CARDIAC OUTPUT MEASUREMENT BY THERMODILUTION AND FLOWMETER METHODS IN LOW FLOW STATES

Masters Research Project

by

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INTRODUCTION

Statement of Problem

Critical care nurses assess and treat human responses to illness in critical life situations. Measurement of cardiac output (CO) by the thermodilution method has become an integral part of assessing critically ill patients. Clinicians use this information to assess left ventricular function and to evaluate therapy directed toward stabilization and improvement of patients' cardiac performance.

Because of the importance of the CO measurement, accuracy is paramount. The thermodilution method of CO measurement is based on blood temperature changes over time between the right atrium and pulmonary artery caused by a bolus of fluid injected into the right atrium. However, accuracy of the thermodilution method is dependent on a variety of technical and physiological factors. Technical factors related to the equipment and procedure include the catheter and amount of fluid within its lumen, the type of injectate solution usually sterile 5% dextrose in water (D5W) or normal saline (NS), injectate volume, injectate temperature, duration of injection, timing of injection in relation to the respiratory

cycle, and the mathematical algorithm for integration the thermodilution curve as computed by the bedside CO computer. Physiological factors that affect the accuracy of the thermodilution method include blood temperature, body position, competency of the tricuspid valve, hematocrit, and variations in pulmonary artery temperature associated with the respiratory cycle. An additional factor that affects the accuracy of the thermodilution method is variability in blood flow states. In the practice setting, CO determination is a collaborative function that nurses share with physicians. Nurses, in collaboration with physicians, select specific technical procedures when measuring CO depending on the equipment used and patients' physiological factors.

In the clinical setting, however, there is little consistency in the technique used to obtain CO measurements. Equipment differences exist, as reflected by a variety of thermodilution injectate systems and computers. The area of greatest inconsistency is associated with the injectates used. Critical care nurses typically determine the volume and temperature of injectate used for CO measurements. The use of 5 ml or 10 ml, room or iced temperature injectate varies among institutions and often among critical care units within an institution.

Because of the importance of CO determinations in physiologically unstable patients, the injectate volume combined with the frequency of CO measurement could compromise the hemodynamic status of a fluid restricted patient. Nurses often select 5 ml injectates to minimize the fluid administered during frequent CO measurements. This technique is often utilized in patients with left ventricular failure who experience high pulmonary artery pressures and low COs and cannot tolerate additional fluid volume.

The use of room or iced temperature injectate is often determined by fiscal and time concerns. The room temperature injectate system is less costly in that it does not need a cooling system and requires less setup time. Finally, the injectate solution varies with either D5W or NS being used.

With the amount of variation that exists in the thermodilution method of measuring CO, we questioned which injectate volume and temperature results in the most accurate measurement of CO. Because accuracy is especially important in low flow states, reducing errors associated with injectate temperature and volume is critical.

Therefore, this study was conducted to examine which volume and temperature of injectate results in the most accurate and reliable measurements of CO by thermodilution in

low flow states. Measurements made using 5 ml and 10 ml volumes of injectate at room and iced temperatures were compared to reference values obtained by the flowmeter method of CO measurement.

Review of Literature

Cardiac output, defined as the volume of blood pumped by the heart within a one minute period, is the product of heart rate and stroke volume. Although there is significant variation in what is considered to be the normal CO in an adult human, the normal range is generally quoted to be within 4.1-6.0 L/min. Volumes below 4.0 L/min are considered to be low flow states, and those exceeding 6.0 L/min are considered to be high flow states (Hurst et al., 1986).

Multiple techniques are available to measure cardiac output in humans, including the radioisotope, ultrasonic, electromagnetic flowmeter, Fick, and indicator dilution methods. The latter, in turn, includes the dye dilution and thermodilution methods (De Alsa & Smith, 1981). This review will focus on the Fick method which is a standard for humans; the flowmeter method which is often used in animal studies; and the thermodilution method which is the most common technique used in clinical patient assessment.

Fick Method

The Fick method of CO measurement is based on the principle of uptake and release of a reference substance as the result of blood flow through an organ. The oxygen content of inspired and expired air are calculated, and arterial and

venous blood oxygen levels are determined over a three minute period of time. The quotient of oxygen consumption divided by the arteriovenous oxygen difference is the indicator of blood flow and thus a reflection of CO. This method requires that the patient breathe a known concentration of oxygen from a spirometer with a carbon dioxide absorber, thus measuring oxygen consumption by the changes in gas concentration. Arterial and mixed venous blood gases are drawn to determine the oxygen concentration of blood flowing to and from the lungs. Although the Fick method is considered to be the reference standard in human studies, it is not an instantaneous measure of CO but instead reflects flow over a period of time (Hurst et al., 1986).

Flowmeter Method

Determination of blood flow using an electromagnetic flowmeter is based on the principle of magnetic induction. When surrounded by a magnetic field, blood flow through a vessel produces a sinusoidal voltage signal which in turn can be amplified and then averaged to indicate the rate of flow through the vessel (Cromwell, Weibell, & Pfeiffer, 1980). The rate of flow is expressed in liters per minute and is a direct reflection of CO when the flowmeter is placed on the outflow tract of the heart, the ascending aorta. In contrast to the

Fick method, measurement of CO is relatively instantaneous. This method requires implantation of a flowmeter transducer which precludes its use in humans, but it is a reference standard for CO measurement in animal studies.

Thermodilution Method

The thermodilution method, introduced by Fegler in 1954 using dogs, employed the principle of indicator dilution, using the temperature of a fluid bolus as the indicator. This method was based on blood temperature changes between the heart and the aorta within a certain period of time. Originally, implanted thermocouple sensors were placed in the right ventricle and aortic arch, requiring multiple cannulations at any one time.

In 1968, Branthwaite and Bradley measured CO in humans using a prototype flow directed thermodilution catheter with thermistor beads implanted within the catheter. Blood temperature in the right atrium and pulmonary artery could then be monitored through one catheter. This method became clinically feasible in the early 1970s with the advent of the pulmonary artery catheter with dual thermistor sensors and remains the most common method of CO measurement in clinical practice. A bolus of cold injectate is the indicator signal, while the background fluctuation of pulmonary artery blood

temperature and electrical interference constitutes noise, all of which are sensed by the thermistor (Pool, Vandermoten, Varnauskas, & Wassen, 1970; Swan, Donoso, Marcus, Forrester, & Ganz, 1971). This method requires one cannulation site for placement of a flow directed pulmonary artery catheter and is based on blood temperature changes caused by a bolus of fluid injected into the right atrium and sensed at the distal catheter thermistor positioned in the pulmonary artery. CO is calculated using the Stewart-Hamilton equation (Figure 1). The equation calculates the integral of the temperature change curve that is produced by the injectate bolus and sensed by the distal thermistor.

Correlation Between Flowmeter and Thermodilution Methods

Both the thermodilution and flowmeter methods are relatively instantaneous measures, requiring only a few seconds to calculate the CO. This similarity in CO calculation time makes the two methods more suitable for comparison. Using an in-vitro model with flow rates ranging from 1.0-5.0 L/min, Bilfinger, Lin, and Anagnostopoulos (1982) compared CO values obtained by thermodilution using 3, 5, and 10 ml of room and iced temperature NS injectates to flowmeter results. Their data identified a difference of 7-14% between the thermodilution and the flowmeter methods. High

$$Q = \frac{V_i(T_B - T_i)K_1K_2}{\int_0^x \Delta T_B(t)dt},$$

where:

Q = cardiac output,
V_i = injectate volume,
T_B = blood temperature,
T_i = injectate temperature,
$\Delta T_B(t)dt$ = change in blood temperature as a function of time,
K_1 = density factor:

$$\frac{(\text{sp heat})(\text{sp gravity})_{\text{injectate}}}{(\text{sp heat})(\text{sp gravity})_{\text{blood}}},$$

K_2 = computation constant which takes into account units in liter per minute, catheter dead space, heat change in transit, and injection rate.

Figure 1. The Stewart-Hamilton equation for calculation of cardiac output by the thermodilution method. (From "Thermodilution Cardiac Output: A Critical Analysis and Review of the Literature" by J. M. Levett & R. L. Replogle, 1979, Journal of Surgical Research, 27, p. 392.)

correlations (r=.81-.98) were also found between these two methods in dogs by Meisner et al. (1974) using 10 ml room temperature NS injectates.

Problems Associated With the Thermodilution Method

Initially, the procedure for thermodilution measurements included use of three 10 ml iced injectates, each manually injected within 2-4 seconds, with the measures averaged to derive a single CO value. This procedure is still recommended by American Edwards Laboratories, a major manufacturer of CO catheters and computers, and is commonly utilized in both clinical practice and research (Swan & Ganz, 1972; Forrester, Ganz, & Diamond, 1972; Hodges et al., 1975; Weisel, Berger, & Hechtman, 1975; Venkataraman et al., 1976; Vandermoten et al., 1977).

Unfortunately, several technical problems have been found with the preparation and use of iced systems in the clinical setting. These include the initial delay for cooling the injectate, additional equipment costs, and increased nursing time (Killpack, Davidson, Woods, & Grose, 1981). Another important problem is an increased risk of injectate contamination with an open iced bath (Grose, Adair, & Reim, 1981). These problems can be resolved with the use of a closed injectate system at room temperature. No delay is

needed to cool the solution, the system is less costly, and the risk of contamination is decreased.

Several investigators have studied the correlation between CO determinations made with room and iced temperature injectates and have consistently found high positive correlations (r=.93-.99) between the two injectates (Killpack, Davidson, Woods, & Grose, 1981; Shellock, Reidinger, Bateman, Matloff, & Gray, 1982; Elkayam, Berkley, Azen, Weber, Geva, & Henry, 1983; Shellock & Reidinger, 1983; Vennix, Nelson, & Peirpoint, 1984). However, these studies did not include comparisons with a standard reference method of CO measurement. Because the room temperature injectate values were compared only to iced thermodilution CO determinations and not to a different reference method, the accuracy of results could be questioned.

Stawicki, Holford, Michealson, and Josephson (1979) compared room temperature thermodilution CO determinations to the Fick method and found correlations of r=.68-.70 ($p<.001$). However, Hoel (1979), when comparing room temperature injectates to the Fick, found a higher correlation of r=.97. Both Hoel and Stawicki et al. used 10 ml D5W injectates. More recently, Daily and Mersch (1987) found a higher correlation between the Fick method and 10 ml of NS injectate at room

temperature ($r=.84$, $p<.001$) than that obtained with the iced injectate ($r=.72$, $p<.001$) in patients undergoing cardiac catheterization.

Postulated sources of error with iced injectates include warming of the injectate during infusion and the presence of preexisting warm fluid within the catheter itself (Wong, Skulsky, & Moon, 1978; Kadota, 1986). In addition, previous research has shown a 3-12% error or variability with repeated iced injectates. This is thought to be due to progressive cooling of the catheter with the first injection providing the highest measurement, thus overestimating the averaged CO (Wong et al., 1978; Kadota, 1986). The major manufacturer of cardiac output equipment, American Edwards Laboratories, recommends that the first output determination be discarded (American Edwards Laboratories, 1982).

Volume overload is a potential physiological problem associated with frequent CO determinations using 10 ml injectates. For example, if CO is measured every two hours, averaging three to five determinations and using 10 ml injectates, a total of 360-600 ml of solution would be administered in a 24 hour period. This additional volume cannot be tolerated by patients with high pulmonary artery pressures and low COs. The problem of fluid volume overload

can be minimized by decreasing the injectate volume to 5 ml. However, some researchers have postulated that a reduction in the signal-to-noise ratio with the smaller injectate volume makes it less accurate than the 10 ml volume. The 5 ml volume produces a smaller signal thus allowing for extraneous noise to interfere with the reception and interpretation of the signal (Wessel, James, Grahn & Paul, 1971; Merrick, Hessel, & Dillard, 1980).

Enghoff and Sjogren (1973) reported a 5 ml room temperature NS injectate to be reliable indicator for measuring CO in humans. However, lack of clarity about the method used for comparison and the small sample size (N=4) coupled with the lack of reported correlations, leave the study results open to question. Stawicki et al. (1979) compared COs using both 5 ml room and iced temperature injectates to the Fick method and found a moderate correlation ($r=.638$, $p<.001$) for both methods combined; individual correlations were not reported. Bilfinger et al. (1982) found 8 and 12% differences, respectively, between an in-vitro flowmeter and the thermodilution method using 5 ml room and iced NS injectates.

Thermodilution Determinations in Low Flow States

A low flow state is defined as a CO below 4.0 L/min in human adults (Hurst et al, 1986). The reliability of the thermodilution method in measuring CO has been questioned when CO is below this level. Studies using both human and animal models have shown that the thermodilution method can overestimate CO in low flow states by as much as 35% in comparison to reference methods (Levine & Sirinek, 1981; van Grondelle et al., 1983; Woog & McWilliam, 1983; Dyson, Allen, & McDonnell, 1985). Animal studies using miniature swine and cats utilized 2 ml room and iced temperature D5W injectates (Levine & Sirinek, 1981; Dyson et al., 1985), while human studies utilized 10 ml room and iced temperature D5W injectates (van Grondelle et al., 1983; Woog & McWilliam, 1983). No research could be found that assessed the validity of 5 ml injectates in relation to a reference method in either humans or animals with comparable blood volumes in low flow states. Therefore a study is needed to assess the accuracy and reliability of 5 and 10 ml room and iced temperature injectates at low flow states.

Conceptual Framework

Cardiac output is the volume of blood pumped by the heart within a set period of time and is the product of heart rate and stroke volume (Hurst et al., 1986). Alterations in CO result in either high or low flow states. Reduction in left ventricular contractility and stroke volume result in high pulmonary artery pressures and low CO. This phenomena is characteristically seen in critically ill patients experiencing left ventricular heart failure. Accurate and reliable measurement of the CO is critical in these patients since it is an important physiological indicator from which therapy is determined. Accuracy, or validity, and reliability of the thermodilution method of CO measurement is related to a variety of physiological and technical factors that may result in systematic or random error.

Systematic and Random Error

Two types of measurement error occur with the thermodilution method, systematic and random. Both types of error result from physiological and technical factors that influence the accuracy and reliability of the thermodilution method. Figure 2 offers a schematic representation of the factors that influence the process of obtaining CO measurements.

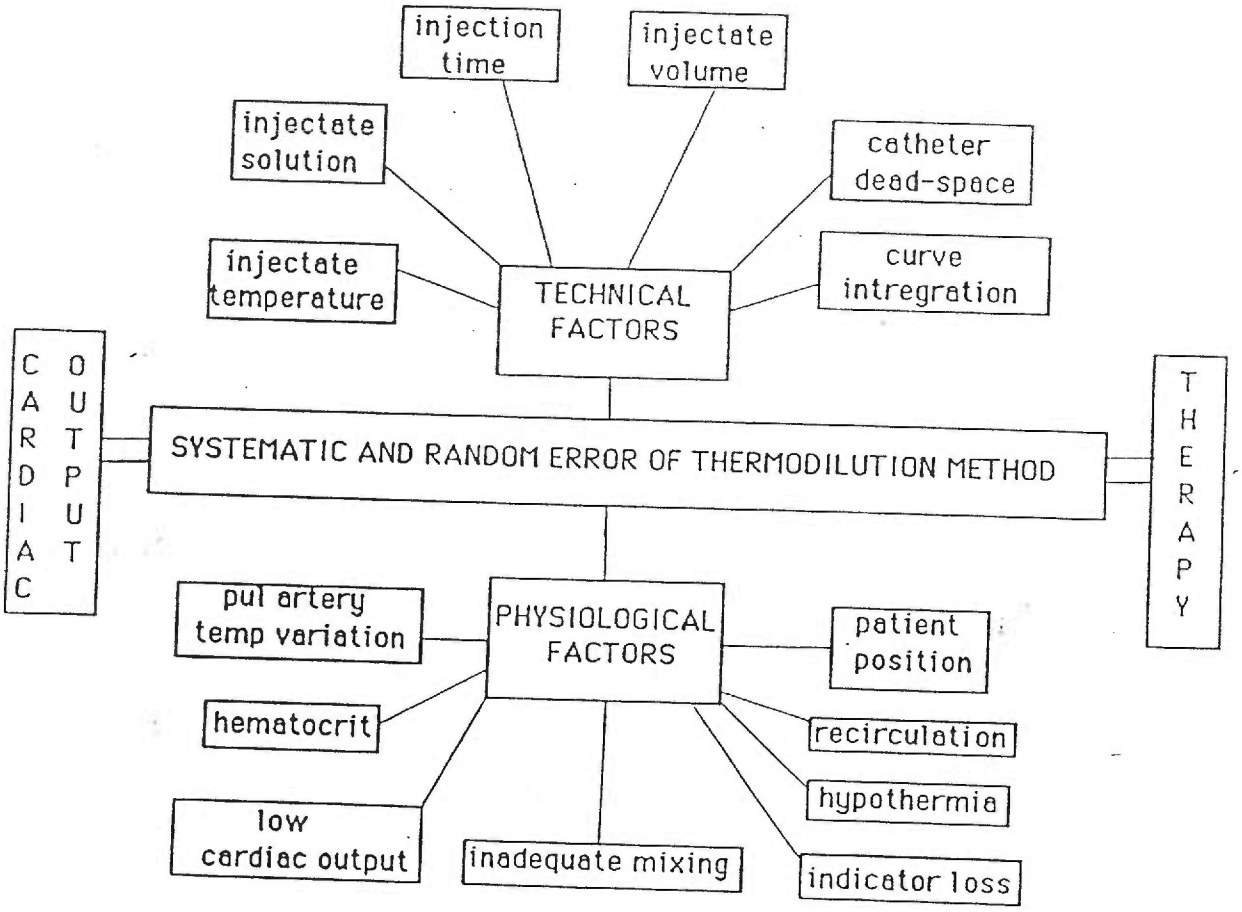

Figure 2. Factors influencing in the reliability and accuracy of the thermodilution method. (Adapted from "Thermodilution Method of Measuring Cardiac Output" by H. Meisner et al., 1974, Annals of Thoracic Surgery, 18, p. 512.)

Systematic error refers to the difference between measurements obtained with the thermodilution method and the reference method to which it is compared and reflects the accuracy of the thermodilution method. The accepted amount of systematic error between the thermodilution and flowmeter methods is approximately 10% within a normal range of CO (San Marco, Philips, Marquez, Hall, & Davlia, 1971; Meisner et al., 1974; Merrick, Hessel, & Dillard, 1980; Bilfinger, Lin, & Anagnostopoulos, 1982). For accuracy in comparing two methods, it is critical that they be measured near simultaneously.

Random error refers to variations that occur within the thermodilution method itself and reflects the reliability of the method. In obtaining a thermodilution CO, the results of a series of three measurements are averaged to derive the stated output value. The repeated individual values are never exactly the same, and random error refers to the amount of difference between them. The accepted range of difference for a series of three thermodilution measurements is between 4 and 10% (Stetz, Miller, Kelly, & Raffin, 1982; Weil, 1982).

Physiological Factors

Pulmonary artery temperature fluctuations. Physiological factors that produce error may be especially relevant in low

flow states. One of the most significant physiological sources of error is the normal fluctuations in pulmonary artery temperature. The variation of 0.02-0.05 °C that occurs with inspiration and pulsatile blood flow produces a fluctuation in the baseline of the CO curve, resulting in a 1-8% error in the output determination with a normal CO range (Andreen, 1974). The fluctuations in pulmonary artery temperature have a greater effect in low flow states because of slowed pulmonary blood flow and an increased number of respiratory cycles during the prolonged CO determination. Additionally, the 1-8% error has a more significant effect with a low CO. When CO is within the normal range, a 5% error is clinically insignificant; while at lower COs, 5% represents a clinically significant change. To overcome this baseline variation, often referred to as physiologic noise, investigators have recommended the use of a large volume of cold injectate or indicator in order to increase the signal-to-noise ratio (Ganz, Donoso, Marcus, Forrester, & Swan, 1971; Ganz & Swan, 1972; Forrester et al., 1972). Woog and McWilliam (1983) identified reduced systematic and random error for an iced 10 ml D5W injectate when compared to the same volume of room temperature injectate, with dye dilution as the reference method. Additionally, newer CO computers

(Ganz & Swan; 1972; Meisner et al., 1974). Indicator loss decreases the denominator of the equation, thereby overestimating the CO (Woog & McWilliam, 1983; van Grondelle et al., 1983). One could speculate that the use of room temperature injectates would produce less indicator loss in low flow states and thus produce a more reliable CO value. This did not occur, however, in Woog and McWilliam's (1983) research that demonstrated greater systematic and random error with room temperature injectates.

Recirculation of indicator. Recirculation of the indicator occurs when the surrounding pulmonary parenchyma is cooled by the injectate. This produces a reversible temperature change at the distal thermistor that lasts approximately 75 seconds with normal CO (Meisner et al., 1974). Because of the limited number of studies done with low CO, the effect of recirculation in low flow states is unknown. However, the recirculation effect is reduced with the use of room temperature injectates (Levett & Replogle, 1979).

Other physiological factors. Hypothermia and body position are other physiological factors that also affect CO determinations. Hypothermia influences the temperature difference between the indicator solution and the blood thus reducing the signal-to-noise ratio (Kohanna & Cunningham,

1976). While back rest positions do not influence CO determinations, lateral body positioning is thought to affect the reproducibility of serial output measurements (Grose, Woods, & Laurent, 1981; Whitman, Howaniak, & Verga, 1982; Kleven, 1984; Doering & Dracup, 1988).

A final physiologic factor that can affect the accuracy of the thermodilution method is cell content of the blood, or the hematocrit. Calculations using the Stewart-Hamilton equation are based on the specific heat of blood with a hematocrit of 42% (Andreen, 1974). Reduction in the hematocrit level to 30% will reduce the specific heat of the blood and produce a 1% systematic error in the cardiac output calculations (Andreen, 1974; Meisner et al., 1974).

Technical Factors

In normal CO states, the most significant sources of error in the thermodilution method are found with the technical factors (C. Smith, personal communication, August 19, 1988).[1] Recommendations regarding technique, including iced injectates, rapid injection times, limited handling of the injectate syringes, and a series of three measurements one minute apart, are employed to reduce some of the technical

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1. Personal communication with C. Smith, Products Manager, American Edwards Laboratory, Santa Ana, CA.

error. The use of an in-line thermistor which senses the indicator temperature just proximal to the injectate port increases the overall accuracy of the thermodilution method. Other technical factors such as curve integration, computer accuracy, and the computation of the algorithm are not controlled by technique but continues to influence the thermodilution method.

Curve integration. Accuracy in the computer calculation of CO is dependent upon the quality of the output curve. Because of reduced blood velocity in low flow states, the CO curve is increased in duration. Smaller injectate volumes may produce a lower amplitude curve which may result in a poorer quality of curve (Levett & Replogle, 1979). Additionally, baseline variability secondary to pulmonary artery temperature fluctuations can produce irregularities in the thermodilution curve (Andreen, 1974). The newer thermodilution CO computers account for this fluctuation by averaging the blood temperature variations prior to injection (Runciman, Ilsley, & Roberts, 1981b).

Catheter deadspace. Catheter deadspace refers to the fluid that is present within the catheter. This represents a 0.35 ml volume of warm fluid for a 7-French gauge catheter (Levett & Replogle, 1979). Deadspace volume has a greater

effect when smaller volumes and or iced injectates are used. All CO computers take this variation into account by employing a computation constant based on the injectate temperature, volume, and type of catheter used. However, error has been demonstrated with serial iced injectates due to progressive cooling of the catheter, producing an overestimation of CO of 3-12% in normal CO (Wong, Skulsky, & Moon, 1978; Kadota, 1986). Whether this occurs in low flow states has not been examined.

Thermodilution injectate temperature, solution, volume. Several sources of technical error are present in the injectate itself. Within the context of normal CO, 5 ml and 10 ml, room and iced temperature thermodilution injectates have been examined for systematic and random error. Conflicting results exist as to the amount of systematic error for 10 ml volumes in normal CO states. When comparing room and iced temperature injectates, Daily and Mersch (1986) found higher correlations, and thus less systematic error, with room temperature NS injectates when compared to the Fick method. Other studies, however, have found iced 10 ml D5W injectates to be the more valid indicator (Hodges, Downs, & Mitchell, 1975; Stawicki et al., 1979; Hoel, 1978). Del Gizzi and Ward (1988) found that a 10 ml room temperature D5W injectate had

thermodilution results with indicator dye method in low flow states. Both of these studies, however, used only 10 ml iced D5W injectates.

The presence of random error has been examined in normal flow states. Daily and Mersch (1986) found that 10 ml room temperature NS injectate produced a greater standard deviation, thus more random error, than did the iced injectates of the same volume. Similarly, Del Gizzi and Ward (1988) demonstrated that 5 ml room temperature D5W injectates produced greater random error when compared to 10 ml room temperature results.

Limited data are available about the random error present with the thermodilution method of determining CO in low flow states. Woog and McWilliam (1983) found greater random error with room temperature injectates of 10 ml D5W in comparison to the results with similar volume iced injectates.

In summary, while a 10 ml iced injectate appears to provide the most reliable measurement of CO at normal flows, that is the least amount of random error, it is unclear what volume and temperature of injectate provides the most accurate values, that is the least amount of systematic error. Within the context of low flow states, inadequate research has been done regarding varying types of injectates. It has been

the CO measurement in low flow states obtained by the thermodilution method correlate better with the value obtained by flowmeter when a room or iced temperature injectate was used? (c) Was the variability of repeated measures affected by the use of 5 ml and 10 ml volumes of room and iced temperature injectates in low flow states?

normal, high-normal range, and low CO levels. Flowmeter measures were obtained simultaneously with each thermodilution CO.

Subject

Data were collected from a single preinstrumented ewe weighing approximately 70 kg at the Heart Research Laboratory at Oregon Health Sciences University. The ewe was housed and cared for according to the National Institutes of Health guidelines for animal care (1988) with controlled temperature, humidity, and light cycles. The rationale for using this animal model was twofold. First, an animal model allowed manipulation of the venous return to induce a controlled CO and produce low, normal, and high-normal flow states. Second, an adult sheep's cardiac output normally ranges from 5.0-7.0 L/min, which is similar to that of humans, thus making research findings regarding CO measurements comparable (Stowe & Good, 1961; Rosenfield, 1977). In that myocardial hypertrophy had been induced by prior testing of this subject, higher than normal COs were present. Thus, the range of CO in this study was extended to 8.5 L/min in order to include the entire normal CO range for the subject. Other researchers have used miniature swine and cats to test the accuracy of thermodilution methods in low CO states, but because of the

size of the animals, were restricted to 1-2 ml injectate volumes (Levine & Sirinek, 1981; Dyson, McDonnell, & Horne, 1983; Dyson, Allen, & McDonnell, 1985). With a sheep model, use of 5 ml and 10 ml injectates was possible.

The research ewe was preinstrumented with an ascending aortic flow transducer. Stroke volume, as measured by the flow transducer, and heart rate were recorded on a strip recorder. An arterial pressure catheter had also been placed in the aorta. In addition, a C-shaped balloon had been placed around the inferior vena cava which, upon inflation, reduced venous return to the right heart, thereby reducing CO. The ewe was medicated intravenously with 30 mg propranolol and 16 mg atropine sulfate to minimize sympathetic and parasympathetic effects on the heart in response to CO manipulation. Propanolol was administered prior to the initiation of data collection. Atropine sulfate was administered prior to each injectate trial.

Instruments

Procedural consistency was maintained through the use of standardized equipment. All thermodilution measurements were made using an American Edwards #93A-131H-7-F Swan-Ganz^{R} flow-directed thermodilution catheter and the COM-1 analogue cardiac output computer (American Edwards, Santa Ana, CA).

Validity of the computer has been established by American Edwards. Clinical testing of the COM-1 computer demonstrated 9.6% variability from the reference method along with ±2% variability in repeated measures when used with 5 ml and 10 ml injectates of D5W at room and iced temperatures (C. Smith, personal communication, August 19, 1988). A strip chart recorder (Gould-Statham, Hato Rey, Puerto Rico) was used to document adequate thermodilution output curves. The occlusive balloon (In Vivo Metrics Systems, Heraldsburg, CA) placed around the inferior vena cava (IVC) was employed to impede venous return, thereby reducing the CO to desired levels. An ascending aortic flowmeter transducer (In Vivo Metrics Systems, Heraldsburg, CA) connected to a flowmeter (Gould-Statham, Hato Rey, Puerto Rico) determined the reference CO values to which the thermodilution results were compared (Tetirick & Mengoli, 1963).

Prior to implantation, the flowmeter was calibrated with high and low flow rates of normal saline. The survival rates for flowmeters after implantation vary from three to six months (In Vivo Metrics Systems, Heraldsburg, CA). The flowmeter used in this study had been implanted for eleven weeks. After implantation, consistency of the ratio between the flowmeter and a thermodilution measure using 10 ml iced

D5W injectate was periodically checked to demonstrate continued reliability. For this study, a variation within 15% between these two measures was considered acceptable. The flowmeter has been shown to be a valid measure of CO when chronically implanted an animal (Sellers & Dobson, 1967). In addition, correlations of r=.97-.98 have been reported in dogs and calves between the flowmeter and thermodilution methods of CO measurement for both the normal and low CO ranges; injectates varied from volumes of 3, 5, and 10 ml of either NS or D5W for both room and iced temperatures (San Marco, Philips, Marquez, Hall, & Davlia, 1971). The accepted amount of variation between the results from flowmeter and thermodilution methods has shown to be approximately 10% (San Marco, Philips, Marquez, Hall, & Davlia, 1971; Meisner et al., 1974; Merrick, Hessel, & Dillard, 1980; Bilfinger, Lin, & Anagnostopoulos, 1982). In this study, the flowmeter was also used to verify the reduction of CO achieved through inflation of the IVC balloon.

Prefilled 10 ml syringes with 5 ml and 10 ml volumes were measured with a gram scale to the nearest 0.1 gram to ensure consistency of injectate volume by weighing each syringe before and after filling. Sets of three syringes containing

5 ml or 10 ml were kept at either room temperature (21.6 ^{o}C) or enclosed in plastic and immersed in an iced bath (0.0 ^{o}C) for at least one hour prior to testing. Ice was added to the bath as needed and additional filled syringes were available.

Sterile D5W was used as the injectate solution. This was done in compliance with the assumptions of the Stewart-Hamilton equation, which is based on the specific heat and density of D5W (Pool et al., 1970; Swan et al., 1971). To minimize variability, all injections were performed manually by the same investigator and within a 2-4 second period (Ganz & Swan, 1972). In order to prevent warming of the injectate that can result in a 6-12% error in the CO, handling of the syringes was kept to less than 30 seconds (Powner, 1975; Levett & Replogle, 1979).

To measure injectate temperature, the in-line injectate temperature probe of the COM-1 cardiac output computer was used. When connected at the injectate port, this thermistor sensed the injectate temperature just prior to entering the pulmonary artery catheter. Upon completion of data collection, accuracy of the in-line thermistor was tested using both room (21.6 ^{o}C) and iced (0 ^{oC}) temperature solutions while the pulmonary artery catheter thermistor was tested by measuring room temperature solution. Both

thermistors demonstrated accurate temperature sensing when compared to values obtained with an Omega Fastemp ambient thermometer (Omega Engineering Inc., Stamford, CT).

Data Collection Procedure

The ewe was placed in a stanchion cart to prevent free movement. Maintaining minimal activity in an upright weight bearing position assured a steady cardiac output. After locally anesthetizing the insertion site with 1-2 ml of 1% lidocaine, a standard 7-French flow directed pulmonary artery catheter (American Edwards, Santa Ana, CA) was placed by the investigators via the external jugular vein. The proximal injectate port was positioned in the right atrium and the distal tip positioned in the pulmonary artery, as verified by the appropriate waveforms (Ellis, Gold, Rees, & Lillehei, 1972). An open injectate system was connected to the proximal injectate hub. The COM-1 in-line temperature probe was connected to the injectate port.

All thermodilution measurements of CO were calculated by the American Edwards COM-1 standard analogue output computer. Additionally, all CO curves were documented by a strip chart recorder and inspected for technical accuracy, including the presence of a rapid upslope and a smooth downslope to the curve (Fig. 3).

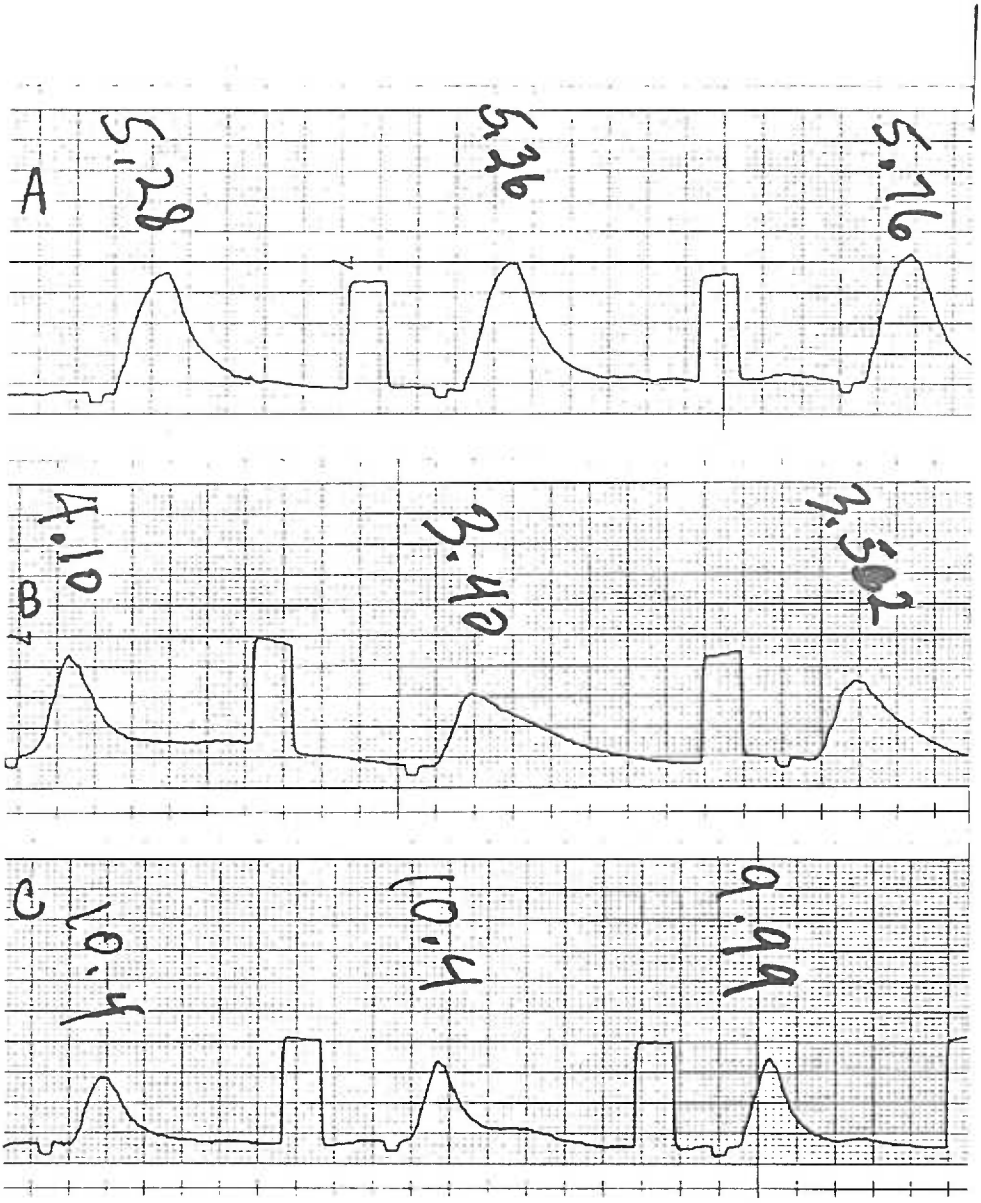

Figure 3. Examples of a (A) normal, (B) low, and (C) high-normal thermodilution curves demonstrating rapid upslopes and a smooth downslopes. Thermodilution CO values obtained from the digital display of the COM-1 CO computer.

Because of the ewe's rapid respiratory rate of 120 breaths per minute, the injections could not be timed in conjunction with end-expiration. Because of this, the injections were bolused randomly during the ewe's respiratory cycle.

A single thermodilution measure of CO consisted of a bolus of one of the four injectates. The recommended 1 minute interval between injections, which allows for removal of the cool injectate from the pulmonary vessels (Meisner et al., 1974; Daily & Mersch, 1987), was waived because the ewe would not withstand a 3 minute period at very low COs. In order to maintain consistency of procedure, all COs were determined in rapid sequence with the time interval between injections only as long as needed to allow the thermodilution computer to calculate the output, which approximated 20 seconds. During this interval, the strip chart recorder provided visual verification of the output curve. The flowmeter measures of $\dot{C}O$ were obtained at the initiation of each thermodilution injection over a four second period.

The range of CO measured in this study was approximately 2.0-8.5 L/min. Decreased levels of COs within the range of 2.0-7.0 L/min were induced by inflating the IVC balloon. Again, the rationale for obtaining normal and high-normal CO

data was to provide sufficient data to correlate the thermodilution and the flowmeter measurements. This allowed any deviation between the two measures at low COs to be easily identified.

Data collection began at 1300 hours after insertion of the pulmonary artery catheter, connection of the aortic pressure line to the transducer, and calibration of the flowmeter. The initial injectate to be tested was the 10 ml iced solution. Using triplicate measures with 10 ml iced injectates, 11 sets of triplicate COs at varying levels. However, secondary to technical problems, one set of measures was deleted. After determining the ewe's normal CO using 10 ml iced injectate, randomly determined but varied levels of low CO were measured with this injectate. The process began with the inflation of the IVC balloon to create the low CO. This was followed by three rapidly determined thermodilution and flowmeter measures. Immediately after obtaining the data for the third injection, the IVC balloon was deflated and normal CO was restored. Upon completion of each series of three measures at low COs, a five minute period was allotted to monitor the ewe for restoration of normal CO. Throughout the data collection at low flow states, the ewe was closely

monitored for loss of motor function and physical collapse characteristically seen with inadequate CO.

The three remaining injectates were randomly sequenced by the toss of a coin prior to data collection. The initial 10 ml iced injectate was followed by the 5 ml iced solution, then the 5 ml room temperature solution, and finally the 10 ml room temperature solution. All four injectates were tested using the same protocol. Table 1 summarizes the sequence of data collection and the number of measurement series for each injectate.

The total volume of fluid administered during data collection was approximately 1350 ml over a 4 hour period. Considering that the normal blood volume for a 70 kg ewe approximates 4000-5000 ml (Hansard, Butler, Comar, & Hobbs, 1953), this amount of fluid was compatible with the ewe's cardiovascular tolerance. Upon completion of the four trials, the pulmonary artery catheter was removed, all invasive monitoring devices disconnected, and the ewe returned to its pen.

Protection of the Subject

In accordance with the standards of the National Institutes of Health (1988), the ewe was housed in a 20 ft^2 pen that permitted freedom of movement and normal posture,

Table 1

Sequence of Injectates and Number of Triplicate Thermodilution and Flowmeter measures at CO levels of 2.0-8.5 L/min

Order of Testing	Injectate Volume	Injectate Temperature	Series of Triplicate Measures
1	10 ml	iced	10
2	5 ml	iced	11
3	5 ml	room	11
4	10 ml	room	11

with bedding of straw or shredded newsprint. Ambient temperature was maintained at 18-29 ^{o}C, with fresh air circulated from the outside. The humidity was that of the outside air, approximately 30-70%. The lighting cycle was 16 hours of light (0600-2200) and 8 hours of darkness (2200-0600). The ewe had free access to hay and water which were placed in metal feeders elevated off the floor (National Institutes of Health, 1988). During the actual data collection period, the ewe was not fed because of the possibility of interfering with the steady state CO.

Prior authorization from the Animal Subjects Committee was obtained by the primary investigator from the Heart Research Laboratory for the instrumentation previously implanted. Authorization for the additional procedures in this study was obtained by the investigators. Throughout the data collection period, arterial pressure, heart rate, and rapidity of recovery from reduced CO was monitored to ensure the ewe's cardiovascular stability. When the one incidence of cardiovascular instability occurred during a period of low CO, as manifested by near loss of motor function, data collection procedures were stopped, the IVC balloon deflated, and resuscitative measures were performed via administration of intravenous fluid and isoproterenol.

Analysis

To answer the research questions, a two part analysis was conducted examining systematic and random error of the thermodilution results. The data were analyzed using the Crunch Statistical Package, Version 3 (Crunch Software Corporation, Oakland, CA).

The initial analysis examined the systematic error for each injectate. This was achieved by correlating the thermodilution results with those obtained from the flowmeter. Lines of regression were calculated for each of the four injectates, comparing the thermodilution and flowmeter measures at varying levels of CO (McCall, 1986; Phillips, 1978). The injectate that had the highest correlation with the results from the flowmeter was judged to have the least amount of systematic error and thus to provide the most accurate thermodilution CO measurement at a given level of CO.

The second part of data analysis defined the random error for each of the four injectates. This was achieved through the use of analysis of co-variance (ANCOVA). For each set of triplicate measures, the mean and standard deviation for both thermodilution and flowmeter measures were calculated. Standard deviations for thermodilution and flowmeter measures for each injectate were then compared using ANCOVA and the

Tukey-A post hoc test. The injectate with the least amount of variation when compared with the flowmeter results was judged to have the least amount of random error and thus presumed most reliable.

CHAPTER III

RESULTS

The accuracy of the thermodilution CO method was determined by correlating results to those obtained by flowmeter. Correlations for the 129 thermodilution and flowmeter measures at CO levels ranging from 2.0-8.0 L/min are summarized in Table 2. In the low CO range of 2.0-4.65 L/min, 9-11 measures were made for each injectate. Correlations between the thermodilution and flowmeter measurements at low COs were consistently high for all four injectates (r=.92-.99), with the 5 ml iced solution having the highest value. Over the entire range of CO tested, however, the 10 ml iced injectate provided measurements with the highest correlation (r=.98). An incidental finding showed that correlations between the thermodilution and flowmeter measures decreased with increasing levels of CO to the extent that all four injectates provided much lower correlations when the CO exceeded 6.50 L/min (r=-.20 to .70), with the 10 ml iced injectate providing the highest correlation.

Reliability was assessed by comparing the standard deviations of triplicate thermodilution and flowmeter results. This was achieved through the use of ANCOVA with the flowmeter

Table 2

Correlations of Flowmeter and Thermodilution Measures of CO

Cardiac Output L/min	Iced Temperature		Room Temperature	
	10 ml	5 ml	10 ml	5 ml
2.00-8.50	.9797*** (n=30)	.9460*** (n=33)	.9428*** (n=33)	.9479*** (n=33)
2.00-4.65	.9181** (n=9)	.9889*** (n=9)	.9759*** (n=10)	.9744*** (n=11)
4.66-6.50	.9140** (n=8)	.6713* (n=15)	.8104** (n=14)	.1383 (n=4)
6.51-8.50	.6996* (n=13)	-.1970 (n=9)	.1133 (n=8)	.5836* (n=17)

***p<.00001 **p<.0005 *p<.01
n= number of paired measures

results as the co-variate. Comparison of the standard deviations from the thermodilution measurements for the four injectates to the those of flowmeter method revealed no statistically significant differences when analyzed by ANCOVA and the Tukey-A post hoc test. The 10 ml iced injectate showed the least amount of variation from the flowmeter (Table 3). Thus all four injectates proved to be reliable measures within the range of CO tested.

Analysis of variance revealed a significant 23% difference in the mean CO values between the first and third injections in the series of triplicate measures. The statistically significant variation ($p<.05$) between the measures was not evident between the first and third flowmeter results.

Table 3

Comparisons of the Mean Standard Deviation for Triplicate Thermodilution Measures with Flowmeter Measures as Co-variate

Injectate	Mean Standard Deviation	p Value
10 ml iced	0.268	NS
5 ml iced	0.349	NS
10 ml room	0.408	NS
5 ml room	0.446	NS

NS=not significant

CHAPTER IV

DISCUSSION

The results of this study indicate that the thermodilution method of CO determination is accurate within the range of 2.0-8.5 L/min. For data analysis, 4.65 L/min was selected as the upper end of the low CO range, the rationale being that a CO of 4.65 L/min when divided by a hypothetical standard BSA of 2.0 m^2 results in a low CI level. Within the range of 2.0-4.65 L/min, all four injectates tested demonstrated very high correlations and thus were highly accurate. The 10 ml iced injectate, however, had a statistically lower correlation ($p<.0005$) than the other three injectates ($p<.00001$). However, this small difference has no clinical implications. Because of the accuracy demonstrated by all four injectates, the clinical decision as to which injectate to use in low flow states may be predicated on other concerns such as patient tolerance of additional volume administration.

Inasmuch as all four injectates had very high correlations with the flowmeter, perhaps the postulated physiological sources of error did not influence the accuracy of the thermodilution technique at low flow states. Pulmonary artery temperature fluctuations, inadequate mixing, and loss of indicator may not

influence low CO determinations as previously speculated in earlier research.

Over the entire range of CO tested, the 10 ml iced injectate was a better indicator. An incidental finding demonstrated that COs of 4.66-6.50 L/min, or normal range of CO, both room and iced temperature 10 ml injectates were the most accurate. Additionally, when CO exceeded 6.51 L/min, all injectates had moderate to poor correlations. However, there was uneven distribution of CO levels when testing the 5 ml room temperature injectates. There were four CO determinations done within the range of 4.66-6.50 L/min and 17 determinations between 6.51-8.50 L/min. Because of the skewed distribution, one must question the validity of the correlations obtained for these two levels. In this study, no single injectate was most accurate over the entire range of CO tested.

This study also demonstrated adequate reliability of the thermodilution method. There was minimal difference between the standard deviations of triplicate thermodilution measures when compared to the flowmeter results. All four injectates then, provided reliable measures of CO. This may also indicate that the clinically noted variability in thermodilution results may be due to physiologic variability rather than to the methodology of the thermodilution technique.

The high degree of accuracy and reliability demonstrated in this study also points to the importance of consistent technique. Without technical consistency, the results from the thermodilution method of CO measurement would be questionable.

Limitations

There are several limitations to this study including the use of a single animal subject. The single ewe, although having hemodynamic responses and blood volume similar to humans, may not reflect the actual human condition. However, it would be unethical to perform this study in humans. In addition, a hypovolemia model was used to create a state of low CO rather than the more common clinical presentation of left ventricular dysfunction resulting in high pulmonary artery pressures. Upon autopsy examination of the subject's heart, there was evidence of left ventricular hypertrophy secondary to partial aortic occlusion from a prior study conducted on this animal. Left ventricular dysfunction, however, was not evident at the time of this study in that the subject's pulmonary artery pressures were not elevated and the CO was higher than normal.

The pharmacologic control of sympathetic and parasympathetic response to alterations of CO do not reflect actual clinical practice. However, inducing a relatively constant heart rate ensured consistent diastolic filling time and

thus stoke volume. This prevented gross alterations in CO secondary to heart rate and stroke volume changes.

The limited number of low flow thermodilution and flowmeter measures also could have influenced the results. The 10 ml iced injectate provided the highest correlations at all CO levels except at low flows. Because of the limited number of low flow determinations, the lower correlation obtained for the 10 ml iced injectate could be questioned. However, the correlations within the low CO range were all very high for all four injectates.

The small number of CO determinations for the 5 ml room temperature injectate over the range of 4.66-8.5 L/min probably influenced the correlation values obtained. Because of this, one must question the results obtained from this injectate.

Clinical Implications

Because no single injectate was consistently most accurate over the range of CO tested, recommending one injectate for determining CO at various flow states may not be appropriate. Selection of the injectate should be predicated on using the volume and temperature with the least amount of error associated with various flow states. The indicator is then tailored to the CO. Because all four injectates proved to be reliable, the selection of which injectate to use should be based on accuracy.

Although the 5 ml iced injectate provided a slightly higher correlation at low flow states, the difference in the correlations of all four injectates was very small and probably clinically insignificant. The use of a smaller volume injectate may be satisfactory and preferable in patients with low COs who are volume restricted.

The use of either room or iced temperature 10 ml injectates is probably appropriate for patients with normal COs. However, when the CO exceeds 6.50 L/min, the 10 ml iced injectate may be the most accurate indicator to use.

Recommendations for Future Study

Replication of this study is warranted because of the single animal subject and the limited numbers of low CO determinations. Verification of these findings is necessary to provide a basis for changing clinical practice. Because of the incidental findings at high-normal CO levels, additional research examining thermodilution CO measurements in high flow states is warranted. Additionally, the accuracy and reliability of the thermodilution method during periods of altered stroke volume and blood viscosity, such that occurs with large volume fluid resuscitation, is indicated. Finally, replication of this study in another animal model such as swine or primates with comparable blood volume and hemodynamics to humans, may be warranted.

Summary

This study asked the question which combination of 5 and 10 ml, room and iced temperature injectate was most accurate and reliable when measuring CO using the thermodilution method. Although a large range of COs were tested, this study focused on low COs. The results indicated that no one injectate was most accurate over the entire range tested, but all four injectates were reliable. At the low levels of CO, all four injectates were consistently accurate. In the clinical setting when patients with low COs are fluid restricted, the use of a smaller volume thermodilution injectate would be satisfactory and preferable in this situation.

References

American Hospital Formulary Service. (1986). Drug Information 86. Bethesda: American Society of Hospital Pharmacists.

Andreen, M. (1974). Computerized measurement of cardiac output by thermodilution: Methodological aspects. Acta Anaesthesia Scandinavia, 18, 297-305.

American Edwards Laboratories. (1982). Understanding hemodynamic measurements made with the Swan-Ganz catheter. Santa Ana, CA.: American Edwards Laboratories.

Bilfinger, T. V., Lin, C. Y., & Anagnostopoulos, C.E. (1982). In vitro determination of accuracy of cardiac output measurements by Thermal Dilution. Journal of Surgical Research, 33, 409-414.

Branthwaite, M. A., & Bradley, R. D. (1968). Measurement of cardiac output by thermal dilution man. Journal of Applied Physiology, 24(3), 434-438.

Cromwell, L., Weibel, F. J., & Pfeiffer, E. A. (1980). Cardiovascular measurements. In Biomedical instrumentation and measurements (2nd ed., pp. 105-172). Englewood Cliffs: Prentice-Hall.

Daily, E. K., & Mersch, J. (1987). Thermodilution cardiac outputs using room temperature and ice temperature injectate: Comparison with the Fick method. Heart and Lung, 16, 294-300.

Daily, E. K., & Schroeder, J. S. (1985). Techniques in bedside hemodynamic monitoring. St. Louis: C.V. Mosby Company.

De Alsa, R. A., & Smith, R. N. (1981). The critical care environment: Instrumentation. In Kinney, M. R., Dear, C. B., Packa, D. R., & Voorman, D. M. N. (Eds.). AACN's clinical reference for critical-care nursing (pp. 1021-1025). New York: McGraw-Hill Book Company.

Del Gizzi, L. & Ward, C. R. (1988). In-vitro determination of the effects of varying room temperature injectate volume on thermodilution cardiac output [Abstract]. Proceedings of the 1988 National Teaching Institute (p. 683). Newport Beach: American Association of Critical Care Nurses.

Doering, L., & Dracup, K. (1988). Comparison of cardiac output in supine and lateral position. Nursing Research, 37, 114-118.

Dyson, D. H., McDonell, W. N., & Horne, J. A. (1984). Accuracy of thermodilution measurement of cardiac output in low flows applicable to feline and small canine patients. Canadian Journal of Comparative Medicine, 48, 425-427.

Dyson, D. H., Allen, D. G., & McDonell, W. N. (1985). Comparison of three methods for cardiac output determination in cats. American Journal of Veterinary Research, 46(12), 2546-2552.

Elkayam, U., Berkley, B. A., Azen, S., Weber, L., Geva, B., & Henry, W. L. (1983). Cardiac output by thermodilution technique: Effect of injectate's volume and temperature on accuracy and reproducibility in the critically ill patient. Chest, 84(4), 418-422.

Enghoff, E., & Sjogren, S. (1973). Thermal dilution for measurement of cardiac output in the pulmonary artery in man in relation to choice of indicator volume and injection time. Upsala Journal of Medical Science, 78, 33-37.

Ellis, R. J., Gold, J., Rees, J. R., & Lillehei, C. W. (1972). Computerized monitoring of cardiac output by thermal dilution. Journal of the American Medical Association, 220, 507-511.

Fegler, G. (1954). Measurement of cardiac output in anesthetized animals by a thermo-dilution method. Quarterly Journal of Experimental Physiology, 39, 153-164.

Fischer, A. P., Benis, A. B., Jurado, R. A., Seeley, E., Teirstein, P., & Litwak, R. S. (1978). Analysis of errors in measurement of cardiac output by simultaneous dye and thermal dilution in cardiothoracic surgical patients. Cardiovascular Research, 12, 10-199.

Ganz, W., Donoso, R., Marais, H. S., Forrester, J. S., & Swan, H. J. C. (1971). A new technique for measurement of cardiac output by thermodilution in man. The American Journal of Cardiology, 27, 392-396.

Ganz, W., & Swan, H. J. C. (1972). Measurement of blood flow by thermodilution. The American Journal of Cardiology, 29, 241-246.

Grose, L., Adair, M., & Reim, M. (1981). Incidence of contamination of thermodilution cardiac output bath. [Abstract]. Circulation, 64, IV-179.

Grose, L., Woods, S. L., & Laurent, D. J. (1981). Effect of backrest position on cardiac output measured by the thermodilution method in acutely ill patients. Heart and Lung, 10(4), 661-665.

Guyton, A. C., Jones, C. E., & Coleman, T. G. (1973) Circulatory physiology: Cardiac output and its regulation. Philadelphia: W.B. Saunders Company.

Hansard, F. L., Butler, W. O., Comar, C. L., & Hobbs, C. S. (1953). Animal Science, 12, 402.

Hodges, M., Downs, J. B., & Mitchell, L. A. (1975). Thermodilution and Fick cardiac index determinations following cardiac surgery. Critical Care Medicine, 3(5), 182-184.

Hurst, J. W., Logue, R. B., Rackley, C. E., Schlant, R. C., Sonnenblick, E. H., Wallace, A. G., & Wenger, N. K. (1986). The heart (p. 51). New York: McGraw-Hill Book Company.

Kadota, L. (1986). Reproducibility of thermodilution cardiac output measurements. Heart and Lung, 15, 618-622.

Killpack, A. K., Davidson, L. J., Woods, S. L., & Grose, B. L. (1981). Effect of injectate volume and temperature on measurement of thermodilution cardiac output in acutely ill patients. [Abstract]. Circulation, 64, IV-165.

Kleven, M. (1984). Effect of backrest position on thermodilution cardiac output in critically ill patients receiving mechanical ventilation with positive end-expiratory pressure. Heart and Lung, 13(3), 303-304.

Kohanna, F. H., & Cunningham, J. N. (1977). Monitoring of cardiac output by thermodilution after open heart surgery. The Journal of Thoracic and Cardiovascular Surgery, 73(3), 451-457.

Larson, C. A., & Woods, S. L. (1982). Effect of injectate volume and temperature on thermodilution cardiac output measurement in acutely ill adults [Abstract]. Circulation, 66 (Supplement II), II-98.

Levett, J.M., & Replogle, R.L. (1979). Thermodilution cardiac output: A critical analysis and review of the literature. Journal of Surgical Research, 27, 392-40.

Levine, B. A., & Sirinek, K. R. (1981). Cardiac output determination by thermodilution technique: The method of choice in low flow states. Proceedings of the Society For Experimental Biology and Medicine, 167, 279-283.

McCall, R. B. (1986). Fundamental statistics for behavioral sciences (pp.64-95, 286-313). San Diego: Harcourt Brace Jovanovich Company.

Merrick, S. H., Hessel, E. A., & Dillard, D. H. (1980). Determination of cardiac output by thermodilution during hypothermia. American Journal of Cardiology, 46, 419-422.

Meisner, H., Hagl, S., Heimisch, W., Mayr, N., Mendler, N., Struck, E., Walther, V., & Sebening, F. (1974). Evaluation of the thermodilution method for measurement of cardiac output after open-heart surgery. Annals of Thoracic Surgery, 18, 504-515.

National Institutes of Health. (1988). Guide for the care and use of laboratory animals (NIH Publication No. 86-23). Washington, DC: U. S. Government Printing Office.

Norris, S. L., King, E. G., Grace, M., & Weir, B. (1986). Thermodilution cardiac output--an in-vitro model of low flow states. Critical Care Medicine, 14(1), 57-59.

Pearl, R. G., Rosenthal, M. H., Nielson, L., Ashton, J. P. A., & Brown, W. Jr. (1986). Effect of injectate volume and temperature on thermodilution cardiac output. Anesthesiology, 64, 798-801.

Phillips, D.S. (1978). Basic statistics for health science students (p. 91). San Francisco: W.H. Freeman Company.

Pool, B. O. J., Vandermoten, P., Varnauskas, E., & Wassen, R. (1970). Validity and reproducibility of determination of cardiac output by thermodilution in man. Cardiology, 55, 136-148.

Powner, D. L. (1975). Thermodilution technic for cardiac output. (1975). New England Journal of Medicine, 293, 1004.

Reidinger, M. S., & Shellock, F. G. (1984). Technical aspects of the thermodilution method for measuring cardiac output. Heart and Lung, 13, 211-215.

Rosenfeld, C. R. (1977). Distribution of cardiac output in ovine pregnancy. American Journal of Physiology, 223(3), H231-235.

Runciman, W. B., Ilsley, A. H., & Roberts, J. G. (1981a). Thermodilution cardiac output--a systematic error. Anaesthesia Intensive Care, 9(2), 135-139.

Runciman, W. B., Illsley, A. H., & Roberts, J. G. (1981b). An evaluation of thermodilution cardiac output measurement, using the Swan-Ganz catheter. Anaesthesia Intensive Care, 9, 208-220.

Sanmarco, M. E., Philips, C. M., Hall, C., & Davila, J. C. (1971). Measurement of cardiac output by thermal dilution. American Journal of Cardiology, 28, 54-58.

Sellers, A. F. & Dobson, A. (1967). Some applications and limitations of electromagnetic flowmeters. Gastroenterology, 52(2), 374-379.

Venkataraman, K., De Guzman, M. C., Khan, A. H., & Haywood, L. J. (1976). Cardiac output measurement: A comparison of direct Fick, dye dilution and thermodilution methods in stable and acutely ill patients. Journal of the National Medical Association, 68, 281-284.

Vennix, C. L., Nelson, D. H., & Pierpoint, G. L. (1984). Thermodilution cardiac output in critically ill patients: Comparison of room temperature and iced injectates. Heart and Lung, 13(5), 574-578.

Weil, M. H. (1982). Measurement of cardiac output. Critical Care Medicine, 5, 117-119.

Weisel, R. D., Berger, R. L., & Hechtman, H. B. (1975). Measurement of cardiac output by thermodilution. New England Journal of Medicine, 292(13), 682-684.

Weisel, R. D., Vito, L., Dennis, R. C., Berger, R. L., & Hechtman, H. B. (1975). Clinical applications of thermodilution cardiac output determinations. American Journal of Surgery, 129, 449-452.

Wessel, H. U., Paul, M. H., James, G. W., & Grahn, A. R. (1971). Limitations of thermal dilution curves for cardiac output determinations. Journal of Applied Physiology, 30, 643-652.

Whitman, G. R., Howaniak, D. L., & Verga, T. S. (1982). Comparison of cardiac output measurements in 20° supine and 20° right and left lateral recumbent positions. Heart and Lung, 11, 256-257.

Wong, M., Skulsky, A., & Moon, E. (1978). Loss of indicator in the thermodilution technique. Catheterization and Cardiovascular Diagnosis, 4, 103-109.

Woog, R. H., & McWilliam, D. B. (1983). A comparison of methods of cardiac output measurement. Anaesthesia and Intensive Care, 11(2), 141-146.

APPENDIX

Obs.	INJECT	TRIAL	ORDER	FM	TD	VARG
1	1	1	1	36.5	8.57	8.085480
2	1	1	2	36.0	8.00	7.974720
3	1	1	3	36.0	7.53	7.974720
4	1	2	1	32.0	7.56	7.088640
5	1	2	2	31.0	6.63	6.867120
6	1	2	3	31.0	7.32	6.867120
7	1	3	1	26.0	6.02	5.759520
8	1	3	2	27.5	6.25	6.091800
9	1	3	3	25.5	5.99	5.648760
10	1	4	1	19.0	3.48	4.208880
11	1	4	2	19.0	4.11	4.208880
12	1	4	3	19.0	3.78	4.208880
13	1	5	1	34.0	7.68	7.531680
14	1	5	2	36.0	7.37	7.974720
15	1	5	3	36.0	7.56	7.974720
16	1	6	1	28.0	6.73	6.202560
17	1	6	2	29.0	6.24	6.424080
18	1	6	3	29.0	6.14	6.424080
19	1	7	1	9.0	2.18	1.993680
20	1	7	2	9.0	2.33	1.993680
21	1	7	3	9.5	2.32	2.104440
22	1	8	1	23.0	5.55	5.094960
23	1	8	2	24.0	5.66	5.316480
24	1	8	3	24.0	5.48	5.316480
25	1	9	1	12.5	2.60	2.769000
26	1	9	2	14.0	3.37	3.101280
27	1	9	3	13.0	2.27	2.879760
28	1	10	1	32.0	6.76	7.088640
29	1	10	2	33.0	6.68	7.310160
30	1	10	3	33.0	6.77	7.310160
31	2	1	1	32.5	8.07	7.199400
32	2	1	2	32.5	6.87	7.199400
33	2	1	3	32.5	7.43	7.199400
34	2	2	1	32.5	6.53	7.199400
35	2	2	2	33.0	6.27	7.310160
36	2	2	3	33.0	7.20	7.310160
37	2	3	1	25.0	5.72	5.538000
38	2	3	2	24.0	5.38	5.316480
39	2	3	3	24.0	5.27	5.316480
40	2	4	1	30.0	6.37	6.645600
41	2	4	2	30.0	6.05	6.645600
42	2	4	3	30.0	6.94	6.645600
43	2	5	1	31.0	8.57	6.867120
44	2	5	2	31.5	7.81	6.977880
45	2	5	3	31.5	7.37	6.977880
46	2	6	1	23.0	5.87	5.094960
47	2	6	2	23.0	5.97	5.094960
48	2	6	3	22.5	4.83	4.984200
49	2	7	1	11.0	2.63	2.436720
50	2	7	2	8.0	2.00	1.772160
51	2	7	3	7.5	1.83	1.661400
52	2	8	1	24.0	5.80	5.316480
53	2	8	2	24.0	5.29	5.316480
54	2	8	3	24.0	6.02	5.316480
55	2	9	1	16.0	3.76	3.544320

Obs.	INJECT	TRIAL	ORDER	FM	TD	VARE
56	2	9	2	16.0	3.60	3.544320
57	2	9	3	16.5	3.63	3.655080
58	2	10	1	23.5	5.48	5.205720
59	2	10	2	24.0	5.15	5.316480
60	2	10	3	24.0	5.36	5.316480
61	2	11	1	22.0	4.43	4.873440
62	2	11	2	22.0	4.35	4.873440
63	2	11	3	21.0	4.48	4.651920
64	3	1	1	33.0	8.76	7.310160
65	3	1	2	33.0	8.21	7.310160
66	3	1	3	33.0	7.10	7.310160
67	3	2	1	31.0	5.74	6.867120
68	3	2	2	32.0	7.96	7.088640
69	3	2	3	32.0	7.56	7.088640
70	3	3	1	30.0	7.60	6.645600
71	3	3	2	30.0	8.28	6.645600
72	3	3	3	30.5	7.53	6.756360
73	3	4	1	24.5	7.41	5.427240
74	3	4	2	25.0	6.89	5.538000
75	3	4	3	24.0	6.21	5.316480
76	3	5	1	10.0	2.84	2.215200
77	3	5	2	10.0	2.65	2.215200
78	3	5	3	11.0	2.57	2.436720
79	3	6	1	26.0	6.61	5.759520
80	3	6	2	26.5	6.64	5.870280
81	3	6	3	25.5	6.36	5.648760
82	3	7	1	20.0	5.54	4.430400
83	3	7	2	19.0	4.40	4.208880
84	3	7	3	20.0	4.57	4.430400
85	3	8	1	12.0	2.62	2.658240
86	3	8	2	10.0	2.54	2.215200
87	3	8	3	9.5	2.67	2.104440
88	3	9	1	30.5	6.50	6.756360
89	3	9	2	31.5	7.62	6.977880
90	3	9	3	31.5	7.01	6.977880
91	3	10	1	26.0	7.58	5.759520
92	3	10	2	27.5	7.07	6.091800
93	3	10	3	28.0	7.14	6.202560
94	3	11	1	18.0	4.62	3.987360
95	3	11	2	18.0	4.41	3.987360
96	3	11	3	18.5	4.41	4.098120
97	4	1	1	26.0	7.76	5.759520
98	4	1	2	25.5	6.86	5.648760
99	4	1	3	26.0	7.07	5.759520
100	4	2	1	26.5	6.38	5.870280
101	4	2	2	28.0	8.29	6.202560
102	4	2	3	28.0	7.81	6.202560
103	4	3	1	30.0	7.42	6.645600
104	4	3	2	29.0	7.20	6.424080
105	4	3	3	28.5	6.65	6.313320
106	4	4	1	20.5	4.89	4.541160
107	4	4	2	20.5	4.92	4.541160
108	4	4	3	20.0	4.43	4.430400
109	4	5	1	11.0	3.17	2.436720
110	4	5	2	10.0	2.60	2.215200

Obs.	INJECT	TRIAL	ORDER	FM	TD	VAR6
111	4	5	3	9.0	2.67	1.993680
112	4	6	1	23.5	5.13	5.205720
113	4	6	2	24.5	5.64	5.427240
114	4	6	3	25.0	5.15	5.538000
115	4	7	1	20.0	5.14	4.430400
116	4	7	2	19.0	4.57	4.208880
117	4	7	3	17.0	4.22	3.765840
118	4	8	1	15.5	4.68	3.433560
119	4	8	2	18.0	4.65	3.987360
120	4	8	3	17.0	4.69	3.765840
121	4	9	1	14.0	4.67	3.101280
122	4	9	2	17.0	4.71	3.765840
123	4	9	3	16.5	4.13	3.655080
124	4	10	1	10.5	2.57	2.325960
125	4	10	2	8.5	2.70	1.882920
126	4	10	3	8.0	2.17	1.772160
127	4	11	1	21.0	5.27	4.651920
128	4	11	2	20.5	5.38	4.541160
129	4	11	3	20.0	4.86	4.430400

ABSTRACT

CARDIAC OUTPUT MEASUREMENT BY THERMODILUTION AND FLOWMETER METHODS IN LOW FLOW STATES

Laura E. Renner & Gail Y. Sakuma

The purpose of this study was to examine which volume and temperature of thermodilution injectate (5% dextrose in water) produced the most accurate and reliable CO measurement in low flow states (CO 2.00-4.65 L/min). Data was collected from a single preinstrumented ewe at the Heart Research Laboratory at the Oregon Health Sciences University. Simultaneous measurements of CO were made by thermodilution and flowmeter over a range of approximately 2.00-8.50 L/min with each of the four volume-temperature combinations of injectate (5 and 10 ml volumes, each at iced and room temperatures). CO was lowered from the ewe's baseline by inflating an inferior vena cava occulder, after which a rapid succession of three paired thermodilution and flowmeter measurements were made. This sequence of triplicate measures was repeated at 10-11 levels of CO for each injectate.

Accuracy of thermodilution determinations was determined by correlations to the reference flowmeter measurements. Over the entire range of CO, the 10 ml iced injectate provided the highest correlation. In low flow states, all four injectates provided CO values which correlated highly to the flowmeter results, with the 5 ml iced injectate producing the highest value. All injectates provided poor to moderate correlations at high COs with the 10 ml iced solution providing the highest value.

CO L/min	ICED 10 ml	ICED 5 ml	ROOM 5 ml	ROOM 10 ml
2.0-8.5	0.9797***	0.9460***	0.9479***	0.9428***
2.0-4.6	0.9181**	0.9889***	0.9744***	0.9759***
6.5-8.5	0.6996**	-0.1970	0.5836*	0.1133

***p<.00001 **p<.0005 *p<.01

Reliability of the four injectates was assessed by analysis of variance which showed no significant difference in the variability of repeated measures between the thermodilution and flowmeter methods of CO measurement in relation to any of the four injectates. The clinically noted variability between repeated thermodilution measurements may be due to the dynamic

nature of CO rather than the thermodilution methodology.

This study suggests that a smaller cold volume of injectate rather than the traditional 10 ml injectate may be satisfactory in patients with low COs who are volume restricted. Perhaps no single thermodilution injectate should be used exclusively, but instead, the selection of injectate volume and temperature should be tailored to the patient's CO.