
Original Article***In Vitro Evaluation of the Medtronic™ Cardioplegia Safety System®***

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ABSTRACT

Myocardial preservation demands the precise and accurate delivery of cardioplegic solutions to provide nutritive delivery and metabolic waste removal. The purpose of this study was to evaluate the performance characteristics of the Medtronic® CSS™ Cardioplegia Safety System in an *in vitro* setting.

The CSS™ was evaluated under the following conditions: blood to crystalloid ratios of 1:0, 1:1, 4:1, 8:1, 0:1; potassium concentrations of 10, 20, and 40 mEq L⁻¹; volumetric delivery collection at 100, 250, 500, 750, and 990 mL/min; pressure accuracy at 100 and 300 mmHg; and system safety mechanisms. Measured and predicted values from the CSS were compared using one way ANOVA, with statistical significance accepted at $p \leq 0.05$.

The measured values for the tested ratios and volume collections were all within the manufacturer's technical parameters. Potassium concentration results were all within expected values except at 100 mL/min, where the measured value of 17.1 ± 2.1 mmol was lower than the expected 20.0 ± 0.2 mmol ($p < .034$). As flow rates changed, the CSS line pressure error was constant (0.5 to 3.7%), and the only significant difference was observed at 100 mmHg, 500 mL/min (102.3 ± 1.7 vs. 100.0 ± 0.0 mmHg, $P < .003$). The device performed accurately and reliably under all simulated safety conditions, including bubble detection, over pressurization and battery backup. In conclusion, the performance of the CSS was within the manufacturer's specifications for the majority of the tested conditions and operated safely when challenged under varying conditions.

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INTRODUCTION

The primary goal of myocardial protection is to prevent reversible damage from progressing into irreversible injury while maintaining viable myocardial cells. Decreasing the oxygen and nutrient demands of the heart reduces the vulnerable period of injury during surgical intervention. Several methods of cardioplegic protection have been developed to preserve the physiologic function of the myocardium during cardiopulmonary bypass (CPB). Despite the significant improvements in cardioplegic delivery systems, inadequate myocardial protection is still a primary cause of cardiac mechanical failure, resulting from perioperative myocardial ischemia or reperfusion injury (1).

Various advances in myocardial protection techniques, both pharmacological and mechanical, have occurred since first described in 1955 by Melrose et al. Administering a hyperkalemic solution directly into the coronary circulation, Melrose et al. successfully arrested the heart by altering the extracellular potassium concentrations of patients undergoing the repair of congenital heart defects (2). In 1973, Gay and Ebert reintroduced hyperkalemic cardioplegia, emphasizing a lower concentration of potassium to avoid direct myocardial injury (3). This modification has proved to be the model by which the current extracellular solutions have been formulated.

In the late 1970s, Follette and colleagues introduced the concept of cold, hyperkalemic blood cardioplegia (4). The improved buffering and oxygen-carrying capacity of blood provides the myocardium with the nutrients and oxygen needed for tissue repair. Lazar and Roberts reported that by manipulating flow, pressure, volume, and distribution of cardioplegia, better intraoperative myocardial protection can be achieved (5).

Most contemporary cardioplegia delivery devices function to mix blood and crystalloid solutions in fixed ratios, regulate thermal delivery via an integral heat exchanger, and deliver cardioplegia to the coronary circulation (6, 7). Despite improvements in such systems, the need for systems capable of allowing greater refinements in cardioplegia administration still remains (8, 9). Industry has begun to recognize these concerns with the development of new generation cardioplegia delivery devices (10–12). The most recent device introduced is the Medtronic® Cardioplegia Safety System® (CSS).^a The purpose of this study was to quantitatively assess, using an *in vitro* model, the ability of the CSS to deliver expected volumes and concentrations of cardioplegia solutions accurately and precisely.

MATERIALS AND METHODS

The functional characteristics of the CSS were examined

using an *in vitro* model previously described, which was modified to evaluate the CSS (9–11). This model was designed to mimic a range of clinical environments and challenge available safety systems. The accuracy and precision of the CSS was determined by evaluating a number of variables that could be encountered with cardioplegia delivery during CPB. Trials involving volumetric collections, pressure determinations, varying ratios of blood and crystalloid solutions, and end potassium delivery concentrations were conducted. The results were compared to calculated values and evaluated for significant differences. The integral safety systems were tested, including ultrasonic gross air detectors, pressure monitoring, emergent power supply, and various safety alarms.

DEVICE DESCRIPTION

The CSS is a microcomputer-controlled device designed to deliver arterialized blood mixed with cardioplegic solution using the CSS-specific disposable set. The CSS employs two independent roller pumps to deliver desired blood to crystalloid ratios based on the relative speeds of each pump. The console displays flow and volume data, line and external pressure monitoring, alarm and alert systems status, two temperature monitors, and two timers. An accessory syringe pump^b is connected to the CSS console for control of potassium administration.

The two independently rotating pumps deliver flow up to 990 mL/min, either combined or individually. Ratios between 0:1 to 9:1 or 1:0 to 1:9 can be selected. The console displays the flow rate in 10 mL/min increments. In addition, the monitor displays the volume delivered, the total volume delivered, and the volume limit (0–9990 mL in 10 mL increments). The former feature allows the user to program the volume of solution to be delivered.

Both line pressure and external pressure are measured by the CSS. The line pressure is measured at an integral modulus on the console, into which the CSS disposable set is loaded. The external pressure measurement system requires a sterile, disposable pressure measurement system between the internal pressure transducer and the pressure line. Both systems measure pressures between 0 and 500 mmHg (0 to 70 kPa) and are displayed on the console. The system includes programmable overpressure alarms and alerts. The CSS has the ability to deliver cardioplegia at a fixed, user-defined pressure by varying flow. The system attempts to maintain the selected pressure by varying the flow.

In addition to the overpressurization alert and alarm safety features, the CSS includes air detectors and an emergent power supply. The two ultrasonic gross air detectors are located on inlet of the blood and crystalloid pumps. Sensitive to bubbles as small as 134 μ L, detection of air can sound an alert and/or shut off the pumps (user defined). The CSS uses lead acid

^a Medtronic Cardiopulmonary, Minneapolis, MN

^b Model 3400, Graseby Medical Ltd., Munich, Germany

batteries as an emergent power supply, and their use and status are displayed on the monitor.

Potassium (K^+) delivery can be accomplished in one of two ways: use of kalemic crystalloid solution or use of an anesthesia syringe pump. The syringe pump infuses K^+ into a port distal to the pumps, where the blood and crystalloid lines converge. It is interfaced with the CSS, and allows variable delivery of K^+ between 0 and 50 mEq/L.

The CSS requires the use of a compatible disposable set. The tubing is made of polyvinylchloride (PVC), except the regions within the pump raceways, which are silastic. The set includes a heat exchanger, air detector fittings, line pressure fittings, and a syringe line connector. The disposable set can be transferred to a roller pump under emergency conditions.

CIRCUIT PREPARATION

A circuit was constructed using PVC tubing and the CSS disposable set to mimic a clinical sanguineous cardioplegia delivery system (Figure 1). A 20-liter PVC container was con-

nected to a twin roller pump^c (RP) that served as the blood source for the cardioplegia reservoir. A 40-micron arterial line filter^a was placed in the blood source circuit. The blood was recirculated for 30 min before sample collection and throughout the test period. A heat exchanger^a was placed proximal to the arterial line filter, and blood temperature was set at $30 \pm 2^\circ\text{C}$. A hemoconcentrator^d was placed distal to the heat exchanger via a bypass line and utilized to adjust blood source hematocrit to the desired starting range of $25 \pm 2\%$. The remaining side was connected back to the 20-L blood reservoir and served as a recirculation line, and the cardioplegia circuit was connected to the blood source.

The blood source and cardioplegia circuits were gravity primed with 0.9% saline solution and thoroughly debubbled. Thirty thousand units of bovine lung heparin were added to the prime. Bovine blood, collected the morning of the experiment,

^c Model 7400, Sarns/3M Health Care, Ann Arbor, MI

^d HPH 1000, Minntech, Minneapolis, MN

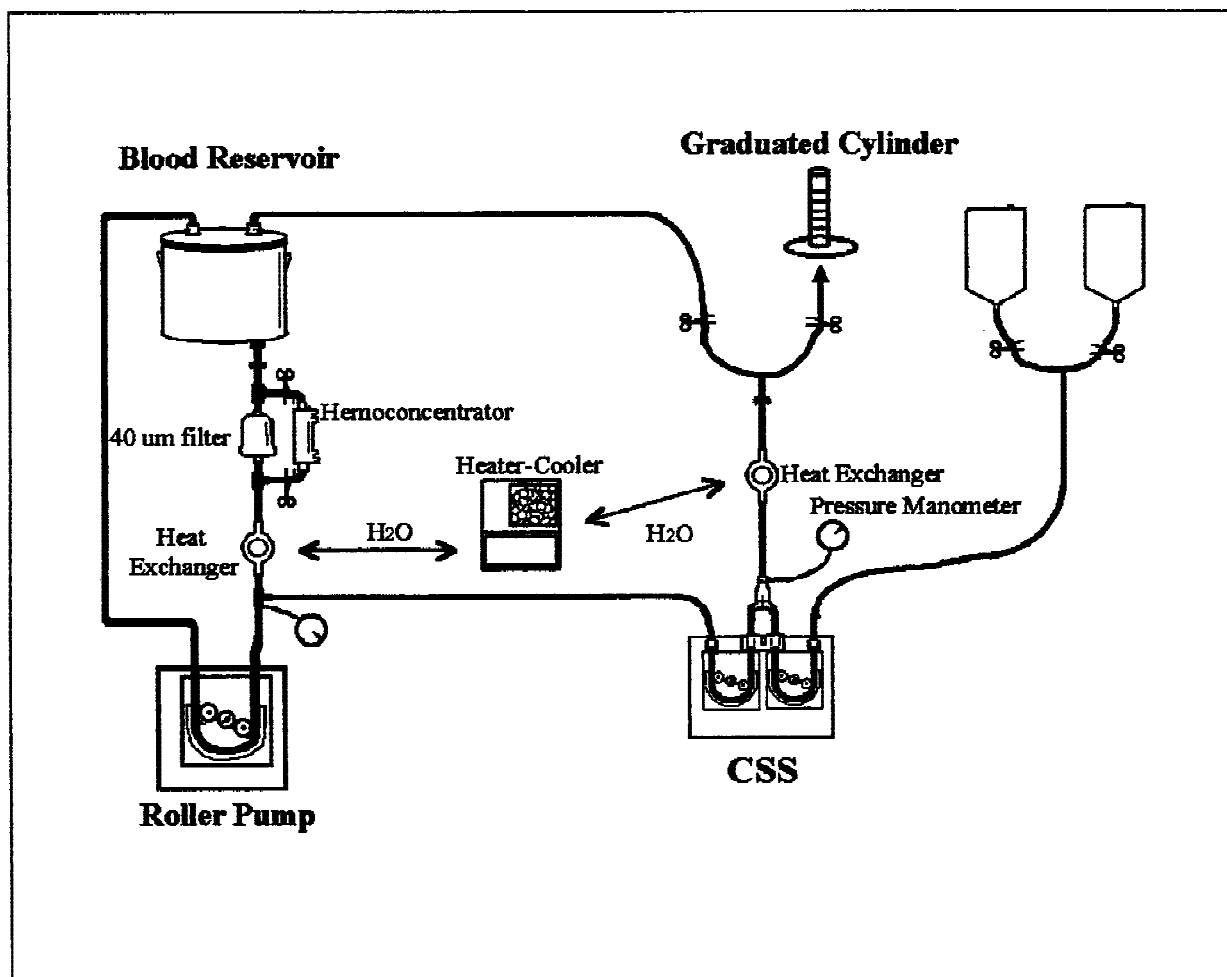


Figure 1.: Cardioplegia safety system test circuit.

was heparinized with 5 units of bovine lung heparin per mL, and the hematocrit was adjusted to $25 \pm 2\%$. Acid base balance was maintained with a pH of 7.40 ± 0.05 , base excess at 0 ± 5 mEq, and temperature at $30 \pm 2^\circ\text{C}$. The potassium concentration of the blood source was adjusted to 5 ± 1 mEq before the start of the end potassium delivery concentration determinations.

The cardioplegia test circuit^a was set up and primed according to manufacturer specifications. A crystalloid base solution (0.9% NaCl) was connected to the CSS crystalloid pump with a hydrostatic pressure of 100 cm H₂O. During volumetric determinations, one side of the wye connector was directed to appropriate sized graduated cylinders, and the other side was directed into a separate container to avoid altering the starting characteristics of the blood source solution.

VOLUMETRIC DETERMINATIONS

The accuracy of the CSS flow rate was determined by measuring the volume delivered by the device at the outlet in timed collections. The test conditions included 100, 250, 500, 750, and 990 mL/min flows, 4:1 blood to crystalloid, and 100 and 300 mmHg line pressure. After 30 sec at the tested flow, the amount of volume collected in 1 min was measured using a graduated cylinder and compared to the reported flow rate of the CSS. All tests were performed in quadruplicate, using a different disposable set each time.

BLOOD TO CRYSTALLOID RATIOS

The blood and crystalloid pump accuracy were tested by measuring the volume delivered by each pump at the outlet in timed collections. The tested ratios of blood to crystalloid solutions were 0:1, 1:0, 1:1, 4:1 and 8:1 at flow rates of 100, 250, and 500 mL/min. After 30 sec at the tested flow, the amount of volume collected in 1 min was measured using a graduated cylinder and compared to the reported flow rate of the CSS. All tests were performed in quadruplicate, using a different disposable set each time.

PRESSURE ACCURACY

The accuracy of the CSS line and external pressure readings were assessed by simultaneous measurement with a fluid-filled pressure-recording system. Following mercury calibration of both measurement devices, measurements were made at 100, 250, and 500 mL/min flow and line pressures of 100 and 300 mmHg.

The constant pressure mode was tested by cutting in a series of five 1/8-inch lines into the test circuit. The flow was set at 300 mL/min with four lines closed, and the constant pressure function was engaged. The 1/8-inch lines were progressively opened, and the pressure and the flow were measured.

In addition, the pressure safety alarm and shut-off were tested by setting the line pressure to 250 and 500 mmHg. These pressures were programmed as the maximum pressure allowed for the system. A Hoffman clamp was utilized to increase the pressure until the safety system disengaged the pump. At the

time of alarm and disengagement, the pressure recorded on the CSS was compared to the pressure registered on the fluid-filled manometer to assess the accuracy of the safety system. All pressure evaluations were performed in quadruplicate.

POTASSIUM DELIVERY

The precision of K⁺ concentration ([K⁺]) delivery was evaluated by measuring the end concentration and comparing it with the expected values. The initial [K⁺] of 5 ± 1 mEq was measured by a real-time gas analyzer at the beginning of each set of ratio trials. The CSS was programmed to deliver [K⁺] of 10, 20, and 40 mEq/L at three flows: 100, 250, and 500 mL/min. When beginning a trial and changing to a new flow rate, the circuit was flushed with 500 mL of cardioplegia corresponding to the new flow or concentration. The end [K] was measured using both a real-time blood gas analyzer and traditional laboratory procedures. All tests were performed in quadruplicate using different disposable sets.

SAFETY SYSTEMS

Battery life was evaluated using a fully charged battery (24-h charge time before evaluation) with a flow rate of 300 mL/min and a back pressure of 150 mmHg. Volume measurements were made at 5-min intervals to determine accuracy of flow delivery over the battery discharge period. The evaluation was performed in duplicate.

The reliability of the integral bubble detectors was determined by introducing gaseous emboli into the circuit from both the blood and crystalloid lines. Air was introduced via a Tuberculin syringe in volumes of 0.1 mL, 0.2 mL, 0.4 mL, 0.5 mL, and 1.0 mL and flow rates of 100, 250 and 500 mL/min. All tests were performed in quadruplicate.

Timer accuracy was evaluated by comparing the recorded elapsed time on the CSS to independent stop watches at 1, 5, and 10 min. All measurements were taken in quadruplicate.

STATISTICAL ANALYSIS

All data were loaded onto a desktop computer in standard spreadsheet format. Comparison of differences between expected and measured values was determined using one way analysis of variance (ANOVA). When significant differences were determined ($p \leq .05$), an additional multiple comparison test was performed (Fishers least significant difference test). All data are expressed as mean \pm 1 standard deviation of the mean.

RESULTS

There were no significant differences seen between the measured and expected total cardioplegia delivery or delivery from the individual pumps. The percentage difference in total cardioplegia delivery from expected ranged from $2.7 \pm 2.1\%$ (750 mL/min and 300 mmHg line pressure) to $4.4 \pm 3.3\%$ (990 mL/min and 100 mmHg line pressure). The percentage differ-

ence in delivery from the blood pump from expected ranged between $4.9 \pm 3.5\%$ (250 mL/min and 8:1 blood to crystalloid) and $8.0 \pm 0.0\%$ (100 mL/min and 1:1 blood to crystalloid). The percentage difference in delivery from the crystalloid pump from expected ranged from $2.5 \pm 1.9\%$ (100 mL/min and 1:1 blood to crystalloid) to $10.8 \pm 5.4\%$ (100 mL/min and 8:1 blood to crystalloid). No noticeable trends were observed for percentage differences in total cardioplegia delivery by flow rate, ratio, or line pressure, although the higher flow rates were associated with greater total difference in delivery (Figures 2–5).

Significant difference between measured and expected end $[K^+]$ were found for 20 mEq/L at a flow rate of 100 mL/min (2.9 ± 2.1 mEq/L, $p = .0190$). The percentage difference between measured and expected end $[K^+]$ ranged from $3.7 \pm 2.1\%$ (10 mEq/L and 100 mL/min) to $14.4 \pm 10.6\%$ (20 mEq/L and 100 mL/min) (Figure 6).

No significant differences were observed between the CSS pressures and the measured pressures. The average difference between the displayed internal line pressure and the measured pressure ranged from 1.5 ± 1.7 mmHg (300 mmHg and 100 mL/min) to 3.75 ± 3.3 mmHg (100 mmHg and 250 mL/min) (Table 1). The average difference between the displayed external pressure and the measured pressure ranged from 2.5 ± 2.4 mmHg (300 mmHg and 500 mL/min) to 6.25 ± 1.3 mmHg (100 mmHg and 250 mL/min) (Table 1). When the constant pressure mode was examined, the CSS maintained a steady pressure, staying within 1% of the set point. As expected, the CSS increased flow in response to increased lumen size, and decreased flow in response to decreased lumen size, to accurately maintain the set pressure.

DISCUSSION

Even with four consecutive decades of improvement, inadequate myocardial protection remains as a primary cause of cardiac mechanical failure (13). As a result of hypoxia, isch-

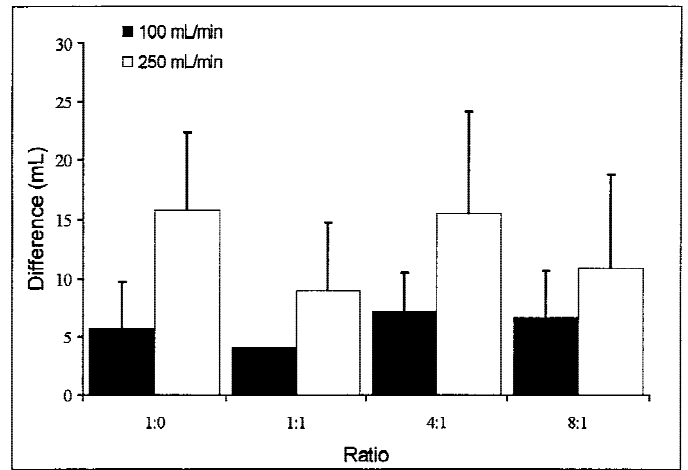


Figure 3.: Difference in blood pump delivery from expected, by flow rate and ratio.

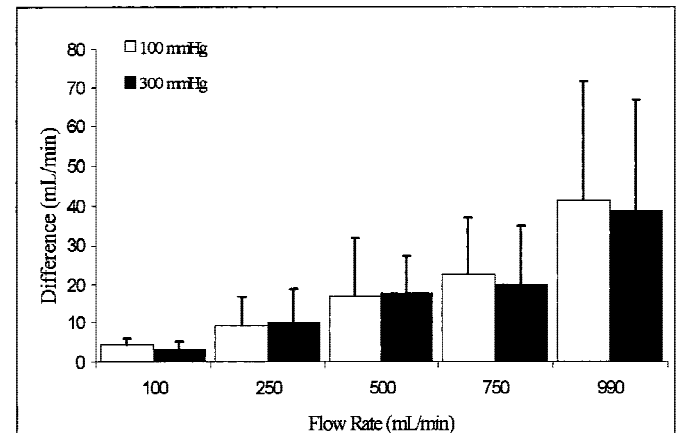


Figure 4.: Difference in total cardioplegia from expected, by flow rate and line pressure.

emia, and reperfusion injury, we see low output syndrome and cardiac failure, typically resulting in the use of inotropic agents and assist devices.

Ebert was compelled to state that the proper application of mechanical delivery may be more important than the specific pharmacological support used (14). Through manipulation of flow, pressure, volume, and distribution, better myocardial protection can be achieved. Myocardial protection is only effective when there is safe, precise, and accurate delivery of cardioplegic solutions. This is accomplished by a precise interface between the disposable and nondisposable elements of the delivery system.

Since the mid-1980s, the positive displacement twin roller pump, delivering cardioplegia at a fixed ratio under pressure, has been the standard cardioplegia delivery system. However, these systems were not designed specifically for cardioplegia delivery. Although they are considered industry standards, they

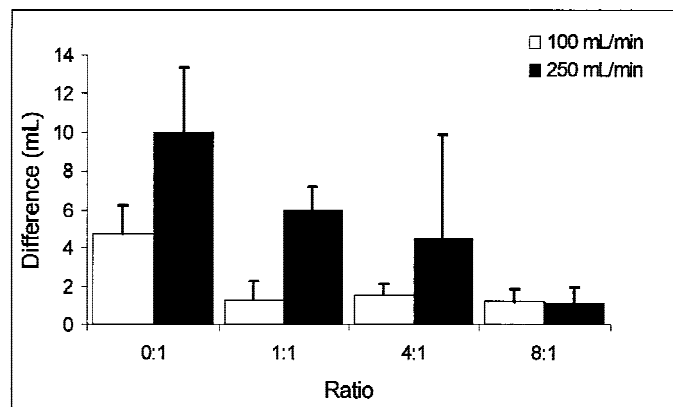


Figure 2.: Difference in crystalloid pump delivery from expected, by flow and ratio.

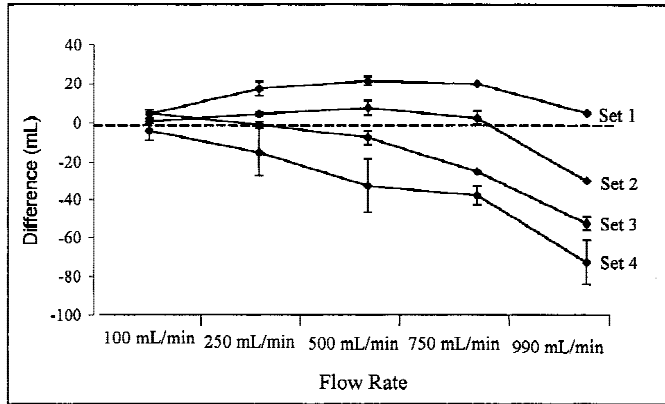


Figure 5.: Difference in delivery by flow rate and disposable set.

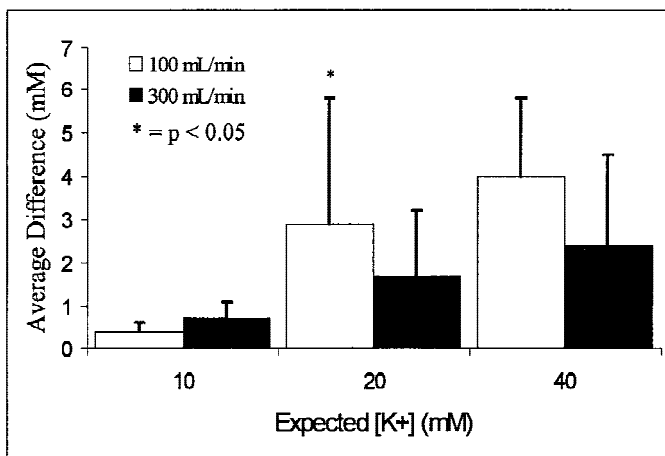


Figure 6.: Difference in end [K⁺] delivery by flow rate and expected [K⁺].

Table 1: Difference in pressure readings from expected

	Internal Line Pressure		
	100 mL/min	250 mL/min	500 mL/min
100 mmHg	2.5 ± 1.7%	3.7 ± 3.2%	2.2 ± 1.6%
300 mmHg	0.5 ± 0.6%	1.2 ± 0.7%	1.2 ± 0.6%
	External Pressure		
	100 mL/min	250 mL/min	500 mL/min
100 mmHg	5.8 ± 4.1%	6.2 ± 1.3%	3.3 ± 1.6%
300 mmHg	0.8 ± 0.9%	1.3 ± 0.9%	0.8 ± 0.8%

do not offer the flexibility required to alter blood or crystalloid components, and they limit the ability to manipulate pharmacological delivery.

Although there is no consensus on the optimum myocardial protection strategy, it is clear that cardioplegia delivery devices that can rapidly alter cardioplegia composition and hemodynamic delivery conditions are needed. The need for improved

cardioplegia delivery systems has prompted the introduction of four new generation devices. These devices allow more regulated control of flow and pressure; more accurate, precise, and flexible delivery of chemicals and nutrients; the ability to alter blood to crystalloid ratios; and enhanced safety systems. The CSS is the latest device offered. It was designed to permit changes in the blood:crystalloid ratio; to offer flexibility in the manipulation of flow, pressure, and end [K⁺] delivery; and to feature an enhanced user interface through various safety systems.

To evaluate the capability of the CSS to deliver set ratios of blood:crystalloid accurately, volume delivered by the two pumps were evaluated independently of each other across different flow rates, ratios, and line pressures. These values were compared to expected values, and significant differences were seen between measured and expected volumes of crystalloid collected across all flow rates at ratios of 0:1 and 1:1 (Figure 2). It should be noted that these differences were within the manufacturers' technical specifications of ±10%. No significant differences were seen in the blood pump or total cardioplegia delivery (Figures 3 and 4). Each trial was performed with a different disposable set, and each set showed considerable variation in total cardioplegia delivery. One set consistently delivered higher than expected volumes, averaging +13.7 mL/min; whereas, another set consistently delivered less than expected with an average of -32.3 mL/min (Figure 5). Generally, these differences became more pronounced as flow rates increased.

The CSS also has the ability to vary the end [K⁺] delivery via the accessory Grasby syringe pump. Potassium delivery was tested by sampling the end [K⁺] with a point of care analyzer and traditional laboratory analysis (Figure 6). The difference at 20 mEq and 100 mL/min flow fell outside the manufacturer's tolerance of + or -2 mEq. It should be noted that the use of the syringe pump is not absolutely necessary, and K⁺ can be delivered via the crystalloid bag(s). This is especially attractive in light of the possibility for syringe pump failure.

The CSS measures both internal line pressure and external pressure. No statistically significant differences were found for the pressure reading across all pressures and flows (Table 1).

The CSS safety systems performed according to the manufacturer's instructions for use. On auxiliary power, the CSS accurately delivered cardioplegia until the time of extinction, which averaged 33 min at full flows. The bubble detectors consistently detected air as small as 100 μL across flows. The overpressurization alert and alarm and the timers were found to function accurately and reliably.

The limitations of this study can be divided into two parts. First, it was an *in vitro* evaluation, and, therefore, translation into the clinical setting should be taken with caution. Second, it was not practical to test some of the devices used with the CSS. For example, potassium delivery was tested with the

syringe pump and the CSS working in conjunction. The syringe pump was not evaluated independent of the CSS, and, therefore, any error in end $[K^+]$ delivery could not be attributed to the CSS or the syringe pump alone.

In conclusion, our evaluation of the Medtronic Cardioplegia Safety System showed this device to be both precise and accurate in delivering specified volumes and ratios of blood and crystalloid solutions and performed according to the manufacturer's specifications for the majority of tested conditions.

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