

Agreement between radial and femoral arterial blood pressure measurements during orthotopic liver transplantation

Matthew Lee, Laurence Weinberg, Brett Pearce, Nicholas Scurrah, David A Story, Param Pillai, Peter R McCall, Larry P McNicol and Philip J Peyton

Maintenance of cardiovascular stability during orthotopic liver transplantation (OLTx) is a significant challenge to the anaesthetist. Patients with advanced liver failure typically have peripheral vasodilatation and a hyperdynamic circulation.¹ Intraoperative blood loss is often substantial due to collateral portal circulation and coagulopathy, and patients may become more haemodynamically unstable from haemorrhage, clamping of major blood vessels, graft reperfusion and early graft dysfunction. Accurate real-time monitoring of the circulation is essential for the optimisation of blood volume and the titration of vasopressors to minimise circulatory instability and perioperative risk. Therefore, invasive monitoring of systemic arterial and venous filling pressures is standard practice.

Poor agreement between arterial blood pressure (BP) measurements at different measurement sites has been shown in vasodilatory states during cardiac surgery²⁻⁴ and in critically ill patients on vasoactive drugs.^{5,6} In OLTx, this has occurred briefly after graft reperfusion in a small number of studies.⁷⁻¹⁰ It is not clear whether measurement discrepancies are more significant for mean arterial pressure (MAP) or systolic arterial pressure (SAP). This has important implications for anaesthetic practice, as measured arterial pressure is a primary determinant of fluid and vasopressor administration. We compared arterial pressure measurements in the radial and femoral arteries during OLTx to measure any clinically significant differences between them, and to establish whether arterial pressure measurements at the two sites can be used interchangeably.

Methods

Our study was approved with a waiver of patient consent from the local human research ethics committee (H2012/04546) because arterial pressure measurement at both radial and femoral sites is standard care in our institution for this surgery. The severity of liver disease was assessed with the Mayo Model for End-Stage Liver Disease (MELD) score (United Network for Organ Sharing modification). Patients were excluded if they had contraindications or if there were technical barriers to successful radial and femoral arterial cannulation or pulmonary arterial catheterisation. Patients

ABSTRACT

Objective: To study agreement between radial and femoral arterial pressure measurements in orthotopic liver transplantation (OLTx) surgery to determine whether arterial cannulation sites are interchangeable.

Design, setting and participants: Prospective observational study of 25 patients undergoing OLTx surgery.

Methods: Radial and femoral arteries were cannulated with standardised arterial line kits. Radial and femoral mean arterial pressure (MAP), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and pulse pressure (PP) were measured at four time points (30 minutes after induction of anaesthesia, 30 minutes after the start of the anhepatic phase, 30 minutes after liver graft reperfusion and 30 minutes after the start of bile duct anastomosis).

Main outcome measures: The bias, precision and limits of agreement between radial and femoral arterial pressures were calculated in accordance with Bland–Altman statistics.

Results: Radial–femoral differences in MAP (mean difference, 4.8 mmHg [SD, 4.5 mmHg]), limits of agreement (–13.6 and 8.8, $P < 0.001$) and DAP showed clinically acceptable agreement between measurement sites across all time points. However, clinically significant differences between radial and femoral SAPs (mean difference, –14.9 mmHg [SD, 24.8 mmHg]) and limits of agreement (–63.5 and 33.7, $P < 0.001$) occurred overall. This difference started after portal vein clamping and remained significant throughout the remainder of the operation.

Conclusion: Radial artery SAP underestimates femoral artery measurements significantly but unpredictably. As femoral measurement is more likely to reflect central arterial pressure, radial SAP measurement is not reliable in adults undergoing OLTx.

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undergoing liver transplantation for indications other than liver failure were also excluded (MELD score < 10). We conducted the study between 22 March 2012 and 30 September 2013.

Table 1. Arterial pressure measurements and measures of agreement at four surgical time points and overall

Time point (n)	Mean radial arterial pressure, mmHg (range; SD)	Mean femoral arterial pressure, mmHg (range; SD)	Mean difference, mmHg (SD [=precision])	Limits of agreement, mmHg	P
MAP					
T1 (24)	74.2 (53–125; 16.8)	77.4 (56–126; 16.9)	–3.2 (3.5)	–10.1 to 3.7	0.0004*
T2 (24)	61.9 (36–80; 11.7)	67.4 (48–83; 10.8)	–5.5 (3.8)	–13.0 to 2.0	<0.0001†
T3 (25)	60.0 (46–87; 9.1)	65.0 (54–91; 21.9)	–5.0 (4.1)	–13.0 to 3.0	0.0001*
T4 (25)	63.4 (39–95; 13.1)	68.8 (49–100; 12.0)	–5.4 (4.8)	–14.8 to 4.0	<0.0001†
Overall	64.8 (36–125; 13.9)	69.6 (48–126; 13.1)	–4.8 (4.5)	–13.6 to 8.8	<0.0001*
SAP					
T1 (23)	109.3 (80–178; 21.5)	113.0 (82–175; 22.9)	–3.7 (14.7)	–35.5 to 25.1	0.1029
T2 (22)	86.2 (45–128; 20.4)	107.0 (61–130; 16.9)	–19.1 (19.5)	–57.3 to 19.1	0.0001†
T3 (23)	91.9 (60–143; 19.7)	111.0 (75–146; 20.8)	–18.3 (25.4)	–68.1 to 31.5	0.0017†
T4 (24)	94.8 (48–137; 21.1)	113.5 (80–141; 15.8)	–18.6 (26.2)	–70.0 to 32.8	0.0020†
Overall	95.6 (45–178; 21.4)	111.2 (61–175; 19.1)	–14.9 (24.8)	–63.5 to 33.7	<0.0001*
DAP					
T1 (23)	54.5 (37–78; 10.8)	55.0 (38–80; 11.3)	–0.5 (3.6)	–7.6 to 6.6	0.0584
T2 (22)	47.3 (30–62; 8.7)	50.0 (33–66; 8.7)	–2.6 (3.0)	–8.5 to 3.3	0.0004†
T3 (23)	44.9 (32–61; 7.1)	46.0 (35–71; 7.3)	–1.1 (2.4)	–5.8 to 3.6	0.0217
T4 (24)	47.1 (30–72; 13.5)	48.1 (27–73; 10.5)	–1.0 (1.6)	–4.1 to 2.1	0.0066†
Overall	48.5 (30–78; 10.2)	49.8 (27–80; 10.0)	–1.3 (3.0)	–7.2 to 4.6	<0.0001*
PP					
T1 (23)	56.9 (43–138; 19.4)	58.0 (33–95; 14.9)	–1.1 (17.5)	–35.4 to 33.2	0.3606
T2 (22)	38.9 (15–67; 13.9)	57.0 (17–77; 15.4)	–18.1 (19.0)	–55.3 to 19.1	0.0005†
T3 (23)	47.0 (25–82; 13.4)	64.1 (27–109; 21.9)	–17.1 (26.6)	–69.2 to 35.0	0.0109†
T4 (24)	47.7 (17–70; 13.5)	65.3 (33–105; 16.8)	–17.6 (26.6)	–69.7 to 34.5	0.0073†
Overall	47.7 (15–138; 16.3)	61.2 (17–109; 17.6)	–13.5 (25.5)	–63.5 to 36.5	<0.0001*

MAP = mean arterial pressure. T1 = 30 minutes after skin incision. T2 = 30 minutes after portal venous clamping. T3 = 30 minutes after graft reperfusion. T4 = 30 minutes after start of bile duct anastomosis. SAP = systolic arterial pressure. DAP = diastolic arterial pressure. PP = pulse pressure. * Using Wilcoxon signed-rank test with Bonferroni correction. † Using student *t* test with Bonferroni correction.

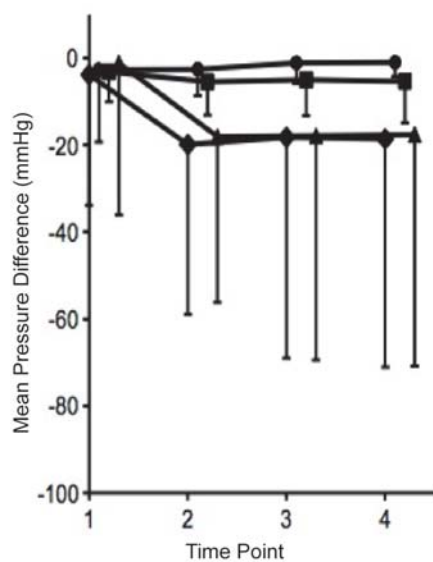
Induction of anaesthesia consisted of a balanced technique combining intravenous midazolam 0.02–0.03 mg/kg, propofol 1–3 mg/kg, fentanyl 1–2 µg/kg and a neuromuscular blocker. Anaesthesia was maintained with isoflurane at inspired concentrations of 0.5–1.5 minimum alveolar concentration in a 50% oxygen–air balance and an infusion of fentanyl 2–5 µg/kg/hour. Ventilation was via a low-flow circle-breathing system with the ventilator set to provide a tidal volume of 7–8 mL/kg using volume-control mode without positive end expiratory pressure. The end tidal partial pressure of carbon dioxide measured by capnography was maintained at 30–40 mmHg.

Routine monitoring included continuous electrocardiography, pulse oximetry and capnography. In accordance with routine practice, invasive radial artery and femoral artery pressure, central venous pressure, pulmonary artery pressure, mixed venous oximetry, urine output and core body temperature monitoring were established after induction of

anaesthesia. A vasopressor infusion of intravenous noradrenaline was administered, according to routine practice, at a rate determined by the attending anaesthetist on the basis of patient haemodynamics (arterial pressure, cardiac output and ventricular preload).

The radial and femoral arteries were cannulated with identical 18-gauge, 18-cm long arterial catheterisation sets (Leader-Cath, Vygon). The two catheters were connected to identical pressure transducers with identical connecting tubing of standard 180 cm length. The two transducers were mounted side by side on a manifold at the midaxillary level and simultaneously calibrated for atmospheric pressure (zeroed). The square wave test was performed after initial setup and at each subsequent measurement time point to confirm that the damping and dynamic responses of the two measurement systems were similar.

MAP, SAP and diastolic arterial pressure (DAP) were recorded during clinical steady-state conditions (in which

Figure 1. Arterial pressure difference v time*

■ = MAP. ◆ = SAP. ● = DAP. ▲ = PP. * Measurements taken from radial and femoral sites at four surgical time points: 1 (30 minutes after skin incision), 2 (30 minutes after portal venous clamping), 3 (30 minutes after liver reperfusion), and 4 (30 minutes after the start of bile duct anastomosis). Two standard deviations are indicated by the vertical error bars.

MAP varied by less than 10% over the preceding 3 minutes) at four time points: 30 minutes after skin incision (T1), 30 minutes after portal vein clamping (T2), 30 minutes after liver graft reperfusion (T3) and 30 minutes after the start of bile duct anastomosis (T4). Pulse pressure (PP) was calculated by subtraction of DAP from SAP. Systemic vascular resistance index (SVRI) was calculated, at each time point and overall, from the MAP–CVP difference, body surface area and the measured cardiac output from bolus thermodilution (using an average of five 10 mL boluses of saline at room temperature). The noradrenaline infusion rate at each time point was also recorded.

The primary end point was the difference in MAP between radial and femoral sites across the four time points and overall. The differences between radial and femoral SAP, DAP and PP were secondary end points.

Bias, precision and limits of agreement were calculated using the Bland–Altman method with correction for multiple measurements,^{11,12} and were used to compare radial and femoral MAP, SAP, DAP and PP. Bias represents the systematic difference between both methods and was calculated as the mean difference between radial and femoral measurements. Precision represents the random error or variability in agreement between the two techniques and was calculated as the SD of the bias. The limits of agreement represent the range in which 95% of the

differences between methods are expected to lie and was calculated as the bias \pm 2 SD.^{13,14}

The statistical significance of differences in MAP, SAP, DAP and PP was calculated by averaging the values for each patient from all four time points, then applying the student *t* test for paired data after testing for normality with the Shapiro–Wilk test. Non-normal data were analysed using the Wilcoxon signed-rank test. $P \leq 0.05$ was considered statistically significant, with Bonferroni correction for multiple measurements. Because of the association between haemodynamic derangement and severity of liver disease in this population, the relationship between the radial–femoral pressure difference and MELD score was determined using the Pearson correlation coefficient (*r*).

Assuming a mean MAP of 70 mmHg and an SD of 5 mmHg, the estimated sample size to provide a 90% power to show a 10% difference between radial and femoral sites was 22 patients. To allow for data loss due to technical difficulties or unacceptable haemodynamic instability at the time of some measurements, 28 patients were recruited.

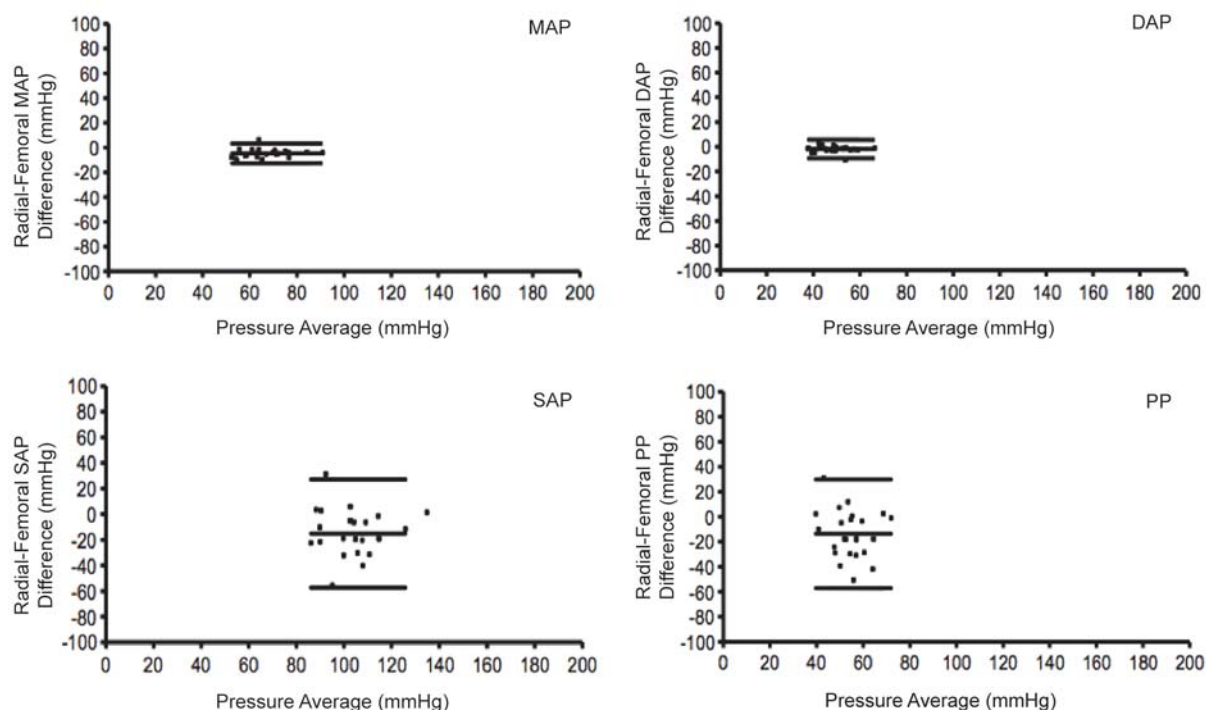
We conducted the statistical analysis using Excel 2008 (Microsoft) and Stata 2012 (Statacorp). Bland–Altman comparisons were conducted and computed with LabVIEW (National Instruments).

Results

Twenty-eight patients were enrolled in our study. Three patients were excluded, as the indication for their surgery was hepatocellular carcinoma rather than liver failure. Of the remaining 25 patients, nine were women and 16 were men. Their mean age was 46 years (SD, 11.8 years), mean weight was 81 kg (SD, 19.8 kg), mean height was 172 cm (SD, 7.5 cm), and mean body surface area was 1.96 m² (SD, 0.3 m²). Indications for OLTx were hepatitis C cirrhosis ($n = 10$), alcoholic cirrhosis ($n = 3$), non-alcoholic steatohepatitis ($n = 3$), autoimmune hepatitis ($n = 2$) and others ($n = 7$). The average MELD score was 24/40 (SD, 7.2). Seven right radial arterial lines and 10 right femoral arterial lines were inserted. All other arterial lines were left-sided. All patients received a noradrenaline infusion (mean, 4.6 μ /minute [SD, 5.0 μ /minute]).

There was acceptable agreement between radial and femoral MAP. Overall, radial MAP underestimated femoral MAP (–4.8 mmHg [SD, 4.5 mmHg]), which was a difference of minimal clinical significance (Table 1). The scatter in agreement between the two sites was acceptable, with limits of agreement between –13.6 mmHg and 8.8 mmHg at all time points. This level of agreement fulfils the accuracy criteria stipulated by the Association for the Advancement of Medical Instrumentation (AAMI) for BP measurement

Figure 2. Arterial pressure difference v arterial pressure average: Bland–Altman plots showing pressure difference in paired measurements from radial and femoral sites plotted against the average of the paired measurements*



MAP = mean arterial pressure. DAP = diastolic arterial pressure. SAP = systolic arterial pressure. PP = pulse pressure. * Upper horizontal lines = upper limits of agreements (two SDs). Lower horizontal lines = lower limits of agreements (two SDs). Middle horizontal lines = mean bias.

devices.¹⁵ These criteria are not specific for systolic, mean or diastolic pressure measurements, but devices are considered comparable if the mean difference between them is ≤ 5 mmHg (SD, ≤ 8 mmHg). Acceptable limits of agreement are therefore ± 15.7 mmHg by these criteria.

For SAP, statistically and clinically significant differences between radial and femoral pressures occurred after portal vein clamping and persisted throughout liver graft reperfusion and bile duct anastomosis. Overall, there was poor agreement between radial and femoral SAP, and wide scatter. Unlike SAP, DAP showed excellent agreement between radial and femoral sites at all time points. The variation in SAP was reflected in a large bias and limits of agreement for PP. These results are shown in Table 1, and graphically in Figure 1 and Figure 2.

There were weak correlations between noradrenaline infusion rates and the radial–femoral SAP difference ($r = -0.28$, $P < 0.01$), and between noradrenaline infusion rates and the radial–femoral PP difference ($r = -0.29$, $P < 0.01$), which were statistically significant after Bonferroni correction for multiple measurements per patient. The noradrenaline infusion rate correlated with radial MAP ($r = -0.36$,

$P < 0.001$), femoral MAP ($r = -0.31$, $P < 0.01$), radial SAP ($r = -0.35$, $P < 0.001$) and radial PP ($r = -0.38$, $P < 0.001$). Raw data are shown in Table 2. There was no relationship between noradrenaline infusion rates and SVRI, cardiac index or MELD score. There was no statistically significant correlation between MELD score and radial–femoral difference for any BP parameter (MAP, SAP, DAP or PP). Of a range of preoperative and intraoperative variables, on multivariate regression analysis, increasing age, decreasing body mass index (BMI) and increasing total intraoperative fluids were found to predict increasing radial–femoral MAP difference (increasing age, $P = 0.044$; decreasing BMI, $P = 0.001$; increasing total intraoperative fluids, $P < 0.001$) and radial–femoral SAP difference ($P = 0.047$, $P = 0.001$, $P = 0.022$ respectively). In addition, decreasing SVRI ($P = 0.013$) and decreasing cardiac index ($P = 0.043$) predicted increasing radial–femoral SAP difference as did markers of reduced ventricular preload (increased stroke volume variation ($P = 0.043$) and decreased central venous pressure ($P = 0.007$)). Noradrenaline infusion rates and MELD score were not significant predictors of radial–femoral difference for MAP or SAP.

Table 2. Haemodynamic data and noradrenaline infusion rates at each time point and overall

Time point	Mean PAC thermodilution CI, L/min/m ² (SD)	Mean SVRI using radial MAP, mmHg/L/min/m ² (SD)	Mean SVRI using femoral MAP, mmHg/L/min/m ² (SD)	Mean noradrenaline infusion rate, µg/min (SD)
T1	5.1 (1.4)	13.5 (6.1)	14.1 (6.1)	0.2 (0.4)
T2	4.3 (1.6)	13.6 (5.4)	15.3 (5.8)	4.3 (4.5)
T3	5.2 (1.7)	10.6 (4.7)	11.7 (5.1)	7.8 (5.1)
T4	5.9 (1.7)	9.5 (3.4)	10.5 (3.7)	6.1 (4.9)
Overall	5.1 (1.5)	11.8 (4.9)	12.9 (5.2)	4.7 (5.0)

PAC = pulmonary artery catheter. CI = cardiac index. SVRI = systemic vascular resistance index. MAP = mean arterial pressure. T1 = 30 minutes after skin incision. T2 = 30 minutes after portal venous clamping. T3 = 30 minutes after graft reperfusion. T4 = 30 minutes after the start of bile duct anastomosis.

Discussion

Our findings showed unacceptable accuracy and precision of agreement between radial and femoral SAP measurements after portal vein clamping, demonstrating that arterial cannulation sites are not interchangeable for most of the surgery. These findings differ considerably from previous studies in OLTx patients, for whom only brief differences between radial and femoral SAP measurements occurred after graft reperfusion. Arnal and colleagues found that radial SAP measurements only underestimated femoral SAP measurements immediately after liver graft reperfusion, with wide scatter in agreement.⁵ This underestimation was less pronounced in patients not receiving vasoconstrictor infusions. By 10 minutes after liver reperfusion, this difference was no longer present. Shin and colleagues observed high intraclass correlation between radial and femoral invasive arterial pressures before liver reperfusion and moderate correlation immediately after reperfusion.⁸ They did not use Bland–Altman statistics in their analysis, which makes comparison with other studies difficult.

The reasons for the differences in our results from previous studies are unclear, and this highlights potential limitations in generalising study findings between treatment centres. Arnal and colleagues conducted their investigations in Spain, which has an opt-out program for organ donation. Potentially, the patients in our study had more advanced liver disease due to the poorer availability of donor organs in Australia, and all patients in our study required vasoconstrictor treatment after reperfusion. The association that Arnal and colleagues found between radial–femoral SAP differences and vasoconstrictor use is reflected in our data, which showed a weak correlation between noradrenaline infusion rate and radial–femoral differences for SAP and PP. However, on multivariate regression analysis, noradrenaline infusion rate did not predict radial–femoral SAP or MAP difference. The persistent and large radial–femoral SAP difference that we found may reflect the severity of cardiovascular derangement rather than vasoconstrictor use, as suggested by the relationship with SVRI and cardiac index. We confirmed the findings of

Arnal and colleagues of no association between MELD score and radial–femoral SAP or MAP differences. Our findings of acceptable agreement in MAP are in keeping with previous studies in liver transplantation and sepsis,^{6–9} but these studies did not examine differences in SAP.

Our finding of acceptable agreement in all arterial pressure parameters at baseline excludes the possibility that our differences were due to equipment-related measurement artefact. Overall, radial SAP underestimated femoral measurement by about 15–20 mmHg, but this was unpredictable, as seen in the wide within-patient limits of agreement. This finding was similar to the radial PP measurement, which was also lower than the femoral measurement with wide limits of agreement. These differences could not be predicted from indices expected to be associated with a more vasodilated state such as noradrenaline infusion rate, SVRI or MELD score. The acceptable agreement between radial and femoral MAP and DAP throughout surgery suggests that monitoring sites are interchangeable for these measurements during OLTx. The underestimation of MAP by the radial site by about 5 mmHg was clinically insignificant and the scatter in agreement was acceptable.

Our criteria for acceptability of agreement were interpreted in accordance with the AAMI criteria for acceptable accuracy and reproducibility of BP measuring devices. It is possible to interpret the agreement between the two sites using a tolerability index approach, as suggested by previous authors.¹⁶ However, to avoid potential bias from the arbitrary nomination of tolerability thresholds, we chose to use the AAMI criteria. Although these criteria were developed for comparing sphygmomanometers, they are the most specific criteria related to BP measurement available and we therefore consider them a useful independent standard for the purpose of this study.

These findings have important implications for the interpretation of arterial BP measurements and subsequent management by the anaesthetist during OLTx. This operation presents the challenge of a high-risk patient population undergoing major surgery, characterised by cardiovascular instability due to the circulatory derangements that accom-

pany the underlying disease process, blood loss, vascular clamping and reperfusion sequelae. Arterial pressure measurements must accurately reflect perfusion pressure to vital organs. The effect of cannula site on the accuracy of arterial pressure measurements has been studied in numerous settings. A central-to-peripheral arterial pressure gradient has been shown at the end of cardiopulmonary bypass,¹⁷ deep hypothermic circulatory arrest,¹⁸ and in patients with presumed sepsis treated with high-dose vasoconstrictors.^{5,6} In these settings, peripheral arterial pressure appears to underestimate central arterial pressure, with postulated mechanisms for this gradient being differences in arterial elasticity,¹⁷ flow,¹⁹ or waveform characteristics.²⁰ The effect of arterial pressure on the management of a patient's haemodynamics is significant. In a prospective study of critically ill patients with septic shock on high-dose noradrenaline, SAP and MAP were significantly higher when measured from the femoral artery compared with the radial artery, enabling a reduction in noradrenaline infusions with no subsequent change in cardiac output or pulmonary artery occlusion pressure observed.⁵ Similarly, during cardiopulmonary bypass, an aortic and radial arterial pressure disparity of up to 11 mmHg has been described, which is a difference deemed sufficient to lead to unnecessary therapy.²¹ Assuming that femoral arterial pressure most closely reflects central arterial pressure,²²⁻²⁵ our findings imply that reliance on radial SAP may lead to inappropriate haemodynamic intervention, such as excessive fluid and vasopressor therapy.

In contrast to SAP, the uniformity of agreement of DAP between radial and femoral sites in our study was remarkable and suggests that, despite wide variations in the degree of vasodilatation in patients, diastolic pressure is relatively consistent throughout the arterial tree. The variations in SAP that we observed may reflect differences in arterial compliance and the resistance of the microcirculation distal to the measurement point at each site. The decreased liver metabolism and subsequent accumulation of vasoactive mediators may also explain the increase in SAP difference observed from the commencement of the anhepatic phase. Arterial compliance and resistance are governed by factors such as arterial diameter, physical characteristics of the microcirculation and levels of inflammatory mediators. We did not aim to investigate the effects of liver transplantation on vascular reactivity. There are potential implications in our findings for other patient populations in which profound vasodilatory states are commonly encountered, eg, critically ill patients with septic shock. The methodology of our observational study could be used in other clinical settings to investigate whether similar patterns exist. Despite all patients receiving an infusion of noradrenaline, we did not specifically investigate the effects of vasopressors on BP measurements at the two sites. Further studies would be

useful to determine the accuracy of BP measurements in situations of vasopressor-induced or vasodilator-induced changes in systemic vascular resistance.

In conclusion, SAP measurements from the radial artery in patients undergoing OLTx underestimate measurements from the femoral artery significantly but unpredictably, which makes radial artery SAP an unreliable parameter for guiding haemodynamic management in these patients. These measurement discrepancies were not confined to the period immediately after liver reperfusion but began with the anhepatic phase and persisted through the remainder of the operation. For MAP and DAP, radial and femoral sites are interchangeable.

Competing interests

None declared.

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