

Correlation between radial and femoral arterial blood pressure during reperfusion in living donor liver transplantation

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ABSTRACT

Background and Aims: Accurate blood pressure measurements are the mainstay for the efficient management of abrupt cardiovascular changes during reperfusion in liver transplant. We sought to compare the femoral and radial pressures during reperfusion and at **T1**:baseline, **T2**: 1 h in dissection: **T3**:portosystemic shunt, **T4**:reperfusion, **T5**: at bile duct anastomosis. **Methods:** A retrospective study was performed amongst 102 adult patients who underwent R lobe living donor liver transplantation. Mean arterial pressure (MAP) and systolic arterial pressure (SAP) at 10 s intervals at reperfusion and at five fixed time points were compared by intraclass correlation coefficient (ICC) and limits of agreement by Bland–Altman statistics. **Results:** MAP by both routes had a good correlation at all time points during reperfusion (overall ICC: 0.946 [0.938, 0.949]) in comparison with SAP (overall ICC: 0.650 [0.6128, 0.684]). At the lowest reperfusion pressure (reperfusion point), MAP showed high levels of agreements (ICC: 0.833 [0.761, 0.885]), whereas SAP showed only a poor level of agreement (ICC 0.343 [0.153, 0.508]). The Bland–Altman analysis for MAP showed a bias of 7.18 (5.94) mmHg and limits of agreement of – 4.5 mmHg to + 18.8 mmHg and for SAP a bias of 25.2 (22.04) mmHg and limits of agreement of – 18.0 mmHg to + 68.4 mmHg at the reperfusion point. The incidence of post-reperfusion syndrome (PRS) was 52.94% by femoral and 57.84% by radial routes. **Conclusions:** Radial MAP correlated well with femoral MAP during reperfusion and at predefined time points and can be used interchangeably for intraoperative monitoring. A high incidence of PRS was noted by our technique of measurement.

Key words: Blood pressure, femoral artery, liver transplant, radial artery, reperfusion

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INTRODUCTION

Cirrhotic cardiomyopathy associated with advanced liver disease may manifest only at times of stress such as during reperfusion. Cardiac complications are reported as the most important cause for early mortality following liver transplant.^[1] An efficient arterial line that correlates well with central arterial pressures is vital in the successful management of liver transplantation surgery. Radial arterial pressures can underestimate pressures when extreme haemodynamic changes occur.^[2]

The haemodynamics during reperfusion phase during liver transplantation is marked by instability of varying

severity, and accurate blood pressure measurements are crucial for the efficient management of sudden cardiovascular changes during this period. Numerous studies have reported inconsistencies between

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femoral and radial arterial pressures during liver transplantation.^[3,4] In the context of limited literature reported in India, we sought to compare femoral arterial blood pressure (FABP) with radial arterial blood pressure (RABP) during the reperfusion phase of living donor liver transplantation with a view to predict the relationship and optimise management amongst our patient profiles.

Our primary aim was to analyse the agreement between simultaneous radial and femoral arterial pressure measurements during reperfusion of liver transplantation surgery. The secondary objectives were the comparison of the pressures at specified time points during surgery.

METHODS

Following approval from the institutional ethics committee, a retrospective observational study was conducted amongst 102 adult patients who had undergone elective living donor liver transplantation between April 2016 and December 2017. Transplants for acute liver failure, paediatric transplants and technical difficulty in femoral cannulation were excluded from the study. All patients had a 20G arterial cannula (Becton Dickinson Infusion Therapy Systems Inc., Sandy, UT, USA) placed in a radial artery under local anaesthesia prior to the induction of anaesthesia. Following intubation, a 5 Fr femoral arterial cannula (Cook Medical Inc., Bloomington, IN, USA) was placed under ultrasound guidance. Monitoring during transplant included pressures measured from radial and femoral sites and a central venous pressure with a 9 Fr triple-lumen catheter with sheath (Edwards Life Sciences, Irvine, CA, USA). The radial artery connected to FloTrac/EV 1000 platform (Edwards Life Sciences, USA) was used for the measurement of cardiac output (CO) and systemic vascular resistance (SVR).

Induction and maintenance of anaesthesia was by standard protocols. Induction protocols were intravenous lorazepam 0.05 mg/kg, fentanyl 2 µg/kg and propofol titrated to a loss of verbal response. Intubation was accomplished at 1-min following administration with 1.0 mg/kg rocuronium. Anaesthesia was maintained with 50% oxygen-air mixture and isoflurane at 0.7–1.0 minimum alveolar concentration (MAC). Ventilation was via a low-flow, circle-breathing system with a tidal volume of 7–8 mL/kg using volume-control mode with a positive end expiratory pressure of 5 mmHg. The end-tidal partial

pressure of carbon dioxide measured by capnography was set to a target of 30–35 mmHg.

We standardised the record of reperfusion on a mobile camera, and data points noted every 10 s as per the protocol were entered in the database. Post-reperfusion syndrome (PRS) was defined as more than a 30% decrease in mean arterial pressure (MAP) versus pre-reperfusion baseline for at least 1 min during the first 5 min after reperfusion.^[5] We also compared the pressures at defined time points from the data records, T1: baseline at the start of surgery, T2: 1 h in dissection phase, T3: time of creation of portosystemic shunt, T4: reperfusion time point and T5: at bile duct anastomosis. Reperfusion point was defined as the lowest radial systolic arterial pressure (SAP) and MAP, and its corresponding femoral pressures were noted.

Using intraclass correlation (ICC) coefficients to compare femoral and radial arterial pressures in the study by Shin *et al.*^[6] with an expected reliability of (ICC) 0.9758, the minimum sample size was calculated to be 87 with 90% power of test, 5% level of significance and minimum acceptable reliability of 0.95.

Categorical variables were presented as proportions, whereas continuous variables were either presented as mean with standard deviation (SD) and median with interquartile range. The agreements between FABP and RABP were measured with ICCs. ICC level of 0.75 and above was considered high agreement, 0.40–0.74 as moderate and <0.40 as poor level of agreement.

The bias, precision and limits of agreement between radial and femoral arterial pressures were calculated in accordance with Bland–Altman methods. The limits of agreement were calculated as the bias \pm 1.96 SD and represent the range in which 95% of the differences between the two methods are expected to lie.

To evaluate diagnostic agreement concerning the presence of PRS, kappa statistics was used to compare FABP and RABP. A kappa statistic of 1.0, \geq 0.75, 0.40–0.74 and <0.40 denoted absolute, high, moderate and poor agreements, respectively. Continuous variables were compared using the Student's *t*-test and Mann–Whitney test for non-parametric test for two variables. Categorical variables were compared by Fisher's exact test or Pearson's Chi-square test. Repeated measures analysis was used to see the changes in parameters over time. All statistical tools were two tailed and $P < 0.05$ was considered

statistically significant. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) for Windows version 23.0. Armonk, NY: IBM Corp.

RESULTS

A total of 102 adults (100/2 M:F) undergoing R lobe living donor liver transplants were included in our analysis, and 3876 readings were obtained [Appendix 1]. Indications for liver transplant were alcoholic cirrhosis (n = 49), cryptogenic (n = 24), hepatocellular carcinoma (n = 15), non-alcoholic steatohepatitis (n = 6), viral (n = 4) and others (n = 4). The baseline characteristics of these patients along with perioperative variables, transfusions and postoperative stay are provided in Table 1.

Simultaneous comparisons were performed on the pressures measured at the two sites. The MAPs measured showed a very high correlation at all points during reperfusion (overall ICC: 0.946 [0.938, 0.949]), [Table 2].

The SAPs, however, showed a moderate correlation at the corresponding time points during reperfusion (overall ICC: 0.650 [0.6128, 0.684]) [Table 3].

Comparison of the pressures at the defined time points was done by ICC [Table 4]. At the T4 ‘reperfusion point’, the MAP measured from both sites showed high levels of agreements (ICC: 0.833 [0.761,0.885]), whereas SAP measured from the two sites showed only a poor level of agreement (ICC: 0.343 [0.153, 0.508]). The pressures measured at T4 were significantly lower than the preceding time point [Table 4].

The incidence of PRS using the mean FABP was 52.94% (54/102) and using RABP was 57.84% (59/102). The measurements from both the sites of monitoring had a high agreement in detecting PRS (kappa values of 0.901).

In a subgroup analysis of patients with and without PRS, we found that the MELD, age, weight, haemoglobin, serum creatinine, ascites drained and blood products transfused were comparable in the groups with and without PRS, but pre-operative sodium was lower in patients who developed PRS (P = 0.024) [Figure 1]. Alcoholic cirrhosis was the most common aetiology in groups with and without PRS (33 vs. 16, P = 0.058), whereas the other causes were comparable between the groups.

We compared the limits of agreement by Bland–Altman method at baseline, at the onset of reperfusion and at the reperfusion point [Figure 2].

Table 1: Pre-operative and perioperative variables

	Mean±SD/median (IQR)
Pre-operative variables	
Age (years)	48.82±7.99
MELD score	22.3±6.766
CTP (A/B/C)	5/14/83
Weight (kg)	71.22±13.70
Haemoglobin (g/dL)	9.38±1.71
Platelets×10 ⁹ /L	68.47±37.15
INR	2.25±0.83
Serum albumin (mg/dL)	2.84±0.74
Sodium (mmol/L)	130.87±6.79
Creatinine (mg/dl)	1.020 (0.82, 1.32)
Total bilirubin (mg/dl)	3.885 (2.03,7.315)
Peri-operative variables	
PRBC (units)	3.00 (2.0,4.0)
FFP (units)	5.00 (3.0, 6.0)
SDP (units)	2.50 (0.50, 5.00)
Cryoprecipitate (units)	10.00 (10,13)
20% albumin (100 ml)	4.0 (3.0, 5.0)
Crystalloids (ml)	6160.42±2348.8
Cell saver	414.46±333.00
EST blood loss (ml)	2909.38±1116.86
Duration of surgery (h)	9.56±1.18
LOICU (days)	7 (6, 9)

MELD – Model for End-Stage Liver Disease; INR – International normalised ratio; PRBC – Leucocyte-depleted packed red blood cells; FFP – Fresh frozen plasma; SDP – Single-donor platelet concentrate; LOICU – Length of ICU stay postoperatively; ICU – Intensive care unit; SD – Standard deviation; IQR – Interquartile range; CTP – Child–Turcotte–Pugh; EST – Estimated

Table 2: Mean radial and femoral artery pressures at reperfusion

Mean arterial pressure between femoral and radial arteries			
Seconds	MAP femoral mm Hg	MAP radial mm Hg	ICC
0	84.52±12.62	79.52±12.79	0.901* (0.857, 0.932)
10	80.74±14.32	75.35±14.07	0.874* (0.819, 0.913)
20	73.48±15.25	68.64±14.96	0.860* (0.800, 0.903)
30	64.86±15.35	59.68±14.95	0.895* (0.848, 0.928)
40	59.91±14.66	54.94±15.10	0.949* (0.925, 0.965)
50	58.25±15.00	52.70±15.60	0.948* (0.925, 0.965)
60	57.94±4.96	52.15±16.90	0.943* (0.917, 0.961)
70	58.32±16.32	52.30±16.89	0.948* (0.924, 0.965)
80	57.76±15.81	52.50±16.61	0.943* (0.915, 0.962)
90	58.60±16.56	52.01±17.58	0.942* (0.913, 0.962)
100	59.11±16.89	52.12±17.53	0.941* (0.910, 0.962)
110	58.84±16.91	52.61±18.31	0.951* (0.923, 0.970)
120	60.74±16.44	53.18±17.38	0.948* (0.916, 0.968)
130	62.25±17.30	54.07±17.53	0.937* (0.895, 0.963)
140	62.88±16.65	55.24±16.94	0.948* (0.910, 0.970)
150	64.89±17.38	57.44 (17.21)	0.950* (0.913, 0.972)
160	63.08±16.56	58.65±17.14	0.957* (0.917, 0.977)
170	59.35±14.59	63.23±16.08	0.964* (0.922, 0.984)
180	61.50±14.53	69.71±16.74	0.966* (0.923, 0.985)
Overall	64.77±18.21	58.57±18.72	0.943* (0.938, 0.949)

*High levels of agreement. Values in parentheses are 95% CIs. CI – Confidence interval; MAP – Mean arterial pressure; ICC – Intraclass correlation

At the baseline T1, SAP showed a mean difference of 5.2 mmHg (SD 9.57) (limits of agreement, –13.57–

Table 3: Systolic radial and femoral arterial pressures at reperfusion

Systolic arterial pressures between femoral and radial arteries			
Seconds	SAP femoral mm Hg	SAP radial mm Hg	ICC
0	125.54±17.61	114.82±18.57	0.688 (0.571, 0.778)
10	121.55±19.43	110.23±19.06	0.710 (0.599, 0.794)
20	113.25±21.71	96.24±24.31	0.643 (0.513, 0.744)
30	103.03±21.20	82.66±23.24	0.645 (0.516, 0.746)
40	97.95±20.80	75.96±23.92	0.614 (0.477, 0.722)
50	95.99±21.63	73.15±24.70	0.621 (0.486, 0.727)
60	95.63±21.47	72.25±25.86	0.630 (0.497, 0.734)
70	96.49±23.08	72.30±27.87	0.668 (0.543, 0.764)
80	95.68±21.44	71.80±26.93	0.622 (0.481, 0.731)
90	96.61±22.21	72.25±28.48	0.631 (0.488, 0.742)
100	97.65±21.17	72.70±28.55	0.643 (0.496, 0.754)
110	99.04±22.11	72.17±29.46	0.618 (0.449, 0.744)
120	100.68±21.14	74.55±28.06	0.631 (0.460, 0.756)
130	102.98±22.18	76.02±28.67	0.660 (0.480, 0.786)
140	102.94±20.17	78.29±27.97	0.691 (0.513, 0.812)
150	104.92±19.68	81.73±28.91	0.715 (0.542, 0.829)
160	106.57±18.88	84.63±28.71	0.646 (0.402, 0.804)
170	110.56±19.43	87.68±19.08	0.687 (0.457, 0.831)
180	117.56±17.61	92.77±18.56	0.698 (0.476, 0.836)
Overall	104.20±23.52	82.96±29.63	0.650 (0.612, 0.684)

Values in parentheses are 95% CIs. ICC ≥0.75 – High agreement; 0.4-0.74 – Moderate agreement; <0.4 – Poor agreement; CI – Confidence interval; SAP – Systolic arterial pressure; ICC – Intraclass correlation

Table 4: Comparison of radial and femoral pressures at specific time points during surgery

Time points	Femoral MAP mmHg	Radial MAP mmHg	ICC
T1	80.12±11.76	83.94±11.20	0.866* (0.765, 0.924)
T2	78.04±10.08	83.66±9.46	0.824* (0.691, 0.900)
T3	78.47±10.72	82.87±11.22	0.849* (0.616, 0.929)
T4	49.38±15.34†	56.51±14.83†	0.833* (0.761, 0.885)
T5	73.03±9.96†	79.1±12.69†	0.751* (0.481, 0.881)

Time points	Femoral SAP mmHg	Radial SAP mmHg	ICC
T1	114.96±16.49	120.16±17.42	0.889* (0.806, 0.882)
T2	111.28±12.24	118.5±13.50	0.714 (0.498, 0.837)
T3	112.75±15.96	121.27±15.33	0.738 (0.536, 0.853)
T4	69.44±25.42†	94.07±21.48†	0.343 (0.153, 0.508)
T5	106.096±16.79†	116.68±15.89†	0.677 (0.335, 0.843)

ICC; ≥0.75 – High agreement; 0.4-0.74 – Moderate agreement; <0.4 – Poor agreement. *High levels of agreement, †P<0.05 versus preceding value. Values in parentheses are 95% CIs. T1 – Baseline; T2 – 1 h in dissection phase; T3 – Start of portocaval shunt; T4 – Reperfusion point; T5 – Bile duct anastomosis; CI – Confidence interval; ICC – Intraclass correlation; MAP – Mean arterial pressure; SAP – Systolic arterial pressure

23.97 mmHg, *P* = 0.483) and the MAP showed bias of 3.82 mmHg (SD 7.08) (limits of agreement, -10.07 to +17.71 mmHg *P* = 0.398).

At the onset of reperfusion, the SAP showed a mean difference of 10.76 mmHg (SD 14.29) (limits of agreement, -17.29 to +38.73 mmHg, *P* = 0.938) and the MAP showed bias of 5.1 mmHg (SD 5.64)

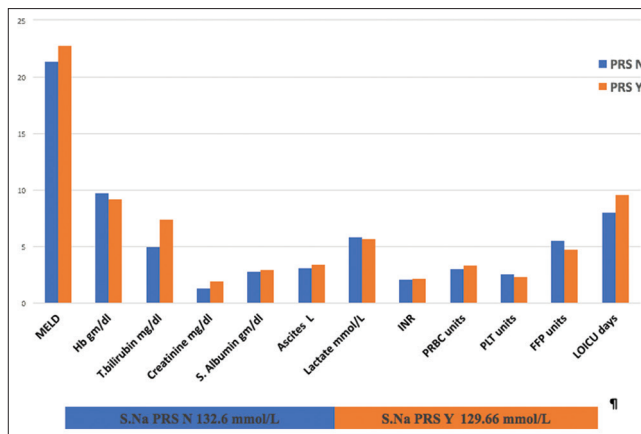


Figure 1: Variables in patients with and without post-reperfusion syndrome

(limits of agreement, -6.06 to +16.16 mmHg, *P* = 0.483).

At the critical reperfusion point, the SAP showed a bias of 25.2 mmHg (SD 22.04) (limits of agreement, -18.0 mmHg to +68.4 mmHg) (*P* = 0.036). However, the MAP only showed a mean difference or bias of 7.18 mmHg (SD 5.94) (limits of agreement, -4.5 mmHg to +18.8 mmHg), (*P* = 0.287) at the same time [Table 4 and Figure 2].

DISCUSSION

We found that a good correlation exists between the MAPs measured by both femoral and radial routes at all time points during reperfusion (overall ICC: 0.946 [0.938, 0.949]), but there was only a moderate correlation between the systolic pressures measured at the same time (overall ICC: 0.650 [0.6128, 0.684]).

The comparisons of mean and systolic blood pressures at defined time points using femoral and radial arterial pressures also yielded the same result. The systolic correlation was poor at the reperfusion point, ICC: 0.343 (0.153, 0.508). The incidence of PRS by our measurement was higher than that of the earlier reports in living donor transplantation.

Although the correlation between radial and femoral arterial pressures during living transplantation has been studied,^[3,4] frequent comparisons at the time of reperfusion are not available. Excessive fluid administered to treat hypotension can cause destruction of the endothelial glycocalyx layer that prolongs recovery after surgery.^[7]

We had devised a recording of reperfusion using a mobile camera and plotted readings at 10 s intervals

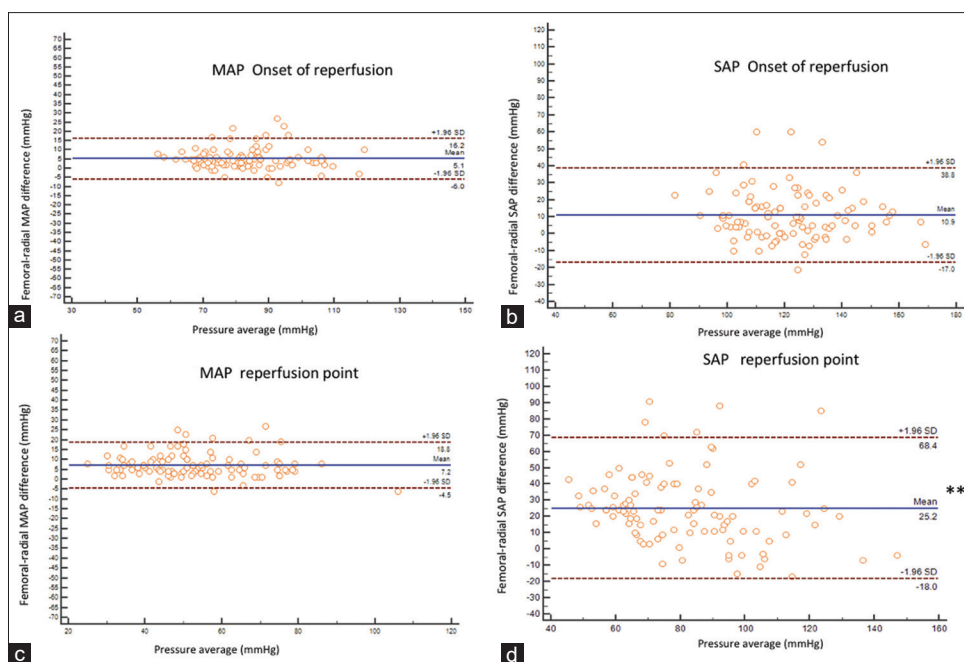


Figure 2: Bland–Altman plots at the start of reperfusion and at reperfusion point. 2a,b: MAP and SAP at onset of reperfusion. 2c,d: MAP and SAP at reperfusion point. ** $P < 0.05$

between femoral and radial pressures to determine correlations and for the accurate measurement of the incidence of PRS. This was entered in the transplant database and maintained with intraoperative records.

Reperfusion is associated with a fall in the SVR, decrease in heart rate and an increase in pulmonary artery pressures,^[8] which can often be severe enough to progress onto cardiac arrest. An accurate assessment of pressures is crucial for an optimal management of reperfusion.

All patients in our study were pre-emptively administered phenylephrine in aliquots of 100 μg increments at the start of reperfusion. Typically, the fall in blood pressures was noted 30 s following the release of the portal clamp, and incremental doses given were guided by the SVR and CO displayed on the CO monitor. When phenylephrine doses exceeded 500 μg , adrenaline was added in increments of 10 μg . We believed that blood pressure measurements from the femoral artery could reduce the vasopressors needed and provide scope for fast-tracking extubation,^[9] but the mean pressures from both sites were found to be comparable.

Literature has suggested that the incidence of PRS can vary between 12% and 77%,^[8] with contributions from inflammatory mediators from perfused graft, donor factors and ischaemia reperfusion injury.^[10] Vital

sign recordings during surgery performed at 5-min intervals can overlook changes from haemorrhage, vasopressor administration or volume resuscitation.^[11] The wide range for the incidence could perhaps be due to underdiagnosis of PRS, particularly when analysing retrospective data.

We noted a high incidence for PRS (52.94% and 57.84%) from the femoral and radial pressure recordings, respectively, similar to the studies by Ryu *et al.*^[12] Arnal *et al.*^[3] opined that mean pressures were better correlates and concurrent vasoconstrictor usage increases the femoral to radial differences. A large number of our patients (89.2%) were on vasopressors at anhepatic phase prior to reperfusion. As part of protocol during surgery, noradrenaline was the first vasopressor and beyond a dose of 0.2 $\mu\text{g}/\text{kg}/\text{min}$, vasopressin to a maximum of 1.8 U/h and then adrenaline at doses 0.02–0.2 $\mu\text{g}/\text{kg}/\text{min}$ was used. We did not find an association with the use of vasopressors on femoral to radial systolic or mean pressure differences by multivariate analysis ($P = 0.284$) in our study.

The median dose of vasopressors used at reperfusion in those with and without PRS was phenylephrine 500 (0, 500) versus 350 (200, 500) μg and adrenaline 50 (30, 100) versus adrenaline 0 (0, 20) μg , respectively. This was used until the pressures showed an increasing trend and was stopped at that point. Our use of vasopressors appears to be higher than that mentioned

by Ryu *et al.*,^[12] however none of the patients had an overshoot above the basal value in our study. We believe that the use of vasopressors was guided by the MAP and SVR and that PRS occurred despite the higher use of vasopressors and inotropes.

Shin *et al.*^[6] have shown a marked difference in the PRS incidence between femoral and radial arteries, 50% and 80.6%, respectively. We did not find any difference between the incidence of PRS measured by both sites, perhaps due to varying patient profiles and vasopressor usage.

Unlike other studies,^[6,13,14] we did not find correlates with higher MELD, lower haemoglobin and creatinine with the occurrence of PRS. However, a lower pre-operative sodium (129.72 ± 7.55 vs. 132.47 ± 5.24 , mEq/L, $P = 0.024$) in the PRS versus non-PRS group was seen in our study [Figure 1]. Interestingly, we noted that the nadir of blood pressure, the reperfusion point, occurred at 80 s (60, 100) in the PRS group versus 60 s (50, 70) in the non-PRS groups.

We had looked at ICCs for the comparison of continuous variables with differing mean and included the Bland–Altman analysis^[15] to strengthen our observations. Similar to the study by Lee *et al.*,^[16] we noted that the correlations were better preserved between the MAPs at the time of reperfusion. Unlike their observations, we noted that although the differences were more at the time of reperfusion, this returned towards normal at the time of bile duct closure.

Femoral arterial cannulation is not a universal protocol at all transplant centres and complications relating to its use in the context of coagulopathic patients have been reported^[17] although the availability of the ultrasound has reduced its incidence.^[18] Femoral arterial pressures can be useful as reliable central arterial pressures in the context of cardiovascular complications including cardiomyopathy that are reported postoperatively in these patients.^[19]

By linear regression from our data, we were able to predict the femoral MAP from the radial MAP by the following equation: femoral MAP = $0.91 \times$ radial MAP + 11.8. This may provide an accurate estimation of a central arterial pressure even in the absence of a femoral arterial line.

We acknowledge some limitations in our study. Although the frequency and damping coefficients

were similar, the size of the cannula varied as per the arterial size, and this may have influenced our readings. We did not correlate the CO and stroke volume variations at the time points of reference, and this may have provided more insights on the study.

The reperfusion data evaluated in our study is unique and systematic and has looked at occurrence of PRS in a specified population. We documented a higher occurrence of PRS, and we believe that PRS can be missed unless looked for accurately. Nonetheless, we were not able to find associations other than a low pre-operative sodium for PRS in our study group. We also found a prediction for femoral MAPs by regression analysis that may be useful in circumstances without a femoral arterial line.

CONCLUSIONS

The MAPs measured at the radial artery correlated reliably with the femoral MAPs at baseline, 1 h in the dissection at portosystemic shunt, reperfusion and at bile duct anastomosis and specifically at all points of reperfusion and can be used interchangeably with femoral MAPs during liver transplant. A high incidence of PRS was seen with this technique of measurement.

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Nil.

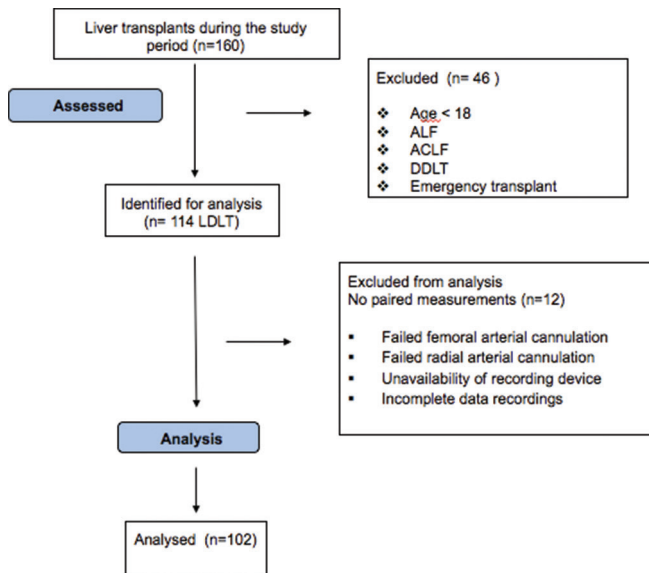
Conflicts of interest

There are no conflicts of interest.

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Appendix 1: Flow diagram of transplant recipients studied