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Normothermic cardiopulmonary bypass: effect on the incidence of persistent postoperative neurological dysfunction following coronary artery bypass graft surgery

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Abstract: We retrospectively reviewed the records of 250 consecutive patients undergoing coronary artery bypass graft surgery (CABG) from January 1994 through January 1996 to determine the incidence of persistent postoperative neurological dysfunction after CABG and to compare normothermic and moderate hypothermic cardiopulmonary bypass (CPB). Normothermic CPB was used in 128 patients (36°–37°C) and hypothermic CPB (27°–28°C) in 122 patients. Postoperative neurological dysfunction included focal motor deficits, delayed recovery of consciousness (>24 h) after surgery, and seizures within 1 week postoperatively. Persistent neurological dysfunction was diagnosed if complete resolution had not occurred within 10 days of surgery. The incidence of persistent postoperative neurological dysfunction was 4.1% in the hypothermic CPB group and 2.3% in the normothermic CPB group. There were no statistically significant differences between the two groups (P = NS). These results suggest that normothermic CPB did not increase the incidence of persistent postoperative neurological dysfunction compared to hypothermic CPB.

Key words: Postoperative complication, Neurological dysfunction, Temperature, Hypothermia, Cardiopulmonary bypass, Coronary artery bypass graft surgery

Introduction

Hypothermic cardiopulmonary bypass (CPB) has been used during cardiac surgery for nearly 40 years to facilitate myocardial and cerebral preservation. It has been demonstrated that normothermic CPB improves post-CPB cardiac function, reduces the incidence of perioperative myocardial infarction (MI), and reduces the incidence of low-output syndrome and the need for intraaortic balloon counter-pulsation [1]. Normothermic CPB in the presence of cardioplegia also results in a reduction of markers of myocardial ischemia [2,3].

Normothermic CPB may predispose to or increase the central nervous system (CNS) injury because of the lack of hypothermic cerebral protective effects [4]. The purpose of this retrospective study is to compare the incidence of persistent postoperative neurological dysfunction between normothermic and hypothermic CPB for coronary artery bypass graft surgery (CABG).

Materials and method

After Institutional Review Board approval, the records of 250 consecutive adult patients undergoing CABG between January 1994 and January 1996 were retrospectively reviewed by one investigator (K.N.). Normothermic CPB was used in 128 patients (36°–37°C) between February 1995 and January 1996, and hypothermic CPB was used in 122 patients (27°–28°C) between January 1994 and January 1995. All patients were operated on by a single cardiothoracic surgeon. Patients who had had previous CABG, CABG without cross-clamping of the ascending aorta, previous or concomitant valve replacement, thoracic aortic aneurysectomy, or ventricular aneurysectomy were excluded. Patients who died within 3 days of surgery and could not be neurologically evaluated were also excluded. All those patients died of cardiac dysfunction, not neurological dysfunction and brain death.

Premedication consisted of diazepam 10 mg PO, famotidine 20 mg PO, and morphine sulfate 5–10 mg i.m. Anesthesia was induced with intravenous midazolam 0.1–0.2 mg·kg^{-1} and fentanyl 10–15 μg·kg^{-1}; tracheal intubation was facilitated by pancuronium 0.10–0.15 mg·kg^{-1}. Anesthesia was maintained with

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supplemental fentanyl (up to 30μg·kg^{-1}) and midazolam. Isoflurane was used as needed.

The bladder temperature was continuously monitored with a thermal, sensor-equipped catheter. Arterial cannulas were placed in the aortic root (n = 242) or the femoral artery (n = 8). Membrane oxygenators with 40μm filters and a nonpulsatile pump were used in all patients. CPB flow rate was maintained at 2.6L·min^{-1}·m^{-1} and the perfusion pressure between 50 and 60mmHg.

Bladder temperature was maintained at 27°–28°C and at 36°–37°C in the hypothermic and normothermic groups, respectively. $Paco_2$ was maintained (uncorrected to temperature) in the range of 30–40mmHg. Cold or warm blood cardioplegia was instituted in the hypothermic and normothermic groups, respectively. Additional cardioplegic solution was infused at 30-min intervals. Weaning from CPB was accomplished with the use of dopamine and dobutamine, with norepinephrine as needed.

Patient characteristics including age, sex, preexisting conditions (diabetes, hypertension), and ejection fraction were recorded. Operative considerations recorded included duration of surgery, anesthesia, CPB, and aortic cross-clamping.

Postoperative neurological dysfunction were defined as a focal motor deficit, disturbance of consciousness defined as a two- or three-digit code of consciousness level using the Japan Coma Scale (24h postoperative), or seizures within 1 week of surgery. Postoperative neurological dysfunction was considered transient if resolution occurred by the tenth postoperative day. In patients with preoperative cerebrovascular disease (CVD), postoperative neurological dysfunction was considered new only if it included a new neurological symptom or exacerbation of the preexisting symptom.

Data are expressed as the mean ± standard deviation. Values were compared between normothermic and moderately hypothermic CPB using the unpaired t-test, Fisher's test, or chi-square analysis. A P value of less than 0.05 was considered statistically significant.

Results

Patient characteristics are summarized in Table 1. There were no significant differences in age, sex, diabetes, hypertension, or ejection fraction between the normothermic and hypothermic groups. The duration of surgery, anesthesia, and CPB was significantly greater in the hypothermic group (Table 2).

There was one patient in each group with transient postoperative neurological dysfunction. Five patients in the hypothermic group and three patients in the normothermic group had a focal motor deficit, which meant persistent postoperative neurogical dysfunction (Table 2). The diagnosis was confirmed by postoperative computed tomography (CT) and neurological consultation. No seizures were noted in any patient within 1 week of surgery.

The incidence of persistent postoperative neurogical dysfunction was 4.1% in the hypothermic CPB groups

Table 1. Patient characteristics

Characteristic	Hypothermic CPB (n = 122)	Normothermic CPB (n = 128)
Age (years)	63.9 ± 8.3	64.0 ± 8.37
Male (%)	72.1	70.3
Diabetes mellitus (%)	26.2	23.4
Hypertension (%)	44.3	31.3
Ejection fraction (%)	61.6 ± 11.2	62.2 ± 12.1

CPB, cardiopulmonary bypass.
Values are expressed as the mean ± SD.

Table 2. Surgical characteristics and neurological outcome

Characteristic/outcome	Hypothermic CPB	Normothermic CPB
Temperature during CPB (°C)	27–28	36–37
Operation time (min)	337.0 ± 78.9	302 ± 72*
Anesthesia time (min)	399.0 ± 82.1	344 ± 76*
Total CPB time (min)	116 ± 28	91.0 ± 21.6*
Time of aortic clamping (min)	76.9 ± 24.0	64 ± 12
Persistent postoperative neurological dysfunction (%)	4.1	2.3

Values are the mean ± SD.
*$P < 0.05$, normothermic *vs* moderately hypothermic group.

and 2.3% in the normothermic CPB group. There were no statistically significant differences between the two groups ($P = 0.43 > 0.05$, NS).

Discussion

In this retrospective study, normothermic CPB does not appear to increase the incidence of persistent postoperative cerebral vascular accident compared to that seen with hypothermic CPB. Postoperative neurological dysfunction is a major cause of morbidity after cardiac surgery and occurs in 1%–11% of patients [5–9]. The incidence varies according to the nature of the study and the criteria used to define neurological dysfunction. We report an incidence in both groups that is well within the range of previously reported studies. The number of the patients in this report is enough to comment on the postoperative neurological dysfunction after CABG in one hospital.

The possibility of increasing postoperative neurological deficits after normothermic CPB is of concern. To date, two large randomized trials of warm versus cold heart surgery have been reported [2,3]. The study of Martin et al. identified an approximately threefold increase in cerebral vascular accidents with normothermic CPB [2]. In contrast, the Warm Heart Investigators reported no difference between normothermic and hypothermic CPB [3]. Differences in these two studies that may have affected the results include differences in technique and patient populations in the management of temperature during normothermic CPB. The study of Martin et al. maintained a systemic temperature higher than 35°C during normothermic CPB, whereas the Warm Heart Investigators did not standardize the systemic temperature, which ranged between 33° and 37°C. The effect of mild hypothermia (33°–35°C) on neuroprotection might also have affected the outcomes. There are other important differences in surgical technique and patient populations that may have affected these trials as well. In the normothermic CPB group of Martin et al. the duration of aortic cross-clamping was significantly longer, and more high-risk patients (diabetic and reoperation) were included. These factors could contribute to the poorer neurological outcomes in the normothermic group. Neither study utilized intense cognitive methodology. Thus the reported outcomes of the two studies might be over- or underestimated. Two other prospective, nonrandomized but consecutive historical control studies reported no change in the incidence of postoperative neurological dysfunction with normothermic CPB compared to hypothermic CPB (warm 1.0% *vs* cold 1.3%, warm 0.8% *vs* cold 1.0%, respectively) [10,11].

To compare the incidence of postoperative neurological dysfunction between normothermic and hypothermic CPB, it is necessary to standardize risk factors and criteria for neurological dysfunction. Among the many risk factors we consider preexisting CVD and aortic calcification to be of great importance. At our hospital patients with severe stenosis or occlusion of cerebral arteries undergo an extracranial-to-intracranial bypass before elective CABG. Patients with more than 75% stenosis of a unilateral internal carotid artery undergo carotid endarterectomy prior to CABG. If bilateral carotid disease is present, these patients may undergo combined CABG and carotid surgery. Those patients were excluded from this study. Patients with a severely calcified ascending aorta undergo CABG without aortic cross-clamping; those patients were also excluded from this study.

Long-duration CPB is also a recognized risk factor. In this study total CPB time in the hypothermic group was longer than that of the normothermic group. However, because both were less than 2 h we do not consider this difference to be of clinical significance [8].

The retrospective nature of the present study precluded the use of neurocognitive measures for detailing postoperative neurological dysfunction. One study with a battery of mental tests reported no difference in the incidence of psychological disorders [12].

In summary, we found in this retrospective study that normothermic CPB did not increase the incidence of persistent postoperative neurological dysfunction in patients undergoing CABG.

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