ORIGINAL

Minute distance obtained from pulmonary venous flow velocity using transesophageal pulsed Doppler echocardiography is related to cardiac output during cardiovascular surgery

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Abstract : ***Purpose.*** **We studied the relationship between minute distance calculated from pulmonary venous flow (PVF) velocity tracing and cardiac output (CO) measured with thermodilution method in patients undergoing cardiovascular surgery.**
Methods. **In 32 patients undergoing cardiovascular surgery, simultaneous measurements of hemodynamics including CO and transesophageal pulsed Doppler signals of PVF velocity were performed before and after surgical repair. Minute distance was calculated as the product of the heart rate and the sum of time-velocity integrals of PVF.**
Results. **The minute distance after surgical intervention increased from 1121 ± 347 cm・sec^{-1} to 1764 ± 538 cm・sec^{-1} ($p<0.001$; mean ± SD), while CO increased after surgical intervention from 3.5 ± 0.9 L・min^{-1} to 5.3 ± 1.1 L・min^{-1}. Simple linear regression analysis showed that minute distance was related with CO before and after surgical intervention (r=0.81 and r=0.76, respectively). The changes in minute distance were also related with those in CO (r=0.80).**
Conclusion. **The present study demonstrated that minute distance obtained from the pulsed Doppler tracings of PVF velocity was related with CO during cardiovascular surgery in adults. These results suggest that the changes in CO could be estimated from minute distance in pulmonary vein. J. Med. Invest. 52 : 178-185, August, 2005**

Keywords **:** *pulmonary blood flow, cardiac output, transesophageal echocardiography*

INTRODUCTION

It is important to know the changes in cardiac output (CO) during surgical operation especially in patients undergoing cardiovascular surgery. The intermittent cold bolus thermodilution technique by using pulmonary artery (PA) catheter has been widely applied to measure CO. Some studies indicated that the use of PA catheter in surgical patients decreased mortality (1-4), but other studies demonstrated that PA catheter use had no effect (5-7) or increased morbidity or mortality (8-10). Thus, several approaches to the measurements of CO by transesophageal echocardiography (TEE) have been tried without using PA catheters (11-16), but each has its limitations. For example, success rate with Doppler CO with pulmonary artery approach was 76% (11). Cardiac output derived from pulsed Doppler imaging of pulmonary artery systolic flow velocity modestly correlated with thermodilution CO (r=0.65), but output determined from the mitral valve diastolic flow velocity did not (r=0.24) (12). The good relationship between CO calculated as the product of time-velocity integral of aortic ejection continuous-wave

Received for publication March 22, 2005 ; accepted July 25, 2005.

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Doppler signals and aortic valve area and thermodilution CO existed (r=0.94) (14). However, the success rate with Doppler CO with aortic approach was 97-98% (14, 16). Furthermore, all of the previously reported approaches by using Doppler TEE required at least 2 images that are included blood flow velocity and cross-sectional area.

Recently, we used transesophageal Doppler echocardiography to evaluate the changes in pulmonary blood flow in children with tetralogy of Fallot (17). The pulmonary blood flow were measured in the left upper pulmonary vein and calculated from changes in minute distance (the product of heart rate and the sum of time-velocity integrals of pulmonary venous flow velocity) (17). Then, we demonstrated that intravenous administration of phenylephrine increased arterial blood pressure and pulmonary blood flow as evaluated from the minute distance, resulting in improved systemic oxygenation (17). Pathologically, pulmonary blood flow in tetralogy of Fallot is reduced, but we could obtain the signals of pulmonary venous flow velocity in all children in the previous study. This might be due to the anatomical close relationship between esophagus and pulmonary vein. These results suggest that the success rate of the estimation of CO from minute distance is higher than that of the other Doppler approaches. Moreover, this approach would be easy to obtain minute distance because only one image is required for the calculation. However, there is no report indicating that minute distance calculated from pulmonary venous flow velocity recording is related to CO. We designed this study to assess the relationship between minute distance and CO in adults.

SUBJECTS AND METHODS

Following our Institutional Ethics Committee approval and informed patient consent, we studied 32 patients undergoing elective cardiac or major vascular surgery. Patients were excluded if they had an abnormal heart rhythm without sinus rhythm, a history of a recent gastroesophageal disease (<3 weeks), or a presence of left-to-right or right-to-left shunts.

On the morning of surgery, patients received their usual cardiac medication. Premedication consisted of atropine (0.1 $mg \cdot kg^{-1}$) and either hydroxyzine (1 $mg \cdot kg^{-1}$) or midazolam (0.05 $mg \cdot kg^{-1}$) intramuscularly. In the operating theatre, cannulae were inserted into a peripheral vein and a radial artery. Standard monitoring included pulse oximetry, leads II of the electrocardiogram for heart rate and automated ST-segment trend analysis, and end-tidal capnography.

Anesthesia was induced using intravenous fentanyl (2-4 $\mu g \cdot kg^{-1}$) and thiamylal (2-4 $mg \cdot kg^{-1}$). Neuromuscular blocking was obtained by vecuronium (0.15 $mg \cdot kg^{-1}$). Following tracheal intubation, the lungs were mechanically ventilated with the combination of oxygen (50 %) and nitrous oxide and the tidal volume was adjusted to produce normocapnia (end-tidal carbon dioxide between 30 and 40 mmHg). Anesthesia was maintained with sevoflurane (0-2 %) and fentanyl [50-100 $\mu g \cdot kg^{-1}$ for surgery with cardiopulmonary bypass (CPB) ; 5-20 $\mu g \cdot kg^{-1}$ for surgery without CPB]. After induction of general anesthesia and tracheal intubation, a 7.5 Fr, pulmonary artery catheter (744HF75, Baxter Healthcare, Irvine, CA) was inserted through the right internal jugular vein and advanced into the pulmonary artery. This catheter was connected to a continuous CO monitor (Vigilance ; Baxter Healthcare). After placement of the pulmonary artery catheter, a multiplane TEE probe (21369A Phillips Medical Systems, Andover, MA) was inserted orally, and a routine echocardiographic evaluation was performed.

Measurement of pulmonary venous flow velocity and cardiac output

To measure the pulmonary venous flow velocity, the TEE probe was withdrawn slightly from the position obtaining a four-chamber view in the transverse scan, and the tip was anteflexed and turned to the left, providing a clear view of the left upper pulmonary vein as it emptied into the left atrium. A sample volume was placed 1 cm into the pulmonary vein from its junction with the left atrium. Guided by Doppler color-flow imaging, the multiple imaging angle was adjusted (0 - 20 °) to capture the left upper pulmonary venous flow parallel to the ultrasound beam. Pulmonary venous flow velocities were measured with pulsed Doppler echocardiography. Doppler signals were judged to be optimal when the greatest amplitude and quality of the spectral waveform was achieved through adjustment of the beam position and gain settings. Then, pulmonary venous flow velocity waveforms were recorded on videotape and printed on hard copy.

As described previously (17), we measured peak velocities and time-velocity integrals of the systolic (peak S, TVI-S), early diastolic (peak D, TVI-D), and reversal (peak R, TVI-R) waves with pulmonary venous flow velocity tracings (Figure 1). Three consecutive beats were measured and the results averaged. We measured RR interval from electrocardiogram, which was recorded simultaneously with pulmonary venous flow velocity (Figure 1). Total time-velocity integral (total TVI), heart rate, and minute distance were calculated off-line as follows : total TVI (cm)=(TVI-S)+(TVI-D)-(TVI-R) ; heart rate (beats$\cdot$min^{-1})=60/RR interval (sec) ; minute distance (cm$\cdot$min^{-1})=total TVI$\times$heart rate.

During pulmonary venous flow measurements, standard hemodynamic variables including heart rate, mean arterial pressure, mean pulmonary artery pressure, mean central venous pressure, and mean pulmonary capillary wedge pressure were recorded. Then, 10 ml of normal saline at room temperature was injected manually, and the average of three measurements was used as the thermodilution CO value. Doppler measurements were performed with the interruption of mechanical ventilation, but thermodilution measurements were done during and without interruption (18). Systemic vascular resistance and pulmonary vascular resistance were calculated using standard formulae.

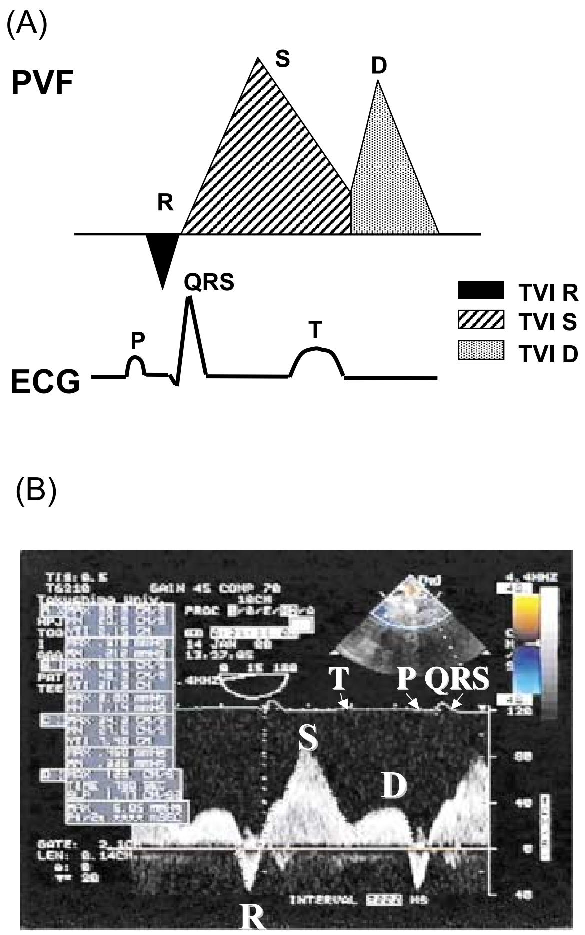

Figure 1. **(A) Graphic illustration of the normal polyphasic pulmonary venous flow pattern and its relative timing in the cardiac cycle. Normal pulmonary venous flow is composed of systolic (S wave) and diastolic (D wave) forward flow with a small component of reverse flow (R wave). Schematics show measurements of time-velocity integrals (TVI). (B) Representative example of pulmonary venous flow velocity recording and measurement of time-velocity integrals of systolic (TVI-S), early diastolic (TVI-D), reversal (TVI-R) flows, and RR interval. Measurements were performed quickly on freeze-frame images. In this example, values of TVI-S, TVI-D, TVI-R, and RR interval were 21.5 cm, 7.46 cm, 2.15 cm, and 0.79 sec, respectively. From these results, total TVI {(TVI-S) + (TVI-D) - (TVI-R)} and minute distance (total TVI × heart rate) were 26.81 cm and 2038 cm$\cdot$min^{-1}, respectively.**

Experimental protocol

Simultaneous measurements of pulmonary venous flow velocity, hemodynamics, and thermodilution CO were made before CPB or cross-clamp of abdominal aorta. Mean arterial pressure had been maintained within 20 % of the value at pre-induction of anesthesia before measurements, adjusting administration of anesthetics, fluid infusion, or bolus intravenous administration of ephedrine (4 mg). However, continuous infusion of cardiovascular drugs had not been made until first measurements, except for nitroglycerin.

After termination of CPB or after either reconstruction of aorta or myocardial revascularization in patients without CPB, measurements were performed again with continuous intravenous administration of dopamine (> 3 μg$\cdot$kg$^{-1}\cdot$min^{-1}) and other cardiovascular drugs including dobutamine, norepinephrine, milrinone, nitroglycerin, nicorandil, prostaglandin E1, or diltiazem. TEE-based measurements were performed on freeze-frame images. We carefully placed a sample volume at the same location in each patient.

Statistical analysis

Results are presented as mean ± SD or absolute values. Hemodynamic data and minute distance were compared using Student's *t*-test. Simple linear regression analysis was performed between thermodilution CO and minute distance. Ten randomly selected pulsed Doppler recordings of pulmonary venous flow were used to assess interobserver and intraobserver variability in measurement of minute distance. Variability was expressed as the ratio of the difference between the two measurements to their mean. A p-value < 0.05 was considered significant.

RESULTS

Preoperative clinical characteristics were shown in Table 1. Simultaneous measurements of minute distance and thermodilution CO were performed in each patient before and after surgical intervention. In all 64 measurements, pulsed Doppler recordings of pulmonary venous flow were accomplished accurately (Figure 1). In the echocardiographic analysis, peak S and peak

Table 1. Patient characteristics and surgical procedures. Values are mean±SD or number.

Patient characteristics	
Male/Female	21/11
Age (yr)	69 ± 6
Height (cm)	158 ± 9
Weight (kg)	60 ±10
Surgical Procedures (on-pump/off-pump)	24/8
Coronary artery bypass grafting	11/2
Aortic valve replacement	6/0
Thoracic aortic aneurysmectomy	5/0
Abdominal aortic aneurysmectomy	0/6
Mitral valve replacement	2/0

on-pump = cardiovascular surgery with cardiopulmonary bypass ; off-pump = cardiovascular surgery without cardiopulmonary bypass.

D increased significantly after surgical intervention (from 40.5 ± 14.4 to 59.2 ± 20.9 cm•sec^{-1} and from 34.8 ± 17.2 to 45.3 ± 13.8 cm • sec^{-1}, respectively), whereas peak R did not change significantly (from 16.1 ± 6.7 to 18.9 ± 7.6 cm•sec^{-1}). TVI-S and TVI-R did not change significantly after surgical intervention, but TVI-D increased, resulting in significant increases in total TVI (Table 2). As heart rate also increased after surgical intervention, the minute distance (total TVI × heart rate) increased significantly after surgical intervention (Table 2).

All patients received continuous intravenous infusion of dopamine (> 3 μg•kg^{-1}•min^{-1}) and other agents to maintain appropriate hemodynamics after CPB or surgical repair (Table 3). Thermodilution CO significantly increased and systemic vascular resistance decreased after surgical intervention (Table 2).

The regression equation representing the relation between minute distance and thermodilution CO before and after surgical intervention were as follows: CO (L•min^{-1})=2.1 × minute distance (cm•min^{-1}) × 10^{-3}+1.14 (r=0.81, p<0.0001) and CO (L•min^{-1})=1.6 × minute distance (cm • min^{-1})×10^{-3}+2.50(r=0.76, p<0.0001), respectively (Figure 2A and 2B). The correlation coefficient obtained between percent changes in minute distance (% of before surgical intervention) and those in thermodilution CO (% of before surgical intervention) were significant (r=0.80, p<0.0001, Figure 3). In all 32 patients, one patient showed that percent changes in thermodilution CO increased (137% of before CPB) while percent changes in minute distance decreased (93% of before CPB). However, remains showed the same direction of both percent changes in thermodilution CO and those in minute distance. Interobserver and intraobserver measurement variability in minute distance were 5.1 ± 3.9 % and 5.6 ± 4.5 %, respectively.

Table 2. Hemodynamic and Doppler echocardiographic variables recorded before and after surgical intervention. Values are mean ± SD.

	Before	After
Hemodynamics variables		
HR (beats•min^{-1})	63 ±13	85 ± 21*
MAP(mm Hg)	79 ±13	76 ± 12
MPAP (mm Hg)	18 ± 8	18 ± 4
CVP (mm Hg)	8 ± 3	8 ± 4
PCWP (mm Hg)	12 ± 6	11 ± 4
SVR	1758 ± 548	1077 ± 345*
PVR	138 ± 84	112 ± 43
CO (L•min^{-1})	3.5 ± 0.9	5.3 ± 1.1*
Pulmonary venous flow velocity integrals		
TVI-S (cm)	11.5 ± 4.5	12.8 ± 5.5
TVI-D (cm)	8.2 ± 2.9	9.8 ± 3.6*
TVI-R (cm)	1.3 ± 0.7	1.3 ± 0.7
TTVI (cm)	18.5 ± 5.3	21.3 ± 6.1*
Minute distance (cm•min^{-1})	1121 ± 347	1764 ± 538*

HR=heart rate ; MAP=mean arterial pressure ; MPAP=mean pulmonary arterial pressure ; CVP = mean central venous pressure ; PCWP=pulmonary capillary wedge pressure ; SVR=systemic vascular resistance ; PVR = pulmonary vascular resistance ; TVI-S = time-velocity integral of systolic wave ; TVI-D= time-velocity integral of early diastolic wave; TVI-R = time-velocity integral of reversal wave ; TTVI=total time-velocity integral
TTVI=(TVI-S)+(TVI-D)-(TVI-R) ; Minute Distance = TTVI•HR
* p < 0.05 versus before surgical intervention

Table 3. Drugs administered before and after surgical intervention. Values are patient's number.

	Before	After
Dopamine	0	32
Dobutamine	0	13
Norepinephrine	0	1
Milrinone	0	5
Prostaglandin E1	0	22
Nitroglycerine	13	24
Nicorandil	0	10
Diltiazem	0	1

DISCUSSION

Intraoperative TEE has been used to formulate the surgical plan, assess cardiac function, and evaluate surgical outcome. It was reported that the information obtained influenced important therapeutic decisions in open heart surgery (19), valvular surgery (20), the repair of congenital heart disease (21), or off-pump coronary artery bypass surgery (22). Thus, intraoperative TEE has been applied widely during cardiovascular surgery. Intraoperative TEE was also reported to be

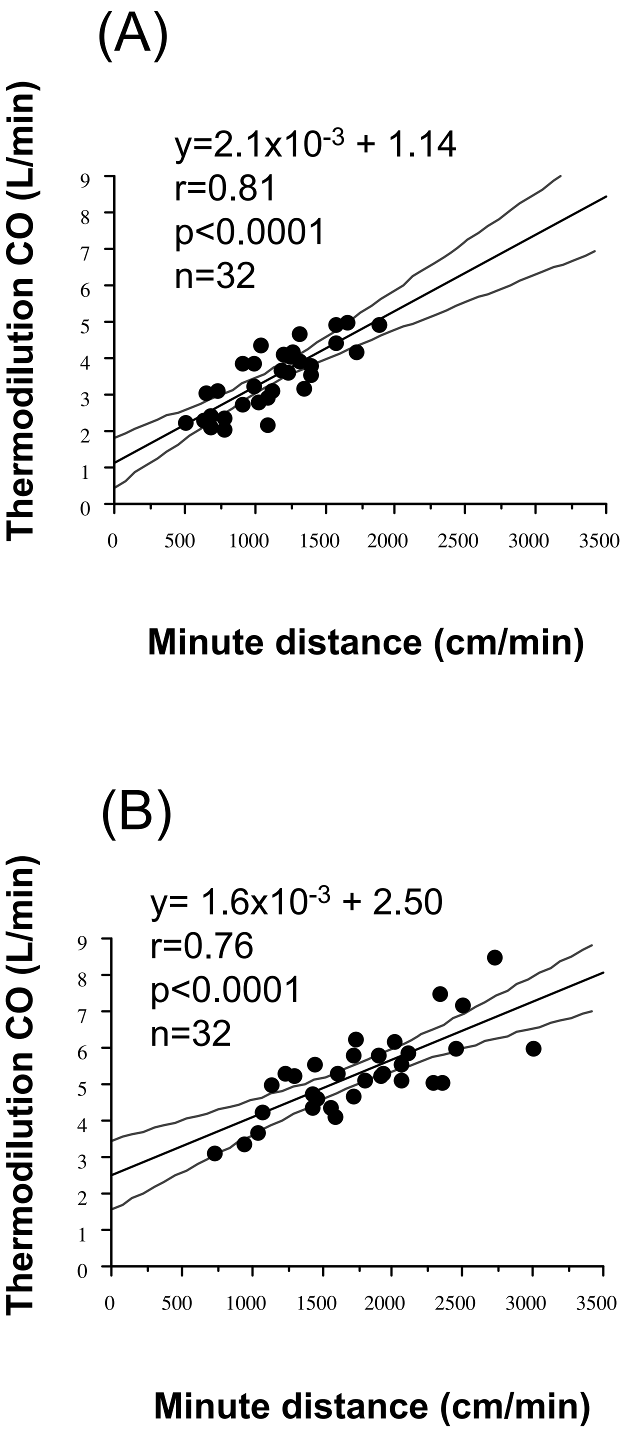

Figure 2. Relationship between minute distance and thermodilution cardiac output (CO) before (A) and after (B) surgical intervention. Dashed line indicates 95% confidence intervals.

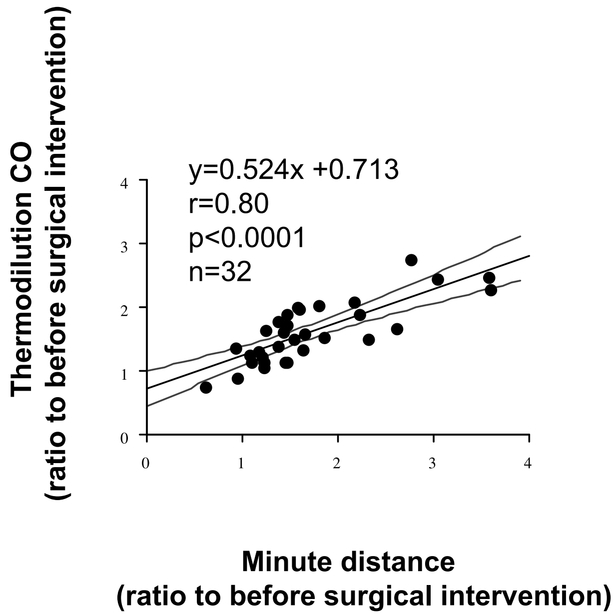

Figure 3. Relationship between the changes in minute distance (% before surgical intervention) and the changes in cardiac output (CO) measured with thermodilution method. Dashed line indicates 95% confidence intervals.

able to measure CO via several approaches (11-16). However, no study reported whether CO was estimated from pulsed Doppler signals of pulmonary venous flow velocity. We demonstrated in the present study that minute distance calculated from the pulmonary venous flow velocity tracings was highly correlated with thermodilution CO both before and after surgical intervention. We further showed that the trend of the changes in minute distance was very similar to that in CO. These results suggest that minute distance in pulmonary vein is strongly associated with CO and that the changes in CO can be estimated from minute distance in pulmonary vein during cardiovascular surgery.

It is important to know the changes in CO during cardiovascular surgery, because CO is one of the determinants for tissue oxygen supply. Thermodilution technique using PA catheter has been popular to measure CO during perioperative period. The information obtained from PA catheter is very useful to assess the function of the circulatory and respiratory systems. The most common serious complications during and after PA catheter insertion include arrhythmias, injury to the lung, thromboembolism, and sepsis (23). The direct complication rates are estimated at 0.1% to 0.5% in surgical patients (23). Although the controversy exists, recent studies indicated that measurements of CO using PA catheter did not improve or worsen the mobility and mortality. These results suggest that PA catheter may be harmful (8-10). In 2000, the US National Heart, Lung, and Blood Institute and the US Food and Drug Administration reported that consensus was achieved regarding the need for a randomized controlled trial of PA catheter use in a cohort of elective, low-risk patients undergoing surgical coronary revascularization (23). Thus, the alternative methods of CO measurements are expected. As intraoperative TEE is useful and applied widely, the measurements of CO with TEE is a good candidate for the evaluation of

CO during cardiovascular surgery. It was reported that correlation coefficients between thermodilution CO and Doppler CO determined by mitral valve flow, pulmonary artery flow, and aortic flow were 0.25, 0.65, and 0.94, respectively (12,14). In the present study, we demonstrated that correlation coefficients between thermodilution CO and minute distance before and after surgical intervention were 0.81 and 0.76, respectively (Figure 2). These results suggest that minute distance in the pulmonary venous flow has the better relationship with thermodilution CO than Doppler CO with mitral valve flow and pulmonary artery, but not Doppler CO with aortic flow.

The minute distance was calculated from only pulmonary venous flow velocity tracing, while the previous approaches require two TEE views for blood flow velocity recording and cross-sectional area measurement (11-16). In addition, TEE is an excellent technique for pulmonary venous flow measurement because of the close anatomical relation between an esophagus and pulmonary veins. In the present study, pulmonary venous flow tracing with TEE was recorded successfully in all 32 patients and all 64 measurements (success rate 100%), whereas the previously reported success rate with Doppler CO with pulmonary artery approach was 76% (11), and that with aortic approach was 97-98% (14,16). These findings may suggest that our approach is easier to estimate CO as compared with the previous approaches.

Recently, we reported that intravenous administration of phenylephrine in children with tetralogy of Fallot improved systemic arterial oxygenation, which was associated with the increases in minute distance in pulmonary vein (17). These results suggested that minute distance in pulmonary vein was strongly influenced with pulmonary blood flow, which is equivalent to CO in normal subjects. Thus, we evaluated the relationship between minute distance and thermodilution CO in the present study and demonstrated the good relationship between minute distance and thermodilution CO. Our findings in the present study implied that minute distance would represent the pulmonary blood flow even during repair of congenital heart disease in children. This is interest because the evaluation of pulmonary blood flow in children with congenital heart disease is difficult in clinical situation. The PA catheters for children are not available for clinical use. Doppler approaches with both aorta and pulmonary artery is disturbed to reveal the precise pulmonary blood flow in children with congenital heart disease by intra-and/or extra-cardiac shunt. Thus, it is likely that minute distance is superior to estimate not only the changes in CO but also pulmonary blood flow in patients with congenital heart disease. In contrast, it is difficult to assess the pulmonary blood flow in children with anomalous pulmonary venous connection. Severe mitral regurgitation flow may also lead misinterpretation as severe mitral regurgitation jet may affect the pulmonary venous flow.

Simultaneous measurement of thermodilution CO and recording of pulmonary venous flow velocity were performed twice in each patient. The low systemic vascular resistance has been shown to occur during and after CPB (24), while pulmonary vascular resistance increased after CPB (25). Hemodynamics sometimes significantly change after reperfusion during cardiovascular surgery without CPB. In the present study, systemic vascular resistance significantly decreased after surgical intervention, but pulmonary vascular resistance did not change significantly. The effects of either CPB or reperfusion in non-CPB surgery and infusion of drugs including at least dopamine significantly increased heart rate and CO. Thus, hemodynamics in the time points for measurements were quite different in the present study. However, the correlation between CO and minute distance before and after surgical intervention were similar (r=0.81 and r=0.76, respectively). Furthermore, the good relationship between the changes in CO and those in minute distance existed. These results indicated that our approach was reliable to estimate the changes in CO during cardiovascular surgery, while we did not evaluate the cross-sectional area of a pulmonary vein.

A limitation of our study design includes the use of thermodilution as the gold standard because it is susceptible to error ; however, it remains a clinical standard for determining CO (26-29). Another limitation is that our study protocol did not consider the cross-sectional area of the pulmonary vein. Therefore, minute distance did not show the accurate pulmonary blood flow. However, it is well known that the accuracy of pulsed Doppler CO measurements strongly depends on the assumed flow area (30). This means that measurements of flow area are possible to make a big error in calculation of pulsed Doppler CO.

In conclusions, minute distance obtained from the pulsed Doppler tracings of pulmonary venous flow velocity was related with CO during cardiovascular surgery in adults. This approach was easy and reliable. These results suggest that our approach is one of candidate to estimate the intraoperative changes in CO.

ACKNOWLEGEMENT

This work was supported in part by a grant-in-aid for scientific research #12770823 from the Ministry of Education, Science, Sports and Culture of Japan.

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