Interactive CardioVascular and Thoracic Surgery 15 (2012) 655–660
doi:10.1093/icvts/ivs294 Advance Access publication 29 June 2012

Decreased incidence of low output syndrome with a switch from tepid to cold continuous minimally diluted blood cardioplegia in isolated coronary artery bypass grafting

Cristian Rosu, Maxime Laflamme, Clotilde Perrault-Hébert, Michel Carrier and Louis P. Perrault*

Department of Cardiac Surgery, Montreal Heart Institute, Université de Montréal, Montreal, Quebec, Canada

* Corresponding author. Montreal Heart Institute, Université de Montréal 5000 Bélanger Street, Montreal, Quebec, Canada H1T 1C8. Tel: +1-514-3763330; fax: +1-514-3761355. e-mail: louis.perrault@icm-mhi.org (L.P. Perrault).

Received 20 September 2011; received in revised form 16 May 2012; accepted 30 May 2012

Abstract

OBJECTIVES: The optimal temperature for blood cardioplegia remains unclear.

METHODS: A retrospective analysis was performed on 138 patients undergoing isolated myocardial revascularization by a single surgeon in our institution over a period of 2 years. Patients operated on early in the study period received tepid (29°C) continuous minimally diluted blood cardioplegia (minicardioplegia), delivered in an antegrade continuous fashion. Later, our surgeon began using cold (7°C) blood minicardioplegia in all patients. Data pertaining to clinical outcomes and postoperative biochemical data were obtained, and the two groups were compared.

RESULTS: Low cardiac output syndrome, defined as the need for intra-aortic balloon pump counter pulsation or inotropic medication for haemodynamic instability, was more frequent in the tepid cardioplegia group than in the cold cardioplegia group (16.0 vs 2.4%, $P = 0.006$). There was no difference in the maximal serum creatine kinase MB between the two groups (cold 25.4 ± 3.21 μg/ml vs tepid 36.5 ± 7.10 μg/ml, $P = 0.62$), in the rates of perioperative myocardial infarction (cold 1.2% vs tepid 6.0%, $P = 0.15$) and the need for postoperative insertion of an intra-aortic balloon pump (cold 4.8% vs tepid 0.0%, $P = 0.3$). There was no other statistically significant difference between the two groups in the measured parameters.

CONCLUSIONS: A higher rate of low cardiac output syndrome in the tepid cardioplegia group suggests inferior myocardial protection with the tepid cardioplegia. Cold cardioplegia may provide better protection than tepid cardioplegia when minicardioplegia is used.

Keywords: Cardioplegia • Myocardial protection • Cardiopulmonary bypass • Coronary artery bypass

INTRODUCTION

Myocardial preservation techniques are an essential element in any successful cardiac operation, and cardioplegia is one of its cornerstones. The ideal temperature of blood cardioplegia remains a contentious issue. Blood cardioplegia was first described as infused at a temperature of 8°C [1], and cold blood cardioplegia continues to be in widespread use. The underlying rationale is that during ischaemic, or anaerobic arrest, hypothermia further reduces myocardial metabolism by 10–15% [2–4]. More recently, the use of warm (37°C) blood cardioplegia has demonstrated advantages compared with cold blood cardioplegia [5]. Unlike its colder variant, however, warm blood cardioplegia requires continuous administration as any interruptions may subject the heart to warm ischaemia and may be associated with more frequent neurological complications. Consequently, operative exposure may be suboptimal due to blood flooding the field. Difficulties in obtaining full electromechanical arrest and significant systemic vasodilation prompting the need for vasoconstrictor agents have been problematic in some studies using warm cardioplegia [6].

With temperature-related disadvantages to both cold and warm blood cardioplegia, studies were undertaken to establish the optimal temperature. Tepid (29°C) blood cardioplegia was introduced by Hayashida *et al*. [7] as an alternative to warm or cold cardioplegia with the potential advantages of both temperatures and without their drawbacks. In the context of this ambiguity over the optimal temperature for blood cardioplegia, we set out to determine the clinical results of the use of tepid blood cardioplegia vs cold blood cardioplegia in the practice of a single surgeon at our institution.

MATERIALS AND METHODS

This study was performed as a retrospective analysis of prospectively collected data. Between 6 April 2006 and 3 October 2008, 138 patients underwent isolated coronary artery bypass surgery by a single surgeon in our institution and were administered cardioplegia of a uniform temperature throughout the operation. From this group, 84 (63%) patients received cold blood cardioplegia and 54 (37%), tepid blood cardioplegia. Data pertaining to

clinical outcomes, including perioperative myocardial infarction (MI), low cardiac output syndrome (LCOS), mortality and postoperative biochemical data were obtained in both study groups.

This study was approved by the ethics and research committee of the Montreal Heart Institute.

Cardioplegia groups

Patients were given either cold (mean temperature 10.1°C ± 1.7) or tepid (mean temperature 27.6°C ± 1.1) blood cardioplegia according to the surgeon's preference. Minimally diluted blood cardioplegia was used as described by Menasché *et al*. [8]. Briefly, standard 1/4" tubing (0.63 cm) is passed through an independent roller pump and is used to bring oxygenated blood directly from the oxygenator to the cardioplegia catheter in the aortic root. Distal to the roller pump, a three-way stopcock is incorporated into the circuit, through which the cardioplegic solution is infused. This solution is prepared by the local pharmacy in 20 and 50 ml ampoules, containing 800 mEq/l potassium chloride and 150 mEq/l magnesium chloride in distilled water. Upon cross-clamping of the aorta, blood is infused into the aortic root at 300 ml/min while a 20-ml bolus of the cardioplegia solution is injected manually over ∼30 s through the side port of the stopcock. When cardiac arrest is achieved, the blood flow rate is reduced to 150–200 ml/min and an electric syringe pump (Baxter, Deerfield, IL, USA) is used to infuse 60 ml of cardioplegic solution at 60 ml/h. Cardioplegia is used exclusively in an anterograde fashion through the aortic root and infused continuously, with interruptions only of the duration of the construction of each distal anastomosis. The rate of infusion of the cardioplegia solution may be reduced if cardiac arrest is maintained at a given infusion rate; conversely the rate may be increased if residual cardiac activity persists. The blood temperature is adjusted by a heater/cooler independent from the main cardiopulmonary bypass (CPB) circuit. A normothermic reperfusion consisting of normokalemic blood was administered for 1–2 min prior to removing the cross-clamp.

Statistical analysis

All statistical analyses were performed using the SPSS statistical software package. Data are expressed as the mean ± SD or the SEM as indicated. Categorical data were analysed using Fisher's exact test. Continuous variables were analysed using the Wilcoxon two-sample test or pooled *t*-test as appropriate. A value of $P \leq 0.05$ was considered statistically significant. LCOS was defined as either requiring an intra-aortic balloon pump (IABP) to be weaned from CPB or being inserted in the intensive care unit (ICU) because of haemodynamic compromise or requiring inotropic medication to maintain the systolic blood pressure at 90 mmHg and the cardiac output at 2.2 l/min/m^2 for 30 min in the ICU after correction of all of the electrolyte and blood gas abnormalities and after adjusting the preload to its optimal value. Cardiac output was measured by the thermodilution method using a pulmonary artery catheter and indexed to body surface area. Perioperative MI was defined as a creatine kinase MB (CK-MB) peak over five times the upper limit of the reference range or new *Q* waves developing postoperatively. Preoperative renal failure was defined as baseline creatinine >150 μmol/l. Postoperative acute renal failure was defined as increase in creatinine of 100 μmol/l over baseline or need for haemodialysis. Pulmonary hypertension was defined as mean pulmonary artery pressure (PAP) >30 mmHg or systolic PAP >50 mmHg. Pulmonary complications included the need for reintubation or prolonged intubation, pneumonia, pulmonary oedema, pleural effusion and/or pulmonary embolism.

RESULTS

Preoperative characteristics

Patient demographic characteristics and risk factors are outlined in Table 1. Both groups were similar in all respects. The majority (81.0–84.0%) of patients suffered from three-vessel disease and a significant proportion of patients in both groups had a left ventricular ejection fraction (LVEF) <30% (29.8% cold group vs 24.0% tepid group, $P = 0.48$). There was no difference between the groups in terms of number of diseased vessels or LVEF. There was a difference that did not reach statistical significance between the two groups in the percentage of patients undergoing coronary artery bypass grafting (CABG) in the context of unstable angina, with more patients receiving tepid cardioplegia (76.0 vs 59.5%, $P = 0.06$) suffering from unstable angina prior to their surgery.

Intraoperative data

Table 2 shows intraoperative data. Blood cardioplegia was infused at a mean temperature of 10.4°C in the cold group vs 27.6°C in the tepid group ($P < 0.001$). CPB times were statistically significantly longer in the cold group (56.4 vs 48.1 min, $P = 0.005$) as were cross-clamp times (29.3 vs 25.4 min, $P = 0.02$). Terminal normothermic normokalemic reperfusion was given before cross-clamp release to 10.0–15.9% patients, which was not statistically significantly different between the groups ($P = 0.44$). Over 96% of patients in both groups received at least one internal mammary artery (IMA) graft, with more patients in the tepid group receiving bilateral IMA grafts than in the cold group (14.0 vs 2.4%, $P = 0.02$). The number of distal anastomoses were also statistically significantly higher in the tepid group (2.96 vs 2.69, $P = 0.03$).

Postoperative outcomes

Table 3 pertains to postoperative outcomes. There was no difference in the maximal serum CK-MB between the two groups (cold 25.4 ± 3.21 μg/ml vs tepid 36.5 ± 7.10 μg/ml, $P = 0.62$). There was also no difference between the two groups in the rates of perioperative MI (cold 1.2% vs tepid 6.0%, $P = 0.15$) or need for postoperative insertion of an IABP (cold 0.0% vs tepid 0.0%, $P = 1$). However, the rate of LCOS was significantly higher in the tepid group than in the cold group (16.0 vs 2.4%, $P = 0.006$). Patients noted to have suffered from LCOS had a statistically significantly lower cardiac index (CI) immediately prior to the initiation of inotropes than the lowest CI measured prior to pulmonary artery catheter removal in patients without LCOS [1.82 l/min × m^2 95% confidence interval (CI) 1.59–2.05 vs 2.41 l/

Table 1: Demographics and risk factors for surgery

Variables	Cold ($n = 84$)	Tepid ($n = 50$)	P-value
Age	65.5 ± 9.7	63.0 ± 10.6	0.15
Sex (% male)	86.9	86	1
Body mass index (kg/m^2)	28.2 ± 4.3	28.9 ± 4.6	0.38
Hypertension	55 (65.5%)	39 (78.0%)	0.17
Diabetes mellitus	20 (23.8%)	19 (38.0%)	0.12
Dyslipidemia	70 (83.3%)	37 (74.0%)	0.27
Smokers	35 (42.2%)	17 (34.7%)	0.46
Preoperative creatinine (mean, µmol/l)	100.4 ± 64.5	92 ± 21.5	0.94
Chronic renal failure	14 (16.7%)	6 (12.0%)	0.62
Requiring dialysis	1 (1.2%)	0 (0.0%)	1
Cerebrovascular disease	3 (3.57%)	2 (4.0%)	1
Stroke	5 (5.95%)	4 (8.0%)	0.73
Peripheral vascular disease	16 (19.0%)	10 (20.0%)	1
Chronic obstructive pulmonary disease	13 (15.5%)	4 (8.0%)	0.29
Unstable angina	50 (59.5%)	38 (76.0%)	0.06
CCS angina class			0.77
I	4 (4.76%)	3 (6.0%)	
II	20 (23.8%)	14 (28.0%)	
III	24 (28.6%)	16 (32.0%)	
IV	23 (27.4%)	13 (26.0%)	
Recent myocardial infarction	29 (34.5%)	17 (34.0%)	1
Past history of myocardial infarction	23 (27.4%)	8 (16.0%)	0.14
NYHA class			0.48
I	47 (56.0%)	32 (64.0%)	
II	23 (27.4%)	11 (22.0%)	
III	13 (15.5%)	5 (10.0%)	
IV	1 (1.2%)	2 (4.0%)	
Preoperative cardiogenic shock	0 (0.0%)	1 (2.0%)	0.37
Preoperative IABP	12 (14.29%)	8 (16.0%)	0.81
Multivessel disease			0.83
Three-vessel disease	68 (81.0%)	42 (84.0%)	
Two-vessel disease	13 (15.5%)	6 (12.0%)	
Left main disease	36 (42.9%)	23 (46.0%)	0.86
Preoperative LVEF (%)	50.8 ± 12.6	47.9 ± 14.0	0.29
			0.48
>45%	56 (66.7%)	34 (68.0%)	
30–45%	25 (29.8%)	12 (24.0%)	
<30%	3 (3.6%)	4 (8.0%)	
Pulmonary hypertension	20 (23.8%)	12 (24.0%)	1
Emergency	1 (1.2%)	1 (2.0%)	0.45
EuroSCORE, logistic (%)	9.8 ± 12.3	9.9 ± 15.2	0.35

Where applicable, data are expressed as mean ± SD.
CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association; IABP: intra-aortic balloon pump; LVEF: left ventricular ejection fraction.

min × m^2 95% CI 2.32–2.50, $P \leq 0.0001$]. However, there was no difference in mean CI in the tepid group compared with the cold group (2.41 l/min × m^2 95% CI 2.27–2.54 vs 2.34 l/min × m^2 95% CI 2.22–2.46, $P = 0.08$). Three patients in the cold group and two in the tepid group did not have a cardiac output measurement postoperatively; these patients were not administered inotropes and had no signs of low output syndrome based on other clinical markers such as central venous oxygenation saturation. Rates of new-onset atrial fibrillation were similar, as were the rates of stroke, other neurological complications, acute renal failure and pulmonary complications. There were no cardiac arrests and only one death (in the tepid group), the result of a perioperative MI leading to low cardiac output and multiorgan failure. There was a trend towards shorter length of stay in ICU and in hospital in the tepid group (3.66 vs 4.96 days, $P = 0.08$, and 6.76 vs 8.45 days, $P = 0.08$, respectively).

DISCUSSION

The major finding of the present study was a lower incidence of LCOS in the cold cardioplegia group despite longer cross-clamp and CPB times. Post-cardiac surgery myocardial dysfunction can be an indicator of suboptimal myocardial protection. Stunning, a phenomenon of temporary, reversible post-ischaemic myocardial dysfunction, was first described 30 years ago [9]. It is a well-recognized and frequent occurrence post-CABG [10], as reported in a study showing transiently depressed postoperative left ventricular and right ventricular function in 96% of patients [11]. Mechanisms that have been implicated in stunning include decreased myofilament responsiveness to the transient increase in intracellular calcium that is responsible for excitation-contraction coupling [12]. In the present study, we found an increased incidence of LCOS in the tepid blood cardioplegia

Table 2: Intraoperative data

Variables	Cold ($n = 84$)	Tepid ($n = 50$)	P-value
CPB time (min)	56.4 ± 17.2	48.1 ± 14.1	0.005
Cross-clamp time (min)	29.3 ± 11.5	25.4 ± 8.2	0.02
Cardioplegia temperature (°C)	10.4 ± 1.7	27.6 ± 1.1	<0.001
Normothermic reperfusion	13 (15.9%)	5 (10.0%)	0.44
Saphenous vein grafts			0.22
1	27 (32.1%)	15 (30.0%)	
2	56 (66.7%)	31 (62.0%)	
≥3	1 (1.2%)	4 (8.0%)	
At least one IMA graft	82 (97.6%)	48 (96.0%)	0.83
Bilateral IMA grafts	2 (2.4%)	7 (14.0%)	0.02
Distal anastomoses (mean)	2.69 ± 0.56	2.96 ± 0.67	0.03

Where applicable, data are expressed as mean ± SD.
CPB: cardiopulmonary bypass; LIMA: left internal mammary artery; RIMA: right internal mammary artery.

Table 3: Postoperative outcomes

Variables	Cold ($n = 84$)	Tepid ($n = 50$)	P-value
CK-MB (max, μg/ml)	25.4 ± 3.21	36.5 ± 7.10	0.62
Reoperation for bleeding complications	3 (3.57%)	3 (6.0%)	0.67
Cardiac complications	31 (36.9%)	23 (46.0%)	0.36
Low cardiac output syndrome	2 (2.4%)	8 (16.0%)	0.006
Cardiac index, mean (l/min × m^2)	2.41 (95% CI 2.27–2.54)	2.34 (95% CI 2.22–2.46)	0.08
Need for postoperative IABP	0 (0.0%)	0 (0.0%)	0.3
Perioperative ischaemia/MI	1 (1.2%)	3 (6.0%)	0.15
Emergency postoperative angiography	0 (0.0%)	0 (0.0%)	1
Acute renal failure	7 (8.3%)	2 (4.0%)	0.48
Atrial fibrillation	28 (33.3%)	16 (32.0%)	1
Stroke	2 (2.4%)	1 (2.0%)	1
Delirium or seizures	9 (10.7%)	5 (10.0%)	1
Pulmonary complications	7 (8.3%)	5 (10.0%)	0.75
Postoperative cardiac arrest	0 (0.0%)	0 (0.0%)	1
Length of hospital stay (days)	8.45 ± 1.12	6.76 ± 0.63	0.08
Length of ICU stay (days)	4.96 ± 1.11	3.66 ± 0.65	0.08
Mortality	0 (0.0%)	1 (2.0%)	0.37

Where applicable, data are expressed as mean ± SEM.
CK-MB: creatine kinase MB; IABP: intra-aortic balloon pump; MI: myocardial infarction; ICU: intensive care unit.

group, despite no difference in biochemical markers of necrosis, suggestive of stunning. Despite significantly more patients in the tepid group suffering from LCOS, mean CI was not different between the two groups. One quarter of patients in the tepid group had a CI >2.64 l/min × m^2, which may have offset the low CIs of the 16% of patients who experienced LCOS. Given that the clinical utility of CI that is more than sufficient for oxygen delivery is unclear when compared with the obvious negative consequences of LCOS, one may argue that the mean CI of each group is of less importance than the presence or absence of LCOS. Accordingly, we ascertained that patients categorized as having suffered from LCOS had statistically significantly lower, abnormal CI than those not experiencing LCOS (1.82 l/min × m^2 95% CI 1.59–2.05 vs 2.41 l/min × m^2 95% CI 2.32–2.50, $P \leq 0.0001$).

In a study of patients undergoing myocardial revascularization by Fiore *et al*. [13], 52 patients were randomized to receive either intermittent antegrade tepid or cold blood cardioplegia. Their findings of a decreased need for postoperative inotropic support and decreased total CK-MB in the tepid group contrasts with ours. However, the CPB and cross-clamp times in their study were markedly longer, perhaps indicating a beneficial effect seen with more prolonged ischaemia. In a more heterogeneous group of patients having undergone a variety of surgeries under CPB, patients receiving tepid blood cardioplegia needed postoperative IABP insertion less frequently and had less atrial fibrillation but had no difference in the rate of perioperative MI, need for postoperative inotropic support, cerebrovascular events or mortality vs the cold blood cardioplegia group [14]. Results were similar in a prospective randomized trial by Elwatidy *et al*. [15] where 128 patients undergoing isolated CABG were allocated to either tepid blood cardioplegia, cold blood cardioplegia with topical cooling or cold crystalloid cardioplegia with topical cooling. There was no difference in the incidence of low cardiac output, use of significant inotropic support, postoperative use of IABP, perioperative or postoperative MI and CK-MB levels between the tepid and cold group. The low risk of adverse outcomes in these patients may make it more difficult to detect a difference between the two groups.

While there was significantly more LCOS in the tepid group, we did not find increased rates of acute renal failure or longer ICU or hospital stays, suggesting either relatively minor dysfunction or excellent compensation through pharmacological support. Likewise, similar rates of postoperative IABP usage suggest that there was no difference in the incidence of severe LCOS.

There was a trend towards difference between the two groups in the percentage of patients undergoing CABG in the context of unstable angina. More patients receiving tepid cardioplegia suffered from unstable angina prior their surgery compared with those receiving cold cardioplegia (76.0 vs 59.5%, $P = 0.06$). Gerber *et al*. [16] demonstrated the presence of persistent myocardial dysfunction in the affected territory in patients with unstable angina due to proximal left anterior descending (LAD) coronary artery disease. These patients had persistent anterior wall motion abnormalities post-percutaneous transluminal coronary angioplasty, with all patients demonstrating LAD artery stenosis of 80% or greater. There was no improvement in wall motion abnormality within the first week and recovery was noted over weeks to months. While the authors describe this phenomenon as 'stunning', the time course and the presence of severe LAD stenosis could lead one to interpret their findings to be more consistent with 'hibernation'. A different study by Jeroudi *et al*. may have better depicted stunning in unstable angina [17]. Patients demonstrating unstable angina and regional wall motion abnormality during their chest pain or immediately after were followed prospectively with serial two-dimensional echocardiography. All patients had marked improvement or resolution of wall motion abnormalities at 24 h. While statistics

on the exact delay between resolution of chest pain and CABG in our patients are not available, there was no difference between the two groups in the frequency of emergency cases or patients requiring a preoperative IABP, making it unlikely that there was a difference in the number of patients operated on during the first 24 h following resolution of their chest pain. Accordingly, one could expect that there should be little residual stunning in most patients at the time of their surgery.

The vast majority of our patients received at least one IMA graft, consistent with current practice in most of the world. However, there were significantly more patients in the tepid group who received bilateral IMA grafts than in the cold group. While bilateral IMA grafting has clearly been shown to have long-term benefits over a single IMA [18], no short-term benefits in terms of perioperative infarction or mortality has been shown [19] and we do not believe this difference between the two groups influenced the outcomes, which focused exclusively on the perioperative period. The patients in the tepid group also had a greater number of distal anastomoses performed, suggesting a more complete revascularization. With the use of antegrade cardioplegia, we would not expect the number of grafts to influence intraoperative myocardial protection; there was also no difference in perioperative ischaemia/MI to explain the higher rate of LCOS. Moreover, the tepid group should have been protected by the more complete revascularization. CPB and cross-clamp times were statistically significantly shorter in the tepid group than in the cold group. Most would agree, however, that this difference (7.3 and 3.9 min for CPB and cross-clamp times, respectively) is probably not of clinical significance, and once again would tend to favour the tepid group. This difference is likely explained by the fact that our surgeon would administer cold cardioplegia when a resident was the primary surgeon.

Our findings contrasted with those of Martin *et al.* [20], who found that patients randomized to continuous warm blood cardioplegia during coronary bypass grafting had more neurological events (4.5 vs 1.4%; $P < 0.005$) and perioperative strokes (3.1 vs 1.0%; $P \leq 0.02$) than those randomized to cold blood cardioplegia. In their study, patients receiving warm blood cardioplegia also underwent normothermic systemic perfusion. Perfusion at normothermia as opposed to moderate hypothermia (32–34°C) may be responsible for increased neurological events, as demonstrated in a Cochrane database review [21], rather than the temperature of the cardioplegia itself. Furthermore, our examination of the literature found no studies demonstrating a difference in neurological events between tepid and cold blood cardioplegia.

One difference that must be noted between our study and many of those cited in this article that compare tepid and cold blood cardioplegia [13–15, 22] is the composition of the blood cardioplegia. The cardioplegia employed in these studies was a mixture of blood from the cardioplegia circuit and a given hyperkalemic cardioplegia solution in a 4:1 ratio, with outcomes tending to favour the tepid cardioplegia. Conversely, our patients received minimally diluted blood cardioplegia, as described earlier. In small studies of tepid blood cardioplegia in which patients were randomized to diluted blood cardioplegia (4:1 blood to crystalloid ratio) or undiluted blood cardioplegia, one study showed improved myocardial oxygen and lactate metabolism, decreased release of myocardial enzyme and free radicals as well as improved left ventricular function in the undiluted cardioplegia group [23], while another showed no difference in clinical endpoints and only minor differences in enzymatic endpoints [24]. However, these studies only used one temperature strategy and the differential effects of temperature with minimally diluted cardioplegia are unclear. Concerns about hypothermia-induced red blood cell sludging in the coronary circulation in the absence of sufficient haemodilution [25] is one potential reason why cold minimally diluted blood cardioplegia has been little studied. However, these concerns may not be warranted, as there is already a certain degree of haemodilution as the blood is derived from the main CPB circuit, with haematocrit usually no higher than 22%. Increased oxygen-carrying capacity due to the higher haematocrit of the cardioplegia and the more important decrease in myocardial oxygen use resulting from the more significant hypothermia induced by cold cardioplegia may provide a better oxygen supply/demand ratio that outweighs the potential benefits of tepid cardioplegia. Further investigation is required as, to our knowledge, our study is the first to compare tepid to cold cardioplegia temperature strategies when using continuous minimally diluted blood cardioplegia.

Limitations

The limitations of this study include those inherent in a retrospective cohort study. The single-surgeon nature of the study provided some homogeneity to the treatment; however, it also limited the number of available patients. While we know that none of the patients who received tepid cardioplegia were operated on by a resident, we do not have data on what proportion of cases our surgeon served as assistant to an operating resident among the cold cardioplegia cases. As a result, there may be differences in the operative technique between the two groups that are not revealed in the collected data. Cardiac output measurements suffered from the limitations inherent in the thermodilution technique, as well the inevitable presence of factors other than myocardial protection that may have influenced cardiac output.

It remains unclear whether cold or tepid blood cardioplegia is the optimal temperature strategy for myocardial protection in coronary bypass surgery. While this study demonstrates a higher rate of myocardial stunning with no change in frank necrosis in the tepid blood cardioplegia group, despite being favoured by a shorter period of global ischaemia, the remainder of the literature remains discordant. Published studies, which favour tepid cardioplegia, are either non-randomized or have relatively small numbers of patients and only examine the results of diluted cardioplegia. As shown in our study, these results may not apply to minicardioplegia strategies. Minimal dilution combined with cold temperature may lead to a significantly better myocardial oxygen supply/demand ratio that outweighs other benefits afforded by tepid cardioplegia. Further studies will be necessary to better define the optimal temperature strategy when employing minicardioplegia. Based on this study, hypothermic continuous minicardioplegia is now the preferred strategy adopted for primary CABG.

Conflict of interest: none declared.

REFERENCES

[1] Barner HB, Laks H, Codd JE, Standeven JW, Jellinek M, Kaiser GC *et al.* Cold blood as the vehicle for potassium cardioplegia. Ann Thorac Surg 1979;28:509–21.

[2] Bigelow WG, Lindsay WK. Oxygen transport and utilization in dogs at low body temperatures. Am J Physiol 1950;160:125–37.
[3] Rousou JA, Engelman RM, Breyer RH, Otani H, Lemeshow S, Das DK. The effect of temperature and hematocrit level of oxygenated cardioplegic solutions on myocardial preservation. J Thorac Cardiovasc Surg 1988; 95:625–30.
[4] Buckberg GD, Brazier JR, Nelson RL, Goldstein SM, McConnell DH, Cooper N. Studies of the effects of hypothermia on regional myocardial blood flow and metabolism during cardiopulmonary bypass. I. The adequately perfused beating, fibrillating, and arrested heart. J Thorac Cardiovasc Surg 1977;73:87–94.
[5] Lichtenstein SV, Ashe KA, el Dalati H, Cusimano RJ, Panos A, Slutsky AS. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
[6] Christakis GT, Koch JP, Deemar KA, Fremes SE, Sinclair L, Chen E *et al*. A randomized study of the systemic effects of warm heart surgery. Ann Thorac Surg 1992;54:449–57; discussion 457–59.
[7] Hayashida N, Ikonomidis JS, Weisel RD, Shirai T, Ivanov J, Carson SM *et al*. The optimal cardioplegic temperature. Ann Thorac Surg 1994;58: 961–71.
[8] Menasché P, Touchot B, Pradier F, Bloch G, Piwnica A. Simplified method for delivering normothermic blood cardioplegia. Ann Thorac Surg 1993;55:177–8.
[9] Braunwald E, Kloner RA. The stunned myocardium: prolonged, postischemic ventricular dysfunction. Circulation 1982;66:1146–9.
[10] Kloner RA, Przyklenk K, Kay GL. Clinical evidence for stunned myocardium after coronary artery bypass surgery. J Card Surg 1994;9(3 Suppl): 397–402.
[11] Breisblatt WM, Stein KL, Wolfe CJ, Follansbee WP, Capozzi J, Armitage JM *et al*. Acute myocardial dysfunction and recovery: a common occurrence after coronary bypass surgery. J Am Coll Cardiol 1990;15:1261–9.
[12] Marban E. Myocardial stunning and hibernation. The physiology behind the colloquialisms. Circulation 1991;83:681–8.
[13] Fiore AC, Swartz MT, Nevett R, Vieth PJ, Magrath RA, Sherrick A *et al*. Intermittent antegrade tepid versus cold blood cardioplegia in elective myocardial revascularization. Ann Thorac Surg 1998;65:1559–64; discussion 1564–65.
[14] Tan TE, Ahmed S, Paterson HS. Intermittent tepid blood cardioplegia improves clinical outcome. Asian Cardiovasc Thorac Ann 2003;11: 116–21.
[15] Elwatidy AM, Fadalah MA, Bukhari EA, Aljubair KA, Syed A, Ashmeg AK *et al*. Antegrade crystalloid cardioplegia vs antegrade/retrograde cold and tepid blood cardioplegia in CABG. Ann Thorac Surg 1999;68:447–53.
[16] Gerber BL, Wijns W, Vanoverschelde JL, Heyndrickx GR, De Bruyne B, Bartunek J *et al*. Myocardial perfusion and oxygen consumption in reperfused noninfarcted dysfunctional myocardium after unstable angina: direct evidence for myocardial stunning in humans. J Am Coll Cardiol 1999;34:1939–46.
[17] Jeroudi MO, Cheirif J, Habib G, Bolli R. Prolonged wall motion abnormalities after chest pain at rest in patients with unstable angina: a possible manifestation of myocardial stunning. Am Heart J 1994;127: 1241–50.
[18] Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R *et al*. Two internal thoracic artery grafts are better than one. J Thorac Cardiovasc Surg 1999;117:855–72.
[19] Gansera B, Schmidtler F, Gillrath G, Angelis I, Wenke K, Weingartner J *et al*. Does bilateral ITA grafting increase perioperative complications? Outcome of 4462 patients with bilateral versus 4204 patients with single ITA bypass. Eur J Cardiothorac Surg 2006;30:318–23.
[20] Martin TD, Craver JM, Gott JP, Weintraub WS, Ramsay J, Mora CT *et al*. Prospective, randomized trial of retrograde warm blood cardioplegia: myocardial benefit and neurologic threat. Ann Thorac Surg 1994;57: 298–302; discussion 302–04.
[21] Rees K, Beranek-Stanley M, Burke M, Ebrahim S. Hypothermia to reduce neurological damage following coronary artery bypass surgery. Cochrane Database Syst Rev 2001;CD002138.
[22] Mallidi HR, Sever J, Tamariz M, Singh S, Hanayama N, Christakis GT *et al*. The short-term and long-term effects of warm or tepid cardioplegia. J Thorac Cardiovasc Surg 2003;125:711–20.
[23] Hayashida N, Isomura T, Sato T, Maruyama H, Higashi T, Arinaga K *et al*. Minimally diluted tepid blood cardioplegia. Ann Thorac Surg 1998;65: 615–21.
[24] el-Hamamsy I, Stevens LM, Pellerin M, Bouchard D, Pagé P, Carrier M *et al*. A prospective randomized study of diluted versus non-diluted cardioplegia (minicardioplegia) in primary coronary artery bypass surgery. J Cardiovasc Surg (Torino) 2004;45:101–6.
[25] Sakai A, Miya J, Sohara Y, Maeta H, Ohshima N, Hori M. Role of red blood cells in the coronary microcirculation during cold blood cardioplegia. Cardiovasc Res 1988;22:62–6.