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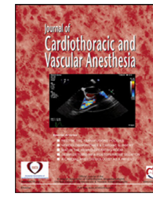

Original Article

Optimal Position of Inferior Vena Cava Cannula in Pediatric Cardiac Surgery: A Prospective, Randomized, Controlled, Double-Blind Study

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Objective: To examine the authors' hypothesis that during the cardiopulmonary bypass (CPB) in children, the inferior vena cava cannula tip placed proximal to the right hepatic vein orifice would produce a higher venous drainage compared with that placed distally.
Design: A prospective, randomized, controlled, double-blind study.
Setting: Single university hospital.
Participants: Thirty-two patients aged <6 years, scheduled for elective cardiac surgery using CPB for congenital heart disease.
Interventions: Participants were randomized to 2 groups: the proximal group with the cannula tip placed proximally within 1 cm of the right hepatic vein orifice and the distal group with the cannula placed distally within 1 cm of the right hepatic vein orifice.
Measurements and Main Results: The primary outcome of this study was the perfusion flow rate at the time of establishment of total CPB with cardioplegia. The authors initially planned to enroll 60 patients, but before reaching the target sample size, the authors terminated this study owing to patient safety, and 18 patients in the proximal group and 14 patients in the distal group finally were analyzed. No significant differences in patient characteristics were observed between the 2 groups. The mean perfusion flow rate in the proximal group was significantly greater (2.55 ± 0.27 L/min/m^2) than that in the distal group (2.37 ± 0.20 L/min/m^2, $p = 0.04$).
Conclusion: The inferior vena cava cannula tip placed in the proximal position was clinically superior, compared with a distal placement, in producing higher perfusion flow in children.
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Key Words: cardiopulmonary bypass; children; inferior vena cava cannula; right hepatic vein; venous drainage; perfusion flow

MAINTENANCE OF OPTIMAL PERFUSION is important during cardiovascular surgical procedures using cardiopulmonary bypass (CPB) to ensure stable circulation dynamics.[1] Perfusion during CPB depends on 2 parameters, flow and pressure, which are linked directly to blood flow to visceral organs, such as the pancreas, stomach, colon, kidneys, and liver.[2−6] Poor perfusion during CPB leads to inadequate tissue perfusion resulting in an increased risk of organ ischemia and postoperative organ dysfunction,[3,5] such as postoperative neurological[7−10] and renal failure.[11−13]

Perfusion flow and pressure during CPB are known to be the most important factors for preventing these adverse effects. Particularly, optimal perfusion flow is more important in children because they require a higher perfusion flow compared with adults for effective organ perfusion owing to their smaller circulating blood volume, higher oxygen consumption rate, higher perfusion flow demand, and immature organ systems.[14−17] The minimum perfusion flow rate most commonly used during CPB under normothermic anesthesia is 2.4 L/min/m^2.[1,15,18]

Venous drainage from a venous cannula is essential to maintaining optimal perfusion flow.[18] Incomplete venous drainage directly affects the hemodynamic support of a patient.[19]

Clinical trial number and registry URL: UMIN000025581, http://www.umin.ac.jp/ctr/index.htm.

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Although venous drainage from a venous cannula is affected by several factors, such as hematocrit, body temperature, cannula size, length of venous drainage line, air in the venous drainage line, low blood volume, and obstruction of the cannula, the inferior vena cava (IVC) cannula position also is considered one of the most important factors.[20−23]

Indeed, the IVC cannula often is misplaced unintentionally in hepatic veins and causes insufficient venous drainage.[22,24,25] Particularly, the right hepatic vein (RHV) is most likely to have the cannula misplaced because it is anatomically the largest hepatic vein and enters the IVC at an oblique angle, and almost 10% of IVC cannulas were found to be placed primarily in the RHV.[24,25] To prevent this, transesophageal echocardiography (TEE)-guided IVC cannulation has been recommended widely.[22,24] However, the optimal tip position of the IVC cannula has not been reported. In the authors' institution, similar to other institutions, IVC cannulas generally are inserted in the proximal side or the distal side to the RHV orifice, which is the IVC at the RHV bifurcation level, depending on the decision of the anesthesiologists who perform the TEE.[24−26] Particularly, in children, the authors occasionally have observed that the IVC cannula tip placed distal to the RHV orifice under TEE-guided IVC cannulation had to be repositioned because of insufficient venous drainage, even if it was not misplaced in the RHV.

Therefore, the authors hypothesized that the IVC cannula tip placed proximal to the RHV orifice would produce a higher venous drainage than placement distal to the RHV orifice. The authors examined this hypothesis in a prospective, randomized, controlled, double-blind study.

Methods

Patients

Ethical approval for this study (approval no. 2706) was provided by the ethics committee of Niigata City General Hospital, Niigata, and the study was registered with the UMIN Clinical Trials Registry (http://www.umin.ac.jp/ctr/index.htm; identifier: UMIN000025581, January 9, 2017). This study was conducted at Niigata University Medical and Dental Hospital (Niigata, Japan), and patients were enrolled between January 2017 and October 2017. Written informed consent was obtained from the guardians of all the patients. The authors enrolled patients aged <6 years who were scheduled for elective cardiac surgery using CPB for congenital heart disease. The authors excluded patients who were not scheduled for IVC cannulation; who did not receive total CPB with cardioplegia; and who had a body weight >15 kg, congenital anomalies of the IVC, and signs of right heart failure.

Anesthetic Management

The children received premedication with a combination of rectal ketamine (5 mg/kg), midazolam (0.3 mg/kg), and atropine (0.03 mg/kg) 45 minutes before the induction of anesthesia. General anesthesia was induced either by inhalation of sevoflurane (5 vol%) or intravenous midazolam (0.3 mg/kg). A tracheal tube was inserted orally after the intravenous administration of atropine (0.01 mg/kg), fentanyl (4-10 μg/kg), and rocuronium (0.6-1.0 mg/kg). Anesthesia was maintained with sevoflurane (1-2 vol%), rocuronium, and fentanyl. An arterial catheter was inserted into the radial or ulnar artery. A central venous catheter was inserted into the right internal jugular vein. A TEE probe was inserted after evacuating air from the stomach with a gastric tube. All TEE examinations in this study were performed with a ProSound SSD α10 sonography machine (Aloka Co., Ltd., Tokyo, Japan), using a biplane probe (UST-52111S, Aloka) or a single-plane probe (UST-52110S, Aloka).

TEE Examination During Cannulation and CPB Procedures

CPB was started with a Staccato heart-lung machine S5 (LivaNova Co., Ltd., Tokyo, Japan) after the attachment of the aortic cannula using a Toyobo NSH heparin-coated cannula (Toyobo Engineering Co., Ltd., Tokyo, Japan) and the superior vena cava (SVC) cannula using the angled-type Toyobo Flexmate (Toyobo Engineering Co., Ltd., Tokyo, Japan). Subsequently, IVC cannulation using the Toyobo Flexmate (Toyobo Engineering Co., Ltd.), which is a commercially available straight cannula with no side hole, was performed under TEE guidance. The TEE operator monitored the view of the IVC inlet and hepatic veins at a transducer angle of 0°. As described previously,[24,27] this view can be obtained easily by turning the probe to the patient's right side (clockwise) from the 4-chamber view and advancing the probe while keeping the right atrium and the orifice of the IVC at the center of the sector. During the insertion of the IVC cannula, the TEE operator checked that the cannula tip was inserted correctly into the IVC and not into the hepatic vein. If the IVC cannula was malpositioned in the hepatic veins, it was repositioned in the IVC. Thereafter, the IVC cannula was placed at the allocated position according to the instructions of the TEE operator. Because the cannula could shift during fixation or connection to CPB, the position of its tip was checked constantly under TEE guidance until the CPB was completely established. During these procedures, the surgical monitor that displayed the TEE image was disconnected to the TEE machine so that surgeons and perfusionists could not see the TEE image at all.

The authors set the target perfusion flow rate as 2.4 L/min/m^2. Venous drainage was performed via gravity-dependent (siphon) drainage. Once all cannulation procedures were finished, and because the authors had not snared the SVC and IVC yet, venous drainage from them was sent to both the CPB and patient's own heart, so the patient's own cardiac output still existed. The authors defined this state as partial CPB. Then, the authors snared the SVC and IVC so that venous return from them was sent completely to the CPB via cannulas and did not return to the patient's own heart at all. This procedure was essential for producing a bloodless field of the heart during surgical procedures. The authors defined this state as total CPB. If the perfusion flow rate under total CPB was less than 1.7 L/min/m^2, which is 70% of the target perfusion flow rate, the authors returned to partial CPB and changed the IVC cannula positioning from the allocated position before measuring the primary outcome to improve the perfusion flow and included these cases in the secondary outcome. If the perfusion flow rate under total CPB could be obtained at least 1.7 L/min/m^2, the authors proceeded to the induction of cardioplegia because the patient's oxygen demand and required perfusion flow rate were satisfied by lowering their body temperature to 32-34˚C and reducing their metabolism and oxygen consumption during surgical procedures under total CPB with cardioplegia.[1]

After that, the authors introduced cardiac arrest by the antegrade administration of cardioplegia. Immediately after cardiac arrest was introduced under total CPB, the authors measured the primary outcome.

Assessments

Patients were allocated randomly to 1 of 2 groups: the proximal group and distal group. The proximal group had the IVC cannula tip placed proximally within 1 cm of the RHV orifice, and the distal group had the cannula placed distally within 1 cm of the RHV orifice under TEE guidance. In this study, the authors defined the RHV orifice as the IVC at the RHV bifurcation level. At a transducer angle of 0˚, the RHV orifice was visualized easily as the position where the IVC and RHV are just joining (Fig 1, *A*). In the proximal group, the tip of the cannula was positioned by pulling the probe slightly to the proximal side within 1 cm of the RHV orifice, where the IVC and RHV join (Fig 1, *B*). In the distal group, the tip of the cannula was positioned by advancing the probe slightly to the distal side within 1 cm of the RHV orifice, where the IVC and RHV separate (Fig 1, *C*). When using a biplane probe, the authors also ascertained whether the cannula was placed correctly in the allocated position at a transducer angle of 90˚ as shown in Fig 1, *D*. Figure 2 shows the actual TEE image where the IVC cannula was placed in each position. All TEE-guided procedures were performed by a single anesthesiologist (Y.S.), skilled in TEE and licensed by the Japanese Board of Perioperative Transesophageal Echocardiography. Randomization was determined using a computer-generated randomization sequence in blocks of 15. The allocations were concealed in sequentially numbered, sealed, opaque envelopes. The TEE operator opened the envelope containing the allocation result at the beginning of the surgery. Surgeons and perfusionists were blinded to the allocation of the patients throughout the study.

The patients' demographic data including age, sex, height, and weight were recorded. Surgical and anesthetic data including hematocrit, rectal temperature, and central venous pressure were recorded at the time of the establishment of total CPB with cardioplegia, and IVC diameter was measured by TEE before the establishment of CPB. CPB data, including aortic cannula size, SVC cannula size, IVC cannula size, priming volume of the circuit, and initial dilution ratio, also were evaluated.

This manuscript adheres to the applicable Consolidated Standards of Reporting Trials guidelines (Fig 3).

Statistical Analysis and Outcomes

Statistical analyses were performed using StatView software (SAS Institute, Cary, NC). Statistical significance was defined as $p < 0.05$ using the 2-tailed Student *t* test for numerical data and the χ^2 test for categorical data.

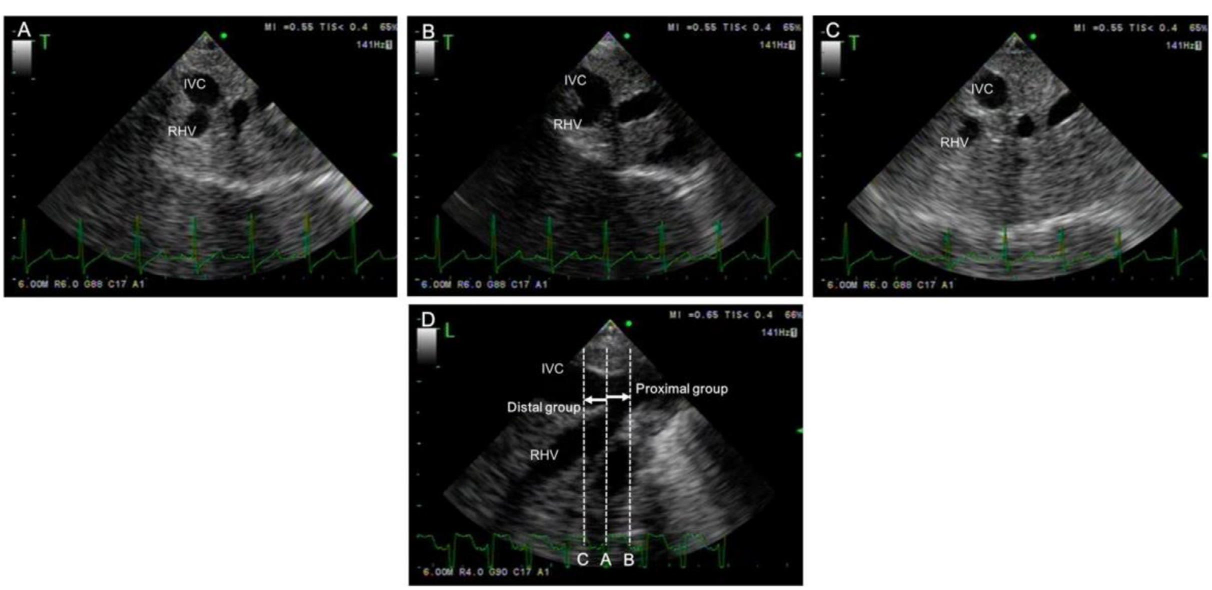

Fig 1. Transesophageal echocardiography image used to determine the cannula tip position. (A) A view of the right hepatic vein (RHV) orifice at a transducer angle of 0˚. (B) The places where the authors guided the tip of the inferior vena cava (IVC) cannula in the proximal group, which was obtained by pulling back the probe proximally within 1 cm of the view of the RHV orifice. (C) The places where the authors guided the tip of the IVC cannula in the distal group, which was obtained by advancing the probe distally within 1 cm of the RHV orifice. (D) The places where the authors guided the tip of the IVC cannula in each group at a transducer angle of 90˚. *Dotted lines* A, B, and C correspond to Fig 1, *A*, *B*, and *C*, respectively, obtained at a transducer angle of 0˚.

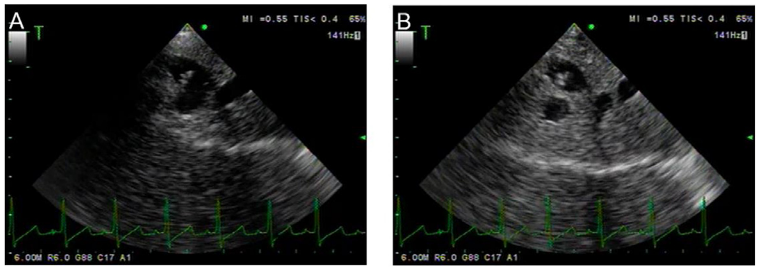

Fig 2. The actual transesophageal echocardiography (TEE) image where the inferior vena cava (IVC) cannula was placed in each position. (A) The actual TEE image with the cannula tip in the proximal group. The authors checked that the TEE image was monitoring the IVC cannula tip correctly by confirming that the cannula disappeared when advancing the probe slightly from this view. (B) The actual TEE image with the cannula tip in the distal group. The authors checked that the TEE image was monitoring the IVC cannula tip correctly by confirming the cannula disappeared when advancing the probe slightly from this view.

According to a retrospective pilot study involving 26 patients, the mean perfusion flow rate (standard deviation) was 2.51 (0.16) L/min/m^2 in the proximal group and 2.25 (0.32) L/min/m^2 in the distal group. The authors regarded a difference of 10% of 2.4 L/min/m^2, which commonly is used as the minimum required perfusion flow rate[1,15,18] as clinically important. Therefore, the sample size calculation was estimated to detect a difference of 0.24 L/min/m^2 in the perfusion flow rate. To demonstrate this difference using a 2-tailed Student *t* test, a sample size of 29 patients per group was the minimum size needed to provide a statistical power of 0.8 and a type I error rate of 0.05. Because of the expected dropout rate, 30 patients per group were enrolled in the study.

The primary outcome of the study was the perfusion flow rate (L/min/m^2) at the time of the establishment of total CPB with cardioplegia. The secondary outcome was the number of patients who needed IVC cannula repositioning before measuring the primary outcome because of insufficient venous drainage. Repositioning of the cannula was performed when the perfusion flow rate was less than 1.7 L/min/m^2 (ie, $<70\%$ of the target perfusion flow rate of 2.4 L/min/m^2).

Results

This study was terminated before the target sample size was reached because the authors observed markedly poor venous drainage relating to their allocated distal position, which occurred only in the distal group, as shown in the secondary outcome. Thus, the authors attempted to open the allocation and analysis although the study had not been concluded because the authors judged that for safety concerns, the study should be discontinued. Consequently, 45 consecutive patients total were assessed for eligibility. The enrollment, randomization, and analysis process are summarized in Fig 3. According to the exclusion criteria, 37 patients in total were randomized and all the patients received their allocated interventions. In the proximal group, 2 patients dropped out from the final analysis because of insufficient venous drainage before the measurement of the primary outcome and were counted in the secondary outcome. The drainage was not related to their allocated proximal position at all because it hardly was improved whether the cannula was pulled toward the proximal or distal side. On the other hand, in the distal group, 3 patients dropped

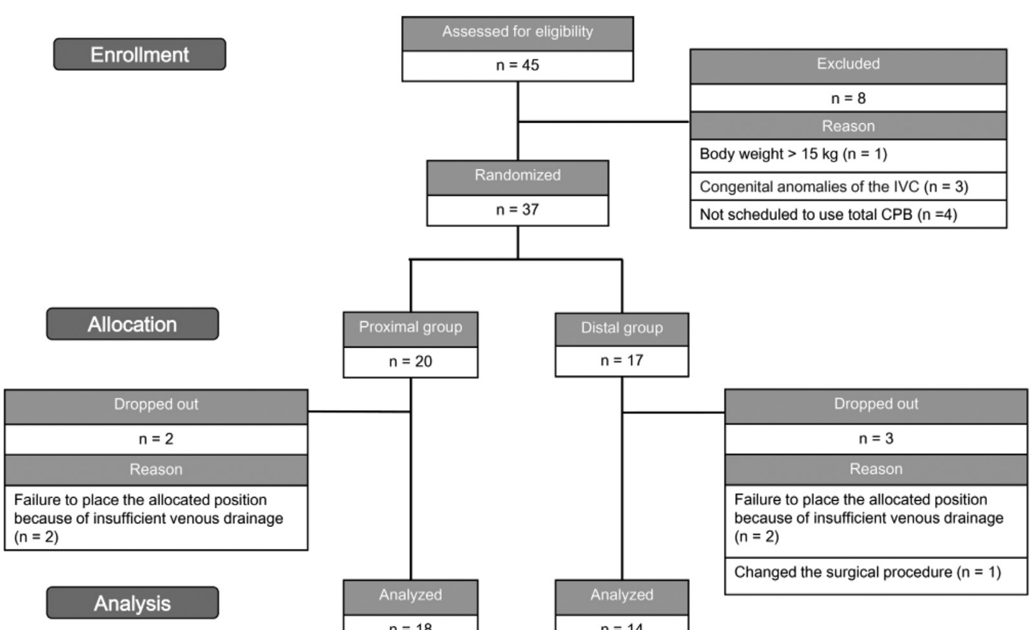

Fig 3. The CONSORT flow diagram of the groups. CONSORT, Consolidated Standards of Reporting Trials.

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out from the final analysis. Two patients dropped out from the final analysis because of insufficient venous drainage before the measurement of the primary outcome and were counted in the secondary outcome. They needed to change the IVC cannula tip from the distal position and they were improved remarkably by pulling the IVC cannula to proximal. One patient dropped out because the surgical procedure was changed and there was no indication for total CPB with cardioplegia. Therefore, 18 patients in the proximal group and 14 patients in the distal group were analyzed finally. No significant differences were observed between the 2 groups regarding patients' characteristics (Table 1). The surgical and anesthetic data are shown in Table 2, and the differences were not statistically significant between the 2 groups.

Figure 4 demonstrates that the mean perfusion flow rate, which was the primary outcome, was significantly greater in the proximal group than in the distal group (proximal group, 2.55 ± 0.27 L/min/m^2; distal group, 2.37 ± 0.20 L/min/m^2; $p = 0.04$; statistical power was calculated to be 0.69 when type I error rate was set to 0.05). The number of patients who required repositioning of the IVC cannula before measuring the primary outcome, which was the secondary outcome, was 2 in both groups and was not statistically significant ($p = 0.99$). However, the cause of the severe venous drainage defect was completely different between the groups. The defect observed in 2 patients of the distal group was related closely to their allocated distal position because it was improved notably when the cannula was pulled back toward the proximal side. On the other hand, contrary to the distal group, that of the proximal group was not related to their allocated proximal position at all because it hardly was improved whether the cannula was pulled toward the proximal or distal side. None of the patients showed any clinical signs of intraoperative or postoperative complications associated with CPB.

Discussion

In this prospective randomized study, the authors revealed that the IVC cannula tip placed proximal to the RHV orifice in children tends to produce a higher perfusion flow rate compared with a placement distal to the RHV orifice; this was the primary outcome. It is generally known that malpositioning of an IVC cannula in the RHV should be avoided for optimal perfusion, but there are no criteria regarding the optimal cannula tip position in the IVC. Therefore, the cannula tip generally is placed in the IVC near the RHV bifurcation level: either proximally or distally to the RHV orifice. Some reports indicate that the tip placed proximal to the RHV orifice is appropriate,[24,25] whereas another report suggested that the tip placed distally is appropriate.[26] Kirkeby-Garstad et al. reported that the IVC cannula placed deep in the IVC, which is approximately 7 cm distal from the RHV orifice in adults, was associated with poor venous drainage.[24] They observed poor venous drainage in 8 patients among the 143 included patients, and 5 of them had the cannula tip placed deep in the IVC. However, these studies involved adults and were not randomized, controlled, or double blind. Moreover, no previous study has investigated the positioning of the IVC cannula at the RHV bifurcation level in children. The position of the IVC cannula for obtaining optimal perfusion is particularly important in pediatric cardiac surgery. Surgical procedures often require bloodless fields; thus, bicaval venous cannulation using IVC cannulas is performed most often.[28] To the authors' knowledge, this study is the first to investigate the optimal position of the IVC cannula, where more venous drainage can be obtained in children using a randomized, controlled, double-blind study. These results indicate that the tip placed proximal to the RHV orifice could be advantageous in producing higher venous drainage. This finding is new and has clinical applicability.

There are plausible mechanisms that support these results. Reports indicate that the proximal side of the RHV orifice in the IVC is less prone to a collapse in intravascular volume than the distal side because the muscular diaphragm protects against the collapse of blood vessels on the proximal side.[29,30] Moreover, it also has been reported that the proximal side of the IVC, where hepatic venous flow enters, is enlarged anatomically.[31] This is consistent with previous findings that suggest that the diameter of the proximal side of the IVC is larger than that of the distal side in healthy volunteers.[32,33] Based on these findings, there is a possibility that the IVC cannula tip placed proximal to the RHV orifice, which is larger and more resistant to collapse, may be less likely to cause position abnormality or stick to the vessel wall when the IVC collapses during CPB.

This study had some limitations. First, it was terminated before the calculated target sample size was reached. The authors judged that this study should not be continued from a safety perspective, considering the severe venous drainage defect relating to their allocated distal position that occurred only in the distal group, as counted in the secondary outcome.

Table 1
Demographic Data of the Groups

	Proximal Group(n = 18)	Distal Group(n = 14)	p Value
Age (mo)	12.6 (11.7)	18.1 (12.7)	0.22
Male/female (number of patients)	9/9	4/10	0.29
Height (cm)	68.7 (12.0)	72.2 (14.1)	0.45
Weight (kg)	7.1 (2.7)	8.0 (3.2)	0.38
Diagnosis (number of patients) ASD[a] / VSD[b] / TOF[c] / other	2 / 8 / 3 / 5	1 / 3 / 4 / 6	

NOTE. Values are mean (SD) or numbers of patients.
Abbreviations: ASD, atrial septal defect; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

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Table 2
Surgical and Anesthetic Data of the Groups

	Proximal Group (n = 18)	Distal Group (n = 14)	p Value
Hematocrit (%)	29.4 (2.5)	31.1 (2.4)	0.07
Rectal temperature (˚C)	34.6 (1.8)	34.8 (2.0)	0.41
Esophageal temperature (˚C)	33.1 (3.0)	33.8 (2.1)	0.46
Aortic cannula size (F)	10.5 (1.7)	11.1 (1.3)	0.29
SVC[a] cannula size (F)	11.4 (1.3)	11.3 (1.3)	0.74
IVC[b] cannula size (F)	14.9 (2.0)	15.4 (1.8)	0.43
CPB[c] priming volume (mL)	236.1 (46.2)	227.1 (21.6)	0.51
Initial dilution ratio (%)	19.2 (4.7)	17.5 (4.0)	0.28
CVP[d] (mmHg)	3.1 (4.7)	3.3 (3.4)	0.91
IVC diameter (mm)	8.4 (1.2)	9.5 (2.1)	0.07

NOTE. Values are expressed as mean (SD). Statistical significance was defined as $p < 0.05$ using the 2-tailed Student *t* test for numerical data and the χ^2 test for categorical data.
Abbreviations: CPB, cardiopulmonary bypass; CVP, central venous pressure IVC, inferior vena cava; SVC, superior vena cava.

However, the authors were able to reveal a significant difference in perfusion flow between the proximal and distal groups with a statistical power of 0.7. Second, the authors used perfusion flow as an indicator to evaluate the optimal position of the IVC cannula. It has been reported that not only perfusion flow but also perfusion pressure is important for venous drainage. Thus, further study to evaluate venous drainage using perfusion pressure might be needed. However, because perfusion pressure is notably dependent on vascular resistance,[18] the authors regarded perfusion flow as a more suitable indicator in this study. Third, the authors used straight cannulas without side holes. Temp et al. reported that straight cannulas tend to cause malposition compared to angled cannulas.[25] The type of IVC cannula might have influenced the results. The authors believe that further studies that would evaluate various kinds of IVC cannula are needed. Finally, the authors could not rule out the effect of minor shunts such as an aortopulmonary fistula on perfusion flow of CPB, which occasionally is observed in children with congenital heart disease. However, these minor shunts were not detected in patients in this study before surgery, and there were no significant differences regarding patients' characteristics between the 2 groups. Therefore, the authors regarded these influences as minimal.

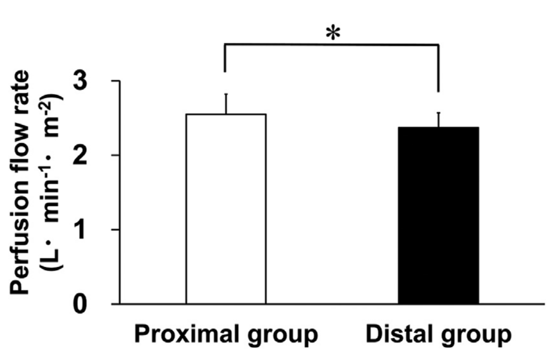

Fig 4. The mean perfusion flow rate (L/min/m^2) at the time of the establishment of total cardiopulmonary bypass with cardioplegia for the groups. Error bars represent the standard deviation. The mean perfusion flow rate in the proximal group was significantly greater than that of the distal group. *$p < 0.05$.

Conclusion

The proximal positioning, compared with the distal positioning, of the IVC cannula tip was clinically superior in producing a higher perfusion flow in children. This result might help to determine the optimal cannula position in children.

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