Comparison of Aortic Pulse-wave Contour Analysis and Thermodilution Methods of Measuring Cardiac Output during Anesthesia in the Dog

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Accuracy and reliability of cardiac output ($\dot{Q}_t$ measurement utilizing computer analysis of the aortic pressure wave (Warner method) were assessed by comparing this technique with a standard thermodilution method in 20 halothane-anesthetized dogs over a wide range of $\dot{Q}_t$ and systemic vascular resistance (SVR) values. Five of the dogs also had electromagnetic flow (EMF) probes placed around the ascending aorta. More than 800 pairs of simultaneous $\dot{Q}_t$ determinations were performed using pulse-wave and thermodilution methods, and more than 150 triplicate measurements made using all three techniques during changes in inspired halothane concentrations (0.5–2.0 per cent) or during infusions of sodium nitroprusside (SNP) and phenylephrine (PE). Cardiac outputs ranged from 0.7 to 5.3 l/min, mean aortic blood pressures ($\overline{BP}$) ranged from 30 to 200 torr, and SVR varied from 70 per cent below to 200 per cent above control values. Correlation of pulse-wave-computed and thermodilution-calculated $\dot{Q}_t$ values was high (r = .91 or better), irrespective of SVR during changes in halothane concentration. Correlation of pulse-wave and EMF methods was equally good during this period (r = .92 or better). Correlation was lower, but still good, with alterations in SVR of 30 per cent or less induced by SNP or PE (r = .90 or better for thermodilution and r = .91 or better for EMF). When SVR was changed from 30 to 50 per cent of control with SNP or PE, correlation between pulse-wave-computed and EMF $\dot{Q}_t$ values remained good (r = .85), but correlation between pulse-wave-computed and thermodilution-calculated $\dot{Q}_t$ values was only fair (r = .79–.77). Correlation of thermodilution-calculated or EMF and pulse-wave-computed $\dot{Q}_t$ values deteriorated significantly with SNP- and PE-induced changes of SVR greater than 50 per cent (r = <.5). These results demonstrate that computer analysis of the aortic pressure wave is a simple and valid method of determining $\dot{Q}_t$ during halothane anesthesia, but must be limited to conditions of only moderate alteration of SVR during infusions of vasopressor or vasodilator drugs. (Key words: Anesthetics, volatile: halothane. Anesthetic techniques: hypotension, induced, nitroprusside. Equipment: electromagnetic flow probes. Heart: cardiac output. Measurement techniques: pulse contour analysis; thermodilution.)

COMPUTATION OF CARDIAC OUTPUT via computer analysis of the central aortic pulse-wave contour, as described by Warner and co-workers,[1,2] is a convenient method for measuring cardiovascular alterations caused by anesthetics and anesthetic adjuvants. The method has recently been criticized[3] for lacking sufficient accuracy and standardization to permit its application to pharmacologic and cardiovascular research questions. The purpose of this study was to compare the accuracy and reliability of the Warner method with those of standard thermodilution and electromagnetic flow (EMF) probe cardiac output measurement techniques over a wide range of alterations in $\overline{BP}$, $\dot{Q}_t$ and SVR induced by changes in anesthetic concentration (halothane) and by infusions of a vasopressor (phenylephrine) or vasodilator (sodium nitroprusside) drug.

Methods

Detailed derivations of the Warner method of measuring cardiac output can be found elsewhere.[1-4] The Warner equation used in these studies is:

$$SV = K(P_{md})\left(1 + \frac{Sa}{Da}\right)$$

where SV is stroke volume and K is a calibration constant determined by making a simultaneous measurement by an independent method (thermodilution), P_{md} is the difference between the average aortic pressure during the last 80 milliseconds of systole and the average aortic pressure during the last 80 milliseconds of diastole and is referred to as the "mean distending pressure" (fig. 1). Sa and Da represent the systolic and diastolic areas. In Warner's original equation,

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ABBREVIATIONS	
$\dot{Q}_T$	= cardiac output
SVR	= systemic vascular resistance
$\overline{BP}$	= mean aortic blood pressure (torr)
$\overline{RAP}$	= mean right atrial pressure (torr)
SNP	= sodium nitroprusside
PE	= phenylephrine
HR	= heart rate
SV	= stroke volume
K	= calibration constant
P_{md}	= mean distending pressure
Sa	= systolic area
Da	= diastolic area
EMF	= electromagnetic flow

calculation of the mean time of transmission required the simultaneous measurement of both a central and a peripheral arterial pressure. The mean time of transmission (tw) was later assumed to be constant at 80 msecs, thus making measurement of the peripheral arterial pressure unnecessary.

Twenty male mongrel dogs (18–22 kg) were anesthetized with thiopental, 25 mg/kg, iv. Endotracheal tubes were placed in their tracheas, and their lungs were ventilated with halothane, 0.5 per cent, in oxygen at rates and volumes necessary to maintain arterial carbon dioxide partial pressure (Pa_{CO_2}) between 30 and 35 torr, as measured in femoral arterial blood every 20 to 30 min. A 5 or 7 Edwards Swan-Ganz (model 93A-132 or 93A-131, depending on the dog's size) quadruple-lumen thermistor-tipped catheter with an injection portal located 20 cm from the catheter tip** was flow-directed from an external jugular vein into a branch of the pulmonary artery and wedged for confirmation of position. Two additional Teflon® catheters were introduced, one (10-Fr) via a femoral vein into the right atrium and the second, a 20-guage catheter 100 cm long (CAP IntraFusor-18®, Sorenson Research Company, Salt Lake City, Utah), via a femoral artery to the thoracic aorta. The long arterial catheter has a natural frequency of 20 hertz and a damping coefficient of 0.25. This catheter was attached to a Statham 923Db transducer. A continuous-flush system was used to keep the catheter patent. The transducer was connected to an Electronics for Medicine oscilloscope for continuous oscilloscopic display. Right atrial pressure, (via another Statham transducer), heart rate and electrocardiogram were also continuously displayed on the oscilloscope. The arterial signal on the oscilloscope was conditioned using a locally designed pressure amplifier. The pressure waveform was sampled by a computer program at 200 samples/sec for a duration of 45 sec. The program selected the first 16 artifact-free pressure contours, computed the pressure pulse parameters for each, and averaged them together. Variables displayed included systolic, mean and diastolic pressures, stroke volume, heart rate, cardiac output, and systemic vascular resistance. An 18-gauge Teflon catheter was placed in a foreleg vein to accommodate drug infusions, and a rectal temperature probe was positioned and connected along with the pulmonary-artery thermistor to an Edwards Laboratories Model 9520 thermodilution cardiac output computer equipped for direct write-out.
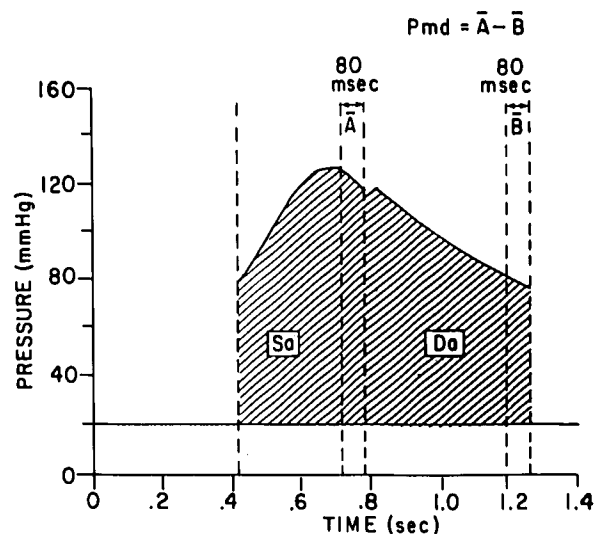

Fig. 1. Variables used in the Warner equation for determining cardiac output. Sa, Da and P_{md} represent systolic area, diastolic area and mean distending pressure, respectively. $\bar{A}$ and $\bar{B}$ represent the average systolic and diastolic pressures 80 msec before the end of systole and diastole, respectively.

Thermodilution cardiac output measurements were made using 10 ml of iced physiologic saline solution injected through the right atrial port of the catheter. In five dogs Biotronex electromagnetic flow probes (14–16 mm), previously calibrated in vitro around excised dog aortas perfused with saline solution, were placed around the ascending aorta and attached to a Biotronex BL-620® flowmeter.

After a 30-min stabilization period, three paired simultaneous determinations of cardiac output were performed using the Warner and thermodilution methods. An identity constant was then calculated and entered into the Warner computer to calibrate the computer so that the pulse-wave contour cardiac output values became standardized to those calculated by thermodilution. Three additional paired simultaneous cardiac output determinations were then performed to confirm that the two methods gave identical cardiac output results. Similar paired evaluations of the two methods were performed every 60–80 min for six hours in three dogs during control conditions (anesthesia with halothane, 0.5 per cent, and oxygen without simultaneous sodium nitroprusside or phenylephrine infusions). In the dogs with both electromagnetic flow probes and thermodilution catheters in place the Warner system was calibrated with the electromagnetic flowmeter as described above.

Following instrumentation and standardization, paired simultaneous cardiac output determinations were performed in the remaining 17 dogs under three sets of conditions using both Warner and thermodilution methods and in five dogs using all three methods
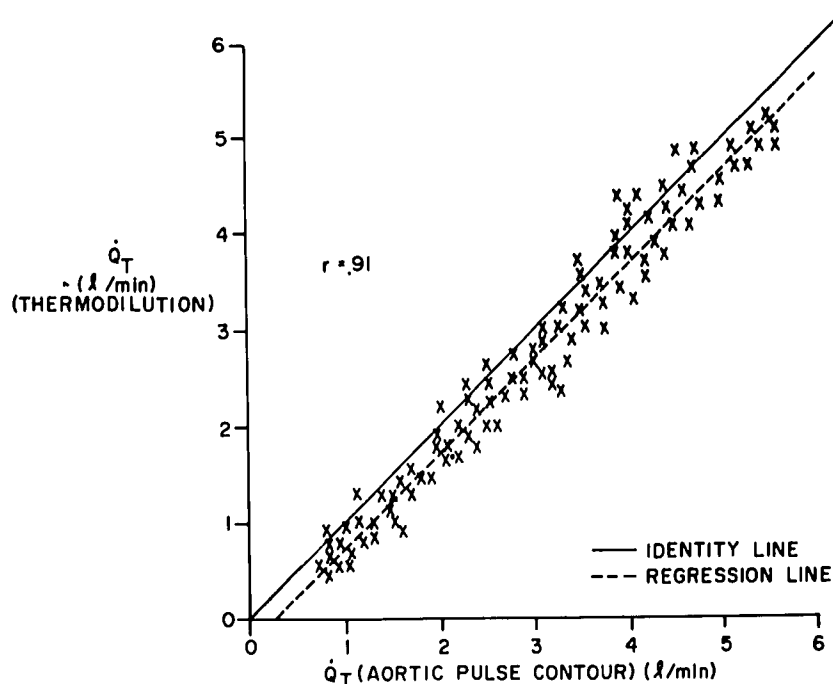
FIG. 2. Correlation of thermodilution and Warner aortic pulse-wave contour cardiac output determinations during changes in halothane concentration from 0.5 to 2 per cent in increments of 0.1 per cent; r = .91.

of determining cardiac output. First, halothane concentration was increased in 0.1-per cent increments from 0.5 to 2.0 per cent, and then it was decreased to 0.5 per cent. Determinations were performed 10 min after each change in halothane concentration. Second, superimposed on the baseline anesthesia with halothane, 0.5 per cent, and oxygen, a sodium nitroprusside, .01 per cent, solution in lactated Ringer's solution was begun and $\overline{BP}$ decreased in 10-torr decrements to 35 torr, then increased to control values. Cardiovascular data were recorded using all techniques 10 min after each 10-torr change in $\overline{BP}$. Third, $\overline{BP}$ was increased in 10-torr increments to 200 torr with a phenylephrine, .0025 per cent, infusion and data recorded 10 min after each change in $\overline{BP}$ as before. Paired values for $\dot{Q}_t$ were determined using each of the two (or three) techniques employed. A difference of 5 per cent or more in any of the pairs of $\dot{Q}_t$ resulted in elimination in all of the pairs.

Correlation coefficients were performed on the paired thermodilution-calculated and computer-calculated $\dot{Q}_t$ determinations for each of the three groups (1, halothane; 2, SNP; 3, PE). In the dogs with electromagnetic flowmeters, separate comparisons were made between computer- and thermodilution-derived $\dot{Q}_t$ and electromagnetic- and computer-measured $\dot{Q}_t$. Systemic vascular resistance coinciding with each set of paired $\dot{Q}_t$ determinations was calculated using the formula:

$$SVR = \frac{\overline{BP} - \overline{RAP} \times 80}{\dot{Q}_t \text{ (thermal dilution or EMF)}}$$
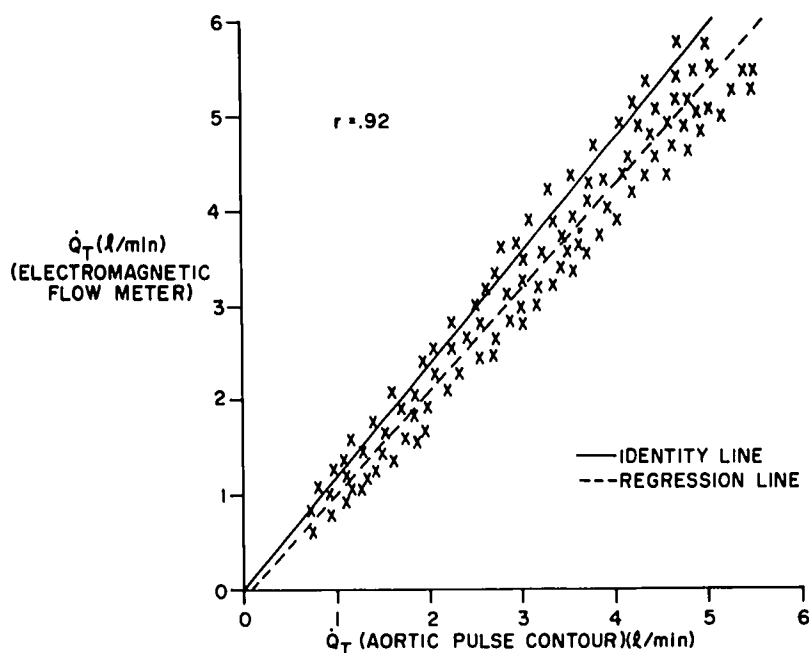
Correlation coefficients were performed on subgroups of paired $\dot{Q}_t$ determinations based on alterations in

SVR expressed as percentage changes from control, in order to evaluate the effects of changes in vascular resistance on the accuracy of the Warner method. For example, all paired cardiac output determinations with SVR changes from control of less than 10 per cent were grouped and correlated. Then all paired cardiac output values with SVR changes of less than 20, 30, 40, 50 and 100 per cent and more than 100 per cent were similarly evaluated. Finally, the absolute difference between the members of each pair of $\dot{Q}_t$ determinations in l/min was determined and resulting values were plotted against SVR.

Results

Calibration of the aortic pulse-wave contour analysis remained stable and $\dot{Q}_t$ determinations utilizing this technique were accurate (within ±5–10 per cent of thermodilution-determined values) over six hours in the three dogs anesthetized with halothane, 0.5 per cent, and oxygen and not subjected to nitroprusside or phenylephrine infusions, so long as continuous flushing was insured (in order to assure a good pulse wave and dicrotic notch) and heart rate remained between 50 and 130 beats/min. When the pulse wave or dicrotic notch became distorted secondary to a small clot on the tip of the catheter, when arrhythmias were present, or when heart rate was less than 60 or more than 140 beats/min, paired Warner method $\dot{Q}_t$ determinations were usually more than 5 per cent different, and were thus discarded. Comparison of the mean of these discarded values with thermodilution or EMF $\dot{Q}_t$ was not attempted in this study. Had such comparison been attempted, differences between techniques would have been much greater than those observed.

FIG. 3. Correlation of electromagnetic flowmeter and Warner aortic pulse-wave contour cardiac output determinations during changes in halothane concentration from 0.5 to 2 per cent in increments of 0.1 per cent; r = .92.

$\dot{Q}_T$ (l/min)
(ELECTROMAGNETIC FLOW METER)

r = .92

——IDENTITY LINE
---REGRESSION LINE

$\dot{Q}_T$ (AORTIC PULSE CONTOUR)(l/min)

Changes in halothane concentration from 0.5 to 2.0 per cent resulted in cardiac output values that ranged from 0.7 to 5.3 l/min (fig. 2) and systemic vascular resistances that ranged from 1,067 to 2,668 dynes.sec/cm[5]. Correlation between Warner method aortic pulse-wave contour-computed and thermodilution-calculated $\dot{Q}_t$ values during changes in halothane concentration utilizing 476 data points was excellent (r = .91) over the entire range of $\dot{Q}_t$ studied. Correlation of Warner method and EMF $\dot{Q}_t$ utilizing 114 data points over the entire range of $\dot{Q}_t$ was also excellent (r = .92) (fig. 3). Deviation of the zero intercept of the regression of both comparisons were small. Neither the correlation coefficients nor intercepts of the regression lines were appreciably altered with changes in SVR (produced by halothane) utilizing either of the methods of comparison (table 1). Absolute differences between Warner method and thermodilution $\dot{Q}_t$ values during changes in halothane concentration were usually less than 0.2 l/min and never more than 0.5 l/min. Absolute differences between Warner method and EMF $\dot{Q}_t$ values during changes in halothane were usually less than 0.2 l/min and never more than 0.4 l/min.

Infusions of sodium nitroprusside and phenylephrine produced ranges of $\dot{Q}_t$ (2.1–5.0 l/min) that were smaller and ranges of SVR (590–8,460 dynes.sec/cm[5]) that were larger than those produced by changes in halothane concentration. Correlations between Warner aortic pulse-wave contour and thermodilution methods and Warner EMF methods of determining $\dot{Q}_t$ were excellent (r = .90 or better and r = .91 or better, respectively) when changes in SVR were 30 per cent or less during infusions of SNP or PE (table 1). When SVR was decreased from 30 to 50 per cent

of control with SNP or PE, correlation between Warner method and EMF $\dot{Q}_t$ remained good (r = .85 or better), but correlation between Warner method and thermodilution $\dot{Q}_t$ was only fair (r = .79 − .75). Correlation of EMF and thermodilution $\dot{Q}_t$ values also decreased (r = .88 − .82) when SVR was altered from 30 to 50 per cent of control values. Correlation of thermodilution or EMF and Warner method pulse-wave-computed $\dot{Q}_t$ deteriorated significantly with SNP- or PE-induced changes of SVR greater than 50 per cent (r = <5). Changes in SVR greater than 30 per cent, and especially those greater than 50 per cent, of control produced significant alterations in the zero intercept and deviations of the slopes of regression lines from identity comparing Warner and thermodilution or EMF methods, irrespective of whether the changes were produced by SNP or PE (fig. 4). Absolute differences between Warner pulse-wave contour and thermodilution of EMF method values during SNP or PE infusions remained small (0.5 l/m or less) so long as SVR remained

TABLE 1. Correlation Coefficients for Thermodilution* and Electromagnetic Flowmeter† vs. Aortic Pulse Contour Paired Cardiac Outputs in 20 Dogs

Percentage Change in Peripheral Vascular Resistance from Control	Halothane		Sodium Nitroprusside		Phenylephrine	
	Therm	EMF	Therm	EMF	Therm	EMF
≤10	.96	.97	.95	.94	.94	.94
≤20	.95	.97	.92	.92	.92	.92
≤30	.94	.96	.90	.91	.90	.92
≤40	.94	.96	.79	.87	.78	.88
≤50	.92	.94	.77	.86	.75	.85
≤100	.91	.92	.46	.48	.34	.44
≥100	—	—	.3	—	.36	.39

* Thermodilution vs. computer = Therm.
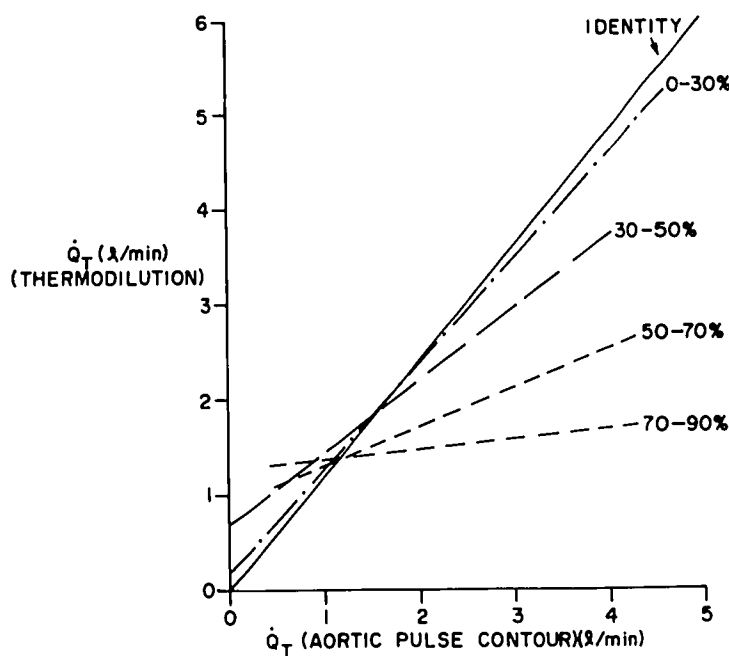† Electromagnetic flowmeter vs. computer = EMF.

Fig. 4. Thermodilution versus Warner aortic pulse-wave contour cardiac output regression lines obtained during increases in systemic vascular resistance of 0–30, 30–50, 50–70, and 70–90 per cent of control values produced by infusion of phenylephrine.

within 0 to 30 per cent of control (calibration) values, but usually increased (as much as 2.3 l/min) in proportion to changes in SVR away from control values.

Discussion

Frequent determinations of cardiac output are extremely valuable in *in-vivo* pharmacologic studies in animals and man and in the monitoring of acutely ill patients during anesthesia. Both Fick and dye-dilution methods provide a relatively accurate estimate of cardiac output; however, these techniques are not practical for applications that require frequent determinations. Thermodilution-measured cardiac output is also a reliable technique, but its is highly invasive and therefore not justifiable for reasonably healthy patients. Thermodilution cardiac output determinations also require infusions of saline solution or other solutions, which can significantly change the volume status of the subjects after frequent cardiac output determinations. Various types of flowmeters can be used to measure aortic blood flow, but their routine use in man is not feasible.

A number of years ago, Warner[1,2,4] and others[5] began investigating a variety of methods of analyzing the central aortic pulse wave for determination of stroke volume and cardiac output. Warner's initial studies suggested that computer analysis of the arterial mean distending pressures was valid and accurate under a variety of clinical and laboratory conditions. Experiments in our animal laboratories and operating rooms suggested that the method was a simple, safe and accurate technique for measuring cardiac output in the clinical setting as well as in the experimental laboratory. However, others[3] questioned its validity when used for anesthetic and pharmacologic investiga-

tions. This investigation was undertaken in an attempt to define the strengths and limitations of the Warner method of cardiac output determination in anesthetized animals undergoing pharmacologic manipulations.

The results of this study demonstrate that correlation of thermodilution and pulse-wave-computed $\dot{Q}_t$ values (according to the Warner method) is excellent so long as SVR remains within 30 per cent of the value present when the computer was calibrated and good when SVR is within 50 per cent of initial values. Correlation of $\dot{Q}_t$ remains good with SVR changes of greater magnitude produced by changing concentrations of halothane, but decreases with greater SVR changes induced by infusions of sodium nitroprusside or phenylephrine.

The reasons changes in SVR greater than 50 per cent of control (computer-calibrated values) induced by peripheral vasodilators or constrictors invalidate the Warner pulse-wave analysis method of computing $\dot{Q}_t$, but similar changes in SVR induced by changes in halothane concentrations do not, are not clear from analysis of our data. However, two possible explanations may be advanced. First, changes in SVR produced by halothane, while on occasion greater than 30 per cent, were never as great as 80 per cent of control, and rarely as great as 50 per cent of control, in this study. On the other hand, SVR changes produced by nitroprusside and phenylephrine were often 100–150 per cent of control. It may simply be that halothane does not alter SVR enough to invalidate the Warner method, and that an anesthetic that produces changes in SVR greater than 50 per cent of control would result in invalidation similar to that produced by nitroprusside and phenylephrine.

A second, and more likely, explanation of the dis-

parity of $\dot{Q}_t$ values found at SVR greater than 50 per cent of calibration values in this study may be related to the pattern of the effects compounds such as halothane have on cardiovascular dynamics versus those produced by infusions of introprusside or phenylephrine. Increasing concentrations of halothane result in simultaneous decreases in $\dot{Q}_t$, $\overline{BP}$, and SVR. In contrast, infusions of SNP decrease $\overline{BP}$ and SVR but usually do not change $\dot{Q}_t$, while infusions of PE increase $\overline{BP}$ and SVR and decrease $\dot{Q}_t$. Cardiovascular changes secondary to SNP and PE infusions undoubtedly alter the pressure–volume relationships of the arterial tree; changes produced by halothane probably do not. Marked alterations of arterial pressure–volume relationships change the size of the arterial tree and probably invalidate the identity or calibration constant entered in the computer during the control period.[6,7] Juardo and co-workers[7] have suggested that significant changes in arterial compliance and elasticity with secondary alterations in arterial pressure–volume characteristics are the principal reasons why all pulse-wave contour methods of determining $\dot{Q}_t$ tend to lose accuracy as elapsed time from initial calibration increases. Kouchoukos et al.[8] came to the same conclusion after demonstrating a good correlation between pulse-wave contour analysis estimates of stroke volume and stroke volume determined by dye-dilution techniques within 24 hours of open-heart surgery, but a poorer correlation during the second 24 hours postoperatively. The same investigators confirmed that Warner's pulse-wave contour analysis determination of $\dot{Q}_t$ was highly correlated with electromagnetic flowmeter determinations of $\dot{Q}_t$ in dogs when SVR remained minimally altered or unchanged but was poorly correlated during infusion of catecholamines.[9] Correlation of pulse contour and thermodilution $\dot{Q}_t$ was not altered by time from initial calibration of the computer in this study. However, the time from initial calibration was only six hours, and there was no significant change in SVR from control values during this interval in the three dogs studied.

The Warner method, like all other aortic pulse-wave contour analysis techniques of cardiac output determinations, is invalidated when a good arterial waveform and dicrotic notch are not present, when arrhythmias occur, and when heart rate is extremely high or low. All of these conditions change or distort the central arterial waveform or cause computer misidentification of important phases of the aortic pulse. Usually the computer recognizes the problem and refuses to analyze the data; however, on occasion this does not happen and the clinician or investigator is presented with inaccurate data.

In our opinion, the data obtained in this investigation demonstrate the validity of the Warner method

of determining cardiac output in pharmacologic investigations involving anesthetics and anesthetic adjuvants. These studies were accomplished, as were our previous investigations in man, in a relatively short period and under strictly controlled experimental conditions. Our findings do not confirm the validity of the Warner method, and, in fact, suggest that it may be invalid in clinical situations in which systemic vascular resistance and arterial pressure–volume relationships may be rapidly and radically changing. Recent findings by our colleagues at L.D.S. Hospital in Salt Lake City (Cundick RM, Gardner RM, unpublished data) confirm the unreliability of the Warner method in patients with frequent and marked changes in cardiovascular dynamics in the operating room or intensive care unit. Unfortunately, these are the precise clinical situations in which a simple technique such as the Warner method would be most valuable.

In conclusion, our findings in this study demonstrate that cardiac output measurements utilizing Warner's computer analysis of the aortic pressure wave is a simple and valid method of determining $\dot{Q}_t$ during pharmacologic investigations involving anesthetic compounds or anesthetic adjuvants. However, the Warner method must be limited to conditions of only modest to moderate alterations of SVR when employed during laboratory or clinical situations that produce changes in arterial pressure–volume relationships after initial calibration.

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