

Effect of Injectate Volume and Temperature on Thermodilution Cardiac Output Determination

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Six combinations of injectate volume (10, 5, and 3 ml) and temperature (0° C and room temperature [RT]) are recommended by the manufacturers of thermodilution cardiac output catheters and computers. We prospectively studied the accuracy and variability associated with these six combinations in critically ill patients requiring intermittent mandatory ventilation. The six methods were similar in their average estimation of cardiac output but differed markedly in their reproducibility. The 10 ml 0° C and 10 ml RT combinations produced the least variability. The 5 ml 0° C and 5 ml RT combinations produced more variability. Variability was much greater with the remaining two combinations. The 3 ml RT combination resulted in an average range of 1.71 l/min within each set of three repeat measurements and an average absolute difference of 1.51 l/min from the values obtained with 10 ml 0° C (each the mean of three injections). We recommend the use of 10 ml 0° C or 10 ml RT for cardiac output determinations in critically ill patients. If it is important to minimize volume administration, the use of 5 ml injectate is acceptable for an estimation of cardiac output. The use of 3 ml injectate volumes is rarely, if ever, justified because the small reduction in volume administration results in a large increase in variability. (Key words: Equipment: catheter, flow-directed. Heart: cardiac output, thermodilution determination.)

THE DEVELOPMENT OF the thermistor-fitted flow-directed pulmonary artery catheter and the solid-state cardiac output computer have made the thermodilution method of cardiac output determination a standard monitoring component in the care of critically ill patients.¹ The use of 10 ml iced injectate has been recommended as the standard method in order to maximize the signal-to-noise ratio in the time-temperature thermodilution curve.¹⁻⁵ Modifications of this technique may use room temperature (RT) injectate or smaller injectate volumes. Possible advantages of RT injectate include immediate availability, convenience of use, stability of injectate temperature,^{3,6} and avoidance of dysrhythmias.^{7,8} Reduction of injectate volume may be advantageous in patients with

compromised cardiac or renal function. The effect of injectate volume and temperature on the accuracy and reproducibility of thermodilution cardiac output determinations has been examined in other published studies.^{5,9-17} However, these studies have usually compared only two or three of the six clinically used volume-temperature combinations (3, 5, and 10 ml of iced and RT injectate) and have frequently been inconclusive or contradictory. We therefore prospectively studied the accuracy and reproducibility of these six volume-temperature combinations in critically ill patients.

Methods

SUBJECTS

Eighteen adult intubated patients were studied. Criteria for entry into the study included: 1) stable rate of administration of intravenous fluids and vasoactive agents for 4 h; 2) stable respiratory function during intermittent mechanical ventilation with a rate of mechanical ventilation of 4-16 breaths/min plus a rate of spontaneous ventilation of 4-20 breaths/min; 3) cardiac output determinations (each the mean of three determinations using 10 ml RT saline) performed at 30-min intervals for 2 h prior to the study varied less than 20%; 4) cardiac output greater than 3 l/min; and 5) no contraindications to the volume administration required by the study (126 ml).

PROTOCOL

Eighteen cardiac output determinations (three blocks of six each) were performed in rapid succession for each subject. Each block of six determinations involved one determination with each of six techniques (10 ml 0° C saline; 10 ml RT saline; 5 ml 0° C saline; 5 ml RT saline; 3 ml 0° C saline; 3 ml RT saline). The order within each block was balanced for each set of six patients. The pulmonary artery catheter was flushed with 2 ml RT saline following the cardiac output calculation for each 0° C saline injection. Injectate temperatures (RT and 0° C) were measured with two separate probes attached to the cardiac output computer through a switching box in order to allow rapid alternation between 0° C and RT injections.

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TABLE 1. Mean Cardiac Output and Within-patient Variance and the Mean \pm SE of the Cardiac Output, Range, and Absolute Difference Relative to 10 ml 0° C for the Six Volume-Temperature Combinations

	10 ml 0° C	10 ml RT	5 ml 0° C	5 ml RT	3 ml 0° C	3 ml RT
Mean cardiac output (l/min)	6.38	6.49	6.71	6.46	6.84	6.61
Within-patient variance (l ² /min ²)	0.25	0.38	0.53*	0.61†	1.30†‡	1.41†‡
Standard deviation of cardiac output (l/min)	0.39 \pm 0.08	0.44 \pm 0.10	0.62 \pm 0.09	0.63 \pm 0.11	0.92 \pm 0.16*§	0.90 \pm 0.17*§
Range of cardiac output (l/min)	0.67 \pm 0.11	0.84 \pm 0.21	1.17 \pm 0.17	1.19 \pm 0.21	1.78 \pm 0.32†§	1.71 \pm 0.34†§
Absolute difference relative to 10 ml 0° C (l/min)	—	0.57 \pm 0.10	0.47 \pm 0.15	0.84 \pm 0.17	0.87 \pm 0.20	1.51 \pm 0.29‡
Correlation coefficient (vs. 10 ml 0° C)		0.94	0.96	0.89	0.90	0.67‡

* P < 0.05 compared with 10 ml 0° C.

† P < 0.01 compared with 10 ml 0° C.

‡ P < 0.01 compared with 10 ml RT.

§ P < 0.05 compared with 10 ml RT.

Pearson product-moment coefficient of correlation (vs. 10 ml 0° C) for the five alternate volume-temperature combinations.

One cardiac output computer (Edwards Laboratories 9520A, Santa Ana, CA) was used for the entire study. All cardiac output determinations were performed by a single investigator (L.N.) using a standardized technique involving injection at the end of a mechanical ventilation.^{18,19} No values were discarded from analysis. Patients' core temperatures ranged from 35.5° C to 39° C and room temperatures ranged from 20.5° C to 22° C. The protocol was approved by our institutional committee for the use of human subjects in research.

STATISTICS

For each volume-temperature combination (e.g., 10 ml RT saline) the 18 sets of three determinations were subjected to a one-way analysis of variance with the patients as groups.²⁰ The resulting estimate of within-group variance is a measure of the within-patient variability using that volume-temperature combination (standard deviation is the square root of the variance). The within-group variances of the six different methods were compared by F test, considering a 0.05 level of probability to be significant.

In addition to this analysis, the three cardiac output determinations for each volume-temperature combination (e.g., 10 ml RT saline) in a given patient were used to calculate a mean value, a standard deviation, and a range (high determination minus low determination) for that individual patient and method. For each of these summary statistics, a repeated-measures design analysis of variance was performed using the six volume-temperature combinations for each of the 18 patients. Differences among methods were then compared by the Newman-Keuls' multiple-comparison test.

An additional parameter, the absolute difference across subjects relative to 10 ml 0° C saline, was calculated for each of the five alternate volume-temperature combinations. For each patient, the absolute (unsigned) differ-

ence between the mean of the three determinations using 10 ml 0° C saline and the mean of the three determinations using the alternate method was calculated. A repeated-measures design analysis of variance was performed on this parameter. Finally, for the five alternate methods, the Pearson product-moment coefficient of correlation with the 10 ml 0° C method was computed using the two paired sets of 18 cardiac output values (10 ml 0° C and the alternate method).

Results

The range of cardiac outputs among patients using 10 ml 0° C saline was 3.38 to 11.98 l/min. The mean cardiac output did not differ significantly among the six methods (table 1). There were significant differences among methods in the within-patient variance with both 3 ml methods having more variability than the other four methods. Both 5 ml methods had more variability than the 10 ml 0° C method. The 10 ml RT method did not differ significantly from the 10 ml 0° C method. There were no differences for any of the three volumes between 0° C and RT injectate. Both the standard deviation and the range of the cardiac output were significantly greater with the 3 ml methods than with the 10 ml methods. The absolute difference across subjects relative to 10 ml 0° C was significantly greater for the 3 ml RT method than for the other four methods. The correlation coefficient versus 10 ml 0° C was significantly lower for the 3 ml RT method than for the 10 ml RT method; the correlation coefficient versus 10 ml 0° C was not statistically different between the 10 ml RT method and any of the remaining three methods.

Discussion

Although the influences of injectate volume and temperature on thermodilution determination of cardiac output have been previously investigated,^{5,9-17} most stud-

ies have compared only two or three methods and have not included critically ill patients. Important aspects of our prospective study of all six volume-temperature combinations are the selection of stable patients receiving intermittent mandatory ventilation, injection at end-expiration, and performance of all injections by one investigator using a standardized, reproducible technique. Although the mean cardiac outputs did not differ among methods, there were significant differences in variability among methods. The three measures of variability (the within-patient variance, the standard deviation, and the range) were similar in their assessment of the reproducibility of the six volume-temperature combinations. Variability increased with the use of smaller injectate volumes but was not significantly affected by the use of RT *versus* 0° C injectate. The use of RT rather than 0° C injectate with the 3 ml method did significantly increase the absolute difference relative to 10 ml 0° C and the correlation coefficient *versus* 10 ml 0° C.

Although our study is the first to evaluate systematically all six volume-temperature combinations, our findings are relatively consistent with other studies. In general, the use of 10 ml 0° C and 10 ml RT injectates have resulted in similar accuracy⁹⁻¹⁵; the use of 5 ml 0° C injectate has produced similar results as well.¹¹ The use of 5 ml RT injectate has resulted in less accurate results.^{11,13} The only published study that examined the use of 3 ml 0° C injectate found it inferior to 5 and 10 ml of iced or RT solution.¹¹ We know of no studies examining the use of 3 ml RT injectate in adults.

In explaining our results, sources of variability in thermodilution cardiac output determination may be considered in three groups. The first group consists of errors in injectate volume, injectate temperature, or injection technique.^{3,5,6,10,19} Minimizing errors in injectate volume favors the use of large volumes because a 0.1 ml error represents 1% of a 10 ml injectate volume and 3.3% of a 3 ml injectate volume; since the dead space of the catheter and connecting stopcock is approximately 1 ml, the volume of injectate is 9 ml or 2 ml and the corresponding errors may therefore be as large as 1.1% and 5%, respectively. Minimizing errors in injectate temperature may favor the use of room temperature injectate because warming of the iced injectate may occur between removal from the bath and injection into the patient.^{3,6,10} The degree of variability introduced by errors in injectate volume and temperature can be minimized by meticulous attention to technique. The second group of errors involves variations in the pulmonary artery blood temperature, which produce noise in the time-temperature curve so that an inappropriate area exists under the curve. These problems are minimized when the signal-to-noise ratio is improved by injecting large quantities of "cold" injec-

tate—either by increasing the injectate volume or by decreasing the injectate temperature. Our finding that the use of 0° C injectate did not improve reproducibility when 10 or 5 ml volumes were used suggests that the signal-to-noise ratio is not a significant problem with these volumes in patients with normal cardiac outputs. The use of 0° C injectate theoretically may be valuable in patients with a low cardiac output. The third group of factors that can produce errors in cardiac output determination are inappropriate points of truncation in calculating the area under the tail end of the temperature-time curve. This is most likely to occur when the shape of the curve deviates significantly from an exponential decay; again, increasing the volume and decreasing the temperature of the injectate may minimize this problem.

We conclude that in patients with cardiac outputs greater than 3 l/min, there is no difference in accuracy or reproducibility between the use of 10 ml 0° C injectate and 10 ml RT injectate. There is more variability with the use of 5 ml 0° C or RT injectate, but the increased variability is less than 0.2 l/min in the cardiac output value (mean of three determinations). The use of 3 ml volumes further increases the variability and results in a cardiac output value (mean of three determinations) with a standard error of almost 0.7 l/min. In addition, the use of 3 ml RT resulted in values that corresponded poorly to the 10 ml 0° C method. Therefore, we recommend the use of 10 ml 0° C or 10 ml RT injectate for cardiac output determination. When it is important to minimize the volume of fluid administered, we recommend the use of 5 ml injectate volumes. The small reduction in volume administration and the large increase in variability that occur with 3 ml *versus* 5 ml injectate volumes suggest that 3 ml volumes are rarely if ever indicated in adults.

References

1. Buchbinder N, Ganz W: Hemodynamic monitoring: Invasive techniques. *ANESTHESIOLOGY* 45:146-155, 1976
2. Ganz W, Donoso R, Marcus HS, Forrester JS, Swan HJC: A new technique for measurement of cardiac output by thermodilution in man. *Am J Cardiol* 27:392-396, 1971
3. Levett JM, Replogle RL: Thermodilution cardiac output: A critical analysis and review of the literature. *J Surg Res* 27:392-404, 1979
4. Wessel HU, Paul MH, James GW, Grahn AR: Limitations of thermal dilution curves for cardiac output determinations. *J Appl Physiol* 30:643-652, 1971
5. Runciman WB, Ilesley AH, Roberts JG: An evaluation of thermodilution cardiac output measurement using the Swan-Ganz catheter. *Anaesth Intensive Care* 9:208-220, 1981
6. Powner DJ: Thermodilution technique for cardiac output. *N Engl J Med* 293:1210-1211, 1975
7. Nishikawa T, Dohi S: Slowing of heart rate during cardiac output measured by thermodilution. *ANESTHESIOLOGY* 57:538-539, 1982
8. Todd MM: Atrial fibrillation induced by the right atrial injection

- of cold fluids during thermodilution cardiac output determination: A case report. *ANESTHESIOLOGY* 59:253-255, 1983
9. Stetz CW, Miller RG, Kelly GE, Raffin TA: Reliability of the thermodilution method in the determination of cardiac output in clinical practice. *Am Rev Respir Dis* 126:1001-1004, 1982
 10. Riedinger MS, Shellock FG: Technical aspects of the thermodilution method for measuring cardiac output. *Heart Lung* 13:215-221, 1984
 11. Elkayam U, Berkley R, Azen S, Weber L, Geva B, Henry WL: Cardiac output by thermodilution technique: Effect of injectate's volume and temperature on accuracy and reproducibility in the critically ill patient. *Chest* 84:418-422, 1983
 12. Nelson LD, Anderson HB: Patient selection for iced *versus* room temperature injectate for thermodilution cardiac output determinations. *Crit Care Med* 13:182-184, 1985
 13. Shellock FG, Riedinger MS, Bateman TM, Gray RJ: Thermodilution cardiac output determination in hypothermic postcardiac surgery patients: Room *vs.* ice temperature injectate. *Crit Care Med* 11:668-670, 1983
 14. Shellock FG, Riedinger MS: Reproducibility and accuracy of using room-temperature *vs.* ice-temperature injectate for thermodilution cardiac output determination. *Heart Lung* 12:175-176, 1983
 15. Vennix CV, Nelson DH, Pierpont GL: Thermodilution cardiac output in critically ill patients: Comparison of room-temperature and iced injectate. *Heart Lung* 13:574-578, 1984
 16. Woog RH, McWilliam DB: A comparison of methods of cardiac output measurement. *Anaesth Intensive Care* 11:141-146, 1983
 17. Pelletier C: Cardiac output measurement by thermodilution. *Can J Surg* 22:347-350, 1979
 18. Stevens JH, Raffin TA, Mihm FG, Rosenthal MH, Stetz CW: Thermodilution cardiac output measurement: Effects of the respiratory cycle on its reproducibility. *JAMA* 253:2240-2242, 1985
 19. Woods M, Scott RN, Harken AH: Practical considerations for the use of a pulmonary artery thermistor catheter. *Surgery* 79:469-475, 1976
 20. Winer BJ: *Statistical Principles in Experimental Design*. New York, McGraw-Hill, 1971, pp 149-257