

Aortic Surgery without Infusion of Cardioplegic Solution at Total Circulatory Arrest

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Background: Minimal infusion of cardioplegic solution (CPS) during aortic surgery using total circulatory arrest (TCA) may reduce several potential side effects: clamping on a diseased aorta, insult of coronary ostia, and edema. **Materials and Methods:** From 2006 to 2009, 72 patients underwent aortic surgery without infusion of cardioplegic solution at the initiation of circulatory arrest. The diagnoses were acute aortic dissection (44), aneurysm (22), and intramural hematoma (6). **Results:** The duration of TCA, the lowest nasopharyngeal temperature, bypass time, and aortic clamp time was 45 minutes, 16.4°C, 162 minutes, and 100 minutes, respectively. The amount of CPS was 1,050 mL, and 15 patients underwent surgery without CPS. The average inotrope score was 113 points (range, 6.25 to 5,048.5 points) corresponding to the dopamine infusion of 5 mcg/kg/min for 1 day. Seven patients showed a level of creatine kinase-MB above 50 ng/mL, postoperatively, compared with the average of 12.75 ng/mL. The ischemic change was found on electrocardiogram in 5 patients, postoperatively. There was no cardiac morbidity requiring mechanical assist. The average of intensive care unit stay and postoperative hospital stay was 40 hours (range, 15 to 482 hours) and 11 days, respectively. **Conclusion:** Minimal infusion of only retrograde CPS during rewarming without initial infusion at TCA in aortic surgery is feasible and can be used with acceptable results.

Key words: 1. Aorta
2. Aortic, surgery
3. Heart arrest, induced
4. Myocardial protection

INTRODUCTION

In general, aortic surgery using total circulatory arrest (TCA) requires myocardial protection using hypothermia and cardioplegic solution (CPS), causing decrease of oxygen demand and metabolism in myocardial cell-like routine open heart surgery. At this point, if omission or minimal infusion

of CPS is achieved, several potential side effects may be prevented: systemic embolization or aortic rupture by clamping on the diseased ascending aorta, insult of coronary os during direct ostial CPS infusion, myocardial edema and hemodilution by fluid overloading, long time operation and anesthesia-induced complications by prolongation of bypass time and ultrafiltration. The aims of this study are the clinical out-

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Table 1. Disease and operative characteristics

Characteristic	Group	No. of cases
Disease entities	Acute aortic dissection	44
	Aortic aneurysm	22
	Intramural hematoma	6
Urgency	Elective	19
	Urgency	10
	Emergency	43
Repair of extent	Ascending aorta	9
	Aortic arch	50
	Bentall operation	7
	Valve sparing root remodeling	5
	Aortic valve replacement	3
	Descending aorta or elephant trunk	5

comes and safety of aortic surgery without initial infusion of cardioplegic solution at the moment of TCA and minimal infusion of only retrograde CPS during rewarming.

MATERIALS AND METHODS

1) Patient demographics

We retrospectively reviewed the medical records and laboratory data of 72 patients who underwent aortic surgery using TCA without initial CPS infusion from January 2006 to June 2009. There were 44 male patients and 28 females. The mean age was 59 years (range, 34 to 84 years). The diagnoses were 44 acute aortic dissections, 22 aortic aneurysms, and 6 cases of intramural hematoma (Table 1). There were 4 mortality cases.

2) Surgical techniques

After general endotracheal anesthesia, TCA was applied by cooling the body temperature using cardiopulmonary bypass (CPB), and the topical method was achieved using arterial cannulation via the ascending aorta or right axillary artery and venous cannulation via the superior and inferior vena cava under median sternotomy. We did not apply aortic cross clamping or initial CPS infusion at the moment of TCA antegradely by direct ostial infusion after aortotomy or retrogradely via the coronary sinus in the cases that were expected to require circulatory arrest times of about 30 minutes due to procedures such as ascending aorta, hemiarch, and to-

tal arch replacement. In the case of aortic valve surgery or valve sparing root replacement, we infused only retrograde 4°C blood CPS intermittently during rewarming of the body temperature using restart of CPB after distal anastomosis. CPB was weaned and ultrafiltration was applied routinely after the main procedure. We performed isolated replacement of the ascending aorta in 9 cases, ascending aorta and arch replacement in 50 cases, the Bentall operation in 7 cases, aortic valve sparing root replacement (the David procedure) in 5 cases, ascending aorta replacement with aortic valve replacement in 3 cases, and descending aorta replacement with elephant trunk insertion in 5 cases. In addition, the concomitant procedures were femorofemoral artery bypass, right gastroepiploic artery bypass, and coronary artery bypass grafting in 1 case each. There were 43 cases that underwent emergent operations (Table 1). The institutional review board approved this study and waived the requirement to obtain the individual patient's consent.

RESULTS

The mean TCA time and the lowest nasopharyngeal temperature was 45 minutes (range, 14 to 110 minutes) and 16.4°C (range, 12.2°C to 20°C), respectively. The mean CPB time and aortic cross clamping time was 162 minutes (range, 81 to 331 minutes) and 100 minutes (range, 34 to 219 minutes), respectively. A total CPS of 1,050 mL (range, 0 to 3,900 mL) was infused on average. In 15 cases, CPS was not infused. The total amount of free water removed by ultrafiltration was 2,600 mL (range, 800 to 6,000 mL), and the postoperative weight loss was 0.3 kg (range, 4.7 kg loss to 5.7 kg gain) on average.

The assessment of inotropic support was evaluated using the 'inotrope score,' a variable calculated as (dopamine or dobutamine dose×hour×1)+(epinephrine or norepinephrine dose×hour×100)+(milrinone dose×hour×10), wherein the dose of each inotropic agent were expressed as mcg/kg/min. The average score was 113 points (range, 6.25 to 5,048.5 points), corresponding to the dopamine infusion of 5 mcg/kg/min for 1 day, and the score exceeded 240 points in 16 patients. We administered inotropic agents for an average of 26 hours (range, 1.5 to 482 hours) and under 6 hours postoperatively in 28 patients.

Table 2. Clinical results

Variable	Average (note)
Duration of TCA (min)	45
The lowest nasopharyngeal temperature (°C)	16.4
CPB time (min)	162
ACC time (min)	100
Total amount of CPS (mL)	1,050 (15 cases without CPS)
Ultrafiltered free water (mL)	2,600
Postoperative body weight loss (kg)	0.3
Inotrope scores ^{a)} (point)	113 (16 cases above 260 points)
Peak level of CK-MB (ng/mL)	12.75
Ischemic change on ECG (case)	5
Arrhythmia (case)	10 (atrial fibrillation: 7 cases)
Mechanical circulatory assist (case)	0
ICU stay (hr)	40 (15-482)
Hospital stay (day)	11

TCA, total circulatory arrest; CPB, cardiopulmonary bypass time; ACC, aortic cross clamping time; CPS, cardioplegic solution; CK-MB, creatine kinase MB; ECG, electrocardiogram; ICU, intensive care unit.

^{a)}A variable calculated by (dopamine or dobutamine dose×hr×1)+(epinephrine or norepinephrine dose×hr×100)+(milrinone dose×hr×10), wherein the dose of each inotropic agent is expressed as mcg/kg/min.

The average creatine kinase MB fraction peak level was 12.75 ng/mL, and 7 cases showed a higher level at above 50 ng/mL. There were postoperative ischemic changes of the electrocardiogram (ECG) in 5 cases. A total of 10 cases of arrhythmia presented with atrial fibrillation (7 patients), sinus arrhythmia (2 patients), and right bundle branch block (1 patients). There was no case that required a mechanical circulatory assist device. The postoperative intensive care unit stay and hospital stay were 40 hours (range, 15 to 482 hours) and 11 days on average, respectively (Table 2). There was no cardiogenic mortality, but there were 4 non-cardiogenic mortality cases including ischemic necrosis of the bowels due to embolism, hypoxic brain damage, sepsis, and a sudden death suspected of aortic rupture.

DISCUSSION

In the basic concept, there exists a safe period during cir-

culatory arrest in open heart and aortic surgery when the cellular function and integrity are intact during the early and late postoperative phase. The safety of the procedure is limited by organ temperature during the safe period in relationship to hypothermia [1]. Since Bigelow et al. [2] reported on the usefulness of hypothermia in cardiac surgery in 1950 [3], Boerema et al. [4] demonstrated that experimental animals had recovered without any remarkable abnormalities after circulatory arrest for the maximum of 15 minutes after cooling using cooling coils via a femoral arteriovenous shunt. In 1960, Guiot et al. [5] and Weiss et al. [6] were the first to report successful applications of hypothermia and circulatory arrest to a human. Contemporary partial bypass, hypothermia, and circulatory arrest were introduced by Lillehei et al. [7] in 1969, and Griep et al. [8] applied them to arch aneurysm surgery in 1975.

In addition, inducing ischemic myocardial arrest using deep hypothermia at the lowest temperature has been achieved at 22°C for 45 to 60 minutes as a safe period without myocardial dysfunction, clinically [9]. The biochemical reaction, essential to cellular metabolism, depends on the body temperature [10]. Hypothermia supports the recovery of normal cell structure and function in the reperfusion phase using declination of metabolism during the ischemic period induced by circulatory arrest. At this point, metabolism is directly related to oxygen consumption; therefore, minimization of oxygen consumption and temperature is closely associated with a safe period during arrest [11-13].

Furthermore, hypothermia reduces the release of excitotoxic amino acids (aspartate and glutamate) [14], calcium influx, and promotes recovery of protein synthesis [15]. It has also been reported as decreasing membrane-bound protein kinase C activity [16] and extending the onset time of ischemic depolarization [17].

Because it is clear that hypothermia reduces oxygen consumption, the application of hypothermia for myocardial protection is now performed universally. The protective effects of hypothermia changes according to the temperature coefficient, the Q_{10} effect, describing the metabolic rate of tissue altered by temperature; theoretically, for every myocardial temperature fall of 10 degrees, the myocardial oxygen consumption (MVO_2) should reduce by half.

In 1982, Rosenfeldt [18] reported moderate hypothermia, down to 25°C, could reduce over 50% of the MVO_2 , but there was no additional benefit to lowering temperature to 22°C. In 1980, Swanson et al. [19] demonstrated the safety of maintaining deep hypothermia at 4°C, and English et al. [20] presented a rationale for hypothermic myocardial preservation in heart transplantation.

Regional vascular occlusion can be induced by hypothermia and then can result in the 'no reflow phenomenon.' Ultimately, Blocking of microcirculation inhibits tissue reperfusion followed by tissue damage despite resumption of circulation. However, Norwood et al. [21] proved by experimentation that this phenomenon is not caused by only circulatory arrest itself but by the combined circumstance of severe hypoxia and that low hypothermia to 20°C even protects it. Hypoxia induces endothelial damage, followed by this phenomenon due to activate release of endothelin-1, the most powerful vasoconstrictor, brings a vicious cycle of insults on the cell. In this hypoxic status, hypothermia was proved to prevent endothelial damage [22].

If both hypothermic circulatory arrest and CPS were applied simultaneously, the merits of each could offset the other. First, because declination of MVO_2 is not remarkable during the initial phase of circulatory arrest regardless of CPS, the hyperkalemic CPS effect is subtle and second; continued CPB could rewarm or inappropriately reperfuse the myocardium. For these reason, application of only hypothermia without CPS has merit. However, Fremes et al. [23], Weisel et al. [24], and Yau et al. [25] have suggested several faults of hypothermia such as 1) delayed myocardial recovery due to a decrease of fluidity and transmembrane transport of the plasma membrane, ionic imbalance due to an increase of intracellular edema and Na accumulation, and cellular injuries such as protein denaturation, 2) postoperative bleeding tendency, and 3) a long operation time affected by a prolonged bypass time.

Therefore, we believe that hypothermia can be complemented by CPS infusion, but the previously described counterbalance must be considered. Clamping of the diseased ascending aorta or ostial injury induced by the direct coronary ostial CPS infusion catheter after aortotomy may be replaced with retrograde infusion via the coronary sinus; edema

and hemodilution that develops from fluid overloading may be controlled by ultrafiltration.

We reviewed postoperative cardiac enzyme and ECG changes to assess the adequacy of myocardial protection. However, the parameters used were not sufficient, and mild myocardial damage may be controlled by postoperative inotropic administration. Therefore, in this study, we quantified the cardiovascular function using the inotrope score as a parameter to distinguish between the damaged and protected myocardium after TCA. The inotrope score was originally introduced by Wernovsky et al. [26] as a quantitative measurement of cardiovascular support. Gaies et al. [27] suggested that the inotrope score can be used as an independent predictor of short-term outcomes of illness severity, morbidity, and mortality in patients suffering from low cardiac output syndrome after open heart surgery.

On a side note, this trial is not a first of all. From a historical perspective, the timing of CPS infusion has changed from just before TCA to just after TCA, and even after distal anastomosis during aortic surgery. Although the timing might be changed according to surgeon's preference or for the purpose of procedural ease, it is our opinion that myocardial protection cannot be absolutely guaranteed based on the timing of CPS infusion. Furthermore, prompt restoration of myocardial perfusion after short TCA may permit infusion of delayed CPS or even omission.

In conclusion, we suggest that only hypothermia can protect the myocardium, avoiding complications induced by CPS infusion in aortic surgery using TCA without initial CPS, according to our clinical cases retrospectively reviewed showing favorable outcomes of the intraoperative and postoperative period.

As a matter of course, a simple proximal anastomosis performed by a skilled surgeon or a more advanced operative technique using an artificial graft or substitute can be accomplished without myocardial damage during the short rewarming period due to the aftereffects of hypothermia alone and without inessential CPS infusion. However, there are some limitations of single hypothermia for myocardial or organic protection without CPS infusion; therefore, further evaluation of more complex procedures, such as the aortic root remodeling combined with aortic surgery described above, will be

required. In addition, further study will be required to explore myocardial evaluation using other diagnostic tools such as echocardiography, single photon emission computerized tomography, and cardiac magnetic resonance imaging.

While the faults associated with conventional CPS infusion may be considered a limitation of our study, if a “golden time” for deep hypothermia alone without the need for the negative effects of myocardial function can be identified by scientific and clinical research, it may become routine to not insert a catheter for CPS infusion. We suggest that if some procedure could be omitted, it would be more effective and scientifically sound.

CONCLUSION

Minimal infusion of only retrograde CPS during rewarming without initial infusion in aortic surgery using TCA is feasible and can be used as a safe surgical modality with acceptable results on the additional basis of large scale clinical studies.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

- Kirklin JW, Barratt-Boyes BG. *Cardiac surgery: hypothermia, circulatory arrest, and cardiopulmonary bypass*. 3rd ed. New York: Churchill Livingstone; 2003.
- Bigelow WG, Lindsay WK, Greenwood WF. *Hypothermia; its possible role in cardiac surgery: an investigation of factors governing survival in dogs at low body temperatures*. *Ann Surg* 1950;132:849-66.
- Bigelow WG, Lindsay WK, Harrison RC, Gordon RA, Greenwood WF. *Oxygen transport and utilization in dogs at low body temperatures*. *Am J Physiol* 1950;160:125-37.
- Boerema I, Wildschut A, Schmidt WJ, Broekhuysen L. *Experimental researches into hypothermia as an aid in the surgery of the heart*. *Arch Chir Neerl* 1951;3:25-34.
- Guiot G, Rougerie J, Arfel G, Dubost C, Blondeau P. *“Extreme cold” in neurosurgery: possibilities and future perspectives: reflections apropos of the 1st case of vascular malformation operated on with success under prolonged circulatory arrest and hypothermia at 10 degrees*. *Neurochirurgie* 1960;6:332-46.
- Weiss M, Piwnica A, Lenfant C, et al. *Deep hypothermia with total circulatory arrest*. *Trans Am Soc Artif Intern Organs* 1960;6:227-39.
- Lillehei CW, Todd DB Jr, Levy MJ, Ellis RJ. *Partial cardiopulmonary bypass, hypothermia, and total circulatory arrest: a lifesaving technique for ruptured mycotic aortic aneurysms, ruptured left ventricle, and other complicated cardiac pathology*. *J Thorac Cardiovasc Surg* 1969;58:530-44.
- Griep RB, Stinson EB, Hollingsworth JF, Buehler D. *Prosthetic replacement of the aortic arch*. *J Thorac Cardiovasc Surg* 1975;70:1051-63.
- Conti VR, Bertranou EG, Blackstone EH, Kirklin JW, Digerness SB. *Cold cardioplegia versus hypothermia for myocardial protection: randomized clinical study*. *J Thorac Cardiovasc Surg* 1978;76:577-89.
- Fuhrman GJ, Fuhrman FA. *Oxygen consumption of animals and tissues as a function of temperature*. *J Gen Physiol* 1959;42:715-22.
- Fuhrman FA. *Oxygen consumption of mammalian tissue at reduced temperatures*. In: Dripps RD, editor. *The physiology of induced hypothermia*. Washinton (DC): National Academy of Sciences, National Research Council; 1956. p. 50.
- Field 2nd J, Belding HS, Martin AW. *An analysis of the relation between basal metabolism and summated tissue respiration in the rat: the post-pubertal albino rat*. *J Cell Comp Physiol* 1939;14:143-57.
- Fuhrman FA, Fuhrman GJ, Farr DA, Fail JH. *Relationship between tissue respiration and total metabolic rate in hypo- and normothermic rats*. *Am J Physiol* 1961;201:231-4.
- Busto R, Globus MY, Dietrich WD, Martinez E, Valdes I, Ginsberg MD. *Effect of mild hypothermia on ischemia-induced release of neurotransmitters and free fatty acids in rat brain*. *Stroke* 1989;20:904-10.
- Widmann R, Miyazawa T, Hossmann KA. *Protective effect of hypothermia on hippocampal injury after 30 minutes of forebrain ischemia in rats is mediated by postischemic recovery of protein synthesis*. *J Neurochem* 1993;61:200-9.
- Busto R, Globus MY, Neary JT, Ginsberg MD. *Regional alterations of protein kinase C activity following transient cerebral ischemia: effects of intracerebral brain temperature*

- modulation*. J Neurochem 1994;63:1095-103.
17. Nakashima K, Todd MM, Warner DS. *The relation between cerebral metabolic rate and ischemic depolarization: a comparison of the effects of hypothermia, pentobarbital, and isoflurane*. Anesthesiology 1995;82:1199-208.
 18. Rosenfeldt FL. *The relationship between myocardial temperature and recovery after experimental cardioplegic arrest*. J Thorac Cardiovasc Surg 1982;84:656-66.
 19. Swanson DK, Dufek JH, Kahn DR. *Improved myocardial preservation at 4 degrees C*. Ann Thorac Surg 1980;30:518-26.
 20. English TA, Cooper DK, Medd R, Wheeldon D. *Orthotopic heart transplantation after 16 hours of ischaemia*. Proceedings of the British Cardiac Society. British Heart J 1980; 43:721-2.
 21. Norwood WI, Norwood CR, Castaneda AR. *Cerebral anoxia: effect of deep hypothermia and pH*. Surgery 1979;86:203-20.
 22. Zhang JX, Wolf MB. *Effect of cold on ischemia: reperfusion-induced microvascular permeability increase in cat skeletal muscle*. Cryobiology 1994;31:94-100.
 23. Fremes SE, Weisel RD, Mickle DA, et al. *Myocardial metabolism and ventricular function following cold potassium cardioplegia*. J Thorac Cardiovasc Surg 1985;89:531-46.
 24. Weisel RD, Mickle DA, Finkle CD, Tumiaty LC, Madonik MM, Ivanov J. *Delayed myocardial metabolic recovery after blood cardioplegia*. Ann Thorac Surg 1989;48:503-7.
 25. Yau TM, Ikonomidis JS, Weisel RD, et al. *Ventricular function after normothermic versus hypothermic cardioplegia*. J Thorac Cardiovasc Surg 1993;105:833-43.
 26. Wernovsky G, Wypij D, Jonas RA, et al. *Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants: a comparison of low-flow cardiopulmonary bypass and circulatory arrest*. Circulation 1995;92:2226-35.
 27. Gaies MG, Gurney JG, Yen AH, et al. *Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass*. Pediatr Crit Care Med 2010; 11:234-8.