Aortocoronary bypass grafting: a comparison of HTK cardioplegia vs. intermittent aortic cross-clamping

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Abstract

Objective: Intermittent, hypothermic aortic cross-clamping (IAC) with myocardial fibrillation and cardioplegic arrest (CA) have been established both as effective methods for coronary artery bypass surgery (CABG). Nevertheless, there exists controversy about the more beneficial cardioprotective effect of one of these procedures in CABG-patients. Methods: In this prospective study we compared the clinical outcome, ischemic serum-markers (CK, CK-MB, Troponin I), electrocardiogram (ECG)-changes, and hemodynamic data of 103 patients. Randomization in group I (IAC; n = 52) or group II (CA; n = 51) was done consecutively, all data were compared by Student’s t-test or χ²-test and P < 0.05 was regarded as significant. The Bretschneider–HTK solution was used for cardioplegic arrest. Data were collected before operation, before ischemic arrest, after 5 and 60 min of reperfusion, 1 and 6 h after operation, 1, 2 and 10 days postoperatively.

Results: There were no significant differences between both groups regarding general patient data: age (IAC: 64.8 ± 9.2 vs. CA: 63.8 ± 9.0 years), left ventricular function (ejection fraction: IAC: 62 ± 14 vs. CA: 64 ± 13%), the amount of bypassed vessels (IAC: 3.4 ± 0.5 vs. CA: 3.6 ± 0.5), total bypass time (IAC: 113 ± 31 vs. CA 108 ± 20 min). The total time of ischemia was significantly less in the IAC group with 37 ± 10 vs. 48 ± 10 min in the CA group. In the IAC-group, a higher mortality was noticed (7.7 vs. 3.9%; N.S.). This was combined with a significantly higher amount of patients with peak serum-values of CK-MB (>40 U/l) and troponin I (>50 ng/ml), 17 in the IAC-group (33%) vs. eight in CA-group (16%). Cerebral strokes were seen in two IAC-patients and none in CA-patients (NS). ECG-changes occurred in 22 IAC patients (42%) vs. 16 CA patients (31%); persistent ischemia related ECG-changes in six IAC (11.5%) vs. five CA-patients (9.8%).

Conclusions: Both cardioprotective methods, IAC and HTK-cardioplegia, seem to offer sufficient myocardial protection in normal CABG-procedures. Although neurologic disorders and mortality rates were higher in patients with intermittent aortic cross-clamping, the differences to the cardioplegia group were not significant. According to the analysis of increased ECG-changes, higher CK-MB and troponin I values, which occurred especially in patients with myocardial ischemia time longer than 40 min, we conclude that cardioplegic arrest with HTK seems to offer more beneficial effects in procedures with prolonged ischemia.

Keywords: Coronary surgery; Intermittent aortic cross-clamping; Cardioplegia; Troponin I

1. Introduction

Improvements in intraoperative myocardial protection amended posts ischemic hemodynamic function, attenuated the prevalence of perioperative infarction, and decreased mortality. Numerous modifications of cardioplegic solutions, after the introduction of the cardioplegic principle by Melrose et al. [1] in 1955, have been applied. The multitude of different methods and techniques clearly demonstrate the persistent inadequacy of all of them because none have shown a satisfactory solution for all ischemia related effects.

A respectable minority of surgeons is still using intermittent aortic cross-clamping (IAC) for myocardial protection. This concept includes ventricular fibrillation and moderate hypothermic perfusion. In particular the new insights into the phenomenon of ischemic preconditioning has also revived the protective concept of intermittent ischemic arrest [2], despite uncertain results in human myocardium [3]. Nevertheless, controversy still exists with regard to cardioplegic solutions or non-cardioplegic techniques for myocardial protection in coronary bypass surgery. There are only a few prospective, randomized studies comparing both techniques [4–8].

In our institution both techniques are commonly used for coronary artery bypass surgery (CABG)-procedures. For cardioplegic protection the Bretschneider–HTK solution is applied. The low sodium and low calcium concept of this
solution, buffered with histidine and mannitol has been clearly approved by a number of studies [9–11].

In a prospective randomized trial the efficacy of myocardial protection between the two different methods was determined by clinical course, electrocardiographic changes and serial measurements of serum markers for myocardial damage, i.e. troponin I.

2. Materials and methods

2.1. Patients

One hundred and three patients undergoing coronary artery bypass grafting were studied over a period of 6 months. Patients were randomized to the mode of myocardial protection at the time of referral. All patients had recurrent angina managed with nitrates, calcium antagonist or beta-blocking agents. Twelve patients had unstable angina and underwent urgent surgical procedure, seven in the IAC-group and five in the cardioplegic arrest (CA)-group. Patients undergoing either emergency, redo- or concomitant procedures were excluded. The study was approved by the Ethics Committee of the Heinrich-Heine University Düsseldorf, and informed consent was obtained from the patients.

2.2. Operative procedure

The criteria for surgical eligibility was more than 70% obstruction in at least two coronary arteries with clinical manifestation of angina or heart failure (or both). Anesthetic technique was standardized for all patients. Thiopental (1–3 mg/kg) was used for induction with 3–5 μg/kg fentanyl, and volatile agents were delivered in 50% air–O2 mixture for maintenance. Neuromuscular blockade was achieved by 0.1–0.15 mg/kg pancuronium bromide.

After internal thoracic artery and long saphenous veins were harvested, heparin was administered and total cardiopulmonary bypass was established. For unloading the left ventricle in both groups the hearts were vented via a canula inserted through the upper right pulmonary vein. The patients blood temperature was cooled down to 30°C before the aorta was clamped. In the cardioplegic group, after aortic cross-clamping the Bretschneider–HTK solution was infused via a roller pump into the aortic root with a perfusion pressure (aortic root pressure) of 60 mmHg. The composition of the solution was NaCl 15 mmol/l, KCl 9 mmol/l, MgCl2 4 mmol/l, histidine 180 mmol/l, His–HCl 18 mmol/l, tryptophane 2 mmol/l, K-ketoglutarate 1 mmol/l; osmolality 310 mosmol/l. Only initially at the beginning of ischemia the solution was infused for a period of 6 min (1760 ± 180 ml were administered), no further cardioplegic perfusion was necessary. All distal anastomoses were performed before release of the clamp. Rewarming was initiated during the final anastomosis.

In the IAC group after reaching moderate hypothermia of 30°C blood temperature, ventricular fibrillation was induced electrically and the aorta was cross-clamped. Each distal anastomosis was constructed during a single period of aortic occlusion, no flowresters or intraluminal shunts were used. During the reperfusion periods blood temperature was kept at 27°C. The time for reperfusion between the intermittent cross-clamping periods was 5 min. After final occlusion the heart was reperfused at 37°C and the heart defibrillated and was allowed to beat during partial aortic occlusion for completion of proximal anastomoses.

Patients were weaned from cardiopulmonary bypass (CPB) when the rectal temperature reached 35°C. There were no differences in postischemic hemodynamic and anesthetic management. Inotropic support was given only when systolic blood pressure was below 90 mmHg and central-venous pressure over 16 mmHg.

Baseline studies included systemic blood pressure, mean right atrial pressure, heart rate and the electrocardiogram were collected prior to surgery, before CPB, 1 h after release of aortic clamp, 1 and 6 h after surgery and on the 1st, 2nd and 10th day after operation. Early death was defined as death within 30 days after operation or during the same hospital admission.

2.3. Analysis

2.3.1. Biochemical analysis

Serial venous blood samples were collected. Laboratory measurements of serum enzymes indicative of myocardial cell damage were creatine kinase (CK) and its MB fraction. An enzyme linked immunoassay was used to measure the serum troponin I (Abbott Laborotories, AxSYM® System) concentrations.

2.3.2. Electrocardiogram

A 12-lead ECG was recorded prior to surgery, at 1 and 6 h postoperatively and on the 1st, 2nd and 10th day after the operation. Diagnostic criteria for perioperative myocardial infarction or ischemia were new Q waves of 0.04 mm or more, a reduction of R waves of more than 25% in at least two leads, ST segment changes of at least 1 mm and lasting over 15 min, T waves abnormalities and bundle branch blocks.

2.3.3. Statistical analysis

All continuous data are expressed as mean ± SD of the mean, except when indicated otherwise. The differences between the preoperative characteristics and between the intraoperative variables in the two groups of patients were analyzed by Student’s t-test for non-paired values, since for these sample sizes the means are sufficiently normally distributed, and by Fisher’s exact test for 2 × 2 tables and the χ2 test. The differences between the variations in hemodynamic and enzymatic parameters in the two groups were analyzed by the Student’s t-test for the differences of pre- and postoperative values. All analyses were performed with
the aid of a statistical software package (SPSS for Windows, SPSS Inc, Chicago, IL). Probability values of less than 0.05 were considered significant.

3. Results

Clinical data of the patients and comparisons are shown in Tables 1 and 2, respectively. With the exception of history of prior myocardial infarctions, age, sex distribution, ejection fraction, the New York Heart Association class, and the number of grafts per patient were not significantly different between the groups. The cardioplegia group had a significantly longer total aortic cross-clamp time than the IAC group. The mean time of aortic cross-clamping in the IAC group was 10.3 ± 2.6 min per single anastomosis, total CPB-time was not significantly different between the IAC group with 117 min vs. the CA group with 107 min.

Low cardiac output syndrome was seen in three patients of the IAC group and in two of the cardioplegic group. One patient of the IAC group developed low cardiac output due to myocardial infarction. The other four cases with low cardiac output were related to poor preoperative condition and coronary anatomy rather than to the operative technique or myocardial protection.

There were two early deaths in the cardioplegic group (3.9%) because of the low cardiac output syndrome. In the IAC there were four deaths (7.7%); two of them died of low cardiac output with the need of the intraaortic balloon-pump, one after hemorrhage and one after therapy-refractant ventricular fibrillation. Two patients of the IAC group had cerebrovascular incidences, one of them with preoperative evidence of cerebro-vascular disease, none in the cardioplegic group.

Inotropic support was defined as any infusion of inotropic drugs for more than 30 min in the early postoperative period. In the IAC group 11 patients needed inotropic support postoperatively, five of them for more than 24 h, in the cardioplegic group there were 14 patients with inotropic support with seven of them for more than 24 h. A more detailed analysis about dosages and different kinds of inotropic drugs, did not show any differences between the two groups. The patients with unstable angina who underwent urgent surgical procedures did not show any different peri- and postoperative outcome compared with the overall performance.

3.1. Biochemical analysis

The levels of serum enzymes and troponin I were identical before surgery and CK-MB and troponin I levels were all below the upper limit of the reference interval (<6 U/l for CK-MB and <0.6 U/l for troponin I). In both groups the levels of CK and its MB fraction raised significantly after operation, with peak concentration 6 h after operation. The peak concentration of troponin I was reached 1 h postoperatively. More pronounced elevations were observed in the IAC group (Figs. 1 and 2, Table 3) with no statistical significance between the groups. In Fig. 3, total time of ischemia was plotted to the peak value of troponin I. As also shown in Table 4, for a time of ischemia <40 min, in the CA group 2 of nine patients (22%) have increased levels of troponin I (>50 ng/ml) and CK-MB (>40 U/l), compared with four of 18 (22%) in the IAC group. For a time >40 min, the corresponding data are six of 42 (14%) in the CA group compared with 13 of 34 (38%) in the IAC group. This demonstrates, that in procedures with myocardial ischemia longer than 40 min, there is a significant higher percentage of patients with elevated troponin I and CK-MB levels in the IAC group compared with the CA group.

### Table 1
Preoperative clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardioplegia (n = 51)</th>
<th>Intermittent aortic cross-clamping (n = 52)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>43</td>
<td>41</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.9 ± 9.2</td>
<td>64.8 ± 9.0</td>
<td>NS</td>
</tr>
<tr>
<td>History of prior myocardial infarction</td>
<td>21</td>
<td>28</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>Angina</td>
<td>16</td>
<td>18</td>
<td>NS</td>
</tr>
<tr>
<td>Unstable</td>
<td>5</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>30</td>
<td>27</td>
<td>NS</td>
</tr>
<tr>
<td>Ventricular function (%)</td>
<td>64 ± 14</td>
<td>62 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>2.56 ± 0.5</td>
<td>2.65 ± 0.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Data presented as mean ± SD. NS, difference not statistically significant.

### Table 2
Surgical data and results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardioplegia (n = 51)</th>
<th>Intermittent aortic cross-clamping (n = 52)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft/patient</td>
<td>3.6 ± 0.5</td>
<td>3.4 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>IMA to LAD graft (n)</td>
<td>49</td>
<td>49</td>
<td>NS</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>48 ± 10</td>
<td>37 ± 10</td>
<td>0.02</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>108 ± 20</td>
<td>113 ± 31</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction (ECG)</td>
<td>3</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Temporary AV dissociation</td>
<td>9</td>
<td>3</td>
<td>0.007</td>
</tr>
<tr>
<td>Inotropic support (n)</td>
<td>14</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>Cerebrovascular incidence</td>
<td>0</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>4</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Data presented as mean ± SD. NS, difference not statistically significant; IMA, internal mammary artery; LAD, left anterior descending artery; AV, atrioventricular.
3.2. Electrocardiogram

Definite perioperative myocardial infarctions, according to ECG-changes (new Q waves or R reduction) and significant increases of total peak CK-MB >50 U/l, troponin I >50 ng/ml, were seen in five patients (9.6%) for the IAC group and in three (5.9%) for the cardioplegia group, transient ECG-changes were seen in 22 patients (42%) of the IAC group and in 17 patients (33%) of the cardioplegia group. Episodes of transient ST-segment deviation were found in 11 IAC patients (21%) and in seven CA patients (14%).

New postoperative supraventricular rhythm disturbances (atrial fibrillation or flutter) were seen in 11 IAC-patients and in 16 cardioplegic patients. Episodes of transient bundle branch blocks or conduction defects occurred in a total of 39 patients (38%) with a significant majority in the cardioplegic group (23 patients, 45%). Episodes of ventricular tachycardia or fibrillation with the need of electrical countershocks postoperatively were one patient in each group, the patient of the IAC group, died due to the therapy-refractant ventricular fibrillation.

4. Discussion

The concept of cardioplegic arrest has been widely investigated and approved in numerous clinical studies. The protective mechanism is based on immediate electromechanical interruption and reduction of cellular metabolism, which preserves cellular energy stores. Attempts to improve myocardial protection have been focused on cardioplegic composition, i.e. blood cardioplegia, its distribution through the coronary system and the early reperfusion phase. In our institution we are using the cardioplegic solution of Bretschneider, first introduced 1964 [12] and modified in the early 1980s [9]. A number of studies showed excellent results with the Bretschneider–HTK solution [11], which is widely used in European centers.

The method of intermittent aortic cross-clamping is based on moderate hypothermia (27–30°C) with a decrease of oxygen demand, which allows the effects of ischemia, lasting less than 20 min, to be rapidly reversible by adequate reperfusion with normal blood, and the oxygen debt is more rapidly repaid in a decompressed ventricle. So far, it is necessary to stress the technical aspects that 5 min of hypothermic perfusion is mandatory before each ischemic period, and that effective decompression of the left ventricle is essential. Studies of Anderson [4], Bonchek [13] and Antunes [14] showed that IAC provides a simple and safe protective method for coronary artery bypass grafting.

There are only a few prospective randomized trials in the literature dealing with the comparison of both different methods. In the early 1980s the study of Pepper et al. [15] revealed no significant differences in myocardial preservation between these methods in patients at least with a good left ventricular function. These results were confirmed by the study of Bonchek et al. [13] and more recently by echocardiographic analysis of systolic and diastolic function by Casthely [16]. Also Taggart [17] and Cohen [5] showed by determining troponin T release and accessing the free radical activity that both techniques provide a similar degree of myocardial protection.

In our study, the clinical course and hemodynamic response were not significantly different in both groups. Small differences were observed concerning the higher hospital mortality and more frequent ECG changes for the IAC group, without reaching significance. There was a higher incidence of rhythm disturbances postoperatively in the cardioplegic group, mainly atrioventricular conduction or bundle branch blocks. Most of these conduction problems did not persist for more than 2 or 3 days, but one must be
aware of them. Due to our very stringent criteria for definition of perioperative myocardial infarction or ischemia, we found a higher, non-significant infarction rate in the IAC group.

Previous studies [8,14,18] reported a low mortality of 1–3%. They all reported that operative deaths occurred mainly in high-risk patients. Compared with these data our mortality rate seems to be high. Analysis of our patients via a risk score (EURO-score) revealed a higher risk score of the patients included in this study (6.5 points) compared with the score from a multicenter analysis (4.8 points), with higher amount of points meaning an increased perioperative risk for morbidity in coronary surgery. In our study, the mean predicted and observed mortality rate were 5.5 and 5.8%, respectively. Further analysis of the patients showed that both deaths in the cardioplegic group and three deaths in the IAC group revealed a high risk score. Regarding this analysis, the higher mortality might be explained by the higher risk profile of the patients included in this study rather than by problems related to the intraoperative protective technique.

Neurologic disorders were seen in two patients of the IAC group (one stroke and one TIA), none in the cardioplegia group. Aortic clamping and particular by repeated aortic clamping is considered one of the major risks for perioperative stroke in patients with atherosclerotic disease of the ascending aorta. Bonchek [18] reported of 1.1% transient and 1.8% permanent neurologic events in a series of 3000 patients operated with repeated aortic cross-clamping. Musumeci [7] showed that, in patients with no preoperative evidence of aortic or cerebro-vascular disease, the repetitive clamping of the aorta in intermittent ischemic arrest is not associated with a higher rate of cerebro-vascular events compared with the single clamp technique. In consent with other studies [8,18], when diffuse arteriosclerotic plaques are found, the risk of thromboembolic complications is markedly higher and the operative techniques eventually should be changed towards application of cardioplegia. Nevertheless, even the single cross-clamp used in cardioplegic arrest may be unsafe in patients with severe diffuse aortic arteriosclerosis, thus special methods with not clamping the aorta and local control of the coronary arteries should be performed.

To assess the degree of myocardial damage, CK and its

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardioplegia (n = 51)</th>
<th>Intermittent aortic cross-clamping (n = 52)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK (h postoperatively)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>113.7 ± 66.8</td>
<td>142.6 ± 63.8</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>217.9 ± 148.8</td>
<td>287.1 ± 260.4</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>293.7 ± 228.5</td>
<td>323.8 ± 266.2</td>
<td>NS</td>
</tr>
<tr>
<td>CK-MB (h postoperatively)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12.7 ± 3.6</td>
<td>17.7 ± 7.9</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>12.4 ± 9.4</td>
<td>22.1 ± 14.7</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>13.7 ± 11.1</td>
<td>18.7 ± 12.4</td>
<td>NS</td>
</tr>
<tr>
<td>Troponin I (h postoperatively)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>24.6 ± 13.4</td>
<td>37.5 ± 14.8</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>41.2 ± 18.7</td>
<td>60.5 ± 36.4</td>
<td>NS</td>
</tr>
<tr>
<td>12</td>
<td>22.7 ± 45.1</td>
<td>41.7 ± 57.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data presented as mean ± SD. NS, difference not statistically significant.

Fig. 3. Relation between peak-value of troponin I and total time of ischemia of each patient operated with cardioplegic arrest (A) and intermittent aortic cross-clamping (B).
MB-fraction as well as troponin I were measured. Troponins (T, I and C) are regulatory proteins of the contractile apparatus of the myocardium and offer a high specificity and sensitivity for myocardial damage [19,20]. Our data demonstrate a significant release of cardiac troponin I even in clinically uncomplicated coronary bypass operations. This implicates that there is some reversible ischemic myocardial damage in at least all patients. The lower level of troponin I measured after cardiopulmonary procedures indicates that the Bretschneider cardioplegia prevents more effectively the onset of ischemia-induced myocardial damage. However, the data-analysis of patients with increased levels of troponin I or CK-MB showed, that particularly in procedures with an aortic cross-clamp time >40 min intermittent aortic cross-clamping seems to be less effective compared with cardioplegic arrest.

So far, our data are consistent with results of Flameng et al. [6], comparing the intermittent aortic cross-clamping vs. use of St. Thomas cardioplegia. They showed that the clinical outcome was essentially the same. However, detailed analysis of biochemical and ultrastructural alterations demonstrated that myocardial protection was less effective with intermittent cross-clamping and early functional recovery was impaired. In contrast to our results, studies from Musumeci [7] and Anderson [4] found even lower levels of CK-MB and troponin T in patients with intermittent aortic cross-clamping compared with cold blood cardioplegic arrest. These results may be related to the significantly shorter ischemic time in patients with aortic cross-clamping than in patients with cardioplegic arrest.

In conclusion, the present study shows that for routine procedures intermittent aortic cross-clamping is as effective as the use of crystalloid cardioplegia (Bretschneider–HTK solution) in protecting the myocardium from ischemic injury induced by global ischemia during CABG-procedures. Nevertheless, the larger number of patients in the IAC-group with increased CK-MB and troponin I levels, in patients who had a total time of ischemia longer than 40 min, suggests that aortic cross-clamping seems less effective for longer ischemia duration compared with cardioplegic techniques using the HTK solution.

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**Table 4**

<table>
<thead>
<tr>
<th>Total time of ischemia</th>
<th>Cardioplegia (n = 51)</th>
<th>Intermittent aortic cross-clamping (n = 52)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>≤40 min</td>
<td>2 (22)</td>
<td>4 (22)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;40 min</td>
<td>5 (14)</td>
<td>13 (38)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* Number of patients (%) with a peak-value of troponin I postoperatively >50 ng/ml and CK-MB >40 U/l, dependent on total time of ischemia. NS, difference not statistically significant.

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**References**


Appendix A. Conference discussion

Dr M. Antunes (Coimbra, Portugal): I was interested in your report; unfortunately the small numbers do not allow you to reach statistical significance in many aspects. There are some points that I would like to raise. Early in 1990, I stopped using cardioplegia for coronary surgery, whether isolated or accompanied by other procedures such as valve procedures. I started with intermittent aortic cross-clamping, but it took me only a couple of months to realize that we don’t need the aortic cross-clamping. We can control the coronary flow locally and do the anastomoses very safely, very easily, and we have had excellent results. We dropped the usage of inotropes by about three-fourths, and we have now surpassed 5000 procedures with a mortality which is close to 1%. I was surprised to see your mortality of about 6%, and I wonder whether there wasn’t a technical factor there, because I couldn’t see any significant risk factors for operative mortality in your series. Can you comment on this, please?

Dr Sunderdiek: A lot of patients included in this study had a very severe coronary artery disease with a low ejection fraction, furthermore the peri-operative risk stratification revealed a higher risk score of these patients compared to other studies. As we have also seen in the study presented before, there are some other countries which have the same incidence of mortality. I think the higher mortality is depending on other problems of the patients population rather than the intraoperative protective technique.

Dr D. Rocco (Lecce, Italy): I had the opportunity of reviewing more than 100 cases operated on with intermittent aortic cross-clamping at the same institution. In some patient subgroups results, which were comparable with the data you just presented could be documented, whereas in other patients better results, comparable with the ones obtained with other conventional methods of myocardial protection (i.e. warm cardioplegia), could be demonstrated. In that experience I noticed some technical differences according to the surgeon’s preferences. My question is: was your series performed by several surgeons?

Dr Sunderdiek: Each technique was used by different surgeons, so in each group three experienced surgeons performed the operations. We did not include operations which were done by a surgeon in his less experienced manner.

Mr K. Dhital (London, UK): With regard to your caution against using cross-clamp fibrillation when you are expecting a longer ischemic time, is that caution based on any particular strategy you have used in the sequence with which you graft the vessels?

Dr Sunderdiek: We did not use a particular strategy in the sequence with which we graft the vessels. With regard to these results, when we expect more bypass vessels, more than four or five for instance, with a particular morphology of the coronary artery disease, then we will prefer the cardioplegic method. Also, in patients with poor left ventricular function when we also expect that more than three bypass vessels will be necessary, then we also prefer the cardioplegic method.

Professor T. Treasure (London, UK): Thank you for the nice study. There are few randomized trials. I think you should be complimented. Would you agree that having shown this difference at 40 min, you should form a policy, to use the safer technique, the more protective technique, for all patients, rather than guess which ones are going to need 40 min or longer or less?

Dr Sunderdiek: Thank you. To form a policy from these results is not easy because the amount of patients included in this study is rather small. However, when we expect a longer time of ischemia, then we favour the cardioplegic method. To form a real policy we have to perform a study with a larger patient population.

Dr E. Gams (Dusseldorf, Germany): I am a co-author on this paper. I might add to Tom Treasure’s question that, of course, the policy is to make a decision towards the safer method, and that might be, of course, using cardioplegia. In this regard I might quote one sentence of Norman Shumway. He said, ‘cardioplegia is a bad surgeon’s best friend’. Our study could show that it is also a good surgeon’s best friend.