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Blood pressure monitoring during liver transplantation: the method of measurement does matter

M.L. Katin*, A.M. Dzyadz`ko, M.Yu. Gurova, O.O. Rummo

Minsk Scientific and Practical Center of Surgery, Transplantation and Hematology,

8 Semashko St., Minsk, 220045, Republic of Belarus

*Correspondence to: Maksim L. Katin, Head of Anesthesiology and Intensive Care Unit № 2 at the Minsk Scientific and Practical Center of Surgery, Transplantation and Hematology, e-mail: katinml@gmail.com

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Introduction. *Accurate blood pressure (BP) measurements are the mainstay for the efficient management of abrupt changes of hemodynamics and perfusion during orthotopic liver transplantation (OLT).*

Material and methods. *The prospective study included 39 patients. We compared the BP values measured in the femoral and radial arteries during the different phases of the OLT.*

Results. *The central systolic arterial pressure (SAP) and mean arterial pressure (MAP) were significantly higher than those measured in the peripheral artery during the anhepatic phase (95.1±10.6 vs. 84.5±9.9 mm Hg, and 66±8.8 vs. 59.7±7.1 mm Hg, respectively), after 5 minutes of reperfusion (91.1±17.3 vs. 78.5±18.4 mm Hg, and 63.9±13.1 vs. 57.7±13.6 mm Hg, respectively), and after 15 minutes of reperfusion (102.2±16.8 vs. 88.1±14.4 mm Hg, and 67.7±10.7 vs. 62.5±10.4 mm Hg, respectively). We found a strong correlation between the differences of SAP and MAP and the dose of norepinephrine administered during the anhepatic phase (r=0.76*

and r=0.77 for SAP and MAP, respectively), and after 5 minutes of reperfusion (r=0.71 and r=0.52 for SAP and MAP, respectively). The difference between central and peripheral BPs after 15 minutes of reperfusion mainly depended on the changes in the potassium concentration (r=0.55 for SAP and MAP) and base deficiency (r=0.73 and r=0.82 for SAP and MAP, respectively).

***Conclusion**. Thus, it was proved that the invasive measurement of BP in the femoral artery is a more accurate method compared with that in the radial artery as it is less exposed to high doses of vasopressors and variations in the acid-base state during OLT.*

Keywords: blood pressure, orthotopic liver transplantation

Conflict of interests. Authors declare no conflict of interests

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Abbreviations

BP = blood pressure

DAP = diastolic arterial pressure

SAP = systolic arterial pressure

MAP = mean arterial pressure

IVC = inferior vena cava

OLT = orthotopic liver transplantation

BE = base excess

SD = standard deviation

MELD = Model for End-Stage Liver Disease

Introduction

Invasive blood pressure (BP) monitoring is the standard in providing anesthesia during orthotopic liver transplantation (OLT) surgery. The number and location of arterial lines vary between centers [1]. The most frequent access site for blood pressure monitoring is the radial artery because this access is easy to get and associated with low complication rates [2]. Many clinical decisions in everyday practice are based on the blood pressure measurement, especially during large surgical interventions, such as OLT. Systolic arterial pressure (SAP) measured in the radial artery is usually slightly higher than that in the aorta, while the mean arterial pressure (MAP) remains constant at any level of the arterial vascular tree [3]. The inverse ratio of the central and peripheral pressures is observed after artificial circulation [4, 5] and in other clinical situations, including sepsis and vasopressor infusions [6]. The data on such changes in the ratio of central and peripheral pressures during OLT have already been published [7], but they have not been confirmed for restrictive strategy of perioperative fluid therapy in volemic support during surgery.

The study purpose

The purpose of the study was to compare the "invasive" BP pressure values measured in the radial and femoral arteries in patients who were managed using the protocol of restrictive fluid therapy for liver recipients and to assess the impact of various hemodynamic and metabolic factors on the accuracy of measuring the "invasive" blood pressure during OLT.

Material and methods

After receiving the approval from the local Ethics Committee and obtaining a signed informed consent, 39 patients with end-stage liver cirrhosis were enrolled in a prospective observational study to investigate the impact of restrictive perioperative infusion therapy on patients' hemodynamics during OLT (Table. 1).

Table 1. Patient characteristics

Total number	39
Age, years	50 (10)
Gender, m:f	20:19
Body Mass Index, kg/m^2	24 (4.2)
Child – Pugh A,%	12
Child – Pugh B,%	60
Child – Pugh C,%	28
MELD	16 (3.5)
Ascites, %	59
Hepatorenal syndrome, %	26

Note: MELD denotes the assessment of liver cirrhotic patient's severity by MELD score (Model for End-stage Liver Disease, 2016)

Patient characteristics are shown in Table 1. The causes of liver cirrhosis included viral hepatitis in 62% of patients, primary biliary cirrhosis in 10%, non-alcoholic steatohepatitis in 5%, Wilson's disease in 5%, cryptogenic cirrhosis of the liver and others in 18%. Among all the patients, the liver cirrhosis severity was assessed as Child–Pugh A in 12% of cases, Child–Pugh B in 60%, and Child–Pugh C in 28% of cases. The mean MELD of the patients was 16. Hepatorenal syndrome before surgery was observed in 26%, ascites were seen in 59% of recipients.

Liver transplantation was performed using the "classical" technique with complete clamping of vena cava [8] at the stage of making vascular

anastomoses without using veno-venous bypass. Standard monitoring included electrocardiography, pulse oximetry, capnometry, and non-invasive blood pressure measurement. The following agents were used for induction into anesthesia: fentanyl 2 μg × kg^{-1}, propofol 2 mg × kg^{-1}, and rocuronium 0.6 mg × kg^{-1}. After orotracheal intubation, the patients' lungs were ventilated, keeping SpO_2 and $EtCO_2$ within normal range. The maintenance phase of anesthesia involved fentanyl 1–2 μg × kg^{-1} × h^{-1}, atracurium 0.3–0.6 μg × kg^{-1} × h^{-1}, and inhalation anesthesia with sevoflurane 0.7–1 vol.%. The depth of anesthesia was controlled by monitoring the bispectral index.

After induction into anesthesia, the radial artery was catheterized on the right with a 20G catheter, 8 cm long (Vygon arterial leadercath 115.090, Vygon, France). The catheter was connected to a rigid line, 150 cm long, filled with physiological solution, which was attached to a compatible transducer system (TrueWave™ T100209A, Edwards Lifesciences LLC, USA) that was positioned at the level of the patient's midaxillary line. All the patients also underwent a left femoral artery catheterization with a 5F catheter, 20 cm long (PiCCO Catheter PV2015L20N, Pulsion Medical Systems SE, Germany). The catheter was connected to a rigid line, 100 cm long, filled with physiological solution attached to a compatible transducer system (PiCCO Monitoring Kit PV8215CVP, Pulsion Medical Systems SE, Germany) that was positioned at the level of the patient's midaxillary line. The systems were reset by the level of atmospheric pressure before surgery. The blood pressure curves were displayed on a patient monitor (IntelliVue MP70, Phillips Healthcare, Netherlands) with the recording of systolic (SAP), mean (MAP), and diastolic (DAP) arterial pressures in the radial and femoral artery. The data were analyzed and registered at the end of anesthesia. The femoral artery catheter was attached to the central

hemodynamics measurement system (PiCCO2, Pulsion Medical Systems SE, Germany) for continuous measurement of cardiac index and derived parameters: global end-diastolic index, stroke volume variability, and systemic vascular resistance index. The body temperature was measured by the thermistor of the femoral artery catheter.

The data of "invasive" BP were recorded

- at the beginning of surgery (just before the skin incision);
- in the pre-hepatic phase (at 90 min after skin incision after skin incision);
- in the anhepathic phase (at 10 min after applying the clamps on the inferior vena cava [IVC]);
- in the reperfusion phase (on the 5th and 15th minutes after removing the clamps from the IVC);
- in neohepatic phase (at 90 min after reperfusion).

The parameters that were registered included the lowest SAP, MAP, and DAP obtained from the radial and femoral arteries at the indicated time points before the measurement of the cardiac output, since the rapid temperature changes occurring during the PiCCO2 monitor calibration process could have had an effect on the BP measurement.

Perioperative infusion therapy, vasopressor and cardiotonic support were carried as guided by the algorithm of restrictive fluid therapy for a perioperative period. The basic infusion rate was maintained at 2 ml × kg^{-1} × min^{-1}. Colloid boluses (4% gelofusin, 5% albumin solutions or fresh frozen plasma, depending on the clinical case) were administered in case a preload deficiency was detected (stroke volume variability ≥13%, global end-diastolic volume index ≤ 500 ml/m^2). Vasopressor support was administered

from the start of surgical intervention. Doses were chosen to maintain MAP at a level higher 65 mm Hg.

Statistical analysis was performed using "Statistica 10" Sofware. Clinically significant difference in BP was defined as a difference of 10 mm Hg or higher for SAP, and 5 mm Hg or higher for MAP and DAP. The t-test for dependent samples and Bland–Altman analysis were used to assess the statistical difference in the measurements of "invasive" blood pressure between the radial and femoral arteries [9]. Linear regression was used to determine the relationship between hemodynamic and metabolic (norepinephrine dose, potassium ion concentration, and base excess) variables and the BP difference value at different time points. Independent variables included the age, body mass index, liver cirrhosis severity as assessed by Child –Pugh score [10], and the norepinephrine dose. The dependent variables included the differences between SAP and MAP at different phases of OLT. Data are presented as mean values (standard deviation [SD]).

Results

A total of 468 blood pressure measurements were obtained from the 39 patients included in the study. SAP and MAP data obtained from the radial and femoral arteries at different phases of surgery are presented in Table 2.

Table 2. Blood pressure in the orthotopic liver transplantation phases

OLT phase	SAP, mm Hg		MAP, mm Hg	
	Radial artery	Femoral artery	Radial artery	Femoral artery
Start of surgery	108.1 (12.9)	107.6 (11.4)	78.4 (10.3)	78 (11.3)
Pre-anhepathic	102.9 (9.1) *	104.7 (8.4)	75.6 (8.1)	76.4 (8.5)

Anhepathic	84.5 (9.9) **	95.1 (10.6)	59.7 (7.1) **	66 (8.8)
Reperfusion 1	78.5 (18.3) **	91.1 (17.3)	57.7 (13.6) **	63.9 (13.1)
Reperfusion 2	88.1 (14.4) **	102.2 (16.8)	62.5 (10.4) **	67.7 (10.7)
Neohepatic	99.5 (9.6) **	109.4 (9.3)	69.3 (18.5) *	71.9 (15.6)

* Statistically significant difference, $p < 0.05$
** Statistically significant difference, $p < 0.01$

At the beginning of surgery SAP and MAP in the radial and femoral arteries were not statistically different. During the pre-hepatic period, a statistically significant difference in SAP was found between the radial and femoral arteries (102.9 ± 9.1 mm Hg versus 104.7 ± 8.4 mm Hg, $p = 0.04$), which had no clinical significance. During the anhepathic phase, the central SAP and MAP were significantly higher than those measured in the peripheral artery (95.1 ± 10.6 versus 84.5 ± 9.9 mm Hg; $p = 0.005$ for SAP, and 66 ± 8.8 versus 59.7 ± 7.1 mmHg; $p = 0.007$ for MAP). A similar pattern was observed after 5 minutes of reperfusion (91.1 ± 17.6 versus 78.5 ± 18.3 mm Hg; $p = 0.006$ for SAP, and 63.9 ± 13.1 versus 57.7 ± 13.6 mm Hg; $p = 0.009$ for MAP), and after 15 min of reperfusion (102.2 ± 16.8 vs. 88.1 ± 14.4 mm Hg; $p = 0.005$ for SAP, and 67.7 ± 10.7 versus 62.5 ± 10.4 mm Hg; $p = 0.007$ for MAP). During the neohepatic phase, statistically significant differences were found in SAP and MAP between their values obtained in the radial and femoral arteries (99.5.5 ± 9.6 versus 109.4 ± 9.3 mm Hg; $p = 0.003$ for SAP, and 69.3 ± 18.5 versus 71.9 ± 15.6 mm Hg; $p = 0.04$ for MAP); however, only the former difference was clinically significant. Bland-Altman plots for anhepatic phase and a 15 min reperfusion time-point are shown in Fig. 1 and Fig. 2.

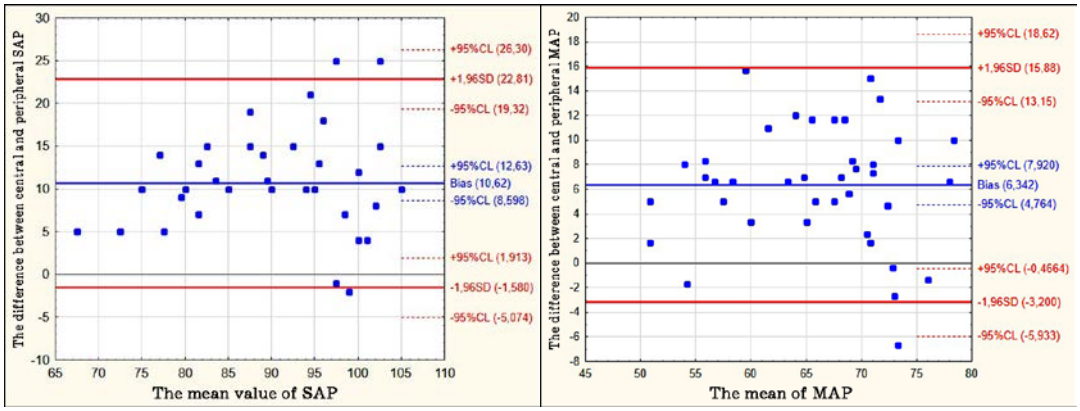

Fig. 1. The difference in SAP and MAP between their values obtained in the radial and femoral arteries in the anhepatic phase of orthotopic liver transplantation. Horizontal lines show the mean bias and the upper and lower limits of agreement 1.96 × SD

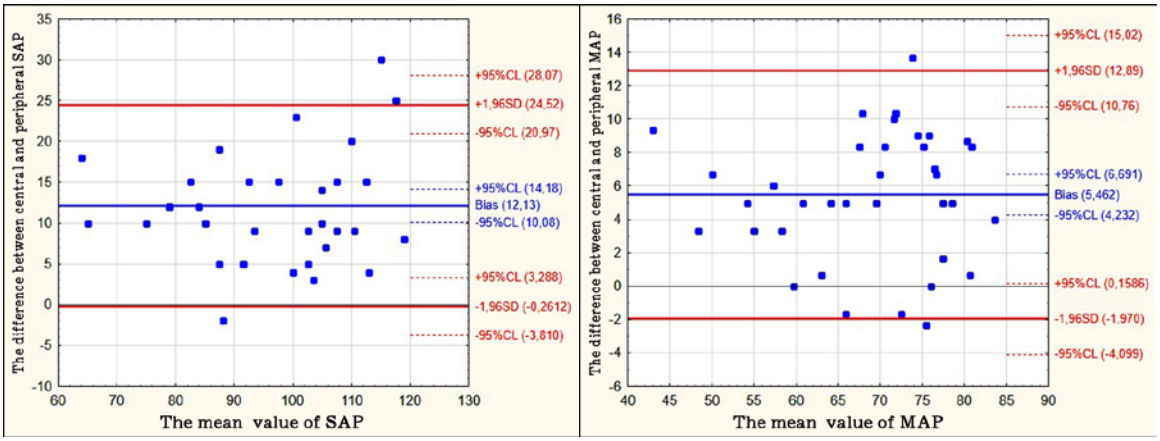

Fig. 2. The difference in SAP and MAP between their values obtained in the radial and femoral arteries after 15 minutes of reperfusion. Horizontal lines show the mean bias and the upper and lower limits of agreement 1.96×SD

In the anhepathic phase, there was a decrease both in the central and peripheral SAP and MAP. However, the extent of peripheral SAP reduction (18.4 ± 10.9 mm Hg) between the pre-hepatic and anhepathic phases was

statistically significantly higher than that in the central SAP reduction (9.64 ± 10.1 mm Hg; p = 0.008). A similar pattern was observed in the extents of peripheral and central MAP reductions (13 ± 9.5 mm Hg vs. 7.2 ± 8.9 mm Hg; p = 0.009) (Table 3).

Table 3. Arterial pressure changes during the liver transplantation surgery

OLT phase	SAP, mm Hg		MAP, mm Hg	
	Radial artery	Femoral artery	Radial artery	Femoral artery
Pre-anhepathic	102.9 (9.14)	104.7 (8.4)	75.6 (8.1)	76.4 (8.5)
Anhepathic	84.5 (9.9) **	95.1 (10.6)	59.7 (7.1) **	66 (8.8)
Difference	18.4 (10.9) **	9.64 (10.1)	13 (9.5) **	7.2 (8.9)

* Statistically significant difference, p <0.05
** Statistically significant difference, p <0.01

All patients required various doses of norepinephrine infusion during OLT. The correlation analysis revealed a strong correlation between the central, peripheral systolic (ΔSAP), the mean arterial pressure (ΔMAP) and the dose of norepinephrine administered during the anhepatic phase (r = 0.76; p = 0.00000 and r = 0.77; p = 0.00000, respectively), as well as on the 5th minute of the reperfusion phase (r = 0.71; p = 0.00000 and r = 0.52; p = 0.0006, respectively) (Fig. 3 and Fig. 4).

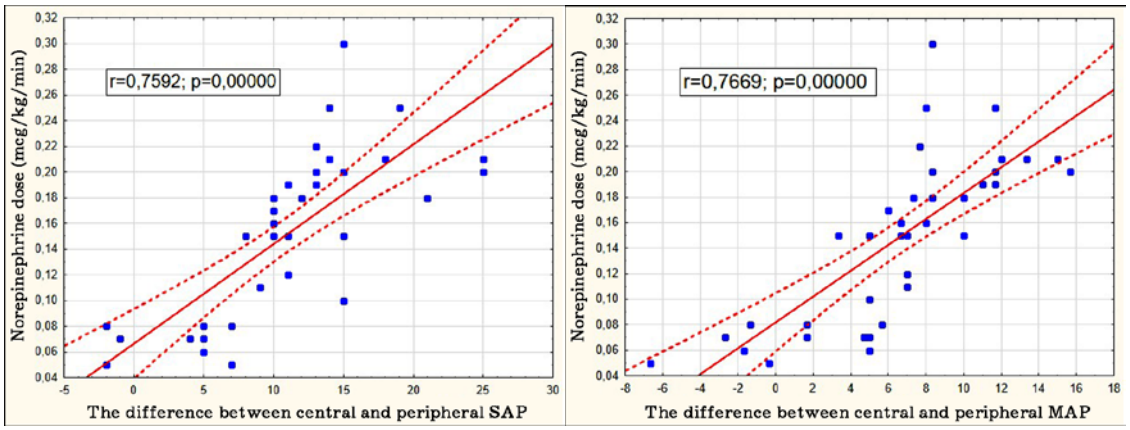

Fig. 3. The correlation between ΔSAP, ΔMAP, and the norepinephrine dose administered during the anhepathic phase

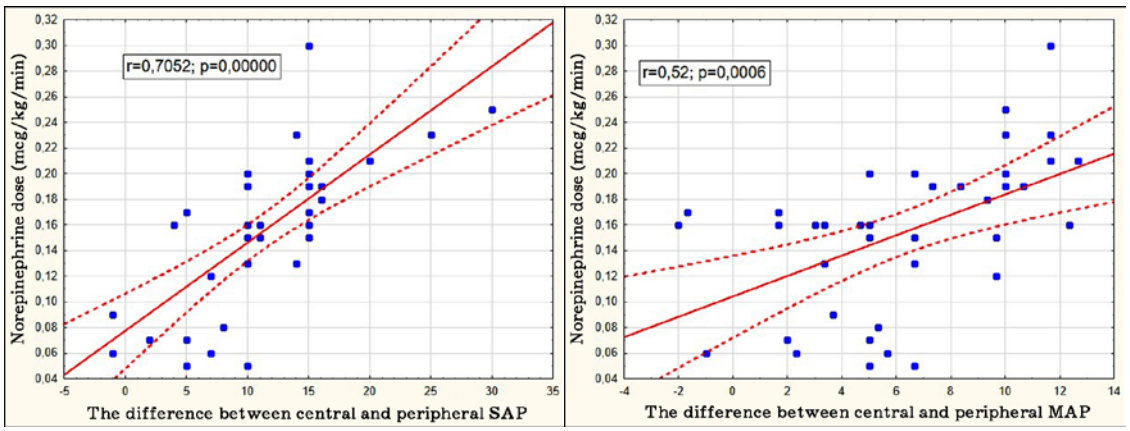

Fig. 4. The correlation between ΔSAP, ΔMAP, and the dose of norepinephrine administered after 5 min of reperfusion

The correlation between ΔSAP and ΔMAP and the dose of norepinephrine on the 15th minute of the reperfusion phase was not so convincing (r = 0.21; p = 0.2084 and r = 0.27; p = 0.0935, respectively), which prompted us to look for other causal factors for this phenomenon. We assumed that changes in the regulation of vascular tone of the peripheral arteries after reperfusion were associated with an excess of anaerobic metabolism products entering the bloodstream. Table 4 shows the dynamic

changes in the blood concentration of potassium ions (K^+) and base excess (BE).

Table 4. Changes in the blood concentration of potassium ions and base excess during the liver transplantation surgery

	Pre-anhepatic phase	Anhepatic phase	Reperfusion 2 (15 minutes)
K^+, mmol/L	3.9	4.1	5.3 **
BE mmol/L	-0.9	-3.4 *	-7.9 **

* Statistically significant difference in the parameter values ($p < 0.01$) between the pre-hepatic and anhepatic phases.
** Statistically significant difference in the parameter values ($p < 0.01$) between the hepatic and reperfusion phases.

During the reperfusion period, we noted a statistically significant increase in the concentration of potassium ions and a statistically significant decrease of BE compared with those parameters recorded in an anhepatic phase. A statistically significant decrease of BE in blood in the anhepatic phase compared with those in the pre-hepatic phase had no clinical significance.

The correlation analysis revealed a strong correlation between the ΔSAP, MAP and the blood potassium concentration ($r = 0.55$; $p = 0.0003$ and $r = 0.55$; $p = 0.0002$, SAP and MAP, respectively), as well as BE in blood ($r = 0.73$; $p = 0.0000$ and $r = 0.82$; $p = 0.0000$, SAP and MAP, respectively) after 15 minutes of the reperfusion phase (Fig. 5 and Fig 6).

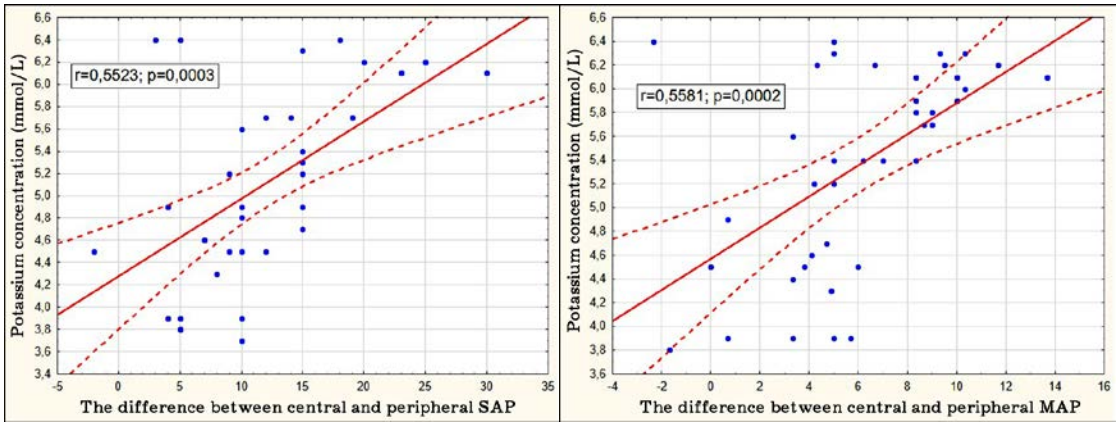

Fig. 5. Correlation between central and peripheral SAP, MAP, and blood potassium concentration after 15 minutes of reperfusion

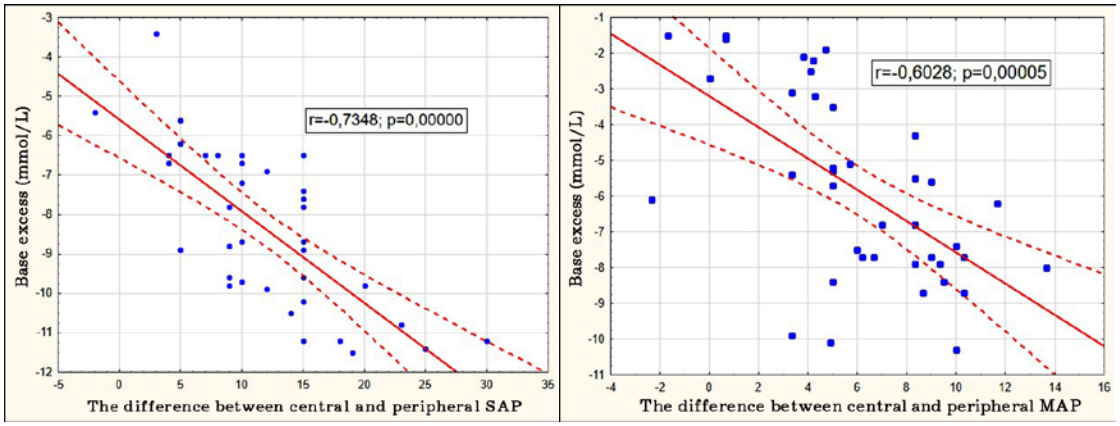

Fig. 6. Correlation between central and peripheral SAP, MAP, and base excess after 15 min of reperfusion

Discussion

This observational study yielded several results. First, statistically significant and clinically relevant differences were obtained in the SAP and MAP between their measured values in the radial and femoral arteries in the anhepatic phase, after 5 minutes of reperfusion, and after 15 minutes of reperfusion. Second, an obvious relationship was revealed in the SAP and MAP between their measured values in the central and periphery arteries in

the anhepathic phase, on the 5th minute of the reperfusion phase and depending on the norepinephrine dose. Third, a strong correlation was demonstrated between the blood potassium concentration, the base excess, and the SAP and MAP measured values after 15 min of reperfusion.

The statistical analysis (t-test for dependent samples) showed a statistically significant difference of 10.6 mm Hg between the central and peripheral SAP, and a statistically significant difference of 6.3 mm Hg between the central and peripheral MAP in the anhepathic phase (Table 2). The differences were verified using the Bland–Altman analysis (a special tool for comparing the results of two measurements, none of which is absolutely reliable), which also showed a statistically significant difference equal to 10.6 mm Hg between the central and peripheral SAP, and the one equal to 6.3 mm Hg between the central and peripheral MAP (Figures 1 and 2). We interpreted these results as the evidence that the accuracy of both the systolic and mean arterial pressure measurements in the anhepatic phase of OLT depends on the location of the monitoring catheter. Under normal conditions, relatively compensated patients have the systolic blood pressure in the radial artery higher compared to its values taken in the femoral and other central arteries. This difference can be explained by an increased pulse as a result of a higher resistance and harmonic resonance in the vessels of the muscle type. At the same time, MAP values in the central and peripheral arteries practically do not differ [6, 11]. Specific circumstances can cause considerable differences between the MAP in the radial artery and the central MAP. When invasive BP measurement through a catheter in the radial artery is taken, such factors as the presence of proximal obstructive vascular lesion, warming after hypothermic artificial blood circulation [4, 5, 12], high doses of vasopressors [6, 13, 14], deep hypothermia [12], cardio-

pulmonary resuscitation [15], and anesthesia with isoflurane [5] may lead to underestimated central BP level. The cause of this discrepancy in obstructive vascular lesion is obvious; however, there are certain contradictions in determining the etiology of this phenomenon during artificial blood circulation and vasopressor therapy. There is a theory that muscular-type arteries are more sensitive to pressure effects than central elastic arterial vessels [16]. This mechanism leads to a significant reduction in blood flow in the radial artery when exposed to vasopressors [5]. The differences observed in the anhepathic phase are apparently related to the titration of high doses of vasopressors to maintain an adequate perfusion in conditions of reduced venous return after clamping the IVC. The studies that had investigated this phenomenon in liver recipients demonstrated conflicting results. Acosta et al. [7] noted no differences between the central or peripheral MAP measurements at any stage of OLT, while Arnal et al. [17] observed the difference in SAP only, but not in MAP during reperfusion. A study examining pediatric OLT, on the contrary, showed a significant difference in both the SAP and MAP when comparing the results of measurements in the femoral and radial arteries in most patients [18].

Interesting data were obtained in a study where the authors compared the results of blood pressure measurements using a cuff on the upper limb and the direct blood pressure measurements in the femoral and radial arteries 3–10 minutes after the venous reperfusion of the graft. The results were significantly comparable for blood pressure measurements made in an indirect way and invasive measurements in the femoral artery, and discrepancies were found when compared those with the BP values obtained by invasive monitoring in the radial artery. Presumably that was due to a

more proximal cuff position for non-invasive blood pressure measurement. [19].

We believe that such a considerably discrepancy in the results may be explained, first, by different approaches to an infusion therapy in each of the centers performing OLT; and second, by analyzing the differences in the invasive BP measurement separately, without taking into account the effect of other factors, such as a vasopressor dose, peripheral vascular resistance status, preload, etc.

The results obtained when analyzing the correlation of central and peripheral BP with a vasopressor dose showed the greatest correlation ($r = 0.76$, $p = 0.00000$ for SAP and $r = 0.77$; $p = 0.00000$ for MAP) observed in the anhepatic phase (Fig. 3). The correlation analysis after 5 min of reperfusion (Fig. 4) showed a moderate correlation of SAP ($r = 0.71$; $p = 0.00000$) and MAP ($r = 0.52$; $p = 0.0006$) to the rate of norepinephrine titration. When comparing the relationship of central and peripheral BP to norepinephrine dose after 15 minutes of reperfusion (Fig. 5), a very weak correlation was found ($r = 0.21$; $p = 0.2084$ for SAP and $r = 0.27$; $p = 0.0935$ for MAP).

Our observations demonstrated lower values of SAP and MAP measured in the radial artery, as compared to the results of those parameter measurements in the femoral artery (Table 2) in the reperfusion phase of OLT. The causes of the revealed central-to-peripheral decrement in the early post-reperfusion period (after 5 min of reperfusion) were quite clear and depended primarily on a significant decrease in the right ventricle preload caused by a decrease in the blood circulating volume as a result of filling the graft with blood, and the associated increase in the vasopressor dose. Meanwhile, we did not observe a strong correlation of the central and

peripheral BP values to the dose of norepinephrine on the 15th minute of reperfusion. The causes of that might become clearer after analyzing the relationship between the peripheral vascular tone impairments and the pathophysiological abnormalities occurring in the recipient's body with blood flow restoring in the liver graft. As a result of reperfusion, significant amounts of anaerobic metabolism products and potassium ions are released into the systemic circulation. These changes lead to an impaired autoregulation of the vascular tone, causing a pronounced decrease in the total peripheral vascular resistance. This phenomenon is based on the mechanisms similar to warming after hypothermic artificial circulation. There is a theory about extreme vasoplegia leading to proximal bypass and distal vasoconstriction of arterial vessels, which is the cause of low peripheral pressure [20]. The results obtained in the analysis of the correlation of central and peripheral BP with the blood potassium concentration after 15 minutes of reperfusion showed a moderately strong correlation of the central-to-peripheral decrement of SAP ($r = 0.55$; $p = 0.0003$) and MAP ($r = 0.55$; $p = 0.0002$) to the concentration of potassium ions. Meanwhile, the results of the analysis of the correlation between systolic and mean BP measured in the central and peripheral arteries and the blood BE showed a strong dependence of the central-peripheral decrement of SAP ($r = 0.73$; $p = 0.0000$), and of MAP, in particular ($r = 0.82$; $p = 0.0000$).

This confirmed our assumptions that the mechanism of the revealed significant difference between the MAP in the radial artery and the central mean BP in the reperfusion period was related to vasoplegia after hypothermic circulation.

Conclusion

Invasive blood pressure monitoring is a mandatory component of patient anesthesia during orthotopic liver transplantation. In some cases, measuring invasive arterial pressure in the femoral artery has several advantages: (1) in infusing high doses of vasopressors to correct low total peripheral vascular resistance and vasoplegia during liver transplantation when the measuring of the “invasive” arterial pressure through a catheter in the radial artery is not a fairly accurate technique; (2) the femoral artery catheterization in critically ill patients with preexisting hypotension and vasoconstriction is technically easier than the radial artery catheterization and has a better chance for success [14]; (3) and the use of ultrasound navigation for femoral artery catheterization makes this technique as safe as the radial artery catheterization [21]. Despite the obvious advantages of the femoral artery catheterization for invasive blood pressure monitoring during orthotopic liver transplantation, it is worth noting the risks of potential complications when performing this intervention. They include a high risk of bleeding, arterial pseudoaneurysm formation, and femoral artery thrombosis [22]. Therefore, when making decision on the method for measuring the “invasive” blood pressure, one must be guided by a balance between relative risk and benefit for each individual patient.

Since the results obtained by measuring the "invasive" blood pressure in the femoral artery are less susceptible to the impact of pathophysiological disturbances and the changes in the volemia and vasopressors balance occurring during the different phases orthotopic liver transplantation, this technique ensures better accuracy of hemodynamic monitoring in liver transplant recipients, and, hence, the timeliness of taking clinical decisions during orthotopic liver transplantation.

In recipients with severe hepatic failure and the resulted hyperdynamic circulation syndrome, the invasive measurement of blood pressure in the femoral artery is a more sensitive tool for displaying the changes in hemodynamics during orthotopic liver transplantation.

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Information about authors

Maksim L. Katin, Head of Anesthesiology and Intensive Care Unit No.2 at Minsk Scientific and Practical Center of Surgery, Transplantation, and Hematology, ORCID:0000-0001-8129-1249;

Alexandr M. Dzyadz'ko, Dr. Med. Sci., Head of Anesthesiology and Intensive Care Department at Minsk Scientific and Practical Center of Surgery, Transplantation, and Hematology, ORCID:0000-0003-1965-1850;

Maryanna Yu. Gurova, Head of Anesthesiology and Intensive Care Unit No.5 at Minsk Scientific and Practical Center of Surgery, Transplantation, and Hematology, ORCID:0000-0003-4923-7204;

Oleg O. Rummo, Corr. Member of NAS of Republic of Belarus, Prof., Dr. Med. Sci., Director of Minsk Scientific and Practical Center of Surgery, Transplantation, and Hematology, ORCID:0000-0001-7023-4767.