

# Deep Hypothermic Circulatory Arrest and the Femoral-to-Radial Arterial Pressure Gradient

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**Objectives:** To determine the femoral-to-radial arterial pressure gradient, as well as the factors associated with them, in patients receiving cardiopulmonary bypass (CPB) with profound hypothermia and circulatory arrest.

**Design:** Retrospective automated hemodynamic record review.

**Setting:** University hospital.

**Participants:** Patients undergoing pulmonary thromboendarterectomy with deep hypothermic circulatory arrest.

**Measurements and Main Results:** The automated hemodynamic records of 54 consecutive patients undergoing pulmonary thromboendarterectomy with deep hypothermic circulatory arrest were reviewed, comparing the femoral and radial arterial pressures throughout the intraoperative period. In 20 of the patients, the hemodynamic data from the first 16 postoperative hours were also studied. Forty-one of 54 (76%) of the patients exhibited a mean arterial gradient of at least 10 mmHg either during or after CPB, femoral being higher. Clinically significant gradients were noted throughout the CPB period and the post-CPB period in these patients. In the 54 patients studied, the systolic blood pressure (SBP) gradient was  $32 \pm 19$  mmHg after CPB (95% confi-

dence limits 28.2 mmHg, 39.0 mmHg), and the mean arterial pressure (MAP) gradient was  $6.3 \pm 4.9$  mmHg (95% confidence limits 5.5 mmHg, 8.6 mmHg). The duration of clinically significant SBP ( $>10$  mmHg) and MAP ( $>5$  mmHg) gradients in the postoperative period were  $5.2 \pm 5.7$  hours and  $5.8 \pm 7.2$  hours, respectively. Advanced age correlated with high post-CPB pressure gradients in this population and was associated with prolonged postoperative resolution of the gradients.

**Conclusions:** The femoral-to-radial arterial pressure gradients, particularly systolic, after CPB, were greater and of longer duration in these patients undergoing deep hypothermic circulatory arrest than gradients previously reported for routine CPB. Central arterial pressure monitoring is recommended for patients undergoing deep hypothermic circulatory arrest, being valuable both for intraoperative and postoperative care.

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**KEY WORDS:** pulmonary thromboendarterectomy, deep hypothermic circulatory arrest, arterial pressure gradients

THE RADIAL ARTERIAL systolic pressure (SBP) is normally higher than aortic, with mean pressure (MAP) constant throughout the arterial tree.<sup>1</sup> A reversal of this systolic pressure relationship, as well as a significant mean gradient after cardiopulmonary bypass (CPB), have been described.<sup>2</sup> Also, significant differences in MAP during the early phase of CPB have been reported, central pressure (aortic, femoral) being higher than peripheral (radial).<sup>3,4</sup> Little work has been done, however, to delineate clinical factors leading to the gradients, such as temperature management, duration of CPB, and individual patient factors. Also, studies to date have included only the intraoperative period. Although hypothermia has been implicated as a contributing factor,<sup>5</sup> its effect has not been studied. Furthermore, the effect of deep hypothermic circulatory arrest on these gradients has not been described. In the authors' clinical practice involving deep hypothermic circulatory arrest (DHCA), dramatic differences have been found between femoral and radial arterial pressures (particularly after CPB), leading to routine use of femoral arterial monitoring as an estimate of central arterial pressure. This study was undertaken to quantify the extent and timing of the femoral-radial gradients, delineate the clinical factors with which they are associated, and determine the time course of resolution in the postoperative period.

## METHODS

After institutional review board approval, the automated records of 54 consecutive patients undergoing pulmonary thromboendarterectomy (PTE) with deep hypothermic circulatory arrest were studied. In all patients, the diagnosis of chronic thromboembolic pulmonary hypertension was established preoperatively by clinical history, physical examination, and pulmonary angiography. The placement and management of invasive monitoring devices, as well as anesthetic manage-

ment, were performed according to institutional protocols. On the morning of surgery, a peripheral intravenous catheter and a 20-gauge 1.88-in radial artery catheter (Becton Dickinson, Sandy, UT) were placed. The radial artery with the stronger pulse was used.

Anesthetic induction consisted of intravenous midazolam, 0.15 mg/kg, fentanyl, 5 to 10  $\mu$ g/kg, and pancuronium, 0.15 mg/kg. Anesthetic maintenance before CPB consisted of isoflurane, 0.5% to 1% in oxygen, with supplemental doses of fentanyl and pancuronium as required. After endotracheal intubation central venous access was obtained, a pulmonary artery catheter was placed. An 18-gauge 6-in femoral arterial catheter was then inserted (Maxxim Medical, Athens, TX).

All pressure lines were transduced separately and simultaneously using flush-transducers (Transpac IV, Abbott Critical Care Systems, Salt Lake City, UT) connected to a Hewlett Packard Component Monitoring System M1046-9100C (Philips Medical Systems, Andover, MA). The 2 arterial catheters each consisted of the indwelling catheter, 72 inches of pressure tubing, and one stopcock. The frequency response and damping coefficients for the systems were determined according to institutional practice,<sup>6</sup> and all lines were "zeroed" immediately before use. When necessary, further flushing and repositioning were per-

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formed. The natural frequency of the pressure monitoring system for both types of arterial catheters is 20.8 Hz. The damping coefficient for the system attached to a 20-gauge 1.88-in catheter is 0.54, that for the system attached to the 16-gauge 6-in catheter is 0.46. All hemodynamic data were stored within the monitoring system and retrieved at the conclusion of surgery. The digital report of hemodynamics at 15-minute intervals was used for the intraoperative period. In the final 20 patients, the postoperative data were retrieved, using hourly intervals for the first 16 hours of the intensive care unit (ICU) stay.

After median sternotomy and heparinization (400 U/Kg), the aorta, superior vena cava, and inferior vena cava were cannulated and CPB was instituted. A roller pump (Cobe 4197, Cobe Cardiovascular, Inc, Lakewood, CO) and membrane oxygenator (Cobe Duo, Cobe Cardiovascular, Inc) were used in all cases. The circuit had been primed with 1,600 mL of plasmalyte, 25 g of albumin, 25 mEq of bicarbonate, 12 g of mannitol, and 30 mg/kg of methylprednisolone. Intravenous phenytoin was administered during cooling (15 mg/kg), and hemodilution was carried out to a hematocrit of approximately 20%. When the bladder temperature reached 20°C and the tympanic membrane temperature approached 17°C, thiopental was administered (6 mg/kg). Thromboendarterectomy was performed with DHCA in 2 steps, first on the right then on the left pulmonary artery, interrupted by a period of perfusion at 18° to 20°C sufficient to achieve a mixed venous oxygen saturation greater than 90%. During rewarming, supplemental doses of midazolam and pancuronium were administered, and a nitroprusside infusion (0.1-0.5  $\mu\text{g}/\text{kg}/\text{min}$ ) was used to facilitate rewarming. Separation from CPB was achieved when the bladder temperature reached 36°C, and the heparin was reversed with protamine. Hematocrit of at least 28% to 32% was achieved with hemoconcentration, diuresis, and infusion of cell saver and packed red blood cells as necessary.

After CPB, dopamine, 3 to 5  $\mu\text{g}/\text{kg}/\text{min}$ , was used for hemodynamic support. Anesthesia was maintained with isoflurane, 0.5% to 1% in oxygen, and supplemental doses of fentanyl. At the conclusion of surgery, the patient was transferred to the ICU intubated and mechanically ventilated. All patients remained intubated for at least 16 hours postoperatively, and sedation with propofol and morphine was provided. Hematocrit of at least 28% was maintained as described earlier.

Descriptive statistics were used to quantify the femoral-arterial systolic and mean pressure gradients at 15-minute intervals during surgery, and, in the last 20 patients, 1-hour intervals for the first 16 hours after surgery. Results are presented as mean  $\pm$  SD, with 95% confidence limits. Linear regression was used to determine relationships between demographic and hemodynamic factors and the magnitude of the gradients at various time points. Independent variables included age, gender, body mass index, cooling time, total cold time, warming time, total CPB time, systemic vascular resistance (SVR), cardiac index before CPB, cardiac index after CPB, and case duration. Dependent variables included maximum mean and systolic gradients during the following time periods: pre-CPB, cooling, cold, warming, and post-CPB. Fisher exact test was used to determine if advanced age (>65 years), obesity (body mass index >35), poor preoperative cardiac function (cardiac index < 1.5 L/min/m<sup>2</sup>), or sex were associated with clinically significant gradients. Clinically significant gradients were defined as systolic gradient >10 mmHg and mean arterial gradient >5 mmHg. When flow was not pulsatile, MAP and SBP were assumed to be equal.

## RESULTS

Of the 54 patients studied, 22 were men and 32 were women. All patients had poor functional status preoperatively (New York Heart Association class III or IV) and suffered severe pulmonary hypertension. Their demographic and clinical characteristics are summarized in Table 1.

**Table 1. Demographic and Clinical Characteristics**

Age	47.6 $\pm$ 17.2
Height (cm)	170.4 $\pm$ 10.5
Weight (kg)	82.9 $\pm$ 22.1
Body surface area (m <sup>2</sup> )	2.0 $\pm$ 0.3
Body mass index	28.0 $\pm$ 6.0
Cooling time (min)	77.0 $\pm$ 15.8
Cold time (min)	64.1 $\pm$ 14.2
Circulatory arrest time (min)	32.9 $\pm$ 10.0
Circulatory arrest bladder temperature (°C)	19.2 $\pm$ 0.9
Warming time (min)	98.6 $\pm$ 18.0
CPB time (min)	265.9 $\pm$ 35.8
Preoperative cardiac index (L/min/m <sup>2</sup> )	1.7 $\pm$ 0.5
Postoperative cardiac index (L/min/m <sup>2</sup> )	3.1 $\pm$ 0.8

NOTE. Cooling time is the time elapsed between initiating CPB and attaining bladder temperature 20°C. Cold time is time spent at bladder temperature 20°C. Circulatory arrest time is total time spent without perfusion.

Forty-one of 54 (76%) of the patients exhibited a femoral-radial MAP gradient of at least 10 mmHg either during or after CPB. The intraoperative femoral-radial artery mean pressure (MAP) gradients are shown in Figure 1 and the systolic (SBP) gradients in Figure 2. The peak MAP gradient during cooling occurred at 45 minutes into CPB and was 10.0  $\pm$  5.0 mmHg. The peak MAP gradient during warming was 8.4  $\pm$  6.5 mmHg and occurred at 60 minutes into the rewarming phase. After separation from CPB, the peak SBP gradient was 32.1  $\pm$  19.7 mmHg (95% confidence limits 28.2 mmHg, 39.0 mmHg), and the peak MAP gradient was 6.3  $\pm$  4.9 mmHg (95% confidence limits 5.5 mmHg, 8.6 mmHg). Fifteen minutes after separation from CPB, 34 of 54 (63%) patients had an MAP gradient  $\geq$  5 mmHg, and 16 of 54 (33%) had an MAP gradient  $\geq$  10 mmHg. Forty-seven of 54 (87%) had SBP gradient  $\geq$  10 mmHg, and 39 of 54 (72%) had an SBP gradient greater than 20 mmHg. Of the factors studied, only age correlated with the femoral-radial arterial pressure gradient. Upon cooling, age showed a negative correlation with the MAP gradient ( $p = 0.0001$ ,  $R^2 = 0.25$ ). After CPB, age showed a weak positive correlation with the MAP gradient ( $p = 0.05$ ,  $r^2 = 0.07$ ), but a correlation between age and post-CPB systolic gradient did not reach statistical significance ( $p = 0.07$ ). Fisher exact test revealed only that age >65 was a weak predisposing factor to clinically significant MAP gradient after CPB ( $p = 0.02$ , chi-square = 5.9) and was associated with a reduced gradient on cooling ( $p = 0.01$ , chi-square = 7.0).

The average time after arrival in the ICU for resolution of the SBP gradient to less than 10 mmHg was 5.2  $\pm$  5.7 hours. The average time for resolution of the MAP gradient to less than 5 mmHg was 5.8  $\pm$  7.2 hours. Sixteen hours after surgery, 6 of 20 (30%) patients still had an MAP gradient greater than 5 mmHg, and 2 of 20 (10%) had an SBP gradient of greater than 10 mmHg. Age positively correlated with duration of mean gradient >5 mmHg ( $p = 0.02$ ,  $R^2 = 0.3$ ). Strong correlations were noted between gradients (MAP and SBP) immediately post-CPB and postoperative duration of the gradients ( $p < 0.0001$  for both). There were no complications from either the femoral or radial arterial catheters in any of the 54 patients studied.

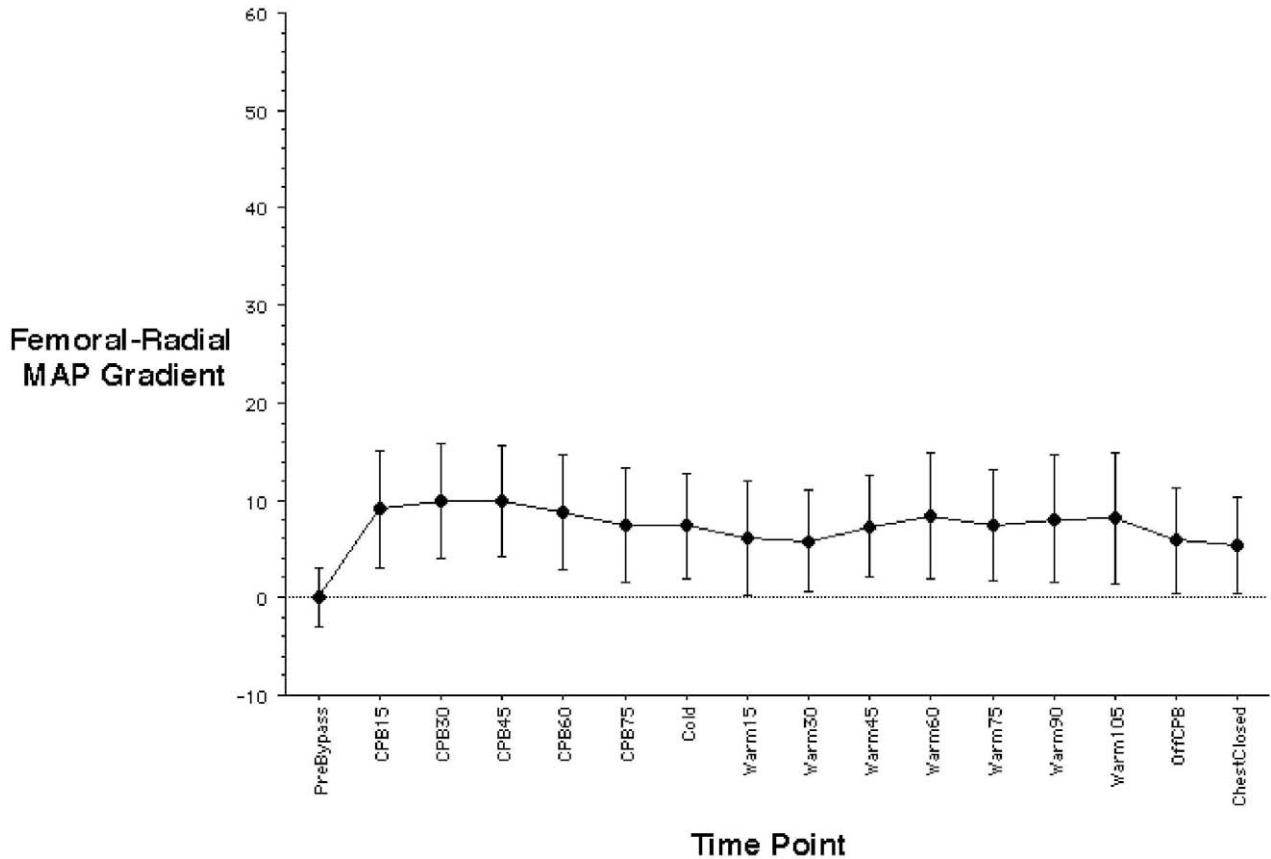


Fig 1. The femoral-radial MAP gradient (mmHg) at various time points during pulmonary thromboendarterectomy. Error bars indicate SD.

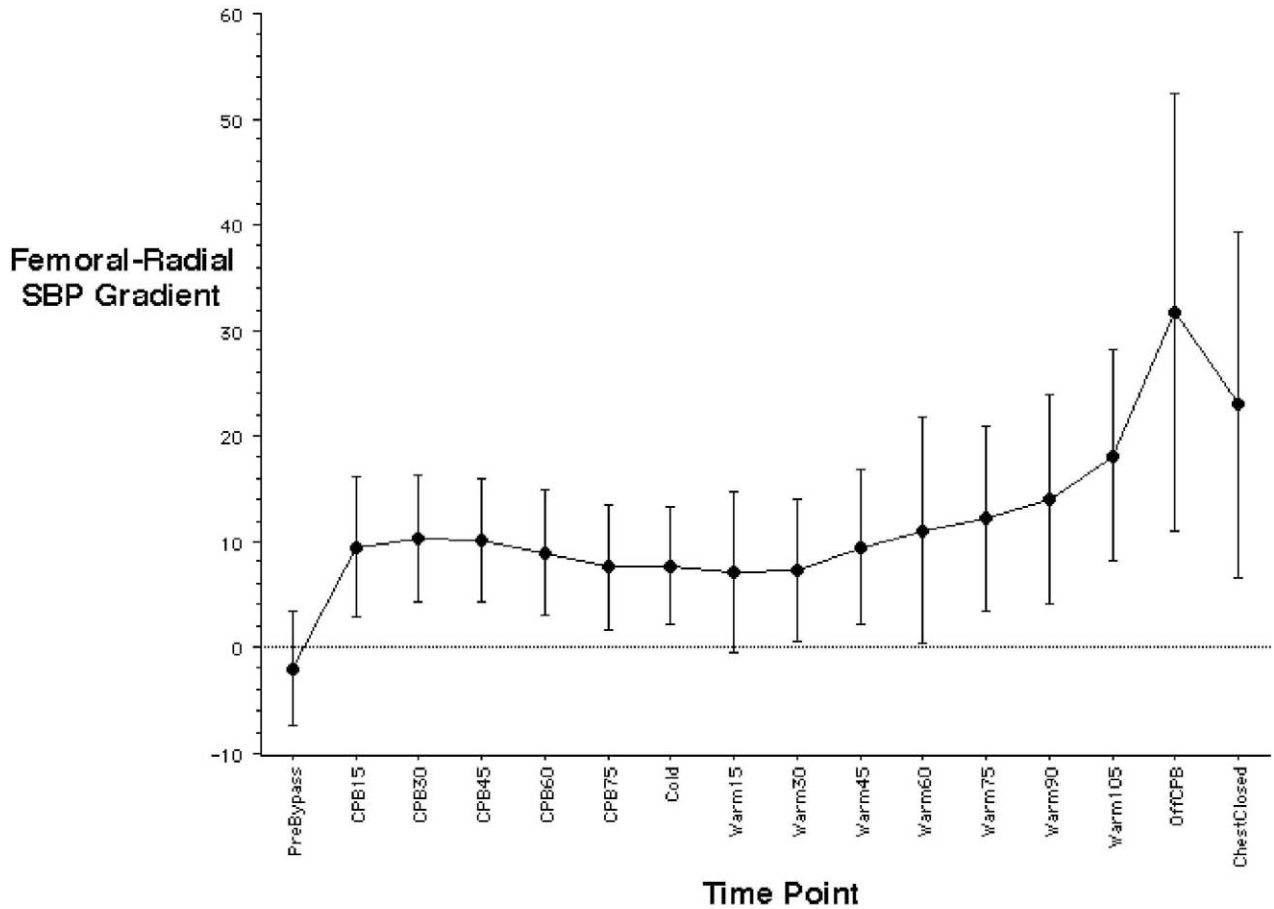
## DISCUSSION

Central-peripheral arterial pressure gradients during or immediately after CPB have received considerable attention. Studies have involved coronary artery bypass graft (CABG) or valve surgery, presumably with mild or moderate hypothermia. Mohr et al<sup>2</sup> studied 48 patients undergoing CABG surgery, with 8 patients (17%) exhibiting an MAP gradient  $\geq 10$  mmHg. SBP data are not specifically reported, although the up-slope (dp/dt) of the arterial pressure wave was decreased in the group of patients with MAP gradient  $\geq 10$  mmHg. Pauca et al,<sup>7</sup> in a study elucidating one of the mechanisms involved in central-peripheral arterial gradients (vasodilatation in the hand), compared aortic with radial artery pressure after CPB in 12 CABG patients. No patients had an MAP gradient  $>10$  mmHg and only 2 (10%) had an MAP gradient  $>5$  mmHg. There was no significant difference in SBP, radial versus aortic, after CPB in this study. Stern et al<sup>8</sup> studied systolic pressure (only) aortic-radial gradients before and after CPB in 18 patients undergoing CABG, finding in 13 patients a systolic gradient of 12 to 32 mmHg immediately after CPB. In their series, the gradient resolved within 60 minutes of separation from CPB (mean = 20 minutes). No specific data regarding temperature management during CPB were reported in these 3 investigations. In a study of 30 CABG patients, Rich et al<sup>4</sup> discovered a systolic aortic-radial gradient of  $\geq 10$  mmHg in 19 (63%) and an MAP gradient  $\geq 5$  mmHg in 18 (60%) on discontinuation of CPB.

These authors were the first to describe a significant MAP gradient early in the CPB period during cooling.

In the present study systolic femoral-radial artery pressure gradients associated with CPB were greater and of higher incidence than those reported by previous investigators. This probably results from one or more factors unique to this population: (1) deep hypothermia; (2) circulatory arrest; (3) prolonged periods of CPB; and (4) other factors unique to PTE, poor preoperative cardiovascular function, or CTEPH. Although it is tempting to assume that DHCA is the predominant factor, it is possible that the necessarily long periods of CPB are responsible.

The mechanisms for the development of the gradient are incompletely understood. Vasodilatation of the arterioles of the hand and proximal arterial-venous shunting have been proposed, as well as vasoconstrictive mechanisms.<sup>2,9</sup> Pauca et al,<sup>7</sup> by occluding the ulnar and radial arteries distal to the radial arterial catheter, were able to substantially raise the radial systolic pressure after CPB. This suggests that hand vasodilatation leads to loss of arterial wave reflection and blunting of the arterial pressure wave.<sup>10</sup> The present authors were unable to show a strong relationship between SVR and pressure gradient, indicating that local redistribution of blood flow may not be reflected by global SVR. It is likely that factors including peripheral vasodilatation, proximal shunting, and blood flow redistribution combine to produce the gradient.



**Fig 2. The femoral-radial systolic pressure (SBP) gradient (mmHg) at various time points during pulmonary thromboendarterectomy. Error bars indicate SD.**

Of all the factors studied, only age correlated with the gradients observed. Elderly patients exhibited slightly greater gradients after separation from CPB than younger patients and, paradoxically, showed a lesser gradient during the cooling phase of CPB. The authors are unable to explain this, but it suggests that the mechanisms involved at the two time points may be different.

It has been argued that, when these gradients occur, the radial arterial pressure is as important as the central pressure because it is this pressure that the periphery “sees.” Few would argue, however, against obtaining accurate central pressures to assess the perfusion pressure of the brain, coronary arteries, and other vital organs. Central arterial pressure measurements can be achieved by cannulation of the femoral or axillary artery. Long radial arterial catheters have been used and are sufficient, provided they extend to the axillary artery.<sup>11,12</sup> Brachial arterial catheters may be ineffective in reliably reflecting central arterial pressure after CPB, although they may provide a better estimate than radial artery catheters.<sup>12,13</sup> All these sites have been shown to be safe for arterial pressure monitoring.<sup>14-16</sup>

There are limitations to this study. No attempt was made to determine the mechanisms for the gradients. Such an effort may involve determination of hand temperature, microcirculation characteristics, radial artery diameter, pressure waveform mor-

phology, and levels of inflammatory mediators. Little is known about the effects of deep hypothermia on vascular reactivity, and it was beyond the scope of this study to investigate them. This population was limited to patients with chronic pulmonary hypertension undergoing PTE. It is possible that some of the results may not apply to patients without pulmonary hypertension undergoing DHCA for other surgeries. Also, the study population and surgical procedures were homogenous. It is possible that studies involving more wide-ranging periods of DHCA, for example, would reveal relationships not apparent in this investigation.

This study shows that DHCA in patients undergoing PTE is associated with exaggerated femoral-radial artery pressure gradients, particularly systolic. There is wide interindividual variation; the gradients are difficult if not impossible to predict and can persist for many hours postoperatively. Thus, central arterial pressure monitoring is recommended in surgeries involving DHCA. If central monitoring is unavailable, clinicians should rely on mean rather than systolic arterial pressure measurements from a peripheral artery.

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