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Instruments and Techniques

Simultaneous determination of the stroke volume and the left ventricular residual fraction with the fiberoptic- and thermodilution method[1]

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Authors' synopsis *Simultaneous measurements of the concentration of dye by a fiberoptic catheter and of the temperature by a thermistor catheter were obtained in dogs. No significant difference for cardiac output and stroke volume was found. The slightly but significant higher residual fraction by thermodilution than by fiberoptic technique is caused by cold transfer between ventricular myocardium and cavity. It becomes evident after the fifth beat.*

Indicator dilution methods have been used to measure ventricular volume for many years. The technique involves ventricular injection of an indicator with measurement of its serial dilution immediately beyond the semilunar valves. Mainly cold or dye as indicators are employed (Holt, 1956; Lüthy, 1962; Rapaport, Wiegand, and Bristow, 1962; Hugenholtz, Gamble, Monroe, and Polanyi, 1965; Krayenbühl, 1969). To our knowledge no comparison of the thermodilution versus the dye method with intravascular measurement at the same sensor site has yet been reported.

Thermodilution is assumed to be complicated by heat exchange between blood and the heart wall because of temperature gradient (Rolett, Sherman, and Gorlin, 1964). The resultant cooling of the inner layers of the ventricular wall may serve as a storage of indicator which is then gradually released to the chamber as the blood temperature gradient is reversed. As a result the indicator decay slope may be prolonged.

The present study was undertaken to compare left ventricular residual fraction and stroke volume of simultaneously recorded aortic thermal and fiberoptic dye dilution curves and to estimate the error from heat transfer complicating the thermodilution method. For rapid sensing of the washout steps the thermistor and the fiberoptic catheters, both with similar time constants, were positioned together in the ascending aorta above the aortic valves.

Methods

Experiments were carried out in five male mongrel dogs, ranging between 21 and 23 kg body weight. After premedication with 2 mg morphine sulphate/kg body weight, the animals were anaesthetized with 90 mg/kg body weight of α-chloralose. Heparin was given in a dose of 300 i.u./kg body weight. The animals were intubated with a cuffed endotracheal tube and ventilated with air by means of an Engström respirator at a rate of 20 c/min. Care was taken to maintain stable normal body temperature throughout the experiment.

Catheters were positioned under fluoroscopic control in the following manner: through the

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left carotid artery a no. 8 F NIH catheter[1] of 50 cm length with six laterally opposed side holes was introduced into the left ventricle. The tips of a no. 4 F catheter with a thermistor bead[2] and of a no. 6 F fiberoptic catheter[3] were fixed together so that the sensing elements were as close as possible. This catheter assembly was located via the right carotid artery in the ascending aorta 1–2 cm above the aortic valves. A no. 8 F NIH catheter[1] was placed in the aortic arch through the left femoral artery for pressure measurements. A no. 6 F bipolar electrode catheter[4] was advanced through the right femoral vein to the upper part of the right atrium or to the apex of the right ventricle for single or paired pacing.

The thermodilution method was employed in the same manner as reported before (Krayenbühl, 1969). A bolus of 5 ml. icecold saline indocyanine green[5] was injected by hand into the left ventricle through the no. 8 F NIH catheter. Immediately after the injection 1 ml. blood was withdrawn in order to eliminate an uncalculable dissipation of thermal indicator to the blood through the wall of the injection catheter. No attempt was made to correct for the dye loss caused by the withdrawal of 1 ml. blood. The amount of cold injected was determined calorimetrically in a model experiment (Krayenbühl, 1969). The thermistor used had a dynamic response of 90% in 0, 1 sec.

Dye dilution curves were recorded with a fiberoptic catheter and the In Vivo Hemoreflectometer equipment (Polanyi and Hehir, 1960; Gamble, Hugenholtz, Monroe, Polanyi, and Nadas, 1965; Hugenholtz, Wagner, and Sandler, 1968). The fiberoptic catheter consists of two bundles of 150 clad glass fibers within the lumen of a standard 6 F cardiac catheter. Contact with the walls of the vessel is avoided by a tripod-like protective tip. One bundle transmits light of selected wavelengths to the distal tip of the catheter (efferent bundle,) the other conveys the reflected light (afferent) to the photoelectric detector. The measurement of dye concentration is derived from the ratio of two reflected light intensities from the blood. The indocyanine green dye concentration is proportional to the quotient of the intensities at 910 mμ and 805 mμ.

Calibration of the dye curves was carried out before and after each experiment. A sample of 3 ml. arterial blood was placed in a cuvette with a magnetic stirrer. The tip of the fiberoptic catheter was placed in the blood-filled chamber and small aliquots of the same dye mixture utilized in the animals were added to blood with an AGLA micrometer syringe[6]. The calibration concentrations were 12·5, 25·0, and 37·5 mg Cardio Green /l. The amount of dye injected into the left ventricle was 0·75 to 1·5 mg Cardio Green in 5 ml. ice-cold saline. The response time of the fiberoptic reflectometer was 95% in 0·1 sec (Hugenholtz *et al.*, 1968).

Cardiac output (CO) was calculated without extrapolation from the planimetrically obtained area of the simultaneously recorded thermal and dye dilution curves. Dilution curves with extrasystoles or arrhythmias were excluded. Stroke volume (SV) was obtained by dividing CO by heart rate (HR). Left ventricular residual fraction (K) was calculated as the average ratio of diastolic concentrations of indicator on successive beats clearly detectable in both curves (Rolett *et al.*, 1964). The ratio of the first two concentration steps after injection (c_2/c_1) was not included in the factor K, since c_1 is based on a different mixing mode with respect to all following concentrations (Krayenbühl, 1969). A comparative analysis of both the average residual fractions (K) and the individual concentration ratios – namely, c_3/c_2, c_4/c_3, c_5/c_4, and c_6/c_5 – was carried out. In order to vary K, CO, and SV the heart rate was changed by single and paired right atrial and right ventricular pacing. In two dogs isoproterenol or noradrenaline was infused intravenously.

Results

1 Cardiac output and stroke volume

Thirty-three simultaneous thermal and dye dilution curves were obtained for the comparison of cardiac output and stroke volume. The mean value for CO_{TH} (thermodilution) was $1{\cdot}358 \pm 0{\cdot}35$ l./min and for CO_{FO} (fiberoptic dye dilution) $1{\cdot}363 \pm 0{\cdot}38$ l./min. (± 1 SE). The difference was not significant ($P < 0{\cdot}90$). The mean values for SV_{TH} ($11{\cdot}2 \pm 0{\cdot}6$) and for SV_{FO} ($11{\cdot}4 \pm 0{\cdot}7$ ml.) also differed not significantly ($P < 0{\cdot}30$) from each other. In Fig. 1 the results are plotted. The correlation coefficient between CO_{TH} and CO_{FO} is 0·62. It is low because of the small variation in the range of CO. The regression equation is $CO_{FO} = 0{\cdot}456 + 0{\cdot}0067\ CO_{TH}$. For the stroke volume the correlation coefficient is 0·95 and the equation $SV_{FO} = -1{\cdot}7 + 1{\cdot}2\ SV_{TH}$.

2 Left ventricular residual fraction

An example of two simultaneously recorded aortic thermal and fiberoptic dilution curves is given in Fig. 2. The results of the comparison of 58 simultaneous determinations of left ventricular residual fraction (K) are plotted in Fig. 3. Only three experimental points are outside the $\pm 10\%$ limits. The correlation coefficient (r) is 0·95, the regression equation is $K_{FO} = 0{\cdot}0625 + 0{\cdot}893\ K_{TH}$. The mean value

[1] USCI, Glens Falls, N.Y./U.S.A.
[2] VECO 32A7, Victory Engineering Corporation, Springfield N.J./U.S.A.
[3] American Optical Company, In Vivo Hemoreflectometer, Bedford, Mass./U.S.A.
[4] GOETZ electrode catheter, USCI, Glens Falls, N.Y./U.S.A.
[5] Cardio Green (Hynson, Westcott, and Dunning, Inc., Baltimore, Maryland, U.S.A.).
[6] Agla micrometer syringe, Burroughs Wellcome, Co., London, England.

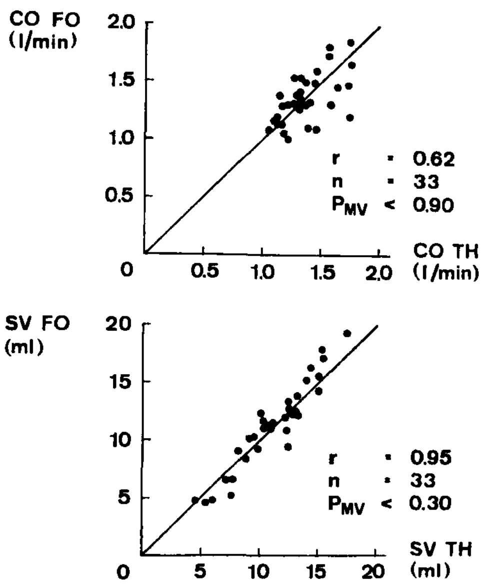
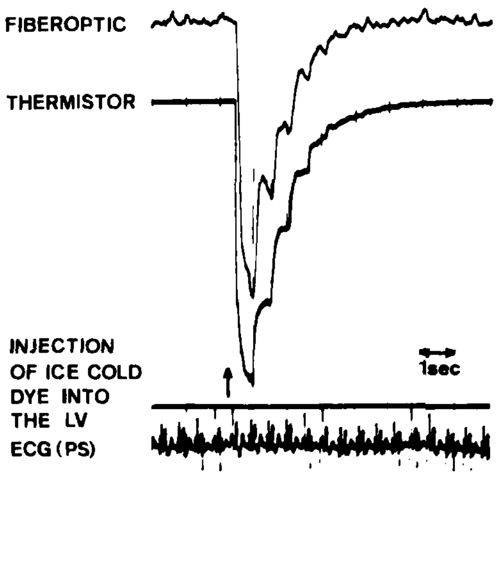


FIG. 1 *Relationship of CO (upper panel) and SV (lower panel) by fiberoptic dye dilution technique (FO) and by thermodilution method (TH). There is no significant difference between both methods. The P-values concern to the comparison of the mean values.*

FIG. 2 *Representative fiberoptic and thermodilution curves simultaneously recorded after injection of cold dye (arrow) in the left ventricle. PS: paired stimulation.*



of the residual fraction by thermodilution is slightly but significantly ($P < 0{\cdot}05$) larger than that obtained by the fiberoptic method:

$$K_{TH} = 0{\cdot}672 \pm 0{\cdot}01 \text{ (SE)}$$
$$K_{FO} = 0{\cdot}661 \pm 0{\cdot}01$$

In Table 1 a comparison of single concentration ratios is made. From the available data the mean values of each concentration ratio was calculated. With respect to c_3/c_2, c_4/c_3, and c_5/c_4 no significant differences between both methods were found. For c_6/c_5, however, the value by thermodilution is significantly higher than by fiberoptic ($P < 0{\cdot}05$). In Table 2, 10 curves where all concentrations between c_2 and c_6 were determined are compared. Again, no differences exist for the ratios c_3/c_2, c_4/c_3, and c_5/c_4, but c_6/c_5 was significantly larger ($P < 0{\cdot}05$) by thermodilution than by fiberoptic.

In Fig. 4 the slope of the stepwise decline of the average indicator concentration is plotted in a semilogarithmic manner. Assuming an average concentration of c_2 for both indicators represented by a deflection of 7 cm the concentrations were calculated from the residual fractions c_3/c_2 to c_6/c_5 in Table 1. The graph shows clearly the deviation of the thermodilution curve from the exponential slope after c_5, whereas the decline in the washout of the dye dilution curve is straight.

The time from the beginning of the thermal and the dye dilution curve till reaching baseline was measured in 58 instances. The duration of the thermal dilution curve ($11{\cdot}4 \pm 4{\cdot}1$ sec, $\pm$SE) was significantly longer ($P < 0{\cdot}001$) than the duration of the dye dilution curve ($9{\cdot}0 \pm 3{\cdot}2$ sec). It has to be considered that the noise in the fiberoptic signal was higher than in the thermodilution curves, which precluded sometimes an accurate determination of the end of the fiberoptic curves.

Discussion

No significant difference between the cardiac output and stroke volume determination by thermodilution and fiberoptic dye dilution technique was found. This is in good agreement with the observations of Weigand and Jacob (1965). These authors compared thermodilution with dye dilution cuvette technique. Comparison of thermodilution or fiberoptic with the FICK method (Goodyer, Huvos, Eckhardt, and Ostberg, 1959; Klussmann, König, and Lütcke, 1959; Wagner, Gamble, Albers, and Hugenholtz, 1968) or with a direct method (right ventricular bypass) (Lüthy and Galletti, 1966) confirms that no difference in cardiac output

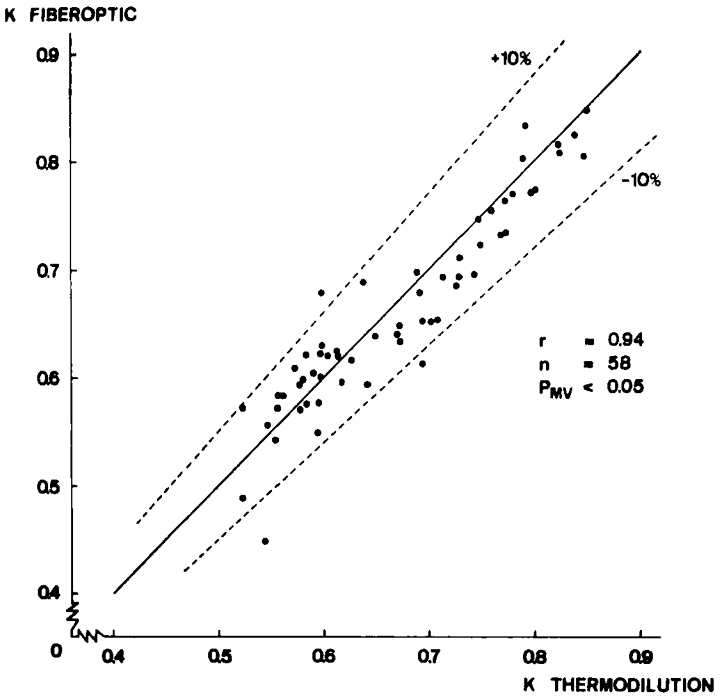


FIG. 3 *Correlation between the residual fraction (K) determined by the fiberoptic method and by the thermodilution technique. Data obtained by Holt's method (ratio of successive steps without c_2/c_1). The mean value of K by thermodilution is slightly but significantly ($P<0{\cdot}05$) larger than that obtained by the fiberoptic method.*

TABLE I *Comparison of single concentration ratios of paired thermal- and fiberoptic dilution curves**

	n	*Thermodilution*	*Signif.*	*Fiberoptic*
c_3/c_2	49	$0{\cdot}663 \pm 0{\cdot}01$	NS	$0{\cdot}650 \pm 0{\cdot}01$
c_4/c_3	55	$0{\cdot}663 \pm 0{\cdot}01$	NS	$0{\cdot}652 \pm 0{\cdot}02$
c_5/c_4	50	$0{\cdot}668 \pm 0{\cdot}02$	NS	$0{\cdot}664 \pm 0{\cdot}02$
c_6/c_5	15	$0{\cdot}750 \pm 0{\cdot}02$	$P<0{\cdot}05$	$0{\cdot}717 \pm 0{\cdot}03$

* A significant difference between the two methods is apparent at c_6/c_5. n = number of observations.

TABLE 2 *Comparison of single concentration ratios of paired thermal- and fiberoptic dilution curves in 10 instances where all concentrations between c_2 and c_6 were obtained**

	n	*Thermodilution*	*Signif.*	*Fiberoptic*
c_3/c_2	10	$0{\cdot}740 \pm 0{\cdot}03$	NS	$0{\cdot}721 \pm 0{\cdot}02$
c_4/c_3	10	$0{\cdot}726 \pm 0{\cdot}03$	NS	$0{\cdot}689 \pm 0{\cdot}04$
c_5/c_4	10	$0{\cdot}732 \pm 0{\cdot}04$	NS	$0{\cdot}775 \pm 0{\cdot}03$
c_6/c_5	10	$0{\cdot}723 \pm 0{\cdot}03$	$P<0{\cdot}05$	$0{\cdot}685 \pm 0{\cdot}03$

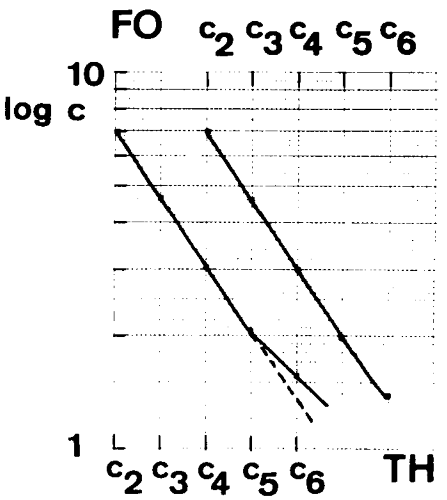
* The residual fraction c_6/c_5 by thermodilution is significantly higher than the same residual fraction by fiberoptic.

and stroke volume determination exists between indicator dilution methods or direct measurements.

The mean values of the left ventricular residual fraction (K) determined with both methods are only slightly but significantly ($P<0{\cdot}05$) different from each other. The value measured by thermodilution is higher than by fiberoptic dye dilution. Similar findings were reported by Weigand and Jacob (1965) with the external dye dilution cuvette technique.

Since cardiac output by both methods showed no significant difference but the slope in the latter part of the thermodilution curves was decreased, it must be anticipated that the initial concentration (c_1) after injection of cold indicator is too low. This may be due to transfer of cold to the wall of the left ventricle. During the subsequent beats when the temperature gradient is reversed probably most of the stored cold in the left ventricular wall is

FIG. 4 *Semilogarithmic plot of the average indicator concentrations of the decline in the thermodilution (left) and the fiberoptic dye dilution (right) curve. Calculations from the residual fractions in Table 1. There is deviation of the thermodilution curve from the exponential slope after c_5, while the dye dilution curve is straight.*



gradually released back to the blood (Rolett *et al.*, 1964). In accordance with this interpretation is the observation that c_2/c_1 is generally larger than K both in dogs and in man (Krayenbühl, Homer, and Galletti, 1966; Krayenbühl, Noseda, De Sépibus, and Fricke, 1968). The delayed washout of the thermal indicator is further documented by a prolonged duration of the thermodilution curves compared with the fiberoptic curves.

An important element in cold exchange is the thermal conductivity of the tissue which is proportional to the rate of tissue flow. In addition to the rate of myocardial blood flow, other factors may be expected to influence the transfer of cold between the ventricular wall and chamber blood. These include the heat capacity of the tissues, the temperature gradient, and the internal ventricular surface area. Cold exchange will also be enhanced at lower values of K, at slower heart rates, and with decreasing ventricular radius (Rolett *et al.*, 1964).

Nevertheless, the error for K introduced by cold exchange is not more than 2–4% of a K of about 0·65. It is even lower when only the second to the fifth beat is analysed. In this range the cold transfer factor appears to be small.

In conclusion, the determination of end-diastolic volume by the thermodilution technique is as valid as by the fiberoptic dye dilution method, provided washout concentrations c_2 to c_5 are used to calculate the residual fraction.

Summary

In five dogs anaesthetized with morphine-chloralose, 5 ml. ice cold saline-indocyanine green were injected through a spray type catheter into the left ventricle. Simultaneous measurements of the concentration of dye by a fiberoptic catheter and of the temperature by a thermistor catheter were obtained in the ascending aorta 1–2 cm above the aortic valves. The sensing elements of both catheters were fixed together.

In 33 simultaneous determinations there was no significant difference for cardiac output and stroke volume. The average residual fraction (K) was obtained from 58 simultaneous measurements. The residual fraction by thermodilution (TH) was slightly but significantly higher ($P < 0{\cdot}05$) than the value obtained by fiberoptic dye dilution technique. The higher K_{TH} is caused by cold transfer, which leads to a prolonged indicator decay slope after the fifth concentration step. When temperature concentrations after the fifth beat were excluded, the thermodilution method revealed the same residual fractions as the fiberoptic dye dilution method.

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References

Gamble, W. J., Hugenholtz, P. G., Monroe, R. G., Polanyi, M., and Nadas, A. S. (1965). The use of fiberoptics in clinical cardiac catheterization. I. Intracardiac oximetry. *Circulation*, **31**, 328–343.

Goodyer, A. V., Huvos, A., Eckhardt, W. F., and Ostberg, R. H. (1959). Thermal dilution curves in the intact animal. *Circulation Research*, **7**, 432–441.

Holt, J. P. (1956). Estimation of the residual volume of the ventricle of the dog's heart by two indicator dilution technics. *Circulation Research*, **4**, 187–195.

Hugenholtz, P. G., Gamble, W. J., Monroe, R. G., and Polanyi, M. (1965). The use of fiberoptics in clinical cardiac catheterization. II. In vivo dye-dilution curves. *Circulation*, **31**, 344–355.

——, Wagner, H. R., and Sandler, H. (1968). The in vivo determination of left ventricular volume. Comparison of the fiberoptic-indicator dilution and the angiocardiographic methods. *Circulation*, **37**, 489–508.

Klussmann, F. W., König, W., and Lütcke, A. (1959). Über die 'thermo-dilution'-Methode zur Bestimmung des Herzzeitvolumens am narkotisierten Hund. *Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere*, **269**, 392–403.

Krayenbühl, H. P., Homer, L. D., and Galletti, P. M. (1966). Methods of calculation of ventricular end-diastolic volume in the dog by the thermodilution technique. *Federation Proceedings*, **25**, 205.

——, Noseda, G., De Sépibus, G., and Fricke, G. (1968). Zur Problematik der Kammervolumenmessung mit Hilfe der Thermodilutionsmethode. *Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung*, **34**, 149–154.

—— (1969). Die Dynamik und Kontraktilität des linken Ventrikels. *Bibliotheca Cardiologica*, **23**, 1–183.

Lüthy, E. (1962). Die Haemodynamik des suffizienten und insuffizienten rechten Herzens. *Bibliotheca Cardiologica*, **11**, 1–168.

——, and Galletti, P. M. (1966). *In vivo* evaluation of the thermodilution technique for measuring cardiac output. *Helvetica Physiologica et Pharmacologica Acta*, **24**, 15–23.

Polanyi, M. L., and Hehir, R. M. (1960). New reflection oximeter. *Review of Scientific Instruments*, **31**, 401–403.

Rapaport, E., Wiegand, B. D., and Bristow, J. D. (1962). Estimation of left ventricular residual volume in the dog by a thermodilution method. *Circulation Research*, **11**, 803–810.

Rolett, E. L., Sherman, H., and Gorlin, R. (1964). Measurement of left ventricular volume by thermodilution: an appraisal of technical errors. *Journal of Applied Physiology*, **19**, 1164–1174.

Wagner, H. R., Gamble, W. J., Albers, W. H., and Hugenholtz, P. G. (1968). Fiberoptic-dye dilution method for measurement of cardiac output comparison with the direct Fick and the angiocardiographic methods. *Circulation*, **37**, 694–708.

Weigand, K. H., and Jacob, R. (1965). Zur Frage der Restvolumenbestimmung des linken Ventrikels im natürlichen Kreislauf. *Archiv für Kreislaufforschung*, **46**, 97–114.