Impact of Perioperative Haemodynamic Monitoring on Cardiac Morbidity after Major Vascular Surgery in Low Risk Patients. A Randomised Pilot Trial

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Objective: to evaluate whether perioperative haemodynamic optimisation influences outcome from infrarenal abdominal aortic aneurysm repair.

Methods: a consecutive series of 100 eligible patients were randomised to either haemodynamic optimisation through the use of a pulmonary artery catheter (CI ≥ 3.0 l/min/m², PWP 10 and 18 mmHg, SVR 1450 dyne/sec/cm², DO2 ≥ 600 ml/min/m²) or conventional treatment.

Results: there were no differences in terms of in-hospital mortality, cardiovascular morbidity, postoperative renal failure or duration of hospital stay between the groups.

Conclusions: in this study perioperative haemodynamic optimisation was not beneficial.

Key Words: Infrarenal aortic aneurysm; Vascular surgery; Perioperative haemodynamic optimisation; Pulmonary artery catheter; Preoperative evaluation of coronary artery disease.

Introduction

It has been suggested that perioperative haemodynamic optimisation through pulmonary artery catheter (PAC) monitoring can improve outcome from aortic surgery.1–8

However, to our knowledge, only one prospective, randomised study has been performed which showed no benefit.9 However, the study included patients with aneurysmal and aorto-iliac occlusive disease.10 Moreover, PAC was used mainly as monitoring device and not to achieve haemodynamic optimisation.

The lack of evidence and the limited ICU resources mean we must identify which patients if any really benefit from intensive perioperative treatment.11,12

We decided therefore to conduct a prospective, randomised pilot study with a limited number of subjects without clinical and echocardiographic evidence of CAD, in order to assess the rate of major postoperative cardiac complications after abdominal aneurysmectomy in relation with the perioperative strategy outlined above. The results could help in evaluating the opportunity to conduct a larger, controlled study.

Materials and Methods

Between 1st April 1996 and 30th March 2000, male patients scheduled for elective infrarenal abdominal aortic aneurysm (AAA) repair were assessed for cardiac risk (Fig. 1). Patients were enrolled if they were aged less than 75 years, asymptomatic for angina and arrhythmias, without significant alterations of ventricular repolarization at resting ecg, without evidence of left ventricular wall motion abnormalities at preoperative transthoracic echocardiography at rest and with an ejection fraction ≥ 50%. Other preoperative risk factors analysed included smoking history, hypertension, diabetes mellitus, chronic obstructive lung
disease, and mild chronic renal failure (serum creatinine level <3 mg/dl).

Acute Physiology And Chronic Health Evaluation (APACHE II)\(^1^3\) was used to measure the severity of illness present preoperatively in order to determine whether control and treatment groups were similar; Sequential Organ Failure Assessment (SOFA)\(^1^4\) score, which takes into account 6 parameters of respiratory, cardiovascular, hepatic, renal, neurological and coagulation systems, was used to describe postoperative individual organ dysfunction/failure in a continuous form, from mild dysfunction (SOFA score \(\leq 2\)) to different levels of failure (SOFA score \(\geq 3\) up to 24).

Criteria for exclusion were presence of advanced chronic renal failure (serum creatinine level \(\geq 3.0\) mg/dl or concomitant continuous or intermittent replacement treatment), severe chronic obstructive lung disease which could anticipate the need for postoperative ventilatory assistance, concomitant aortoiliac obstructive disease.

This study protocol was approved by the Human Ethics Committee of the hospital; informed written consent was obtained from all patients.

Patients eligible were entered consecutively in the order of their scheduled operations and they were randomised in two groups: a computer-generated random number was obtained by phone-call to the Statistical Centre of the hospital on the day before surgery and directed assignment to treatment or control group.

1. **Treatment group** was admitted to ICU on the morning of the day before surgery in order to institute haemodynamic monitoring: radial artery of the non-dominant hand was preferably cannulated and PAC was inserted through the basilic vein under both fluoroscopic and pressure monitoring. Preoperative optimisation of cardiovascular status was defined by the following goals, modified by Shoemaker \(et\ al.^4\) and Berlauk \(et\ al.^5\): Cardiac Index (CI) > 3.01/min/sqm, Pulmonary Wedge Pressure (PWP) >10 and <18 mmHg, Systemic Vascular Resistance (SVR) <1450 dyne/sec/cm\(^5\), Oxygen delivery (DO\(_2\)) > 600 ml/min/sqm.

When not ‘spontaneously’ present, these therapeutic goals were achieved by appropriate treatment: volume-loading, consisting of 9 ml/kg normal saline

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Fig. 1. Protocol of preoperative cardiac risk evaluation for patients scheduled for infrarenal aortic aneurysmectomy; in italics the study project.
0.9% or Ringer’s lactate solution rapidly infused, with additional fluid boluses when requested, until the PWP was >10 and <18 mmHg, followed by intravenous maintenance fluids at 1.5 ml/kg/hr; inotropic drugs: dobutamine initiated in a dose of 2.5 μg/kg/min and titrated upwards to CI > 3.01/min/m²; vasodilator drugs: nitroglycerin 10 μg/min titrated upwards to SVR target.

Patient’s discharge from ICU and transferring to the surgical ward was scheduled at the end of the 2nd postoperative day, if uneventful.

2. Control group remained in the surgical ward during the perioperative period and no haemodynamic monitoring other than central venous pressure and invasive arterial pressure during surgery was instituted.

In both groups, general anaesthesia was administered following the same protocol: induction with propofol 2 mg/kg and atracurium 0.1 mg/kg; IPPV with nitrous oxide in oxygen at a FiO₂ and with a Tidal Volume to achieve SaO₂ > 95% and ETCO₂ = 35 mmHg; maintenance with fentanyl in continuous infusion at a rate of 5 mcg/kg/hour + atracurium when requested.

During postoperative period, in both groups ECG, lactic dehydrogenase (LDH), creatine phosphokinase (CK) and the MB isoenzyme (CKMB) and the serum aminotransferases enzymes AST and ALT were controlled every 6 hours after surgery for the first 48 hours and then daily monitored until the 6th postoperative day and whenever clinically indicated, in order to detect episodes of myocardial ischemia. Whenever high postoperative values of total CK were found, a qualitative troponin I test with a diagnostic cut-off value of 1.5 ng/ml (Spectral’s CARDIAC STATus™ Troponin I Rapid Test – Princeton BioMeditech Corp.) was also performed. Serum creatinine concentration and blood urea nitrogen were also monitored daily until the 6th postoperative day, as biochemical markers of renal failure. Urine output was measured hourly until the end of the 2nd postoperative day, and every eight hours successively.

Duration of surgery, duration of aortic clamping, intraoperative blood loss and replacement, amount of crystalloid (‘balanced’ salt solutions e.g. normal saline 0.9% or Ringer’s lactate) administered perioperatively were registered in both groups.

The primary outcome variable analysed was:

- Cardiovascular morbidity: nonfatal myocardial infarction, based on the existence of at least two of the following criteria: (a) elevated CKMB isoenzyme > 5% and positive simultaneous troponin I test, (b) either new Q-waves or persistent new ST-T wave changes by 12-lead ECG (c) prolonged (>30 minutes) typical chest pain; congestive heart failure (CHF); arrhythmias requiring treatment

Others outcome variables considered were:

- In-hospital mortality
- Postoperative acute renal failure, defined as a worsening of preoperative renal function with accompanying oliguria requiring high doses of furosemide (>250 mg/die) and or continuous or intermittent replacement therapy
- Duration of postoperative hospital stay

Statistics: based on the review of the literature concerning abdominal aneurysmectomy, we found a 10% of major postoperative cardiac complications (non-fatal myocardial infarction, congestive heart failure, arrhythmias requiring treatment). In order to verify the hypothesis that perioperative optimisation of cardiovascular status can improve this endpoint, we considered clinically important a reduction of postoperative cardiovascular morbidity from 10% to 5%. To reveal such reduction, 446 patients in each group would be required, based on the formula for normal theory and assuming a two-sided type II error protection of 0.05 and a power of 0.80. However, the sample size could be even larger, if we consider that perioperative cardiovascular morbidity and mortality rates are probably lower in patients selected as CAD-free. Since it is difficult to enrol such a large number of patients in a single centre, we decided to conduct a prospective, randomised pilot study with a limited number of patients without clinical and echocardiographic evidence of CAD.

Statistical analysis was performed using the appropriate software (SPSS for Windows version 6.1.3). Pre-operative risk factors were compared using Chi-square test with Yates correction with significance level set at p < 0.05; outcomes and perioperative management data were analysed by the chi-square test with Yates correction for categorical data and Mann–Whitney U test for continuous data, with significance level set at p < 0.05.

Results

Hundred consecutive male patients satisfying the entry criteria at the preoperative transthoracic echocardiography were enrolled and randomly divided in treatment and control groups.

Demographic data and medical history for each group are shown in Table 1.

**Table 1. Demographic and medical data.**

<table>
<thead>
<tr>
<th></th>
<th>Treatment group (N = 50)</th>
<th>Control group (N = 50)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>67 (63–75)</td>
<td>68 (62–75)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Smoke history (%)</td>
<td>27 (54)</td>
<td>32 (64)</td>
<td>N.S.</td>
</tr>
<tr>
<td>C.O.L.D. (%)</td>
<td>18 (36)</td>
<td>15 (30)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>5 (10)</td>
<td>7 (14)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>16 (32)</td>
<td>15 (30)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Chronic renal failure (%)</td>
<td>3 (6)</td>
<td>4 (8)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Mean APACHE II preop. (range)</td>
<td>7 (6–10)</td>
<td>7 (5–10)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

**Table 2. Intraoperative data: results expressed as mean (range).**

<table>
<thead>
<tr>
<th></th>
<th>Treatment group (N = 50)</th>
<th>Control group (N = 50)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time</td>
<td>175 (160–250) min</td>
<td>180 (160–245) min</td>
<td>N.S.</td>
</tr>
<tr>
<td>Aortic clamping</td>
<td>75 (55–100) min</td>
<td>65 (55–90) min</td>
<td>N.S.</td>
</tr>
<tr>
<td>Infusions</td>
<td>4500 (3250–6500) ml</td>
<td>4250 (2500–4750) ml</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Blood loss</td>
<td>1000 (450–2750) ml</td>
<td>1100 (500–2500) ml</td>
<td>N.S.</td>
</tr>
<tr>
<td>Cell saver</td>
<td>622 (400–1550) ml</td>
<td>580 (400–1400) ml</td>
<td>N.S.</td>
</tr>
<tr>
<td>PRBC</td>
<td>825 (500–1500) ml</td>
<td>975 (500–2000) ml</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

**Preoperative treatment:** in treatment group, 9 patients developed transient ventricular arrhythmias during positioning of PAC, which did not require treatment. At the preoperative haemodynamic evaluation, 35 patients (70%) met our haemodynamic endpoints without any intervention, whilst 10 patients (20%) in chronic diuretic therapy for hypertension needed volume loading alone and other 5 patient (10%) required additional inotropic treatment with dobutamine at low doses.

**Intraoperative treatment** (Table 2): in treatment group, the total volume of infusions was significantly higher than in control group (p < 0.01). At the declamping, no episodes of arterial hypotension requiring pharmacological treatment were registered in treatment group, whilst in control group of 6 patients needed volume load and/or inotropic drugs (p < 0.05).

**Postoperative treatment** (Table 3): postoperative severity scores did not differ significantly between groups. In treatment group, 5 patient (10%) required inotropic treatment with dobutamine at low doses. Volume of infusions was significantly higher during the 1st postoperative day; urine output remained significantly higher than in control group during 1st and 2nd postoperative day.

In the treatment group at the end of the 2nd postoperative day haemodynamic monitoring was withdrawn in all cases and patients were discharged from ICU and transferred to the vascular-surgical ward.

**Postoperative outcome variables** (Table 4): in both groups in-hospital mortality, non-fatal myocardial infarction and postoperative renal failure rates were null; no significant differences were noted in term of duration of hospital stay between the groups.

Overall cardiac events occurred in 6 patients (6%), two patients of treatment group and four patients in control group; they included arrhythmias (two treatment patients vs three control subjects) and CHF (no treatment patient vs one control subject). In control group there was one case of atrial fibrillation, treated with electrical cardioversion, and two cases of paroxysmal supraventricular tachycardia, requiring pharmacological treatment vs two cases of paroxysmal supraventricular tachycardia in treatment group. In one of these two cases, the episode of paroxysmal supraventricular tachycardia happened during withdrawal of PAC and this was the only complication related to the pulmonary artery catheterization observed in treatment group.

Although control patients tended to have a slightly higher incidence of individual cardiac events, differences between the groups did not achieve statistical significance.

**Discussion**

In any clinical study, statistical significance can be achieved with a relative small number of patients, only if the tested group is at high risk for a bad outcome; preselecting a subset of vascular patients at lower risk for major adverse cardiac complications, as our CAD-free population, any beneficial role of perioperative optimisation of haemodynamic profile is more difficult to define in a relatively small sample, and this was a limitation inherent in the pilot design of our study. Therefore, even if our pilot prospective randomised study could not demonstrate a benefit from the perioperative haemodynamic optimisation in terms of improvement of outcome variables analysed, the risk of a type II statistical error must be acknowledged. The prospective and randomised design of our study, conducted on patients homogeneous in terms of preoperative cardiac risk stratification, in a single vascular surgical centre, represents in any case a correct approach towards a reliable documentation of postoperative cardiac morbidity.

As a matter of fact, reported perioperative cardiovascular morbidity and mortality rates today are lower in comparison with older studies, probably because of better perioperative treatments. Sprung et al., in their recent analysis of 6948 vascular surgical elective and emergency vascular procedures, found a 2.06% incidence of myocardial infarction and a 0.44%
of death in abdominal aortic surgery prosthetic grafts.
If we consider that in the above mentioned study patients with preoperative diagnosis of CAD were 60% in the group without cardiovascular postoperative morbidity, and 85% in the group with postoperative myocardial infarction, our results are not surprising in their very low rate, since they are referring to patients selected as CAD-free.

In recent years the preoperative cardiac evaluation of the patient with vascular disease in order to detect the presence and degree of CAD has gained increased importance for many reasons. 21

First of all, coronary angiography performed before surgery has shown that significant CAD exists in approximately 60% of patients scheduled for major vascular surgery, although asymptomatic and that only 8% are completely CAD-free. 22,23 Moreover, preoperative coronary interventions in symptomatic cases may be indicated to improve long-term survival in patients scheduled for major aortic surgery. 24

Therefore, preoperative cardiac stratification to assess operative risk seems to be the major effort, and several non-invasive techniques have been suggested to improve the preoperative risk stratification in vascular surgical patients. 25,26

The protocol used in our institution is based as first step on transthoracic echocardiography, to detect left ventricular wall motion abnormalities as a significant marker of CAD in formerly asymptomatic patients without significant alterations of repolarization at resting electrocardiogram; ECG treadmill testing has not been chosen as preoperative screening method because most of the vascular patients are not able to perform an adequate physical exercise. For this reason, patients with not significant coronary artery stenosis or with a critical stenosis although less than 85% – which means a reduced coronary artery flow at rest – may have been ignored by our protocol, adopting transthoracic echocardiography.

We cannot exclude that any of these patients could have manifested episodes of myocardial ischemia during intra or postoperative period, which have not been detected by our monitoring protocol. In fact, the diagnosis of postoperative myocardial infarction based on CK-MB isoenzymes in patients undergoing aortic surgery is prone to error; 28 the use of qualitative troponin I test in cases with high postoperative values of total CK, although not as effective as quantitative one, should have improved the diagnostic accuracy of our protocol. In any case, even if these episodes happened, their clinical relevance has been very low and they did not affect the outcome, probably due to their eventually limited severity. At any rate, because there was an equal risk of missed complications in both groups, it is doubtful that the results would have been altered significantly.

Table 3. Postoperative data: results expressed as mean (range).

<table>
<thead>
<tr>
<th></th>
<th>Treatment group</th>
<th>Control group</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(N = 50)</td>
<td>(N = 50)</td>
<td></td>
</tr>
<tr>
<td>SOFA 6 H. AFTER SURGERY</td>
<td>10 (6–12)</td>
<td>10 (6–12)</td>
<td>N.S.</td>
</tr>
<tr>
<td>SOFA 1ST POSTOP. DAY</td>
<td>11 (6–13)</td>
<td>10 (6–12)</td>
<td>N.S.</td>
</tr>
<tr>
<td>SOFA 2ND POSTOP. DAY</td>
<td>8 (6–10)</td>
<td>8 (6–10)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Infusions in 1st postop. day</td>
<td>3480 (3000–4750) ml</td>
<td>2900 (1900–3250) ml</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Urine output in 1st postop. day</td>
<td>2360 (1825–2950) ml</td>
<td>1580 (975–1900) ml</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Infusions in 2nd postop. day</td>
<td>3150 (2750–3600) ml</td>
<td>2980 (2250–3400) ml</td>
<td>N.S.</td>
</tr>
<tr>
<td>Urine output in 2nd postop. day</td>
<td>1523 (1100–2300) ml</td>
<td>1132 (850–2800) ml</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 4. Results on outcome.

<table>
<thead>
<tr>
<th></th>
<th>Treatment Group</th>
<th>Control Group</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>(N = 50)</td>
<td>(N = 50)</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Non fatal m.i.</td>
<td>0</td>
<td>0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>2</td>
<td>3</td>
<td>N.S.</td>
</tr>
<tr>
<td>Congestive Heart failure</td>
<td>0</td>
<td>1</td>
<td>N.S.</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
<td>0</td>
<td>N.S.</td>
</tr>
</tbody>
</table>
| Postoperative Hospital stay | 12 (range 9–17) | 11 (range 8–15) | N.S.
In treatment group, the optimisation of haemodynamic profile on the above mentioned `goal directed' basis, to maintain the left ventricular filling pressure and the cardiac index at the established values, is the reason why no episodes of arterial hypotension at the declamping requiring pharmacological treatment were registered, whilst in control group 6 patients needed volume loading and/or inotropic drugs ($p < 0.05$). For the same reason, a statistically significant higher volume of crystalloids was infused during the first postoperative day and a higher urine output resulted postoperatively. This is a common observation to all the studies that employed PAC in the perioperative management of vascular patients, and probably reflects more confidence to push fluids in, without the fear of causing complications, because of the margin of safety given by knowing the actual PWP.

Recently, some studies have been performed in order to identify cost savings strategies, particularly in terms of bed utilisation and length of hospital stay, for patients scheduled for major vascular surgery, with results that are often contradictory and confusing.

D’Angelo et al. in their retrospective study on 113 patients submitted to infrarenal aneurysm repair compared 74 patients with only a preoperative electrocardiogram and 39 patients with additional testing that included thallium stress test or echocardiogram or cardiac catheterization and concluded that preoperative cardiac testing does not affect postoperative mortality and morbidity and is therefore not usually necessary, whilst perioperative haemodynamic management, with therapeutic end-points similar to those adopted in our treatment group, may be the most important variable in determining outcome.

Opposite conclusions have been drawn by Fleisher et al. who recently reviewed data of Medicare beneficiaries to determine the mortality rate after vascular surgery and noted a reduced perioperative and long-term mortality in patients who had previously undergone preoperative cardiac assessment, in comparison with those not submitted to preoperative cardiac testing.

We think that an accurate preoperative cardiac-risk stratification plays a pivotal role in outlining the perioperative management strategies; in patients selected through our preoperative cardiac evaluation protocol as CAD-free however, the postoperative mortality and cardiovascular morbidity is too low, in our opinion, to justify a controlled randomised study, which would require a considerable effort in selecting and enrolling a quite large number of patients.

The pilot design of our study does not allow any conclusions, but we reasonably speculate that in CAD-free selected patients haemodynamic optimisation is not beneficial. Its role in preventing perioperative cardiovascular mortality and morbidity in different subsets of patients with more severe cardiac impairment at preoperative evaluation must be addressed with further controlled studies.

References


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