

# The influence of extracorporeal circulation on EV1000 monitor hemodynamic parameters at two sites of intravenous cold saline injection

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## Abstract

**Objective:** Previous studies have suggested that transpulmonary thermodilution (TPTD) measurements are influenced by extracorporeal circulation methods, such as blood purification. Using pigs, we investigated the effect of extracorporeal circulation on hemodynamic measurements at two sites of cold saline injection.

**Methods:** Six female outbred pigs were included in the study. A vascular access site was made in the left external jugular vein. Cold saline was injected in the right external jugular vein or the right femoral vein. Hemodynamic monitoring was performed using TPTD (EV1000). Cardiac output (CO), global end-diastolic volume (GEDV), and extravascular lung water (EVLW) values were compared between extracorporeal circulation and no extracorporeal circulation. All data are expressed as median values.

**Results:** The following data were obtained when cold saline was injected into the jugular vein (circulation on vs. circulation off): CO, 2.7 vs. 2.9 L/min ( $P = 0.04$ ); GEDV, 403 vs. 438 ml ( $P = 0.04$ ); and EVLW, 310 vs. 306 ml ( $P = 0.92$ ). The following data were obtained when cold saline was injected into the femoral vein (circulation on vs. circulation off): CO, 2.6 vs. 2.8 L/min ( $P = 0.18$ ); GEDV, 497 vs. 500 ml ( $P = 0.18$ ); and EVLW, 341 vs. 345 ml ( $P = 0.44$ ).

**Conclusions:** Extracorporeal circulation has an effect on the accuracy of measurement of TPTD injection through the jugular vein. In contrast, no effect of extracorporeal circulation was observed when the femoral vein was used.

**Keywords:** Transpulmonary thermodilution, EV1000, Blood purification, Extracorporeal circulation, Cardiac output

## Introduction

Hemodynamic monitoring with transpulmonary thermodilution (TPTD) has been increasingly used among patients with critical illnesses. Using cold saline injection as an indicator, TPTD can measure volumetric hemodynamic parameters, such as cardiac output (CO), global end-diastolic volume (GEDV), and extravascular lung water (EVLW). Measurements are calculated from the area under the thermodilution curve using the Stewart-Hamilton formula.

In patients admitted to the intensive care unit (ICU), the introduction of TPTD has allowed optimization of intensive procedures, such as mechanical ventilation, extracorporeal circulation, and ICU stay, all of which contribute to lower mortality.<sup>1-3</sup> However, blood purification, a type of extracorporeal circulation and commonly used in 8%–10% of ICU patients,<sup>4</sup> may affect the accuracy of TPTD results by influencing blood temperature and flow.

Recently, interference between extracorporeal circulation and TPTD was reported in a clinical research study, but the precise effects remain unknown.<sup>5-9</sup> Specifically, the influence of

cold saline injection site has not been studied. In this report, using a pig model, we investigated whether the site of cold saline injection, jugular vein or femoral vein, affected the influence of extracorporeal circulation on TPTD measurement accuracy in the body of the same pig.

## Methods

### Study subjects

This study was approved by the Institutional Animal Care and Use Committee of Fujita Health University. Six female outbred pigs (age, 3–4 months; body weight, 35–40 kg) were studied. Pigs were anesthetized with sevoflurane and administered Ringer's acetate at 4 ml/kg/h through an ear vein.

### Preparation

Vascular access for extracorporeal circulation was achieved with a GamCath™ HighFlow double lumen catheter (Gambrö Dialysatoren GmbH, Hechingen, Germany) in the left external jugular vein. Extracorporeal circulation was performed using a dedicated machine, the TR-525 (Toray Industries, Inc., Tokyo, Japan). The EV1000 monitor (Edwards Lifesciences, Irvine, CA, USA) with temperature sensing through a VolumeView™ catheter (diameter, 5 Fr; length, 20 cm; Edwards Lifesciences) in the left femoral artery was used for TPTD.

Cold saline (10 ml at 0°C) was injected through central venous catheters (Certofix, B. Braun-Aesculap AG, Tuttlingen,

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Germany) in the right external jugular vein and right femoral vein. All catheter tip positions were over the vascular bifurcation and in the central vein and artery. Both right and left jugular catheters were in the superior vena cava, but the catheter for cold saline injection was placed close to the heart. Only a blood circuit without a filter was used to mimic blood purification (Figure 1).

**Measurement protocol**

The average of three sequential TPTD measurements was used. Cold saline was prepared by shaking in ice just before injection. The EV1000 monitor was used to measure pulse rate (PR), mean arterial blood pressure (MAP), central venous pressure (CVP), body temperature (BT), CO, GEDV, and EVLW. To avoid coagulation of the extracorporeal circuit, 5,000 IU of heparin was administered intravenously. Blood flow rate was 150 ml/min. As hemodynamic parameters were unstable shortly after extracorporeal circulation, circulation was continued for >10 min. After that, initial measurements were taken after injecting cold saline into the jugular vein during circulation (jugular<sub>on</sub>). Circulation was stopped briefly,

and a second set of measurements were taken with circulation off (jugular<sub>off</sub>). Subsequently, we switched from the jugular vein to the femoral vein. Circulation was restarted, and a third set of measurements was taken using the same method (femoral<sub>on</sub>). Circulation was stopped again, and a fourth set of measurements was taken after injecting cold saline into the femoral vein with circulation off (femoral<sub>off</sub>) (Figure 2).

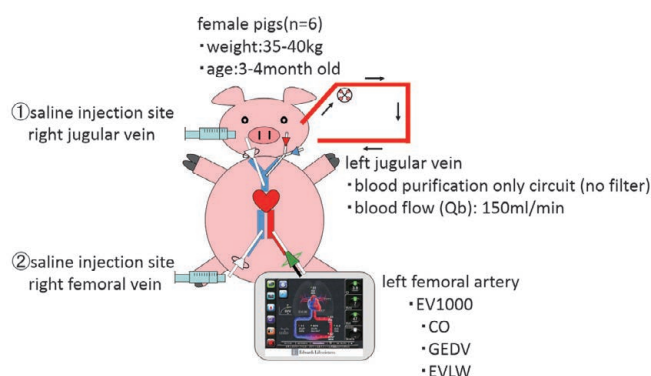
**Statistical analysis**

All data are expressed as median (25–75% interquartile range, IQR). The Wilcoxon signed-rank test was used to compare values between on vs. off conditions (using EZR, Saitama Medical Center, Jichi Medical University, Saitama, Japan). A value of P < 0.05 was considered statistically significant.

**Results**

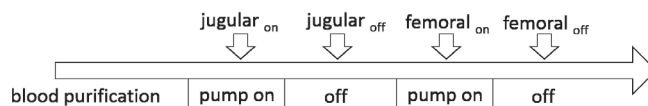
PR, MAP, CVP, and BT results are shown in Table 1. The values obtained were consistent between the jugular and femoral veins. CO was reduced by extracorporeal circulation using the jugular vein, and was restored when the circulation was turned off [2.7 (IQR: 1.8–3.4) vs. 2.9 (IQR: 2.1–3.7) L/min, P = 0.04]. In contrast, the effect of extracorporeal circulation was not observed when the femoral vein was employed [2.6 (IQR: 2.2–3.5) vs. 2.8 (IQR: 2.2–3.6) L/min, P = 0.18]. GEDV significantly increased from jugular<sub>on</sub> to jugular<sub>off</sub> [403 (IQR: 375–454) vs. 438 (IQR: 391–532) ml, P = 0.04]. However, GEDV did not significantly change from femoral<sub>on</sub> to femoral<sub>off</sub> [497 (IQR: 465–533) vs. 500 (IQR: 476–546) ml, P = 0.18]. There was

Figure 1.



Experimental setup. Right jugular vein, right femoral vein and left femoral artery were cannulated for EV1000 measurements. Left jugular vein was cannulated for blood purification.

Figure 2.



Study protocol. Jugular<sub>on</sub>: injecting through the jugular vein under the pump on, jugular<sub>off</sub>: injecting through the jugular vein under the pump off, femoral<sub>on</sub>: injecting through the femoral vein under the pump on, femoral<sub>off</sub>: injecting through the femoral vein under the pump off.

Table 1. Hemodynamic variables and body temperature

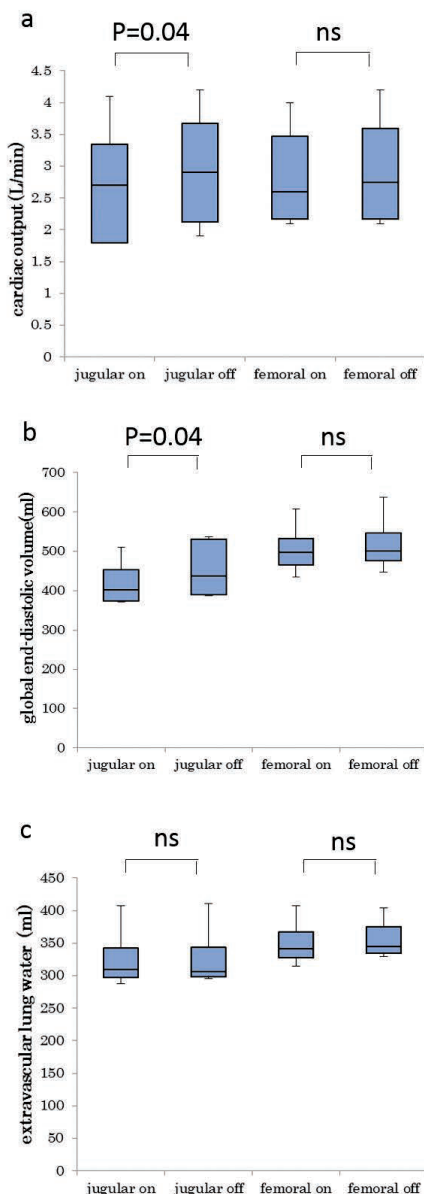
	jugular <sub>on</sub>	jugular <sub>off</sub>	P value	femoral <sub>on</sub>	femoral <sub>off</sub>	P value
PR (/min)	75 (66–88)	75 (67–86)	0.92	75 (65–90)	75 (66–91)	0.15
MAP (mmHg)	60 (58–67)	64 (56–70)	0.59	63 (59–68)	62 (56–70)	0.59
CVP (mmHg)	7 (3–10)	7 (5–9)	0.59	8 (6–11)	9 (6–12)	0.59
BT (°C)	33.1 (31.7–35.4)	33.0 (31.5–35.4)	0.17	33.0 (31.3–35.6)	32.9 (31.3–35.5)	0.15

Results are expressed as median (25%–75% interquartile range).

PR: pulse rate, MAP: mean arterial blood pressure, CVP: central venous pressure, BT: body temperature.

no significant difference between EVLW measured at jugular<sub>on</sub> and jugular<sub>off</sub> [310 (IQR: 297–342) vs. 306 (IQR: 298–344) ml, P = 0.92]. There was also no significant difference between EVLW measured at femoral<sub>on</sub> and femoral<sub>off</sub> [341 (IQR: 328–368) vs. 345 (IQR: 335–376) ml, P = 0.44] (Figure 3).

Figure 3.



Median values of (a) cardiac output, (b) global end-diastolic volume, and (c) extravascular lung water values obtained after injecting cold saline through the jugular vein under circulating on (jugular<sub>on</sub>) and circulating off (jugular<sub>off</sub>) conditions, and through the femoral vein under circulating on (femoral<sub>on</sub>) and circulating off (femoral<sub>off</sub>) conditions.

### Discussion

When we compared jugular<sub>on</sub> with jugular<sub>off</sub>, CO and GEDV were significantly underestimated. In contrast, CO, GEDV, and EVLW were not significantly different between femoral<sub>on</sub> and femoral<sub>off</sub>. Measurements of GEDV in the femoral<sub>off</sub> condition were larger compared with those in jugular<sub>off</sub>. Our results are

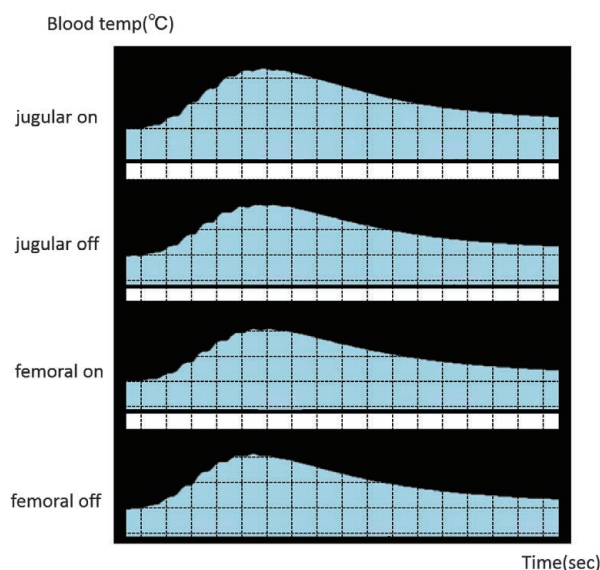
consistent with previous reports by Schmidt et al.<sup>10</sup> and Saugel et al.<sup>11</sup>

Sakka et al.<sup>6</sup> reported statistically significant changes in cardiac index values with blood purification. However, the authors suggested that blood purification does not influence measurements by TPTD in a clinically relevant manner. They also suggested that the position of the dialysis catheter tip used for blood purification does not significantly influence measurement, when cold saline was injected through the superior vena cava. Dufour et al.<sup>7</sup> studied the effect of blood purification on TPTD at a higher blood flow rate than the latter study (250–350 vs. 80–150 ml/min). In this paper, cardiac and GEDV indices did not significantly change with high blood flow and high filtration flow. However, Heise et al.<sup>8</sup> and Nakamura et al.<sup>9</sup> reported that TPTD measurements were influenced significantly by blood purification. These conflicting results show that the matter is still controversial. Our results showed that CO and GEDV were significantly underestimated by extracorporeal circulation in the jugular vein, when cold saline was injected into the jugular vein. In contrast, when cold saline was injected into the femoral vein, CO, GEDV, and EVLW were not significantly changed by extracorporeal circulation. In a study using pigs, Zhang et al.<sup>12</sup> reported that TPTD can accurately measure CO, in accordance with our present results.

Figure 4 shows an example of the thermodilution curve. When jugular<sub>on</sub> was compared with jugular<sub>off</sub>, the thermodilution curve shifted vertically rather than horizontally (Figure 4). Therefore, extracorporeal circulation did not affect transit time, but affected temperature change.

It is known that circuit blood temperature decreases from the beginning to the end of the extracorporeal circuit during blood purification.<sup>13,14</sup> Hence, exothermal blood of the extracorporeal circuit was continuously returned during blood purification. The blood stream from the extracorporeal circulation might affect the diffusion of the injected cold saline. CO and GEDV

Figure 4.



Differences in the thermodilution curve between extracorporeal on and off conditions.

The thermodilution curve was derived from the EV1000 monitor software. Grid lines were applied to the original curve for visual clarity.

were underestimated if the area under the thermodilution curve increased. In contrast, when cold saline was injected into the femoral vein, there was little difference in the thermodilution curve between femoral<sub>on</sub> and femoral<sub>off</sub> (Figure 4).

When cold saline is injected into the jugular vein, it is immediately admixed with extracorporeal circulation blood in the superior vena cava. However, when cold saline is injected into the femoral vein, it becomes adequately mixed and diluted with extracorporeal circulation blood in the right atrium. As a result, the data obtained by injecting through the femoral vein might be consistent with the control value of circulation off.

This study has two limitations. First, we did not assess the position of the dialysis catheter. Although we assessed the injection site for cold saline, injecting cold saline through the femoral vein might distort TPTD measurements. Further study is necessary to clarify the effect of blood purification via the femoral vein on TPTD. Second, we assessed extracorporeal circulation only after stopping. We did not evaluate the restart effect.

In conclusion, extracorporeal circulation has an effect on the accuracy of the measurement of TPTD injection into the jugular vein. In contrast, the effect of extracorporeal circulation was not observed when the femoral vein was used.

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## Conflict of interest

The authors have no conflicts of interest to declare.

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