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Warm Versus Cold Heart Surgery in Diabetics

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Abstract: The aim of the study was to compare the effect of the classic hypothermic perfusion technique with cold crystalloid cardioplegia with the more modern warm heart surgery with warm continuous cardioplegia in a specific risk group, i.e. diabetics. Retrospective study, built around a date (May, 1993) when the technique was uniformly adopted as standard practice in a cardiac surgical unit (Hamilton), at the time a three specialist cardiac surgical unit in a 600-bed central, university-affiliated hospital in Hamilton, New Zealand. Other changes of practice at the time (team, assistance, learning curve, anaesthesia, perfusion, oxygenators) were carefully analysed. No obvious relevant changes were identified in a rigorous analysis. 2198 operations were analysed and 186 consecutive operations on diabetic patients identified. Normothermic (Group W) coronary bypass operations in 117 diabetic patients were compared to 69 similar operations with hypothermia and antegrade crystalloid cardioplegia (Group C). The groups did not differ with regard to age, sex, severity of diabetes or coronary heart disease. There were more urgent operations in Group W (41 vs. 33%). In Group C, mortality was 5.8%, in Group C 2.6%. Stroke rate was 1.4% in Group C and 1.7% in Group W. There were no differences in perioperative myocardial infections. Inotropes were needed less frequently in Group W (13.9 vs. 30.4%, $p<0.05$). Atrial fibrillation was more common in Group W (43,9 vs. 31.9%, $p<0.05$). Heart block was less common in Group W (3.4 vs. 23.2%, $p<0.05$). Transient renal function impairment was significantly more common in Group W (12.8 vs. 4.3%, $p<0.05$). More sternal wound problems were seen after hypothermic surgery (14.5 vs. 5.1%). Warm heart surgery seemed safe, with reduced use of inotropic agents postoperatively, less heart block and fewer infections. However, atrial fibrillation was more common and renal impairment may present a problem in a high-risk population.

Key words: Classic hypothermic, crystalloid, cardioplegia

INTRODUCTION

Since its introduction some ten years ago, warm heart surgery has been routinely employed in more than ten percent of cardiac units worldwide[1]. The initial expectations were optimistic; future cardiac operations were to have "a smooth course…" with "the ability to perform unhurried complex procedures…, virtually all patients could be weaned from bypass with little or no support"[2]. Since then, warm heart surgery has been connected to an increased incidence of stroke[1] and has become generally more controversial and affected by the development of other, competitive techniques, such as off-pump cardiac revascularization.

This study was designed to identify possible clinical benefits and risk factors associated with routine warm heart surgery in a high-risk population of 186 diabetics consecutively operated using the two methods. The chosen cardiac unit offered an ideal setting for comparison, since warm heart surgery was uniformly adopted overnight (May, 1993) by three very experienced surgeons, who performed all operations in the series around the date. Although the study was retrospective in its nature, rigorous analysis of other factors around the time identified no other relevant technical changes.

MATERIALS AND METHODS

Between May, 1993 and June, 1996, 1102 operations were performed using the techniques to be described. Prior to that, from January, 1990 until the beginning of the new era, 1096 operations had been performed employing hypothermic bypass and antegrade crystalloid cardioplegia.

A total of 186 diabetic patients were identified from a prospective database of 2198 consecutive operations.

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They were divided into two subgroups: cold heart surgery (28-32C), Group C and Group W, 35-37C). The division point of the study was the uniform adoption of the new technique, which was accepted by the three operating surgeons simultaneously. The practice was changed overnight.

Patient characteristics: The patient characteristics are presented in (Table 1).

In the cold group, Group C, there were 69 patients, 13 (18.8%) with Insulin Dependent Diabetes Mellitus (IDDM). The median age of the group was 61.1 years. The patients, 18 (26.1%) were female. Sixty patients underwent coronary grafting, the rest had a valve inserted as well (8 aortic, one mitral). The operations, 46 (66.7%) were elective, 23 (33.3%) urgent.

In the warm group (Group W), there were 117 patients. Their median age was 59.7 years. Them, 33 (28.2%) were female. Of these patients, 26 (22.2%) had IDDM, the rest NIDDM. Coronary artery bypass grafting alone was performed on 100 (85.5%) and 17 (14.5%) had a combination of valve insertion (12 aortic, 5 mitral) and coronary bypass grafting. Of the operations, 73 (59%) were elective, 44 (41%) urgent.

The groups did not differ significantly with regard to age, severity of disease (diabes or coronary artery disease), hypertension, previous cerebrovascular events, previous myocardial infarctions, renal function or NYHA classification. There were more emergent operations in the warm group (41 vs. 33.3%).

All patients had undergone cardiac catheterisation to assess ventricular function and the extent of their coronary artery disease. Left ventricular function was estimated from a single-plane ventriculogram. Coronary artery disease was assessed using at least to views of each vessel. A difference of 50% between the narrowing and free lumen was deemed significant.

Anaesthesia: Premedication, induction and maintenance of anaesthesia were similar in both groups. It consisted of weight-dependent doses of fentanyl, isoflurane, midazolam and pancuronium. In addition, propofol infusion was used in later cases.

The patients remained on controlled mechanical ventilation at least four hours postoperatively.

Cardiopulmonary bypass

After median sternotomy and heparinisation (target activated clotting time more than 400 seconds), the heart was cannulated via the ascending aorta and a single two-stage right atrial cannula.

Full cardiopulmonary bypass was instituted using a roller pump (Stöckert, Shiley Inc., Germany) and patients were brought to a nasopharyngeal temperature of 28C to 32C in Group C and 35C to 37C in Group W. During cardiopulmonary bypass, perfusion flow was maintained above 2.4 L min m^2 with a mean arterial pressure of 70 to 80 mm Hg. Moderate haemodilution with haematocrit values between 20 and 25% was used together with alpha-stat acid base balance maintenance.

With the heart empty and beating, a high potassium cold crystalloid cardioplegic solution at 4C in Group C and 37C blood in Group W was introduced into the aortic root via a proximal port after clamping of the aorta. In group W, a 17 Fr retrograde coronary sinus cannula (DLP, Grand Rapids, MI, USA) was inserted as well.

High potassium blood cardioplegia was achieved using a modified St Thomas' solution added to oxygenated blood diluted 4 to 1 with the solution initially, then addition to blood via an IVAC pump. The solution had a haematocrit of 20 to 25% and a potassium concentration of 20 mEq L^{-1}, delivered at an initial rate of approximately 300 ml min. Generally, some 400 ml were needed for arrest.

Thereafter, low potassium (0.9 mmol) solution was infused continuously at a rate of approximately 130 mL h in Group W. If cardiac activity recurred in either group during cross-clamping, high potassium cardioplegia was reinstituted.

In Group C, 1000 ml of cold crystalloid cardioplegia was infused antegradely through the aortic root cannula after cross-clamping.

In all cases, distal anastomoses were performed first. A blower introducing filtered oxygen into the operating area was used to facilitate visualization in the warm group. Proximal anastomoses were performed using a partially occluding clamp in both groups.

The valve operations were performed using standard techniques. The operative parameters are presented in (Table 2).

Data collection: All data were collected in a prospective manner for the Waikato University Cardiac Surgery Database.

Digital standard electrocardiograms were taken preoperatively, on the first day after the operation, after five days and if necessary as deemed by the attending physician.

Blood samples for creatine kinase isoenzymes (CK-MB) were obtained at 24 hrs postoperatively.

Data were collected on myocardial infarction, defined as an elevation in CK-MB greater than 6% of the total amount of the total CK.

The need for inotropic agents to keep systolic blood pressure above 90 mmHg in the presence of optimised filling pressures was recorded.

Table 1: Patient characteristics of 186 diabetics undergoing coronary artery surgery (hypo-or normothermic)

	COLD		WARM	
	(N = 69)	(%)	(N = 117)	(%)
Nature of operation				
-elective	46	66.7	73	59
-emergent	23	33.3	44	41
Hypertension	41	59.4	66	56.4
Previous cerebrovascular accident	5	7.2	6	5.1
NYHA class				
I	42	60.9	65	55.5
II	6	8.7	25	21.4
II	9	13.0	23	19.7
IV	12	12	4	3.4
IDDM	13	18.8	26	22.2
NIDDM	56	81.2	91	77.8

(Abbreviations: NYHA = New York Heart Association. IDDM = Insulin-dependent diabetes mellitus. NIDDM = non-insulin-dependent diabetes mellitus)

Table 2: Perioperative parameters of 186 consecutive diabetics undergoin hypo-or normothermic cardiac surgery

	Cold		Warm	
	N = 69		N = 117	
Number of grafts				
- 3 or more	49	70.4%	86	73.5%
- valve	9	13.4%	17	14.5%
Mean+/-standard deviation				
Age (years)	61+/-9		60+/-9	
Weight (kilograms)	81+/-15		81+/-17	
LVEF (%)	62+/-18		66+/-17	
LVEDP (mmHg)	18+/-7		21+/-8	
CPB (minutes)	85+/-32		84+/-40	
Cross-clamp time (min)	43+/-21		44+/-17	
Lowest temperature (Centigrades)	27.8+/-1.8		34.7+/-1.1	
Blood loss (ml/ 24 h)	955+/-433		11051/-601	

(Abbreviations: LVEF = left ventricular ejection fraction. LVEDP = left ventricular end-diastolic pressure. CPB = cardiopulmonary bypass)

Postoperative bleeding was recorded from theatre until removal of the drains (generally within 24 hrs).

Stroke was identified as any new focal neurological symptoms. A computerized tomography was performed in all suspected cases to identify the cause. It was recorded as temporary, if it was fully resolved within 30 days.

Renal impairment was identified as elevation of serum creatinine of more than 250 micromols L^{-1} with an elevation of at least 50% compared to preoperative values, leading to therapy with diuretics or dialysis.

Any wound discharge with signs of clinical infection leading to antibiotic therapy (with or without bacteria identified in cultures) was recorded as infection. Chest infections were recorded as reported by the radiologists. Any death within 30 days of surgery was recorded as operative death.

Analysis of other factors: Other factors, such as change of assistants, anaesthesia technique, perfusion pressures, oxygenators, postoperative temperatures and possible changes in surgical technique were discussed in detail with each surgeon and anaesthetist.

Statistical methods: Statistical testing was done using BMDP software (Biomedical Data Processing, Sepulveda, California, USA). Results are presented as the mean +/- standard deviation of proportions. Continuous measures were compared by unpaired Students t test and categorical measures by X2 statistical analyses.

RESULTS

The results are presented in (Table 3). The mortality rate was 4 (5.8%) in Group C and 3 (2.6%) in Group W. Temporary or permanent neurologic deficits were observed in 2 (2.9%) in Group C and 3 (2.6%) in Group W. Inotropes were used as previously described in 21 (30.4%) in Group C and 16 (13.9%) in Group W ($p<0.05$). Intra-aortic balloon pulsation therapy was not used in either group.

Reoperations were performed in 3 (4.3%) in Group C and 3 (2.6%) in Group W. Reoperations for other reasons were performed in one (1.4%) and three (1.7%), respectively. The median blood loss was 955 mL 24hrs in Group C and 1100 mL 24hrs in Group W.

Table 3: Results of 186 consecutive diabetics undergoing warm or cold heart surgery

	Cold		Warm	
	N = 69	(%)	N = 117	(%)
Mortality	4	5.8	3	2.6
Stroke	1	1.4	2	1.7
Temporary neurologic deficit	1	1.4	1	0.9
Use of inotropes	21	30.4	16	13.9*
Reoperation for bleeding	3	3.4	3	2.6
Reoperation for other reason	1	1.4	2	1.7
Perioperative myocardial infarction	8	11.6	12	10.3
Arrhythmias				
- atrial fibrillation/flutter	22	31.9	51	43.6*
- heart block	16	23.2	4	3.4*
Infections				
- sternal superficial	10	14.5	4	5.1*
- sternal deep	1	1.4	2	1.7
- vein harvest site	5	7.2	13	11.1
- chest	6	8.7	7	6.0
Renal function impairment	3	4.3	15	12.8*
Dialysis	0	0	4	5.1

(* = $p<0.05$)

Perioperative myocardial infarctions were diagnosed in 8 (11.6%) in Group C and 12 (10.3%) in Group W.

Arrhythmias were observed as follows: in Group C, 22 (31.9%) had atrial fibrillation/flutter, in Group W 51 (43.6%), $p<0.05$. A heart block was identified in 16 (23.2%) in Group C and in 4 (3.4%) in Group W.

Superficial sternal wound infections were diagnosed in 10 (14.5%) in Group C and 4 (5.1%) in Group W ($p<0.05$). Mediastinitis was identified in one (1.4%) and two (1.7%), respectively. Vein harvest site infections were diagnosed in 5 (7.2%) in Group C and 13 (11.1%) in Group W. Chest infections were seen in 6 (8.7%) in Group C and 7 (6.0%) in Group W.

Renal function impairment was recorded in three (4.3%) in Group C and 15 (12.8%) in Group W ($p<0.05$). Four of these patients required haemodialysis. In the others, creatinine returned to preoperative levels within ten days.

DISCUSSION

Warm heart surgery was introduced by Lichtenstein *et al.* in 1991[3,4]. The early reports were optimistic. The new technique seemed physiologically sound, as it was shown that the main factor in myocardial protection is electromechanical arrest of the heart [2-4]. Hypothermia was shown to reduce the oxygen consumption by only additional 10%[2,3]. These findings led to the introduction of normothermic bypass and cardioplegia. Benefits other than enhanced postoperative myocardial performance were expected in postoperative bleeding and arrhythmias[5,6].

Our study compared the two methods in a high risk population of 186 diabetics. A high risk population was used based on the hypothesis that it would reveal more of the possible postoperative problems, such as stroke, renal impairment and infections.

The comparison is retrospective and although it would be unreasonable to presume that the change in temperature was the only change in the performance of the whole team, we still argue that the comparison is valid due to intrinsic, unique factors related to the particular cardiac unit where the study was performed. All operations were done by the same three surgical teams (three surgeons, three anaesthetists). The cutoff point was a day in May, 1993, as after that date, all operations were performed using normothermia and warm blood cardioplegia. The other variables were consciously kept as constant as possible.

Generally, stroke rate after cardiac surgery appears to be approximately 2%[7]. Normothermia has been suspected of producing more strokes than hypothermia. Martin *et al.*[1] reported a significantly increased risk of stroke using warm heart surgery compared to hypothermia (4.5 vs. 1.4%). In our study of a high risk group, no such difference was seen (1.7 vs. 1.4%). Our findings were similar to those of Singh *et al.*[8]. Normothermia has been connected to deterioriation of psychomotorics, but not of memory[9, 10]. The group of Engelman *et al.* was unable to show any neuroprotective effect from moderate hypothermia[11, 12].

Yau *et al.* reported an enhanced postoperative systolic function and myocardial performance using warm heart surgery, as well as Parodi *et al.*[13, 14]. In a randomised study[15], postoperative low output syndrome was less frequent in normothermic patients. Our study showed a significantly reduced need for inotropic agents after warm heart surgery (30.4 vs. 13.9%).

Perioperative myocardial infarction was significantly less prevalent (4.6 vs. 8.0%) in warm heart surgery in a study by Martella *et al.*[16]. We were unable to identify such a difference in diabetics.

A higher incidence (81%) of spontaneous defibrillation at cross-clamp removal was reported by Christakis *et al.*[5]. We noted a significantly increased incidence of postoperative atrial fibrillation after warm heart surgery during the early postoperative period (43.6 vs. 31.9%). Normothermic bypass is known to cause vasodilatation[17], which could mean an increase in the postoperative fluid balance, thus increasing the risk of atrial fibrillation. In our series, heart block was significantly less common in the normothermic group (3.4 vs. 23.2%).

In a report by Yau *et al.*[18], there was a tendency towards less bleeding after warm heart surgery. In our series, no statistically significant difference was seen (1105+/-601 mL vs. 955+/-433 mL), but there was a tendency to more bleeding in the normothermic group, which is similar to the findings of Engelman *et al.*[19].

Renal function impairment has not been reported with warm heart surgery (Tönz *et al.*[20]. In our selected material, warm heart surgery in diabetics was connected to renal failure (12.8 vs. 4.3%). Four patients required temporary haemodialysis, all of them in the warm group. In the others, the elevation of serum creatinine levels lasted less than 10 days. The ischaemic tolerance of organs in normothermia may be decreased. However, mean hospital stay did not differ between the groups.

In our study, more sternal wound healing problems were seen in the hypothermic group (14.5 vs. 5.1%). This may be due to the vasoconstriction caused by hypothermia, as well as its deleterious effects on various immune functions. Diabetes and hypothermia may be a combination favoring infection. However, there was no significant difference in deep infections.

We conclude that warm heart surgery offers the advantage of decreased need of inotropic agents and fewer heart blocks and wound healing problems postoperatively. However, atrial fibrillation is still common and renal impairment may be a problem in diabetics. Stroke is as common in both groups. Neither technique shows an obvious advantage.

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