A Novel Parameter Derived From Photoplethysmographic Pulse Wave to Predict Risk of Postreperfusion Syndrome

Hai-ying Kong (yahoqi@zju.edu.cn)
Zhejiang University School of Medicine First Affiliated Hospital https://orcid.org/0000-0003-4474-6798
Xian Zhao
Zhejiang University School of Medicine
Su-Qin Huang
Zhejiang University School of Medicine First Affiliated Hospital

Research article

Keywords: surgical plethysmographic index, postreperfusion syndrome, transplantation, liver

Posted Date: July 30th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-41789/v1

Abstract

Background

Postreperfusion syndrome (PRS), observed after reperfusion of the grafted liver, was associated with poor outcome. The end-stage liver disease (ESLD) with autonomic dysfunction in the cardiovascular system has greater risk of developing of PRS, due to the poor ability in sympathetic vasoconstriction. Surgical Stress Index (SSI) is a novel parameter derived from photoplethysmographic pulse wave to assess central sympathetic modulation in awake volunteers. In this study, we determined the relationship between SSI values and the risk of developing of PRS during orthotopic liver transplantation.

Methods

We retrospectively studied 163 patients who had undergone OLT, and divided the patients into PRS group and non-PRS group. SSI and related parameters were determined 5min before and after clamping of the inferior vena cava, the occurrence of PRS were recorded during reperfusion.

Results

The clamping of the inferior vena cava modified the SSI significantly, accompanied with significant hemodynamic response. The SSI increased significantly after clamping (47.0 (43.0-49.0) vs.81.0(69.5-89.0), p<0.001). The SSI increased by 45.3% at 5min after clamping of the inferior vena cava in the PRS group, as opposed to 81.7% in the non-PRS group (P = 0.037). PRS occurred in only 19.4% of patients in whom the SSI increased by more than 50%. Based on a multivariate analysis, percentage of the variation in the SSI was associated with a significant increased risk in developing the PRS (OR 2.49, 95% CI 1.15-5.02; P=0.021).

Conclusions

SSI can sensitively indicate the central sympathetic modulation function during liver transplantation procedure. SSI might be a sensitive marker of risk of developing PRS.

Background

Severe hemodynamic instability defined as postreperfusion syndrome (PRS), observed after reperfusion of the grafted liver, is associated with poor outcome[1]. The etiology of this syndrome is not certain with the incidence rate about 8%-30%. In addition to the metabolic acidosis, the release of vasoactive substances by the grafted liver[2], the autonomic dysfunction is responsible for the developing of PRS during reperfusion[3]. The autonomic dysfunction can amplify the haemodynamics instability, characterized as blunt cardiac and pressure compensatory under stressful conditions. Non-invasive tests including lying to standing, valid in diabetics, are introduced to diagnosis the cardiovascular autonomic function before operation[4].] However, most of the cardiovascular autonomic dysfunction in liver cirrhosis is undiagnosed before surgery for asymptomatic. It is urgent to find a sensitive tests of

detecting cardiovascular autonomic dysfunction and ability of coping with severe reperfusion related hypotension during liver transplantation procedure[4].

The surgical stress index (SSI), calculated from normalized analysis of the photoplethysmographic waveform and heart rate, has been regarded as an index of assessing surgical stress reactions[5–8] In addition, the SSI is confirmed to reflect the sympathetic modulation directed to the vessels through gravitational sympathetic stimulation in awake volunteers[9]. Changes in SSI were correlated with the autonomic nervous system modulation in the context of a balanced general anaesthesia undergoing laparoscopic abdominal surgery[10]. To our knowledge, there was no report related the application of SSI monitor during liver transplantation.

Orthotopic liver transplantation (OLT) is known as the key treatment for ESLD. Major haemodynamics changes were frequently observed during clamping and unclamping of the portal vein, hepatic artery, and inferior vena cava (IVC)[11]. IVC clamping caused the decrease of the venous return and subsequent a compensatory baroreflex-mediated increase of peripheral vascular resistance and heart rate to keep proper arterial pressure. Thus, SSI might change significantly after the IVC clamping, and the variation in SSI can partially reflect the central sympathetic modulation function.

The purpose of this study was to evaluate whether variation in SSI values response to the IVC clamping is a sensitive marker of risk of PRS during liver transplantation procedure.

Methods

This was a retrospective observation study performed at the First Affiliated Hospital, Zhejiang University School of Medicine with the approval of the hospitals' Institutional Ethics Committee(2017 – 1095) and registered with the University of Zhejiang School of Medicine's Human Research Ethical Committee. This manuscript adheres to the applicable EQUATOR guidelines.

Study population

All patients undergoing OLT with modified piggy-back technique for the liver cirrhosis from January 2017 to January 2019 were included. Exclusion criteria were: age < 18 or > 65 years, a history of allergy, coronary artery disease and abdomen surgery, preexisting multiorgan failure, and receiving marginal donor liver.

Anaesthesia and monitoring

In addition to the regular monitors including ECG, pulse oximetry, continuous invasive blood pressure (IBP), and central venous pressure (CVP),BIS (BIS-Vista, Aspect Medical Systems, Newton, MA),the SSI was also monitored. In all patients, the SSI sensor was attached to the index finger of the arm. The plethysmographic waveform was continuously recorded. The SSI values were displayed on the S/5 Advance monitor and they were manually recorded. Pulse contour cardiac output monitoring (PiCCO) was

introduced to monitor cardiac output (CO) and guide fluid transfusion. Electrolytes and arterial blood gas analysis were checked periodically and corrected throughout the operation.

Anesthesia was induced with 2 $mg.kg^{-1}$propofol, 5 $\mu g.kg^{-1}$ fentanyl and 0.6 $mg.kg^{-1}$ rocuronium ,and was maintained with propofol,remifentanyl, cisatracurium. The administration of propofol was guided by BIS (40 to 60).The remifentanyl administration was guided by SSI (20 to 50) during the dissection phase, and neohepatic phase. There was no additional fentanil bolus given except continuous infusion of same rate of remifentanil as that before clamping the IVC during the anhepatic stage. Warm blanket and warm fluid or blood were introduced to keep body temperature above 35.5℃.

Fluids (crystalloid, albumin) were preferred during surgery and the transfusion rate was guided by stroke volume variation (SVV). Intraoperative blood and blood products were required according to the measured hemoglobin and coagulation parameters monitored by thromboelastogram(TEG). Hemoglobin value was kept above 7 $g.dl^{-1}$ while $PaCO_2$ was kept at 35–45 mmHg.

Measures to prevent PRS

We used Wisconsin solution as preservative solution in all the grafted livers. The grafted liver was refused before starting the anastomosis of hepatic artery. During anastomosis of the suprahepatic caval vein, the graft was flushed with 500 ml of 5% albumin (0℃) through the portal vein. Appropriate bicarbonate and calcium chloride were administered to prevent hyperkalemia and acidosis.

Record of SSI values and related parameters

SSI and related hemodynamic parameters were determined 5 min before clamping of the IVC(C-5)and 5 min after clamping of the IVC(C + 5).The data included demographic profiles, indications for transplantation, details of comorbidities, cold ischemia times, duration of surgery, monitoring, fluid balance, vasopressin use, PRS, urine output, duration of mechanical ventilation, intensive care unit (ICU) stay and hospital stay, any adverse events noted during the hospital stay were also recorded.

PRS was characterized as a drop of MAP more than 30% for over 1 min during the initial stage after reperfusion.[12]

The primary outcome was the relationship between the variations in SSI values response to the IVC clamping and the occurrence of PRS. The second outcome was the occurrence of PRS, and the variation in SSI values and related parameters response to the IVC clamping.

Statistical analysis

The variables considered are expressed as percentages when measured qualitatively and as means with the standard deviation or median with IQR when measured quantitatively. Chi-square test was used to compare the categorical variables. The Mann-Whitney U-test was used to analyze the proper continuous variables.

The relevant clinical parameters associated with the occurrence of PRS were chose in the univariate logistic regression analysis. Parameters with P values < 0.1 in the univariate analysis were chose in a multivariate logistic regression analysis to determine independent parameters predicting the PRS occurrence. All analyses were performed using SAS release 6.12 (SAS Institute, Cary, NC).

Results

Patient characteristics

185 patients were reviewed in this retrospective study, but 22 patients were excluded for the history of abdomen surgery and cardiac artery disease(n = 5),receiving marginal donor liver(n = 2), performed with partial clamping of the IVC technique(n = 2),the massive blood loss(> 2000 mL,n = 6),receiving vasopressor administration during the dissection phase(n = 7), data from 163 patients were included. PRS was observed in 48 of the 163 patients (29.4%) in our series(Fig. 1). The patient characteristics and relevant intraoperative data in the PRS and non-PRS groups were shown in Table 1. The median duration of surgery, anhepatic phase, the administered of crystalloids and colloids, and etiology for the liver disease were also shown, there was no difference between the two groups. The age, body mass index, model for end-stage liver disease (MELD) scores in the PRS were different from those in the non-PRS groups (P < 0.05).During the dissection phase, there was no difference related to the remifentany adminstration rate and the dose of fentanil requirement between the groups. The requirement of norepinephrine dose was greater in the recipients in the PRS group compared to the non-PRS group [0.53 (0.26–0.83) vs. 0.25(0.05–0.29); 0.43 (0.21–0.62) vs. 0.12 (0.07–0.19) mg. h^{-1}], respectively, for anhepatic and reperfusion phases. No patient suffered hemodynamic shock, the range of administered packed erythrocyte was from one to six units.

Table 1
Baseline and clinical characteristics of the population

	PRS(n = 48)	Non-PRS(n = 115)	p Value
Age, years	48.5 (38.5–53.0)	45 (39–53)	0.3106
Sex: female	22(45.6%)	59(51.2%)	0.2167
BMI(kg m^{-2})	27 (25.0-29.5)	25 (23–27)	0.0054
Underlying disease(n)			
Cirrhosis	40(83.3%)	82 (71.3%)	0.1308
Combined hepatocellular carcinoma	5 (10.4%)	21 (18.3%)	0.2046
Others	3(6.3%)	12(10.4%)	0.4785
Severity of liver disease			
MELD score	27(23–30)	21 (19–23)	0.0002
Comorbidity			
Hypertension	8(16.7%)	18 (15.7%)	0.8551
Diabetes mellitus	5(10.4%)	12 (10.4%)	0.9890
Heart disease	2(4.2%)	3 (2.6%)	0.6027
Surgical time (min)	357.0 (326.5-394.5)	357 (327–394)	0.8670
Anhepatic phase(min)	62.8(6.9)	63.1(6.6)	0.7067
Blood loss during surgery(l)	1118.0 (954.5–1413.0)	1067 (956–1366)	0.5816
Red blood cells(U)	3.0(2.0-4.5)	3 (2–5)	0.2713
Fresh freezing plasma(ml)	827.5(721.0-930.0)	824 (720–927)	0.7582
Donor liver characters			
Cadaveric donor	32(66.7%)	79(68.7%)	0.8582
Cold ischemic time(min)	183.5(127.0-223.5)	184.0 (125.0-225.0)	0.9553
Warm ischemic time(min)	3.9(1.1)	4.0(1.0)	0.2089

Values are mean (SD) or median (range) or number (proportion). PRS,postreperfusion syndrome; BMI, body mass Index; MELD,model for end-stage liver disease

Influence of clamping of the IVC on the SSI values

The SSI values reaction to the IVC clamping recorded from all the patients are shown in the Table 2. SSI increased significantly from C-5 to C + 5.Meanwhile, the heart rate(HR), central venous pressure(CVP),

SVV and systemic vascular resistance index (SVRI) increased significantly from C-5 to C + 5 while the MAP decreased significantly ($p < 0.05$).

Table 2
Surgical stress index and related parameters at 5 min before or after clamping of the inferior vena cava (n = 163)

Variable	C-5	C + 5	P
SSI (%)	47.0 (43.0–49.0)	81.0(69.5–89.0)	< .0001
BIS	46.0(42.0–49.0)	38.0(32.0–40.0)	< .0001
HR(bpm)	88(82.0–91.0)	103(100–109)	< .0001
SVRI (dyn s cm^{-5} m^{-2})	1087 (987.0-1321.0)	1995 (1694–2294)	<.0001
SVV (%)	12(10–12)	19 (18–21)	<.0001
CVP	10(9–12)	6(4–7)	<.0001
MAP (mmHg)	70(69–72)	64(62–68)	<.0001

Values are Mean (SD)or Median (range) SSI, surgical stress index; HR, heart rate; SVRI, systemic vascular resistance; SVV, stroke volume variation; MAP,mean arterial pressure; C-5,5 min before clamping of the inferior vena cava; C + 5,5 min after clamping of the inferior vena cava.

Association with variation in the SSI values and the PRS occurrence

Table 3.showed that percentage of change of the SSI values from C − 5 to C + 5was greater in the patients with non-PRS than those with PRS($P < 0.0001$), as well as the percentage of change of the SVRI values($P < 0.0001$). The HR increased significantly after the IVC clamping, however, there was no difference in the percent of change of the HR from C − 5 to C + 5 between the two groups. The SSI increased by 45.3% at C + 5 in the PRS group, as opposed to 81.7% in the non-PRS group ($P < 0.05$). PRS occurred in only 19.4% of patients in whom the SSI increased at C + 5 by more than 50%.

Table 3
The surgical stress index response to the clamping of the inferior vena cava in patients with PRS and non-PRS groups

	Groups	C − 5	C + 5	%
SSI	PRS	47.0(43.0-49.5)	66.5(63.0–70.0)	45.3
	Non-PRS	46(43–48)	84(79–89)	81.7*
BIS	PRS	45(40–48)	33(31.0-39.5)	-14.2
	Non-PRS	46(42–48)	38(33–40.0)	-11.5
HR(bpm)	PRS	88.5(82.0–90.0)	101(99–103)	23.4
	Non-PRS	86(81–90)	105(100–110)	27.8
MAP(mmHg)	PRS	69(67-71.5)	63(62–68)	-12.1
	Non-PRS	71(69–73)	65(62–68)	-11.7
SVRI(dyn s cm^{-5} m^{-2})	PRS	1021(923–1032)	1623(1321–1823)	51.9
	Non-PRS	1153(995–1403)	2087(1838.5-2320.5)	76.8*
Values are Mean(SD). *P < 0.05 vs. PRS				
SSI, surgical stress index; HR,heart rate; MAP,mean arterial pressure; SVRI,systemic vascular resistance index; C-5,5 min before clamping of the inferior vena cava; C + 5,5 min after clamping of the inferior vena cava; PRS,postreperfusion syndrome; %,percentage of change from C − 5 to C + 5				

Table 4.showed univariate and multivariate regression analysis of clinical risk parameters associated with the PRS occurrence. The factors including age, MELD scores, heart disease, the requirement of red blood cells, percent of the variation in the SSI and the SVRI were the significant determinants of the occurrence of PRS in the univariate logistic regression analysis. Then, multivariate analysis was also introduced to confirm if the variation in the SSI response to the IVC clamping could be an independent risk factor for the PRS occurrence. In addition to the age, MELD scores, the variation in the SSI (OR 2.49, 95% CI 1.147–5.017; P = 0.021) and the variation in the SVRI (OR 2.12,95%CI 1.09–4.95;P = 0.034)resulted as an independent risk factor for PRS(Table 4).

Table 4
Univariate and multivariate regression analysis associated with PRS.

Variable	Univatiate analysis		Multivariate analysis	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Age	1.46(1.13–3.21)	**0.042**	1.59(1.25–2.76)	**0.051**
BMI	1.02(0.96–2.13)	0.712		
MELD score	2.16(1.45–4.05)	**0.036**	2.43(1.30–4.12)	**0.019**
Hypertension	1.05(0.98–2.34)	0.604		
Diabetes mellitus	1.13(1.01–2.26)	0.652		
Heart disease	1.75(1.05-3,15)	0.049		
Surgical time	1.31(1.11–2.76)	**0.479**		
Anhepatic stage	1.12(0.89–1.86)	0.534		
Blood loss	1.29((1.02–2.01)	0.132		
Red blood cells	1.45(0.99–2.37)	0.042		
%,SVRI	1.89(1.65–3.78)	**0.039**	2.12(1.09–4.95)	**0.034**
%,SSI	2.23(1.92–4.32)	**0.026**	2.49(1.15–5.02)	**0.021**

OR,odds ratio; CI, confidence interval;%,percentage of change from 5 min before clamping of the inferior vena cava to 5 min after clamping of the inferior vena cava ; MELD, model for end-stage liver disease; Anhepatic stage,duration from clamping of the portal vein to unclamping of the portal vein and inferior vena cava ;SVRI, systemic vascular resistance index ; SSI, surgical stress index

Outcome

The duration of PRS averaged 5.35 ± 7.02 min. The patients who developed PRS were treated effectively. The length of mechanical ventilation was 1.2 days (day 0 (0–2)). One patient in the PRS group died from multiple organ failure on POD_{11}.The duration of ICU stay was longer in the patients with PRS than those with no PRS (5.9 (2.4), p = 0.031 vs. 2.5(1.8)), while the duration of hospital stay was no statistical significance.

Discussion

The major find in this study was that the frequency of occurrence of PRS in our series was similar to the previous reports[3, 13, 14]. There was significant difference related to the variation in SSI values response to IVC clamping between the recipients with PRS and without PRS. Multivariate analysis showed that the variation in SSI response to IVC clamping was an independent risk factor for the PRS occurrence. These

results suggested that the risk of PRS might be associated with the blunt changes in SSI values response to the IVC clamping.

As we can see from the equation for the SSI value, it is determined by 2 factors, heart beat interval (HBI) and photoplethysmographic amplitude (PPGA). PPGA contributes 66% of SSI values.[9,15] In other words, the SSI reflects sympathetic vasoconstriction reflex and the HR reaction to stimulus including nociception stimuli[10, 15]. The increased SSI values along with the increased HR,CVP,SVV and SVRI were observed after the IVC clamping in our series. The increase of SSI values might be ascribed to the significantly increased HR and SVR, resulting from the compensatory baroreflex for the sudden reduced preload and hypotension. Clamping of the IVC reduced 50% venous return and cardiac output, together with increased systemic vascular resistance and heart rate[11, 16, 17]. The similar change of the hemodynamics had also been reported in the healthy awake volunteers while changing to head-up tilt position[9, 17]. Head-up tilt caused shift of blood toward lower body and reduction of the venous return. These effects induced a compensatory baroreflex-mediated increase of heart rate and peripheral vascular resistance aiming to keep arterial pressure near to the baseline. Thus, variation in the SSI response to the IVC clamping seems to indicate the sympathetic outflow directed to peripheral vessels. The variation of the SSI response to the IVC clamping, might also be helpful to assess the intactness of central sympathetic function.

In recipients with liver cirrhosis, autonomic dysfunction is a common finding; usually it is asymptomatic but it may correlate with increased PRS occurrence[4, 18–20]. Reperfusion of the grafted liver through the portal vein might result in significant cardiovascular collapse, worsening the clinical outcome[12]. To decrease the risk of PRS during liver transplantation, it is advisable to diagnosis the autonomic dysfunction even in the asymptomatic recipients[4]. To date, the autonomic function evaluation of the recipients is another challenging issue because there was no consensus involving the diagnosis of autonomic dysfunction, especially during the procedure[4]. Only a few studies investigated the autonomic dysfunction and its associated with the risk of developing of PRS[3, 4, 18]. The recipients with autonomic dysfunction were at a great risk of hemodynamic instability during the reperfusion of the grafted liver. In one study, sympathetic withdrawal evidenced as lower LF/HF measured before reperfusion of grafted liver was found significantly associated with the risk of developing PRS after reperfusion[18]. The LF/HF of heart rate variability was used as an index of sympathovagal balance, depressed LF/HF was regarded as a relative decline in sympathetic to parasympathetic tone[21]. Another study showed that the variation of the SVRI response to the IVC clamping could be help to assess the intactness of the cardiocirculatory system[3]. Thus, sympathetic dysfunction might be associated with the risk of severe reperfusion-related hypotension. However, it remains not clear whether the PRS may be correlated with the peripheral or central sympathetic dysfunction. This observation indicated that those recipients who had the poor ability of compensatory increase of heart rate and peripheral vascular resistance to keep haemodynamics stability were at greater risk of developing PRS. The SSI values might be a sensitive marker of assess the central sympathetic dysfunction.

Some factors including fluid balance, analgesic and hypnotics can affect the SSI values. All the recipients received similar intraoperative management strategies including fluid, analgesic and hypnotics

transfusion, especially during the dissection stage, thus the effect on the SSI response to clamping of the IVC was similar in all the recipients. The recipients received vasopressive drugs during the dissection stage were also due to the possible effect on the SSI values.

This study was valuable considering the application of a novel parameter during liver transplantation. The response of the SSI value to the IVC clamping might help to detect central sympathetic dysfunction during procedure. The less variation of the SSI showed the blunt baroreflex in case the reduction of preload and hyoptension. The less variation of the SSI might help to remind anesthesiologist to pay more attention to the risk of developing PRS after reperfusion. In addition to correct hypocalcemia and acidosis just before reperfusion of graft liver, active pretreatment with vasoconstrictors should be required to prevent the risk of developing severe PRS.

There were some limitations in this retrospective study. First, it was associated with the usual inherent biases, multiple potential confounders, measured and unmeasured. Second, selecting the MELD scores as the only indicator for evaluation the severity of liver disease to predict the risk of developing PRS might be limited, it was reported that jaundice index, coagulation function, renal function was also associated with the risk of developing PRS[13, 14, 18]. MELD score, however, was a better indicator than individual parameter for evaluating the severity of liver disease, which integrated jaundice index, coagulation function, renal function[27]. Third, we investigated recipients mainly in the setting of LT with the IVC clamping. LT might be performed with partial clamping of the IVC or with VVB in some centers. However, clamping and unclamping of the IVC was associated with more severe hemodynamic instability, especially in the recipients with autonomic dysfunction.

Conclusion

The response of the SSI value to the IVC clamping might help to detect central sympathetic dysfunction. The variation in SSI values response to IVC clamping was associated with the PRS occurrence.

Abbreviations

PRS: postreperfusion syndrome

SSI:surgical stress index

OLT: orthotopic liver transplantation

ESLD: end-stage liver disease

IVC: inferior vena cava

IBP: invasive blood pressure

PiCCO: pulse contour cardiac output monitoring

CO: cardiac output

TEG: thromboelastogram

SVV: stroke volume variation

SVRI :systemic vascular resistance index

C-5: 5min before clamping of the inferior vena cava

C+5: 5min after clamping of the inferior vena cava

CITs: cold ischemia times

ICU: intensive care unit

MAP: mean artery pressure

IQR: inter-quartile range

BMI: body mass index

MELD: model for end-stage liver disease

HR:heart rate

CVP:central venous pressure

OR: odds ratio

CI: confidence interval

POD: postoperative day

HBI:Heart beat interval

PPGA: photoplethysmographic amplitude

LF/HF:Low Frequency / High Frequency

HRV: heart rate variability

LT:liver transplantation

VVB: veno-venous bypass

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Institutional Ethics Committees of the First Affiliated Hospital, Zhejiang University School of Medicine and the Shulan Hospital.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding: None

Acknowledgements

We would like to thank Dr. Ronghui WU, for his help with manuscript revisiting.

Authors' contributions

Hai-Ying Kong:this author helped study design/planning ,study conduct, data analysis, writing paper and revising paper

Xian Zhao: this author helped study conduct, data analysis, and revising paper

Su-Qin Huang: this author helped study conduct and revising paper

Reference

1. Jun IG,Kwon HM, Jung KW, et al.The impact of postreperfusion syndrome on acute kidney injury in living donor liver transplantation:A propensity score analysis.Anesth Analg.2018;127:369-378.

2.Yang Chongwei, Huang Lei, Li Xinyu, Zhu Jiye, Leng Xisheng. Effects of retrograde reperfusion on the intraoperative internal environment and hemodynamics in classic orthotopic liver transplantation.BMC Surg.2018;18: 115-121.

3. Garutti Martinez I, Olmedilla L, Perez-Peña JM, et al.Response to clamping of the inferior vena cava as a factor for predicting postreperfusion syndrome during liver transplantation.Anesth Analg.1997;84:254-259.

4. Di Stefano Cristina, Milazzo Valeria, Milan Alberto, Veglio Franco, Maule Simona. The role of autonomic dysfunction in cirrhotic patients before and after liver transplantation. Review of the literature.Liver Int.2016; 36:1081-1089.

5. Chen X, Thee C, Gruenewald M, et al. Comparison of surgical stress index-guided analgesia with standard clinical practice during routine general anesthesia: a pilot study. Anesthesiology. 2010; 112: 1175–1183.

6. Defresne A, Barvais L, Clement F, Bonhomme V. Standardised noxious stimulation-guided individual adjustment of remifentanil target-controlled infusion to prevent haemodynamic response to laryngoscopy and surgical incision:A randomised contrlled trial.Eur J Anaesthesiol.2017;34:1-11.

7. Colombo R, Raimondi F, Rech R,et al.Surgical pleth index guided analgesia blunts the intraoperative sympathetic response to laparoscopic cholecystectomy. Minerva Anestesiol.2015;81:837-845.

8. Won YJ, Lim BG, Yeo GE.The effect of nicardipine on the surgical pleth index during thyroidectomy under general anesthesia:A prospective double-blind randomized controlled trial.Medicine(Baltimore).2017;96:e6154.

9. Colombo R,Marchi A,BorghiB, et al. Influence of gravitational sympathetic stimulation on the Surgical Plethysmographic Index. Physiol Res. 2015; 64: 183-189.

10. Colombo Riccardo, Raimondi Ferdinando,Corona Alberto, et al. Comparison of the surgical pleth index with autonomic nervous system modulation on cardiac activity during general anaesthesia: A randomised cross-over study. Eur J Anaesthesiol. 2014;31: 76-84.

11.Shih T H, Huang C E, Chen C L, et al. Correlation between changes in end-tidal carbon dioxide concentration and cardiac output during inferior vena cava clamping and unclamping in living-donor liver transplantation. Transplant Proc. 2016;4: 1077-1079.

12. Aggarwal S,Kang Y, Freeman JA, Fortunato FL, Pinsky MR. Postreperfusion syndrome: cardiovascular collapse following hepatic reperfusion during liver transplantation. Transplant Proc.1987; 19:54–55.

13. Umbro I,Tinti F, Scalera I, et al.Acute kidney injury and post-reperfusion syndrome in liver transplantation.World J Gastroenterol.2016;22:9314-9323.

14. Manning Michael W, Kumar Priya A, Maheshwari Kamal, Arora Harendra. Post-reperfusion syndrome in liver transplantation-An overview. J Cardiothorac Vasc Anesth.2019;

15. Ilies C, Ludwigs J,Gruenewald M, et al. The effect of posture and anaesthetic technique on the surgical pleth index. Anaesthesia. 2012;67: 508-513.

16. Mona Rezai Rudnick, Lorenzo De Marchi, Jeffrey S Plotkin.Hemodynamic monitoring during liver transplantation: A state of the art review. World J Hepatol. 2015; 7: 1302-1311.

17.Konur Huseyin, Erdogan Kayhan Gulay, Toprak Huseyin Ilksen,et al. Evaluation of pleth variability index as a predictor of fluid responsiveness during orthotopic liver transplantation. Kaohsiung J Med Sci.2016;32:373-380.

18. Moller S, Mortensen C, Bendtsen F,et al.Cardiac sympathetic imaging with mIBG in cirrhosis and portal hypertension: relation to autonomic and cardiac function.Am J Physiol Gastrointest Liver Physiol. 2012;303: G1228–1235.

19. Dyson JK, Elsharkawy AM, Lamb CA,et al.Fatigue in primary sclerosing cholangitis is associated with sympathetic over-activity and increased cardiac output.Liver Int. 2015;35: 1633–1641.

20.Fede G, Privitera G, Tomaselli T, Spadaro L, Purrello F. Cardiovascular dysfunction in patients with liver cirrhosis.Ann Gastroenterol.2015;28:31-40.

21. Swai Joel, Hu Zixuan, Zhao Xiexiong, Rugambwa Tibera, Ming Gui. Heart rate and heart rate variability comparison between postural orthostatic tachycardia syndrome versus healthy participants;a systematic review and meta-analysis.BMC Cardiovasc Disord. 2019;19:320.

22. Restoux A, Grassin-Delyle S, Liu N, Paugam-Burtz C, Mantz J, Le Guen M. Pilot study of closed-loop anaesthesia for liver transplantation. Br J Anaesth.2016;117:332-340.

23. Soleimanpour H, Safari S, Shahsavari Nia K, Sanaie S, Alavian SM. Opioid drugs in patients with liver disease:A systematic review.Hepat Mon.2016;16:e32636.

24. Bergmann I,Göhner A, Crozier TA, et al.Surgical pleth index-guided remifentanil administration reduces remifentanil and propofol consumption and shortens recovery times in outpatient anaesthesia.Br J Anaesth.2013;110:622-628.

25. Azzam Ammar A H, McDonald John, Lambert David G.Hot topics in opioid pharmacology:mixed and biased opioids. Br J Anaesth. 2019;122:e136-e145.

26. Mastronardi P,Cafiero T, De Cillis P.Remifentanil in anesthesia and intensive care.Minerva Anestesiol.2000;66:417-423.

27. Freeman RB Jr, Wiesner RH, Harper A, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl.2002; 8: 851-858.

Figures

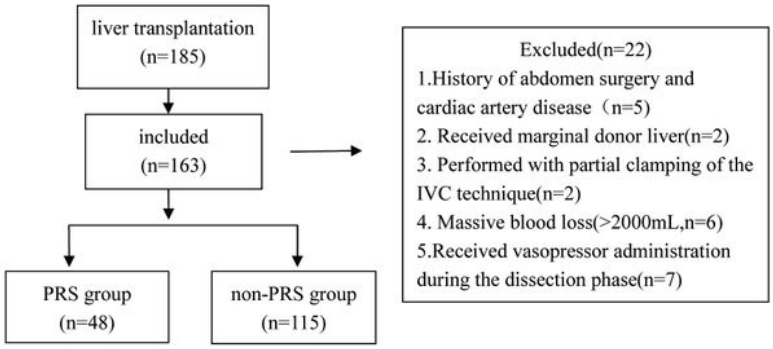

Figure 1

Flow chart of study participants. PRS= postreperfusion syndrome SSI, surgical plethysmographic index IVC, inferior vena cava MELD,model for end-stage liver disease