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Tepid antegrade intermittent blood cardioplegia as an alternative for intermittent crossclamping with Lidoflazine

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ABSTRACT

Background: Blood cardioplegia is a technique with many variations in its use. Intermittent cross clamping with Lidoflazine has proven to deliver good cardioprotection in our center. Question: Is tepid (32˚C) antegrade intermittent blood cardioplegia an efficient, safe and easy-to-use alternative to intermittent crossclamping with Lidoflazine in elective isolated CABG in low-risk patients? Primary outcomes are heart enzymes (cTnI, CK-MB). Secondary outcomes are operation times, length of hospital stay, major complications and in-hospital mortality. Methods: From January 2012 until November 2012, 40 patients with LVEF ≥50%, EuroSCORE II <3.5% and no severe systemic disease underwent elective CABG and were consecutively randomized to intermittent cross-clamping (ICC; n = 20) or blood cardioplegia (BCP; n = 20). All were operated on by the same surgeon. Results: There were no significant differences in age (BCP 65.34 ± 9.76; ICC 65.25 ± 8.42) and EuroSCORE II (BCP 1.25 ± 0.72; ICC 1.04 ± 0.71). There was a significant difference in cross clamp time (BCP 61.10 ± 23.07; ICC 41.30 ± 13.10). No significant differences in ECC-time (BCP 95.85 ± 27.04; ICC 113.80 ± 34.47) and number of distal anastomoses (BCP 2.70 ± 0.73; ICC 2.90 ± 0.72) were found. Values of cTnI 1-day postoperative (BCP 1.50 ± 0.76; ICC 4.50 ± 3.90), maximum cTnI (BCP 2.85 ± 1.73; ICC 6.40 ± 4.30) and maximum CK-MB (BCP 21.10 ± 22.30; ICC 31.35 ± 24.39) differed significantly. No significant differences in postoperative parameters were found: length of hospital stay (BCP 7.95 ± 1.40; ICC 8.25 ± 1.71), atrial fibrillation (BCP 0.20 ± 0.41; ICC 0.45 ± 0.51), major complications (BCP 0.35 ± 0.49; ICC 0.30 ± 0.47). There was no in-hospital mortality. Conclusion: Primary outcomes defined by the cardiac enzymes (cTnI, CK-MB) favour the use of tepid antegrade intermittent blood cardioplegia in low-risk patients undergoing elective CABG-operations. Regarding secondary outcomes, ICC showed shorter cross clamp times.

Keywords: Blood Cardioplegia; Intermittent Cross Clamping; Lidoflazine; Myocardial Protection

1. BACKGROUND

Worldwide, there is a great variation in the techniques used for optimization of myocardial protection during CABG-operations. Despite much research on this topic, no specific protocol has proven superiority [1-3]. For more than 20 years, the use of intermittent cross-clamping with Lidoflazine in our center has proven to deliver good myocardial protection. Blood cardioplegia, on the other hand, is a well-known cardioplegic technique, with many variations in its use regarding the temperature, site and frequency of its injection and composition of the solution. Common principle is the mixture of a cardioplegic solution with blood of the patient.

2. QUESTION

Is tepid (32˚C) antegrade intermittent blood cardioplegia an efficient, safe and easy-to-use alternative to intermittent crossclamping with Lidoflazine in elective isolated CABG-operations in low-risk patients? Primary outcomes are values of postoperative heart enzyme values (cTnI and CK-MB). Secondary outcomes are operation times (extra-corporal circulation time (ECC), cross clamp time (XTC) and total duration of surgery), post-operative length of hospital stay, occurrence of postoperative atrial fibrillation, major in-hospital complications and in-hospital mortality.

3. METHODS AND MATERIALS

From January 2012 until November 2012 forty low risk

patients underwent an elective CABG-operation by one surgeon.

Inclusion criteria were:

- two or three vessels disease with a stenosis >70%.
- Isolated CABG-procedure.
- LVEF ≥50%.
- EuroSCOREII <3.5%.

Exclusion criteria were:

- Urgent CABG.
- Redo CABG.
- Severe renal insufficiency with a GFR <30 ml/min.
- Age <18 years.

Patients were consecutively randomized to intermittent cross clamping (ICC; n = 20) or blood cardioplegia (BCP; n = 20). In the ICC-group, the patients received Lidoflazine (1 mg/kg) systemically after induction of anesthesia [4,5]. The patient's blood was cooled down by the heater-cooler, to a bladder temperature of 28˚C - 30˚C, so hypothermia was another protective measure. Repetitively, the aortic cross clamp was placed in order to perform the distal anastomoses, with a maximum time of 15 minutes for each single anastomosis to limit the time of myocardial ischemia. In the BCP-group, patients were operated on with the use of a modified Calafiore-solution (KCl 1.7 mmol/ml, $MgSO_4$ 0.17 mmol/ml, aqua pi ad 50 ml) with a temperature of 32˚C. This solution was mixed with blood every 15 minutes and 400 cm^3 was delivered into the aortic root during 2 minutes. Other pump characteristics were a declining concentration of the Modified Calafiore solution, starting at a rate of 120 ml/min and a maximum aortic root pressure of 100 mmHg. Postoperative follow up consisted of repetitive measurements of cTnI and CK-MB. In addition, occurrence of major postoperative complications (cfr. infra), atrial fibrillation and length of postoperative hospital stay was noted.

With the use of SPSS Statistics 20, statistical analyses were performed. All values are expressed as mean ± standard deviation. Using the Shapiro-Wilk test, normality was examined. After confirmation, the parameters were analyzed using anunpaired T-test. The parameters where normality was not found were analyzed using the Mann-Whitney U-test. A probability level of 0.05 was chosen as the criterion for statistical significance.

4. RESULTS

As shown in **Table 1**, there were no significant differences in demographic characteristics. The number of patients is identical in both groups (BCP 20; ICC 20). Fewer women than men undergo CABG, which explains the male predominance in this study (sex ratio M/F: BCP 16/4; ICC 17/3). Since coronary heart diseases are mainly a concern for middle-aged or older patients, both groups consist of patients aged 65 years and older (BCP 65.34 ± 9.76; ICC 65.25 ± 8.42). One of the inclusion criteria for this study was a EuroSCORE II < 3.5%, as can be seen in both study arms (BCP 1.25 ± 0.72; ICC 1.04 ± 0.71).

Table 1. Demographic data.

	Blood cardioplegia	Crossclamping with lidoflazine	p-value
Number of patients	20	20	
Sexratio: M/F	16/4	17/3	0.681
Age (years)	65.34 ± 9.76	65.25 ± 8.42	0.695
Mean EuroSCOREII	1.25 ± 0.72	1.04 ± 0.71	0.304

The peroperative parameters that were considered important were the number of distal anastomoses, ECC time and aortic crossclamp time. These are shown in **Table 2**. The number of distal anastomoses was comparable (BCP 2.70 ± 0.73; ICC 2.90 ± 0.72). The mean value of the ECC-time was higher in the Lidoflazine-group, which can be explained by the deeper cooling used with this technique and therefore longer reheating times. This difference however did not prove to be of significance (BCP 95.85 ± 27.04; ICC 113.80 ± 34.47; p-value 0.123). The crossclamp time was significantly longer with blood cardioplegia due to the placement of a single aortic cross clamp compared with the intermittent cross clamping method used with Lidoflazine (BCP 61.10 ± 23.07; ICC 41.30 ± 13.10).

There was no in-hospital mortality. **Table 3** shows the heart enzymes that were followed, cTnI and CK-MB. These enzymes were repetitively measured and the 24-hour postoperative and maximum values during the whole postoperative course were determined. Most of these heart enzyme values showed significant differences, as shown in the following table.

As shown in **Table 4**, other important parameters such as postoperative length of hospital stay and occurrence of atrial fibrillation showed no significant differences. The incidence of major complications was comparable. These included: low cardiac output, arrhythmias, pulmonary-complications (pneumonia, pulmonary embolism, pneumothorax, ARDS), stroke, sternal dehiscence and wound complications, severe renal insufficiency and infections.

5. DISCUSSION

Statistical analysis confirmed the comparability of both groups considering patient characteristics (age, EuroSCORE II) and number of distal anastomoses, thus limiting bias.

The efficiency of myocardial protection was measured by postoperative levels of heart enzymes (cTnI, CK-MB), which have proven to relate to the degree of myocardial damage and are easily detectable [6,7].

Table 2. Peroperative parameters.

	Blood cardioplegia	Crossclamping with lidoflazine	p-value
Number of distal anastomoses	2.70 ± 0.73	2.90 ± 0.72	0.363
ECC-time (min)	95.85 ± 27.04	113.80 ± 34.47	0.123
Crossclamp time (min)	61.10 ± 23.07	41.30 ± 13.10	0.002

Table 3. Levels of heart enzymes.

	Blood cardioplegia	Crossclamping with lidoflazine	p-value
cTnI 1 day postoperative (mmol/l)	1.50 ± 0.76	4.50 ± 3.90	0.000
Max. cTnI (mmol/l)	2.85 ± 1.73	6.40 ± 4.30	0.002
CK-MB 1 day postoperative (mmol/l)	16.95 ± 18.63	26.05 ± 25.85	0.132
Max. CK-MB (mmol/l)	21.10 ± 22.30	31.35 ± 24.39	0.041

Table 4. Postoperative parameters.

	Blood cardioplegia	Crossclamping with lidoflazine	p-value
Postoperative length of hospital stay	7.95 ± 1.40	8.25 ± 1.71	0.499
Occurrence of atrial fibrillation (%)	20 ± 41	45 ± 51	0.096
Major complications	0.35 ± 0.49	0.30 ± 0.47	0.739

Regarding the results of this study, the significant lower value of postoperative cardiac enzymes with blood cardioplegia can be addressed to different mechanisms. Theoretical advantages of blood cardioplegia are the capacity to augment oxygen delivery by the presence of hemoglobin to prevent ischemic injury and the presence of buffers and radical scavengers [8].

Secondly, the hyperkalemia of the solution will lead to a diastolic cardiac arrest making manipulation of the heart easier for the surgeon, thus limiting the perioperative damage to the heart. The cross clamp times however have proven to be significantly longer with the use of blood cardioplegia since this technique requires a single aortic cross clamp. The coronary arteries are derived of blood during the whole operation time, even when it is not strictly required for the surgeon. The main benefit of intermittent crossclamping with Lidoflazine is that the aortic clamp is only placed when making an anastomosis, providing the coronary arteries with blood in between. This limits the ischemia times of the myocardium, which is a target on itself during CABG-operations.

The theoretical downside of this repetitive crossclamping is the greater risk for cerebral embolisms if plaques in the aorta are present. In some institutions however, including ours, this higher incidence of strokes using intermittent crossclamping with Lidoflazine was not seen [9]. Myocardial protection with intermittent aortic crossclamping is economically advantageous when compared to any cardioplegic solution [9].

Tepid blood cardioplegia is defined as a blood cardioplegia solution infused at a temperature of 32˚C. This will lead to hypothermia of the heart and thus a reduced metabolism of the myocytes. Secondarily, a certain degree of systemic hypothermia will be reached, which will vary dependant on the duration of the ECC-time, and the settings of the heater-cooler.

Despite the existence of a protocol for the use of the Modified Calafiore solution in our institution, difficulties in applying this strictly in a clinical setting remains an important issue. This is for example the case when the amount of the cardioplegia solution needs to be adjusted to the myocardial needs in case of remaining or resuming heart activity. The lack of a standardized protocol in these circumstances leads to great individual differences depending on the perfusionist's preferences.

A disadvantage of blood cardioplegia is the longer preparation time needed by the perfusionist. These minutes can be of critical importance in urgent CABG-operations where the damaged myocardium will benefit from early connection to the heart-lung machine because of the reduced workload. Another potential disadvantage of blood cardioplegia is the possible damage by the high potassium concentration to the endothelium of the coronary arteries [10].

A limitation of this study is the small amount of included patients. We expect more pronounced differences in a larger study population. Furthermore, it would be interesting to include high-risk patients in the study design, since they will benefit more from efficient myocardial protection.

6. CONCLUSION

Primary outcomes defined by the cardiac enzymes (cTnI, CK-MB) favour the use of tepid antegrade intermittent blood cardioplegia in low-risk patients undergoing elective CABG-operations. Regarding secondary outcomes, ICC with Lidoflazineonly showed shorter cross clamp times, but other secondary outcomes were comparable.

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ABBREVIATIONS

BCP: blood cardioplegia
CABG: coronary artery bypass grafting
XCT: cross clamp time
ECC: extracorporeal circulation
EuroSCORE: European System for Cardiac Operative Risk Evaluation
ICC: intermittent cross-clamping
LVEF: left ventricular ejection fraction

