A prospective randomized study to evaluate splanchnic hypoxia during beating-heart and conventional coronary revascularization

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Abstract

Objective: Cardiopulmonary bypass (CPB) is associated with gut mucosal hypoxia, which may contribute to gastrointestinal complications. We examined gastric mucosal oxygenation together with whole-body oxygen flux in low-risk patients undergoing coronary artery bypass grafting (CABG) with and without CPB. Methods: Fifty-four patients undergoing primary CABG by the same surgeon were randomized into either on-pump (ONCAB, n = 27) or off-pump (OPCAB, n = 27) groups. The ONCAB group underwent mild hypothermic (35°C) pulsatile CPB with arterial line filtration. Each patient underwent perioperative monitoring with continuous tonometry and cardiac output devices. Gastric intramucosal pH (pHi), gastric-arterial carbon dioxide partial pressure difference (CO2 gap), whole-body oxygen delivery (DO2) and consumption (VO2) and whole-body oxygen extraction fraction were measured at sequential time-points intraoperatively and up to 6 h postoperatively. Anaesthetic management was standardized. Results: Both groups had similar demographic makeup and extent of revascularization (ONCAB 2.6 ± 0.9 grafts versus OPCAB 2.5 ± 0.8 grafts; P = 0.55). The ONCAB group had a mean (± SD) CPB time of 62 ± 25 min and aortic cross-clamp time of 32 ± 11 min. In both groups there was a similar and progressive drop in pHi intraoperatively. Postoperatively, there was a gradual separation between the groups with ONCAB patients showing no further decline in pHi, while further deterioration was observed in the OPCAB group up to 6 h postoperatively. There was a significant difference between the groups over time (P = 0.03). There was a corresponding progressive rise in CO2 gap perioperatively in both groups, with ONCAB patients demonstrating superior preservation of gastric mucosal oxygenation in the early postoperative period. Global oxygen utilization measurements showed superior DO2 and VO2 in the OPCAB group throughout the study. Conclusions: Despite superior global oxygen flux associated with beating-heart revascularization, gastric mucosal hypoxia occurred to similar extents in both groups with worsening trends for the OPCAB patients postoperatively. The splanchnic pathophysiology during beating-heart revascularization should be further explored.

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1. Introduction

Gut mucosal oxygenation, as assessed by non-invasive tonometry, has been shown to be an excellent predictor of patient outcome in a variety of clinical settings, including open-heart surgery and the intensive care [1,2]. This is probably related to the fact that the gut is one of the first organs to undergo ischaemic injury at times of haemodynamic stress [3]. Moreover, the central role of impaired gut barrier function in driving the systemic inflammatory response syndrome and multi-system organ failure would explain why gastrointestinal (GI) integrity is a predictor of outcome. Several retrospective studies have shown that although GI complications are rare after cardiopulmonary bypass (CPB), they are associated with very high mortality [4,5].

Off-pump coronary artery bypass grafting (OPCAB) is currently an accepted modality of surgical coronary revascularization. The continuous improvements in myocardial stabilizers and coronary exposure techniques have
made OPCAB accessible to many surgeons worldwide for the treatment of multi-vessel coronary artery disease. Benefits of OPCAB over conventional coronary artery bypass grafting (CABG) with CPB have been demonstrated, such as reduced perioperative blood loss [6] and attenuation of the inflammatory response [7]. However, OPCAB does not eliminate the potential of significant perioperative organ injury, the magnitude of which may be comparable to surgery with CPB [8,9]. The development of significant perioperative gastric mucosal hypoxia during CPB has been well documented [10,11]. To date a similar evaluation of patients undergoing OPCAB surgery has not been reported. It is therefore important to specifically evaluate the role of OPCAB in gut protection before defining those who may benefit from this strategy. The aim of this study was to evaluate in a prospective randomized fashion global oxygen flux and gastric mucosal oxygenation during CABG with and without CPB.

2. Materials and methods

2.1. Study design

Consecutive patients undergoing primary elective CABG who fulfilled the study criteria (Table 1) were recruited following informed consent. Essentially we studied low-risk patients with normal preoperative cardiac function. All patients were operated upon by the same surgeon. If no contraindications were evident following review of the preoperative coronary angiogram, the patients were randomized into either surgery with CPB (ONCAB group) or off-pump (OPCAB group) by block randomization using a table of random numbers. The study was approved by the Southampton and South West Hants Joint Local Research Ethics Committee.

2.2. Anaesthetic management

The patients’ medications were continued up-the night before the operation except for anti-platelet agents, which were discontinued 7 days prior to surgery. A standardized balanced anaesthetic protocol was utilized in which fentanyl-based anaesthesia was used in combination with benzodiazepine and pancuronium as a muscle relaxant. Anaesthesia was maintained intraoperatively with a mixture of isoflurane and intravenous propofol infusion. Postoperatively the patients remained on propofol infusion until extubation. Active warming techniques were used in the recovery period, to achieve a nasopharyngeal temperature of at least 37°C before extubation. Target haemodynamic values were mean arterial pressure above 60 mmHg and cardiac index over 2.2 l/min per m². Dopamine was used as the first-line inotrope to support a low cardiac output, whilst bolus intravenous injections of phenylephrine or infusion of norepinephrine were used as vasoconstrictors.

2.3. CPB management

A standardized CPB protocol was used for the ONCAB patients. CPB was established using bicaval cannulation and an arterial cannula (Medtronic DLP®; Medtronic Ltd., Watford, UK) placed in the ascending aorta. Pulsatile CPB was conducted under mild core hypothermia (35°C), using a hollow-fibre membrane oxygenator (D903 Avant, Sorin Biomedica, Mirandola, Italy) and arterial line filtration (D734 Micro 40, Sorin Biomedica, Mirandola, Italy). The circuit was primed with 1 l of Hartman’s solution, 500 ml of gelofusine and 5000 IU of sodium heparin. Intermittent antegrade cold blood cardioplegia (4°C) delivered through a 12G aortic root cannula was used for myocardial protection. The cardioplegic mixture consisted of 20% St Thomas’ Hospital No. 2 solution (Martindale Pharmaceuticals, Essex, UK) and 80% autologous blood. A dose of 12 ml/kg was delivered to induce diastolic cardiac arrest and a maintenance dose of 3 ml/kg was administered after completion of each distal anastomosis. The left ventricle was vented through the aortic root during aortic cross-clamping. Flow was maintained at 2.5 l/min per m² during CPB with judicious use of phenylephrine and phenolamine to maintain the mean perfusion pressure between 50 and 80 mmHg. Alpha-stat management of acid-base status was used. Proximal graft anastomoses on the ascending aorta were performed following aortic cross-clamp removal using a partially occlusive clamp.

2.4. OPCAB technique

A median sternotomy was used for surgical access in all cases. Partial systemic heparinization was employed with a target activated clotting time of 300–400 s prior to cardiac manipulation. Trendelenburg posture was employed throughout the period of distal anastomoses and a single suture technique [12] was used to facilitate exposure of the target coronary arteries. A mechanical suction-based myocardial tissue stabilizer (Octopus®3; Medtronic Ltd., Watford, UK) was used to immobilize the operative field during coronary anastomosis. Following arteriotomy, an

<table>
<thead>
<tr>
<th>Table 1: Exclusion criteria*</th>
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<tbody>
<tr>
<td>Age over 75 years</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
</tr>
<tr>
<td>Recent (&lt;3 months) MI</td>
</tr>
<tr>
<td>Intravenous therapy for unstable angina</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Liver failure</td>
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<tr>
<td>Gastrointestinal disease</td>
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<tr>
<td>Peripheral vascular disease</td>
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<tr>
<td>Previous CVA</td>
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</tbody>
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* LVEF, left ventricular ejection fraction; MI, myocardial infarction; and CVA, cerebro-vascular accident.
intraluminal coronary shunt (Flo-Thru; Biovascular Inc., MN, USA) was inserted to maintain distal myocardial perfusion and was removed prior to completion of the anastomosis. Core temperature was maintained at or above 35°C throughout the procedure by minimizing heat loss and active warming techniques. Haemodynamic stability was achieved primarily with preload management (intravenous fluid administration and Trendelenburg posture) and vasoactive agents as required. Construction of the proximal anastomoses to the ascending aorta was performed within a single aortic side-biting clamp period, with the systolic arterial pressure maintained around 100 mmHg to minimize aortic trauma.

2.5. Assessment of gastric mucosal oxygenation

An automated air tonometry technique was used to measure the partial pressure of carbon dioxide in the gastric lumen (PgCO₂), using a 14F nasogastric catheter connected to a Tonocap monitor (Datex-Ohmeda Ltd., Hatfield, Herts, UK). The catheter was inserted during anaesthetic induction. Correct placement was confirmed by auscultating the epigastrium while 20 ml of air was insufflated through the nasogastric tube. Measurements were obtained at the start and end of operation and 2, 4 and 6 h postoperatively. Two additional intraoperative measurements were made; in the ONCAB group at the onset of CPB and 10 min after construction of the proximal anastomoses to the ascending aorta was performed within a single aortic side-biting clamp period, with the systolic arterial pressure maintained around 100 mmHg to minimize aortic trauma.

The following formulae were used:

\[
\text{Blood oxygen content (ml/dL)} = [\text{Haemoglobin (g/dL)} \times \text{blood % oxygen saturation}] \times 1.39 + [\text{Oxygen partial pressure (mmHg)} \times 0.03]
\]

\[
\text{Whole-body oxygen delivery (DO₂) (ml/min per m²)} = \text{arterial blood oxygen content} \times \text{CI (l/min per m²)} \times 0.1
\]

\[
\text{Whole-body oxygen consumption (VO₂) (ml/min per m²)} = (\text{arterial blood oxygen content} – \text{mixed venous blood oxygen content}) \times \text{CI (l/min per m²)} \times 0.1
\]

2.7. Statistical analysis

Patient characteristics and perioperative clinical data in the two groups were compared using a two-sample Student’s t-test or a Mann–Whitney U-test if normal distribution could not be assumed. Categorical variables were compared using the Pearson’s chi-square or Fisher’s exact test as appropriate. Repeated measures analysis of variance was used to assess the effect of time, group and group-time interaction on pH, CO₂ gap, DO₂, VO₂ and Oxygen extraction fraction. Because the data contained subgroups (ONCAB versus OPCAB), the association between different variables was investigated using Spearman’s rank correlation analysis. The Statistical Package for Social Sciences version 10.1 software was used for all descriptive statistics and inferential testing. A P value of less than 0.05 was considered statistically significant.

3. Results

3.1. Demography and clinical outcome

Fifty-four patients were recruited into the study and randomized to two equal groups (ONCAB, n = 27 and OPCAB, n = 27). All patients completed the study protocol and no patient was excluded. No patient allocated to the OPCAB group required the use of CPB.

The demographic variables for the two groups are presented in Table 2. As outlined in the methods, these were low-risk cases and there were no significant differences between the groups. Table 3 summarizes the intraoperative data and clinical outcome. The groups
received similar extent of revascularization using comparable mixture of conduits. There were no differences in operation duration and mechanical ventilation time. Rewarming to a core (nasopharyngeal) temperature of 37°C required a similar period of time in both groups. There was a significant difference between the groups in the use of vasoconstrictors, this was mainly due to the use of phenylephrine during CPB in all but one patient in the ONCAB group. No mortality or major complications, such as myocardial infarction, major neurological deficit or end-organ failure were observed. No patient required the use of an intravascular balloon pump.

### 3.2. Gastric mucosal oxygenation

The perioperative pHi and CO₂ gap in the two groups are displayed in Fig. 1. There were no baseline differences between the groups. A progressive and similar decline in the pHi was observed in both groups intraoperatively. Postoperatively there was a gradual separation between the groups with the ONCAB patients essentially stabilizing, while further deterioration in pHi was observed in the OPCAB group for up to 6 h postoperatively. Repeated-measures ANOVA showed a significant effect of group (ONCAB versus OPCAB) on outcome \( (P = 0.03) \). There was also a significant effect of time \( (P < 0.001) \) and group-time interaction \( (P = 0.02) \) on outcome, indicating that the groups demonstrated different trends across time. The changes in CO₂ gap generally mirrored pHi changes (mucosal acidosis results in a lower pHi and a higher gastric-arterial CO₂ gap). Repeated-measures ANOVA revealed a significant effect of group \( (P = 0.046) \) and time \( (P < 0.001) \) on outcome, although the effect of group-time interaction \( (P = 0.07) \) was not quite significant at the 5% level.

There was a highly significant correlation \( (P < 0.001) \) between pHi and CO₂ gap on Spearman’s rank correlation analysis \( (r = -0.82) \).

### 3.3. Whole body oxygen utilization

Perioperative DO₂, VO₂ and whole-body oxygen extraction fraction are displayed in Fig. 2. There were no...
preoperative differences between the groups. DO₂ was higher in the OPCAB group throughout the study period, this was largely due to the effect of haemodilution during CPB in the ONCAB group (Table 4). There was a significant effect of time ($P = 0.01$) and group ($P = 0.004$) on outcome, however the effect of group-time interaction was not significant ($P = 0.30$), i.e. the difference between the groups did not depend on the sampling time.

There was a significant and similar trend in both groups towards increasing levels of VO₂ during the study ($P < 0.001$ for time and $P = 0.96$ for group-time interaction). OPCAB patients maintained higher levels of VO₂ throughout the study ($P = 0.03$ for the effect of group).

There was also a significant trend towards increasing levels of oxygen extraction fraction with time ($P < 0.001$), however there were no differences between the groups ($P = 0.11$ for the effect of group and $P = 0.59$ for group-time interaction).

Spearman’s rank correlation revealed a highly significant association ($P < 0.001$) between pHi and VO₂ ($r = -0.22$) and pHi and global oxygen extraction fraction ($P = -0.20$).

### 4. Discussion

The absence of GI complications or any major morbidity in our study is not surprising, given the low-risk profile of

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**Table 4**

Perioperative haemoglobin and cardiac index in the two groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline</th>
<th>Operation end</th>
<th>2 h</th>
<th>6 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>ONCAB</td>
<td>11.9 ± 1.2</td>
<td>9.2 ± 1.4</td>
<td>9.6 ± 0.9</td>
<td>10.0 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>OPCAB</td>
<td>11.8 ± 0.9</td>
<td>10.6 ± 1.1</td>
<td>11.0 ± 1.2</td>
<td>10.8 ± 1.0</td>
</tr>
<tr>
<td>CI (/min per m²)</td>
<td>ONCAB</td>
<td>2.51 ± 0.61</td>
<td>2.67 ± 0.51</td>
<td>2.84 ± 0.75</td>
<td>2.99 ± 0.71</td>
</tr>
<tr>
<td></td>
<td>OPCAB</td>
<td>2.48 ± 0.71</td>
<td>2.83 ± 0.80</td>
<td>3.01 ± 0.42</td>
<td>3.08 ± 0.63</td>
</tr>
</tbody>
</table>

a Hb, haemoglobin; and CI, cardiac index. Data is presented as mean ± standard deviation.
the patient population. However, in both groups there was evidence of significant gastric mucosal hypoxia, as demonstrated by a reduction in pH and a corresponding rise in CO2 gap. The optimal way of expressing gastrointestinal tonometry findings has been debated for some time. Currently most experts agree that the gastric-arterial CO2 gap should be regarded as the gold standard measurement [13], while the pHi concept should probably be abandoned. The reason is that the pH calculation is not solely dependent on adequacy of GI perfusion but is also affected by the systemic acid-base status, as the arterial bicarbonate value enters the Henderson-Hasselbach equation. In other words, calculation of the pHi is thought to combine global and gut specific markers. This may explain why the pHi has been found to be a very sensitive early predictor of patient outcome in a variety of clinical settings, including cardiac surgery [1,2]. In this study we elected to document both pHi and CO2 gap results. All studies so far that have monitored gastric mucosal oxygenation in cardiac surgical patients have documented pHi changes and this important clinical and research record cannot be ignored. Equally, it is imperative that the CO2 gap is documented in the context of cardiac surgery. Interestingly, we found that changes in CO2 gap closely mirrored those of pHi so that a progressive perioperative decline in pHi was reflected by a progressive increase in CO2 gap. Correlation analysis confirmed a highly significant inverse relationship between the two variables, which explained 67% of the variation of each other ($r = -0.82$). Statistical analysis revealed a similar effect of group, time and group-time interaction on outcome using either pHi or CO2 gap as a dependent variable. Despite the similarity of the results, we recommend reporting of gut mucosal oxygenation using both parameters until more information on CO2 gap changes during cardiac surgery becomes available.

Our study confirms previous findings of significant perioperative gastric intramucosal acidosis after CPB [10,11]. More interestingly, we observed a similar degree of intraoperative injury to the gastric mucosa during OPCAB, with a worsening trend for OPCAB patients in the early postoperative period. Given the single-surgeon and randomized nature of the study design, the standardized anaesthetic protocol and the absence of any significant differences in the preoperative characteristics of the two groups, these results may at first appear surprising. One would intuitively expect some benefit conferred by the avoidance of CPB. There are certainly factors associated with the use of CPB per se that would partly explain the development of gastric mucosal hypoxia. These factors include the use of subphysiological flow levels during CPB and the release of various endogenous vasoconstrictors, including angiotensin II, with a concomitant rise in systemic vascular resistance [14]. Indeed CPB duration has been shown to be a predictor of gastrointestinal complications [4,5].

However, considering that perioperative gastric mucosal hypoxia has been well described in the context of major abdominal and vascular surgery [15,16], it becomes plainly obvious that factors other than the use of CPB play an important role in its development. The paramount factor that determines gut mucosal oxygenation status is global haemodynamic stability, since the gut is perhaps the first tissue in the body to become compromised at times of haemodynamic stress [3]. The GI tract is known to receive a disproportionately small portion of the cardiac output at times of haemodynamic deterioration [17], and the gut mucosa is especially susceptible to hypoperfusion due to the counter-current flow of its microcirculation [18]. Therefore, it is not surprising that the main predictors of GI complications after cardiac surgery are factors such as older age, perioperative hypoperfusion episodes, peripheral vascular disease and congestive cardiac failure, which indicate the importance of haemodynamic performance and implicate an ischaemic nature of injury [4,5]. This also explains why the use of acid-neutralizing or acid-reducing therapy does not affect the incidence of GI haemorrhage after CPB [19].

Several studies have documented the presence of significant transient haemodynamic impairment during distal anastomoses in OPCAB [20]. Significant drops in cardiac output may occur despite relatively well-preserved systemic arterial pressures. Haemodynamic deterioration is worse during grafting of the less accessible coronary targets that require extensive cardiac manipulation for adequate exposure. Cardiac verticalization results in compression of the right heart chambers against the surrounding fibrous pericardium and pleura and mechanical dysfunction of the right ventricle [21]. Moreover, despite a preserved mean arterial pressure, elevation of the central venous pressure due to a combination of Trendelenburg posture and cardiac elevation results in significant drops in perfusion pressure. It is conceivable that the cumulative effect of these transient episodes of reduced cardiac output and reduced perfusion pressure in the course of distal anastomoses during OPCAB resulted in a degree of ischaemic injury to the gastric mucosa at least comparable to CPB. It is important to note that these transient haemodynamic alterations are not reflected in our global oxygen utilization measurements. These measurements were made at time-points of relative haemodynamic stability, as one of the limitations of continuous cardiac output thermodilution catheters is that they have a long response time when there is an acute change in cardiac output [22]. The acute and often dramatic haemodynamic changes that occur during cardiac manipulation and distal anastomoses in OPCAB would require a continuous real-time cardiac output monitoring technique.

Our results confirm previous findings of a progressive rise in DO2, VO2 and oxygen extraction fraction after cardiac surgery [11,23]. We observed superior DO2 in the OPCAB group, which was largely related to lower haemoglobin levels in the ONCAB patients from CPB-related haemodilution. Despite the disparity in DO2, there was a progressive and similar rise in global oxygen
extractions fraction in the two groups, resulting in higher VO₂ in the OPCAB group. There were no differences in mechanical ventilation time or speed of systemic rewarming postoperatively that would easily account for this difference in VO₂. We are currently investigating the stress hormonal response after OPCAB to obtain more insight into these findings.

A significant inverse relationship between VO₂ and pH has been previously reported [23] and was confirmed in this study. This may partly explain the difference in gut mucosal oxygenation between the groups postoperatively. However, the latter observation may primarily reflect a difference in the accumulated intraoperative ischaemic injury, as there were no clinical differences in the early postoperative period that would provide an alternative explanation. We also found a significant association between pH and global oxygen extraction fraction, with worsening gastric mucosal oxygenation during increased global oxygen extraction.

This finding is similar to the previously reported association between pH and SvO₂ [23] and indicates that the gut becomes particularly susceptible to injury at times of increased global oxygen demand.

The use of pulsatile flow during CPB reflects our current practice but more importantly has been associated with superior perioperative pH and enhanced gastric mucosal perfusion compared to non-pulsatile CPB [10,24]. Pulsatile flow maintains capillary patency by delivering more energy into the vasculature and ameliorates the increase in systemic vascular resistance by reducing the release of vasoconstrictors, such as angiotensin II [14]. Although core temperature during CPB has not been shown to influence gastric pH [25], a systemic temperature of 35°C during CPB was used in this study to avoid the confounding effect of different intraoperative core temperatures in the two groups. It is likely that the choice of CPB protocol, particularly the use of pulsatile flow, had a significant effect on the study findings, and this must be taken into account in future studies.

One limitation of this study is that only low-risk patients with normal cardiac function were studied. This strategy was adopted to ensure homogeneity of the groups, which is essential in prospective randomized studies with small numbers of patients. However, patients with poor left ventricular function or other co-morbidities, such as diabetes mellitus or extracardiac arteriopathy may behave in a rather different manner and the results of this study cannot be extrapolated to such populations. With hindsight, we would also recommend that future studies document postoperative gut mucosal oxygenation beyond 6 h, possibly up to 24 h, to reveal potential differences between ONCAB and OPCAB in the pattern of recovery of pH or CO₂ gap towards baseline values.

In conclusion this study has demonstrated the presence of significant perioperative gastric mucosal hypoxia during CABG either with or without CPB. How these findings may relate to the incidence of GI complications after OPCAB versus surgery with CPB remains to be seen. Whether these findings may be applicable to a high-risk patient population also requires further investigation. However, the results suggest that haemodynamic impairment during OPCAB, though transient, causes significant subclinical end-organ injury.

Acknowledgements

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References


Appendix A. Conference discussion

Dr T. Raychaudhury (Calcutta, India): I’d just like to make a comment which is almost similar to what you are suggesting in your paper. You see, morally, for economic reasons, we have a lot of patients on off-pump, because we use the stabilizers, so almost 90% and over patients are done by off-pump method. So as a result, a large number of patients with poor LV functions are being dealt with upon surgery. We are learning more and more over the last 5, 6 years and now producing acceptable results.

Now, one of the problems is, as you have rightly pointed out, in patients with poor LV function, that they remain with a nasogastric tube for more than 48 h; some of them, quite a large proportion of them. And when – it is now getting rare – when they go on pump because of persistent hypertension or unacceptable arrhythmias, postoperative period, they do better.

And I think we like to think that it has probably a lot to do with the rewarming. Because in the on-pump, we can rewarm the patients to an acceptable temperature. And often patients, particularly during a long operation, when they come out of operating room, the core temperature is high, or reasonable, but the peripheral temperature is pretty low. And they rewarm over a period of 5–6 h. I think this experience universal.

So that is a comment. I think we have to just accept this unacceptable scenario in gut oxygenation, but with the benefit of off-pump surgery.

Dr Velissaris: I can’t give a direct answer to your comments, because actually this study was done on low-risk patients. In fact, we have a study ongoing now in high-risk patients.

With regards to the temperature difference that you mentioned, I have to say that we didn’t actually have this problem in the patients we studied. In fact, there was no difference between the groups in terms of temperature pattern postoperatively. They took a similar time to rewarm.

Dr S. Hagl (Heidelberg, Germany): In the pump group, did you use hypothermia, and if yes, to what degree?

Dr Velissaris: We used a core temperature of 35 degrees. The reason why we did that was to avoid the confounding factor of different intraoperative temperatures between the groups. We had noticed that our off-pump patients usually dropped their core temperature to about these levels.

Dr Hagl: But even with that, let’s say, high temperatures, you may expect changes in the vasomotor activity in the splanchnic area. So it is possible that it is more or less some sort of autoregulation we are looking at?

Dr Velissaris: You mean in terms of intramucosal pH?

Dr Hagl: Yes.

Dr Velissaris: Well, the intramucosal pH, by definition, examines the adequacy of perfusion. So regardless what the levels of perfusion are, when you assess intramucosal pH, you assess essentially adequacy of oxygenation.

Dr Hagl: But oxygen consumption was not different in both groups; is that right?

Dr Velissaris: No. In fact it was higher in the off-pump group.

Dr Hagl: And the next question is, you are looking at, let’s say, a normal patient population, with high ejection fraction, normal cardiac function. May we suggest that these are patients with normal vessels?

Dr Velissaris: Correct.

Dr Hagl: So I think if you really want to say something, you have to select a certain group of patients who are at high risk of, let’s say, decreased flow in the splanchnic area during extracorporeal circulation.

Dr Velissaris: I fully agree that this would be a valid study, and we’re currently doing that. But I think it’s important in a randomized study with small number of patients to keep the study groups as homogenous as possible. And we preferred, naturally, to start from a low-risk patient population and now we’re continuing with a high-risk study.

Dr J. Habicht (Aarau, Switzerland): Both groups were low-risk patients, but you didn’t mention if you used any adrenaline or noradrenaline or any other catecholamines, or if there was any difference between the two groups in this concern.

Dr Velissaris: In terms of vasoconstrictors, all but one patient in the cardiopulmonary bypass group received phenylephrine as a vasoconstrictor during bypass. In the off-pump group, 14, so that’s just over 50% of the patients, received either boluses of phenylephrine or noradrenaline infusion intraoperatively. Postoperatively, seven patients in the off-pump group and four in the on-pump group received vasoconstrictors. And three patients in the on-pump group and two in the off-pump group received inotropes for a low cardiac output.

I think what is important is that this is obviously a clinical study, it’s not an experimental protocol, so you have to treat the patients optimally. And the only thing you can do is to standardize the inotropic agents you give. So we used dopamine as a first-line inotrope for patients who had a low cardiac output, and either boluses of phenylephrine or a noradrenaline infusion for vasoconstriction.

Dr Habicht: Did you investigate if there was a significant difference?

Dr Velissaris: The on-pump patients, as I said, essentially all of them received phenylephrine during bypass, so it’s an inherent part of the protocol. Postoperatively there was no difference in the pH between the patients who received vasoconstrictors and those who didn’t in either group.