on our experience, we can say that by a gradual growth of surgical experience we achieved a shorter operative time and thus in a direct proportion also smaller perioperative blood losses. Coelho et al reached the same conclusion. They compared two transplantation eras at their workplace: the first in 2002–2006 and the second in 2007 and 2011. They found that they had a significantly lower consumption of blood derivatives in the second era than in the first era of transplantations. They attributed it to a growing experience of the surgical and anaesthesiological team and similarly as in our case to mandatory use of the cell saver and autologous erythrocyte concentrate (19).

In the monitoring of the consumption of fresh frozen plasma units during the transplantation and on the 1st postoperative day, we found that the consumption of fresh frozen plasma was significantly higher in the non-venting group than in the venting group. We explained the decrease in the consumption of the fresh frozen plasma in the venting group by the change of the haemostatic management in the period of inclusion of patients in this group and not by the venting technique itself. Its consumption dramatically dropped with a growing experience of surgeons and anaesthesiologists and with the transition from a large volume of plasma to administration of hemocomplettan (fibrinogen). Studies proved that administration of plasma with the aim to correct the coagulation did not reach the desired effect on the coagulation or reduction of erythrocyte concentrate consumption. It was even proved that an excessive supplementation of patients with blood derivatives reduced 1-year survival after the transplantation (20). The significantly higher value of the Quick's time in the venting group was caused by a better haemostatic management of the patient in the second decade of transplantations and not by the technique itself. We have implemented the venting technique at our workplace in 2015, but at the same time we have started to use ROTEM for diagnostics of coagulation, which allowed us a targeted correction and supplementation of coagulation factors.

Conclusion

We can establish on the grounds of our analysis that venting via vena cava inferior did not affect the perioperative and early postoperative course of liver transplantation in the set of monitored parameters. Further analyses are required in the future to evaluate the significance of venting of the preservation solution during reperfusion in liver transplantation, which would include direct invasive measurements of hemodynamic and laboratory parameters in the heart and lungs during reperfusion by means of transoesophageal echocardiogram or a direct sampling of laboratory parameters from the heart and a direct measurement of temperature in the heart.

We have been using venting via vena cava as a standard at our workplace since 2015 during liver transplantation for all the patients. We will continue with the established procedure in the clinical practice, despite the fact that our hypothesis was not confirmed in the group of monitored parameters. We think that the effect of venting via vena cava will show in the group of other prospectively monitored data.

References

1. Skladaný Ľ, Trunečka P. Alokácia štepov na transplantáciu pečene v Slovenskej republike. In: Baláž P. et al. Odběry orgánů na transplantaci. Praha : Karolinum, 2011, 158.

2. Spiegel HU, Palmes D. Organ preservation. Hakim N, Danovitch G. Transplantation surgery. London: Springer, 2001, 265–294.

3. Petrowsky H, Clavien PA. Principles of liver preservation. In: Busuttil RW, Klintmalm GB. Transplantation of the liver. Philadelphia: Elsevier/Saunders, 2015, 582.

4. Porte RJ, Ploeg RJ, Hansen B, van Bockel JH, Thorogood J, Persijn GG et al. Long-term graft survival after liver trans-plantation in the UW era: late effects of cold ischemia and primary dysfunction. European Multicentre Study Group. Transplant International 1998; 11 (S1): S164–S167.

5. Gao WS, Takei Y, Marzi I, Lindert KA, Caldwell-Kenkel JC, Currin RT et al. Carolina rinse solution – a new strategy to increase survival time after orthotopic liver transplantation in the rat. Transplantation 1991; 52 (3): 417–424.

6. Currin RT. Evidence that Carolina rinse solution protects sinusoidal endothelial cells against reperfusion injury after cold ischemic storage of rat liver. Transplantation 1990; 50 (6): 1076–1078.

7. Sanchez-Urdazpal L, Gores GJ, Lemasters JJ, Mekeel H, Schoonhoven R, Lemasters J. Carolina rinse solution decreases liver injury during clinical liver transplantation. Transplant Proc 1993; 25: 1574.

8. Brems JJ, Takiff H, McHutchinson J, Collins D, Biermann LA, Pockros P. Systemic versus nonsystemic reperfusion of the transplanted liver. Transplantion 1993; 55 (3): 527–529.

9. Moreno C, Sabaté A, Figueras J, Camprub I, Dalmau A, Fabregat J et al. Hemodynamic profile and tissular oxygenation in orthotopic liver transplantation: influence of hepatic artery or portal vein revascularization of the graft. Liver Transplant 2006; 12 (11): 1607–1614.

10. Fukuzawa K, Yamada Y, Gologorsky E, Arheart KL, Pretto EA Jr. Hemodynamic recovery following postreperfusion syndrome in liver transplantation. J Cardiothor Vasc Anesth 2014; 28 (4): 994–1002.

11. Xu ZD, Xu HT, Youa HB. Postreperfusion syndrome during orthotopic liver transplantation: a single center experience. Hepatobil Pancreat Dis Internat 2012; 11 (1): 34–39.

12. Chung IS, Kim HY, Shin YH, Ko JS, Gwak MS, Sim WS et al. Incidence and predictors of post-reperfusion syndrome in living donor liver transplantation. Clin Transplant 2012; 26 (4): 539–543.

13. Fukazawa K, Nishida S, Volsky A, Tzakis AG, Pretto EA Jr. Body surface area index predicts outcome in orthotopic liver transplantation. Journal of Hepato-biliary-pancreatic Sciences 2011; 18 (2): 216–225.

14. Hilmi I, Horton CN, Planinsic RM, Sakai T, Nicolau-Raducu R, Damian D, et al. The impact of postreperfusion syndrome on short term patient and liver allograft outcome in patient undergoing orthotopic liver transplantation. Liver Transplantation 2008; 14 (4): 504–508.

15. Siniscalchi A, Dante A, Spedicato S, Riganello L, Zanoni A, Cimatti M, et al. Hyperdynamic circulation in acute liver failure: reperfusion syndrome and outcome following liver transplantation. Transplant Proc 2010; 42 (4): 1197–1199.

16. Garutti Martinez I, Olmedilla L, Perez-Peña JM, Zaballos M, Sanz J, Vigil MD et al. Response to clamping of the inferior vena cava as a factor for predicting postreperfusion syndrome during liver transplantation. Anesthesia Analgesia 1997; 84 (2): 254–259.

17. Zhang WJ, Xia WL, Pan HY, Zheng SS. Postreperfusion hyperkalemia in liver transplantation using donation after cardiac death grafts with pathological changes. Hepatobiliary and Pancreatic Dis Internat 2016; 15 (5): 487–492.

18. Ryu HG, Jung CW, Lee HC, Cho YJ. Epinephrine and phenylephrine pretreatments for preventing postreperfusion syndrome during adult liver transplantation. Liver Transplant 2012; 18 (12): 1430–1439.

19. Coêlho GR, Feitosa Neto BA, de G Teixeira CC. Marinho DS, Rangel ML, Garcia JH. Single-center transfusion rate for 555 consecutive liver transplantation: impact of two eras. Transplant Proc 2013; 45 (9): 3305–3309.

20. Massicotte L, Sassine MP, Lenis S, Seal RF, Roy A. Survival rate changes with transfusion of blood products during liver transplantation. Canad J Anaesth 2005; 52 (2): 148–145.

Received January 18, 2020.
Accepted March 3, 2020.