Comparison of Methods of Cardiac Output Measurements Determined by Dye Dilution, Pulsed Doppler Echocardiography and Thermodilution in Horses

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(Received 15 February 1993/Accepted 19 August 1993)

ABSTRACT. Cardiac output (CO) measurements by the three methods of dye dilution, pulsed Doppler echocardiography and thermodilution in horses under anesthetized conditions were compared. Although CO determined by the thermodilution method was slightly higher than those obtained by the other two methods, the measurements by all methods showed almost similar results. The coefficients of correlation between the dye dilution and thermodilution methods, the dye dilution and pulsed Doppler echocardiography methods, and the thermodilution and pulsed Doppler echocardiography methods were 0.87, 0.89, and 0.88, respectively ($P<0.01$). These results indicate that pulsed Doppler echocardiography and thermodilution methods could be no less useful than the traditional dye dilution method for evaluating of CO in horses. The pulsed Doppler echocardiography method may offer some advantage over other two methods; it is non-invasive and enables continuous measurement of CO.—KEY WORDS: cardiac output, dye dilution, horse, pulsed Doppler echocardiography, thermodilution.

J. Vet. Med. Sci. 56(1): 1–5, 1994

Cardiac output (CO) is a very important indicator for the direct assessment of cardiac functions. Methods for measuring CO include the Fick method, dye dilution, and echocardiography. It is generally believed that the most precise method for CO measurement is applying a magnetic flow meter placed around the aorta. However, this method requires open thoracic surgery.

The pulsed Doppler echocardiography [1, 8, 12] and thermodilution [10, 14] methods are widely used in human by taking invasiveness into consideration. In small animals, CO estimates obtained from M-mode echocardiography are used to discuss effects of anesthetic agents on the cardiovascular system [3].

Although dye dilution method has predominantly been used in the horse [5, 7], it has some shortcomings; difficulty in repetition due to the recirculation of dye, and necessity to ensure the arterial tract. A study on the use of non-invasive echocardiography for assessing CO in the horse has been reported by employing M-mode echocardiography [2]. However, research by the pulsed Doppler echocardiography method has been intended only for evaluating cardiac functions based on measurements of blood flow velocities at a specific location [15]. No study has been reported so far to compare findings by the pulsed Doppler echocardiography method with those obtained by other methods. The thermodilution method, where the measurement is repeatable, is regarded very useful for CO determination in the horse [4, 13]. However, this method also presents problems. In order to achieve precise measurement results, conditions such as the infusion volume, rate and temperature of indicator drugs need to be set appropriately.

The present study evaluated the usefulness of the pulsed Doppler echocardiography and thermodilution methods for the assessment of CO in horses by comparing that of the dye dilution method. CO under pre-anesthesia and anesthetized condition was measured by these three methods almost simultaneously.

MATERIALS AND METHODS

Horses: Four thoroughbreds and 1 angroarabian horse (1 male, 2 geldings and 2 females) were studied. Mean age was 6.2 ± 2.8 (standard deviation: SD) years, and mean body weight was 485.2 ± 26.2 kg. These horses were apparently free from cardiopulmonary disease and had been prohibited from any forms of exercise for two months prior to the start of the study.

Anesthesia: The sedative agents, xylazine (1.0 mg/kg) and midazolam (0.01 mg/kg) were administered separately into the jugular vein. To induce anesthesia, ketamine hydrochloride was injected into the jugular vein with a dose of 2.5 mg/kg of body weight. The horses were anesthetized with halothane and oxygen, and positioned in lateral recumbency. Spontaneous breathing was facilitated by intubating a endotracheal tube which was connected to a semi-closed anesthetic circuit with a 30 *l* breathing bag. Halothane was volatilized intermittently by a Fluotec vaporizer (Floutec 3, Ohmeda, Luisbil, U.S.A.) while oxygen was supplied at 5 to 8 *l* per min.

Anesthesia was maintained for 2 hr. The depth of anesthesia was indicated by the point of disappearance of nystagmus and eyelid reflex and maintained at the two to third phase of the surgical plane. End-tidal halothane concentration was maintained 0.9–1.6%. During anesthesia, lactated Ringer solution was administered in-

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travenously at a dosage of 4 m*l*/kg/hr, in addition to 5% dextrose which was injected for CO measurement by the thermodilution method. No cardioactive agents were used.

Heart rate (HR), electrocardiogram, arterial blood pressure (ABP), pulmonary arterial blood pressure (PAP) and respiratory rate (RR) were monitored by an anesthetic monitoring system (1290 M, Yokogawa Hewlett Packard, Tokyo). ABP was measured by catheterizing the facial artery, and PAP was measured by a balloon-tipped flow-directed catheter (Swan-Ganz catheter, SP5107, Viggo-Spectramed, Tokyo). A pressure transducer (1295A, Yokogawa Hewlett Packard) was used for these measurements. All the data were processed by the computer built in the anesthetic monitoring system.

Measurements of CO:

Dye dilution: The carotid artery, which had been relocated to a subcutaneous position 6 months before this study, was catheterized by a 18G catheter which was then connected to a colorimeter.

Five m*l* of distilled water containing 50 mg of indocyanine green dye was rapidly injected by using a 10 m*l* disposable syringe into the right jugular vein. Following the injection, 50 m*l* of carotid artery blood was withdrawn at a constant rate through a densitometer cuvette connected to a CO computer. The concentration of indocyanine green dye in the blood was determined photometrically by using a Dye Densitograph (EW-90, Erma Optical Works, Ltd., Tokyo).

Pulsed Doppler echocardiography: The SONOS 1000 ultrasound equipment (Yokogawa Hewlett Packard) with a 2.5 MHz transducer was used. The transducer was placed in the left fifth to sixth intercostal space. The aortic anulus diameter was determined by measuring the maximal inner diameter in the systolic phase at the level of the aortic orifice on the long-axis two-dimensional view of the left ventricle. Aortic blood velocities were recorded with a sample volume positioned just distal to the aortic valve in the center of the ascending aorta, and the velocity-time integral was obtained by tracing the outer periphery of systolic blood flow wave forms. The stroke volume (SV) was then calculated by multiplying the integral value. The HR was determined by calculating the interval between the two blood velocity wave form peaks. Collection for the intercept angle between the Doppler beam and flow direction was not done.

Thermodilution: Two different catheters were used; one used for the injection of indicator solution (5% dextrose) and the other for the measurement of temperature fluctuation and CO (7F, Swan-Ganz catheter SP5107, Viggo-Spectramed). After local anesthesia was performed by the subcutaneous injection of 2% lidocaine, 2 catheter introducers (8F, SCC-A400B, Baxter, Tokyo) were placed in the upper and lower sites of the transposed left jugular vein. The catheter for indicator solution injection was introduced into the right atrium through the introducer placed in the upper site. The Swan-Ganz catheter was inserted through the lower introducer. The balloon of the catheter was inflated initially and advanced while pressure wave forms at different sites within the heart being observed. After confirming the characteristic pressure wave forms of the pulmonary artery, the balloon was deflated and the catheter was further advanced by about 10 cm.

Thirty-five m*l* of 5% dextrose at 0°C was used as the thermal indicator and injected into the right atrium within 2 sec by using a pressure injector (Nemoto Kyorindo, Tokyo). The bottles containing the solution were placed in iced water bath during measurement. The pressure injector syringe (100 m*l*) was cooled in a nylon bag which contains crushed ice for 30 min prior to use. CO was measured using a thermodilution cardiac output computer (M1012A, Yokogawa Hewlett Packard).

Protocol for CO measurements: COs were measured before and at intervals of 15 min within 2 hr anesthesia. COs were also measured 180 min after the recovery of horses.

In the dye dilution method, measurements took place at each intended measurement point after confirming the recovery of the densitometoric base line. In the pulsed Doppler echocardiography method, the average CO figure was obtained by measuring 3 consecutive heart beats of clearly recorded systolic wave form three times at each intended measurement point. In the thermodilution method, COs were measured three times at each intended measurement point and at 2 min before and after the point, and then the average figure was calculated.

Statistical analysis: Data obtained by the three methods were processed to produce the coefficients of correlation.

RESULTS

RR and hemodynamic data are shown in Table 1. RR decreased substantially 15 min after the onset of anesthesia, but then increased gradually as time passed. Apnea for more than 30 sec was not observed.

No remarkable changes were observed in the ABP and the PAP. Abnormal conditions were not detected in any of the cases either during anesthesia or after recovery. The horses required 15 to 25 min for recovery after the end of anesthesia.

CO per kg body weight (CO/kg) and SV by the dye dilution, pulsed Doppler echocardiography and thermodilution methods are demonstrated in Fig. 1. CO/kg and SV obtained by the dye dilution and pulsed Doppler echocardiography methods were similar. However, in the thermodilution method higher determinations than those obtained by the other two methods were detected in all the two items. With the lapse of time, CO/kg decreased, and after 75 min reached less than 50% of the preanesthetic value. However, these figures recovered almost to the initial levels within 180 min after the recovery of anesthesia.

Dye dilution outputs were significantly correlated with pulsed Doppler echocardiography and thermodilution ($r=0.89$ and 0.87, $P<0.01$) outputs (Figs. 2 and 3).

Table 1. Changes in heart rate (HR), respiratory rate (RR), arterial blood pressure (ABP) and pulmonary arterial pressure (PAP) during anesthesia

Variables		Pre anesthesia	Time during anesthesia (min) 15	30	45	60	75	90	105	120	Post anesthesia 180 min
HR (beat/min)		34.4[a)] ±5.3	31.2 ±2.4	28.8 ±1.9	30.0 ±2.9	31.6 ±1.5	30.2 ±0.5	29.8 ±2.6	29.2 ±3.1	29.8 ±2.6	34.6 ±0.9
RR (breath/min)		15.2 ±5.3	4.2 ±2.4	6.8 ±1.9	7.0 ±2.9	8.2 ±2.3	7.8 ±3.0	6.6 ±1.7	8.0 ±2.1	9.2 ±2.0	15.8 ±2.5
ABP (mmHg)	systolic	142.8 ±17.3	101.0 ±8.5	101.0 ±3.4	98.0 ±0.7	96.6 ±7.3	96.8 ±7.7	100.4 ±9.3	94.8 ±8.8	93.0 ±10.3	135.6 ±112.5
	distolic	91.4 ±16.3	61.4 ±11.3	56.8 ±5.0	59.2 ±5.6	59.2 ±7.6	67.8 ±9.2	62.0 ±10.6	62.8 ±13.9	61.2 ±14.5	90.2 ±9.2
	mean	117.4 ±12.3	75.2 ±10.6	70.6 ±4.0	72.4 ±4.8	71.6 ±8.7	78.2 ±9.8	72.2 ±10.6	74.0 ±13.0	72.2 ±13.4	109.2 ±8.5
PAP (mmHg)	systolic	41.6 ±9.1	24.6 ±7.1	24.2 ±6.8	26.6 ±4.5	25.4 ±3.7	23.8 ±3.6	24.4 ±1.8	24.6 ±2.7	23.8 ±4.9	40.8 ±6.8
	distolic	19.0 ±5.2	3.2 ±3.6	2.0 ±2.8	2.2 ±4.1	3.6 ±5.1	5.8 ±5.1	6.2 ±3.3	5.0 ±5.5	6.0 ±3.8	16.0 ±5.8
	mean	25.2 ±4.0	11.0 ±4.2	11.4 ±2.4	10.6 ±3.2	11.4 ±4.6	12.2 ±4.3	12.4 ±2.1	14.0 ±2.8	13.2 ±3.4	23.0 ±5.7

a) Mean±standard deviation.

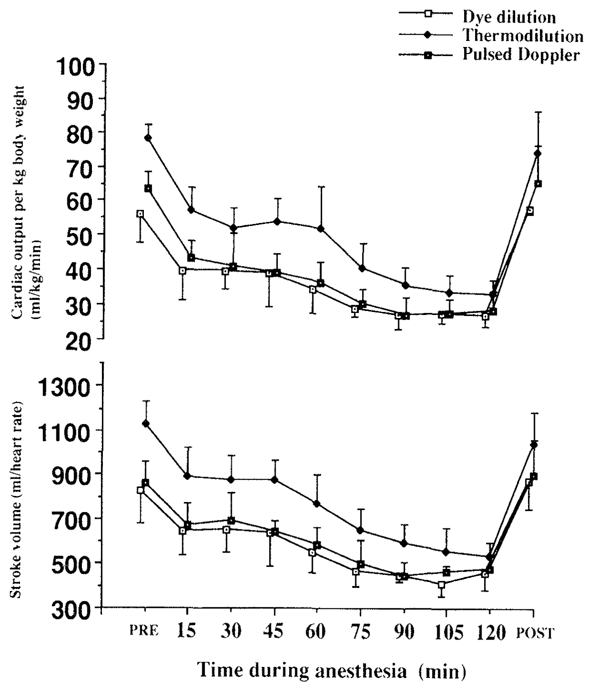

Fig. 1. Changes in cardiac output per kg body weight (CO/kg) and stroke volume (SV) measurements determined by the dye dilution, the thermodilution and the pulsed Doppler echocardiograpy methods during anesthesia.

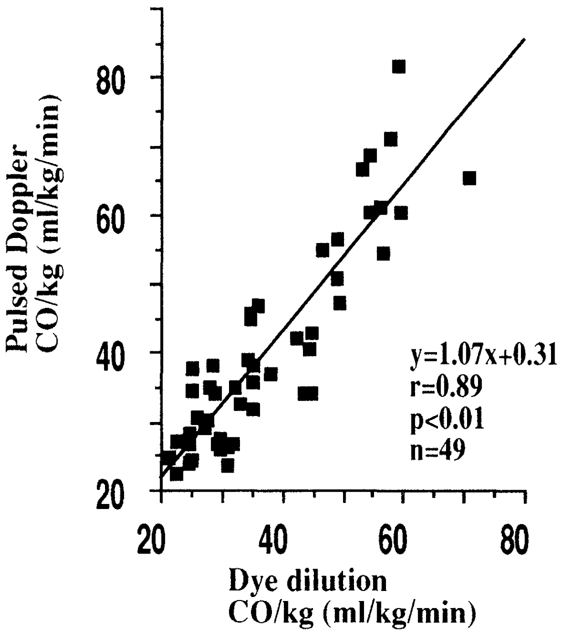

Fig. 2. Pulsed Doppler cardiac output measurements plotted against corresponding dye dilution measurements.

DISCUSSION

The depth of anesthesia is thought to have been almost the same in all the horses studied because HR, RR and the systolic ABP fluctuated within the range of 90 to 100 mmHg.

Pulsed Doppler echocardiography outputs have been reported to be significantly correlated with Fick method and dye dilution outputs in case of human [9], and it is already used at the clinical front to evaluate cardiac functions [6]. In our study, the two dimensional echocardiogram in the long-axis view of the left ventricle was used

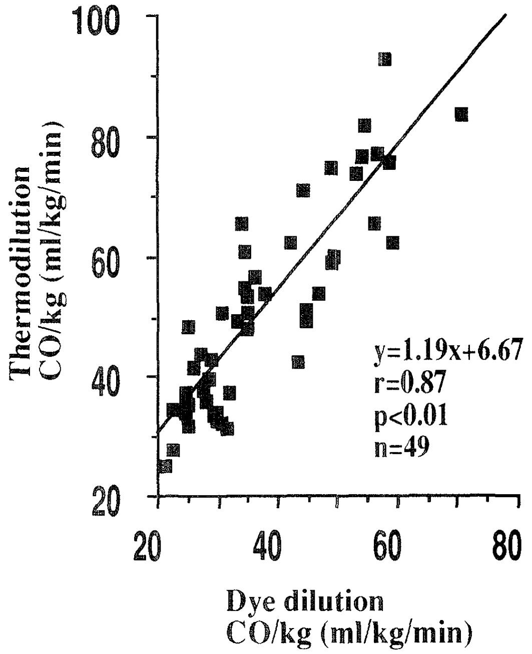

Fig. 3. Thermodilution cardiac output measurements plotted against corresponding dye dilution measurements.

to obtain the image of the aortic anulus section, and the distance between aortic valves was measured to calculate the blood flow area. The aortic anulus diameter was determined by measuring the maximum diameter during systole, although the maximal change in the aortic diameter throughout the cardiac cycle has been shown to be minimal in canine studies [11]. We experienced that the aortic diameter at the level of the aortic orifice measured by two-dimensional echocardiography was very close to that calculated at necropsy in the horses reported here (unpublished data). We believe that our measurement method by echocardiography was reliable.

Aortic blood velocities were recorded in the center of the aortic valve just distal to the aortic valve where in the velocity profiles are considered to be relatively flat in human reports. It was possible to obtain several clear blood velocity wave forms which were free from any influence caused by cardiac beats. The presumed angle of incidence of Doppler beam to blood flow was within 15°C to the X-Y axis, i.e. visualized two dimensions, which could be regarded within the range of biological errors. However, it is necessary to discuss the adjustment of angle to the Z axis, i.e. unseen third dimension, as in our study, the cross sectional image was not obtained from the custodial part but from the middle section of the left ventricle.

Muir *et al.* [13] reported that CO measurements in the horse by the thermodilution method showed significant correlation to those obtained by the dye dilution method when 30 or 40 m*l* of injection material was used. It was also reported that rapid injection was essential to minimize errors [4]. Therefore, a pressure injector used for human angiocardiography was employed to inject 35 m*l* of 5% dextrose (0°C) in 2 sec. For this injection, the 7F, 100 cm catheter placed in the right atrium was used. The arithmetic constant specific to the Swan-Ganz catheter, when employed to inject 10 m*l* of 5% dextrose at 0°C, was used for computer calculation after the constant had been adjusted according to the volume of solution which was actually injected. However, COs measured by the thermodilution method were higher than those obtained by the other two methods in general.

The arithmetic constant is determined by several factors including injection volume, rate, temperature, the dead space of a catheter, and the distance between the indicator injection site and thermister tip [14]. In humans, the rate required to inject 10 m*l* at 0°C by using the Swan-Ganz catheter needs to be faster than 10 m*l* per sec, while the dead space of the catheter is set 0.85 m*l* and the distance between the injection site and thermister tip is 27 cm. In our study, these factors were 17.5 m*l*/sec, 1.35 m*l*, and 40 to 45 cm, respectively.

The ratio of catheters dead space to injection volume is 8.5% for human and 3.9% for the horse. Thus it is less likely that measurement errors occur in horse. However, the distance between the injection point and the thermister tip needed to be extended by more than 13 cm, as two catheters were used in order to facilitate the rapid injection of a large volume of indicator solution. This extension changed the arithmetic constant, reducing the area under the thermodilution curve, which might have led to relatively higher measurements as compared with those by the other methods.

CO/kg before anesthesia was 77.98±4.23 m*l*/kg/min in the present study, which was slightly higher than the reported values of 72.61±8.23 m*l*/kg/min in case of injecting 40 m*l* of the solution at 0°C [13]. It has also been reported that thermodilution outputs = 1.048 × dye dilution [4]. In our study, it was found that thermodilution outputs = 1.19 × dye dilution outputs + 6.67.

Further investigation needs to be conducted to find in what way the distance between the injection point and the thermister tip may affect the arithmetic constant as well as the area under the thermodilution curve, in order to achieve more reliable measurement figures.

Comparing CO measurements obtained by the three methods, pulsed Doppler echocardiography and thermodilution outputs were shown to be significantly correlated with dye dilution outputs. We concluded that the pulsed Doppler echocardiography and thermodilution methods presented in this paper could be useful for evaluating CO in horses, and the former is the most useful for clinical use because of non-invasiveness and capability of continuous measurement.

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