Shimane J. Med. Sci., Vol.9, pp.69-74, 1986

REPRODUCIBILITY OF CARDIAC OUTPUT ESTIMATION BY THERMODILUTION METHOD IN RATS

(reproducibility/thermodilution/conscious state)

Koji WATANABE, Toshikazu NISHIO, Masahiro KIHARA*, and Chuzo MORI

Departments of Pediatrics and *Pathology, Shimane Medical University, Izumo 693, Japan

(Received September 30, 1985/Accepted November 29, 1985)

The reproducibility of the thermodilution method in anesthetized and conscious rats was analyzed. Cardiac outputs in anesthetized state were stable in each procedure. Those in conscious state, especially the first measurement, tended to be underestimated compared with those in anesthetized state. The difference between anesthetized and conscious states might be produced by the increased temperature of saline in the tube placed under the skin of the conscious rat. Therefore, if we exclude the value of the first measurement, the thermodilution method is reliable to measure cardiac output in conscious state.

The thermodilution method is one of the most useful methods for estimating cardiac output in small animals(1-4). However, there have been few reports concerning its reproducibility. Particularly in conscious state, it is very important to estimate the reproducibility of the thermodilution method, because the polyethylene catheter for injection of saline into the right atrium is passed subcutaneously and saline is warmed by body temperature(5).

The purpose of the present study is to analyze the reproducibility of the thermodilution method in anesthetized and in conscious rats.

MATERIALS AND METHODS

Experiment I : anesthetized state

Studies were performed on 10 male normotensive Wistar Kyoto rats (WKY) aged 3-8 months. All rats were anesthetized with

pentobarbital sodium (30 mg/kg). One polyethylene catheter (PE 50 connected to a PE 10 intravascular catheter on the tip) was inserted into the left femoral artery and another catheter into the right atrium (RA) through the right jugular vein. Each catheter was connected to a pressure transducer (TP-101T, Nihon Koden). The thermister was placed in the ascending aorta through the right carotid artery. Cardiac output was determined using a Columbus Cardiotherm 500-R. One hundred microliters of saline at room temperature were injected into the right atrium(6-8). Cardiac outputs were calculated according to the following formula;

$$\text{Cardiac output (ml/min)} = K \cdot \frac{Vs(Tb-Ts)\cdot 60}{\int_0^\infty \Delta\, Tb\, dt}$$

$$K = \frac{Cs \cdot Ss}{Cb \cdot Sb}$$

where cardiac output is in milliliters per minute, Tb is temperature of blood (°C); Ts is temperature of injected saline (°C); Vs is volume of injected saline (ml), $\int_0^\infty \Delta\, Tb\, dt$ is change of blood-temperature, Ss is specific gravity of injected saline (g/ml), Sb is specific gravity of blood, Cs is specific heat of injected saline (cal/g·°C) and Cb is specific heat of blood. The procedure was repeated 3 times at one minute intervals and all results were compared.

Experiment II : conscious state

Measurements of cardiac output were performed in 3 month-old spontaneously hypertensive rats (SHR)(9) and WKY (8 of each) and 6 month-old SHR and WKY (5 of each) (Table I). The right carotid artery, the right jugular vein and the left femoral artery were cannulated in the same way as in Experiment I. These catheters were filled with heparin and their free tips placed on the back of the neck. Twenty-four hours after the operation, measurements were performed in the plexiglass cage to which the rats had been habituated. Each catheter was connected to a pressure transducer. Arterial blood pressure and right atrial pressure were continuously recorded using a Nihon Koden Polygraph. Cardiac output was determined by the same technique as described above.

Table I. BODY WEIGHT (g) AND LEFT VENTRICULAR MASS (g) IN WISTAR KYOTO RATS (WKY) AND SPONTANEOUSLY HYPERTENSIVE RATS (SHR)

	WKY	SHR	WKY	SHR
Age	3M	3M	6M	6M
Number	8	8	5	5
Body Weight (g)	310 ± 26	288 ± 29	413 ± 19	350 ± 6*
Left Ventricular Mass (g)	0.67 ± 0.05	0.91 ± 0.08*	0.80 ± 0.02	1.04 ± 0.07*

*: significant differences from WKY ($P<0.01$)

RESULTS

Experiment I : anesthetized state

The regression equation between cardiac outputs obtained by the first and the second injection was as follows;

$Y = 0.935 X + 0.392$ (Fig. 1)

X: cardiac output in the second injection

Y: cardiac output in the first injection

The regression equation between cardiac outputs measured by the second and the third injection was as follows;

$Y = 1.092 X - 0.631$ (Fig. 1)

X: cardiac output in the third injection

Y: cardiac output in the second injection.

Correlation coefficient was very high (0.997 and 0.986, respectively). The gradient of each formula was approximately 45°, and Y intercept was close to zero.

Experiment II : conscious state

The regression equation between cardiac outputs measured by the first and the second injection was as follows;

$Y = 0.494 X + 2.058$ (Fig. 2)

X: cardiac output in the second injection

Y: cardiac output in the first injection

The correlation coefficient was 0.742.

The regression equation between cardiac outputs measured by the second and the third injection was as follows;

$Y = 0.862 X + 0.970$

X: cardiac output in the third injection

Y: cardiac output in the second injection

The correlation coefficient between the second and the third

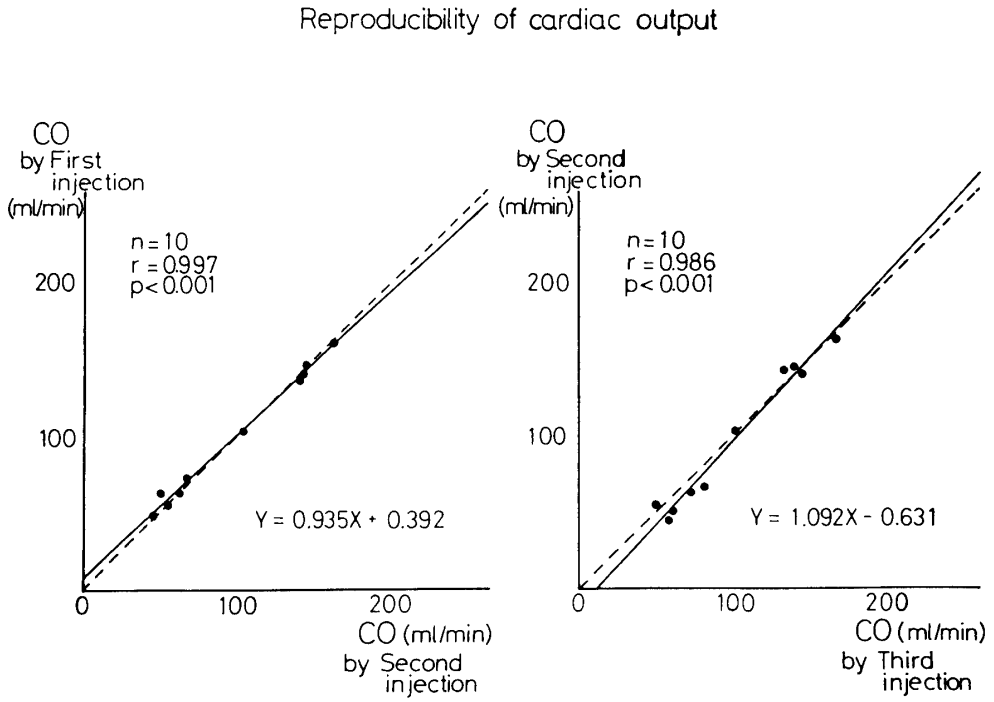

Fig.1. Relationship between cardiac output (CO) rates by each measurement in anesthetized state. The solid line shows the regression equation between cardiac output measured by each injection. The broken line shows an ideal regression equation (Y=X).

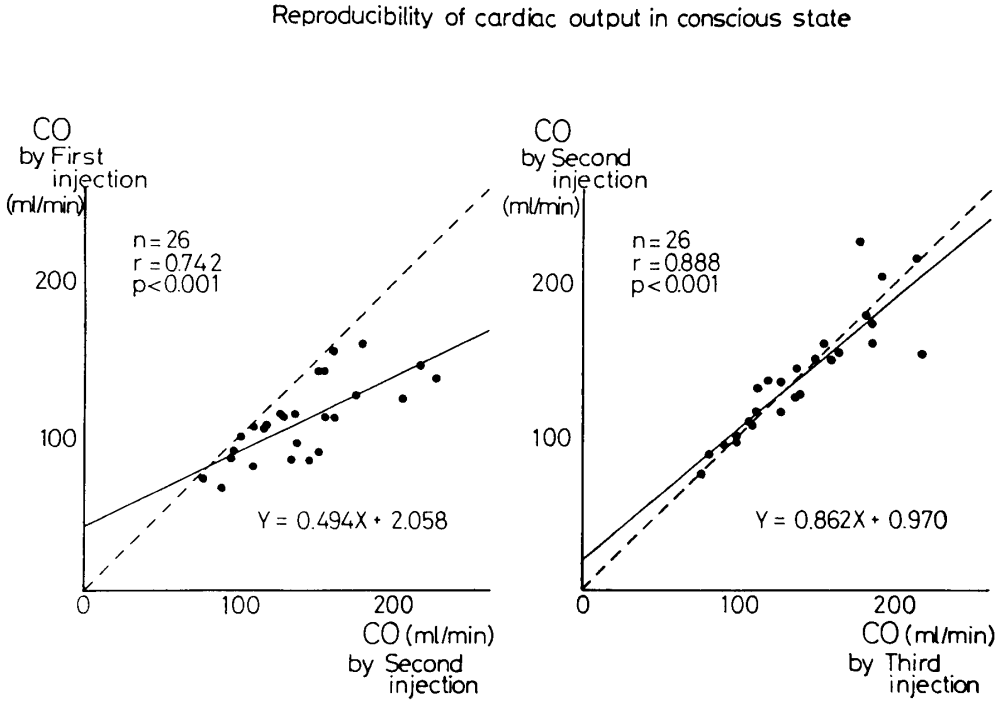

Fig.2. Relationship between cardiac output (CO) rates by each measurement in conscious state. The solid line shows the regression equation between cardiac output measured by each injection. The broken line shows and ideal regression equation (Y=X).

injection (r=0.888) was higher than that between the first and the second (r=0.742) (Fig. 2). The gradient was closer to 45° and Y intercept was also closer to zero than those between the first and the second injection.

DISCUSSION

Reproducibility of output estimation in Experiment I was good in three measurements. However, reproducibility in conscious state was poorer than that in anesthetized state. In the conscious state especially, correlation coefficient between the first and the second procedure was lower than that between the second and the third procedure. The difference may be explained by the increased temperature of saline in the tube passing under the skin (about 4 cm). In the first procedure of Experiment II, the saline in the tube placed under the skin was warmed significantly by body temperature, so the difference between Tb and Ts became smaller. Therefore, output of the first procedure in conscious state may be underestimated. On the other hand, output of the second procedure was almost equal to that of the third one. These data suggest that the injected saline, including the saline in tube placed under the skin, must be kept at constant state. In other words, the injected saline should be maintained at constant temperature(10). Therefore, when measuring cardiac output in conscious rats by thermodilution method, the first measurement should be discarded because the saline in the tube placed under the skin may be warmed significantly. Furthermore it is very important that the measurement should be performed at regular intervals and that the length of the tube under the skin should be kept constant. So long as these problems are kept in mind, thermodilution method using Cardiotherm 500 R is very useful for measuring cardiac output in conscious rats.

REFERENCES

1) Hosie K.F. (1962) Thermal-dilution technics. Circ. Res., 10, 491-504
2) Weisel R.D., Berger R.L., and Hechtman H.B. (1975) Measurement of cardiac output by thermodilution. N. Engl. J. Med., 292, 682-684

3) Lin Y.C., Dawson C.A., Nadel E.R., and Harvath S.M. (1970) Reliability of cardiac output measured by thermodilution method in small animals. Comp. Biochem. Physiol., 34, 245-250
4) Lin Y.C., Dawson C.A., and Horvath S.M. (1970) The expression of cardiac output in the albino rat, *Rattus*. Comp. Biochem. Physiol., 33, 901-909
5) Watanabe K., Nishio T., Mori C., Kihara M., and Yamori Y. (1984) Measurement of cardiac output by the thermodilution method in conscious spontaneously hypertensive rats. Jpn. Heart J., 25, 1051-1058
6) Enghoff E., Michaëlsson M., Pavek K., and Sjögren S. (1970) A comparison between the thermal dilution method and the direct Fick and the dye dilution methods for cardiac output measurements in man. Acta. Soc. Med. UPs., 75, 157-170
7) Evonuk E., Imig C.J., Greenfield W., and Eckstein J.W. (1961) Cardiac output measured by thermal dilution of room temperature injectate. J. Appl. Physiol., 16, 271-275
8) Goodyer A.V.N., Huvos A., Eckhardt W.F., and Ostberg R.H. (1959) Thermodilution curves in the intact animal. Circ. Res., 7, 432-441
9) Yamori Y. (1983) Physiopathology of the various strains of spontaneously hypertensive rats. In: Hypertension-Physiology and Treatment, 2nd ed. (Genest J., Otto K., Hamet P., Cantin M., ed) pp.556, McGraw-Hill, New York
10) Hayes B.E., Will J.A., Zarnstorff W.C., and Bisgard G.E. (1984) Limitations of thermodilution cardiac output measurements in the rat. Am. J. Physiol., 246, H 754-H 760