Right heart assist for beating heart coronary artery bypass grafting

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Abstract

Objective: Cardiopulmonary bypass used in conventional coronary artery bypass surgery (cCABG) entails a risk of complications. Consequently, the trend is moving towards off-pump coronary artery bypass (OPCAB). This procedure, however, may lead to haemodynamic instability due to kinking of the right ventricle when the posterior aspect of the heart is exposed. The aim of the study was to establish if a right-sided circulatory assist device (RHA) was able to maintain haemodynamic stability during OPCAB procedures.

Method: In a prospective study 50 RHA-OPCAB patients and a control group of 50 cCABG patients were examined. Before accessing the marginal arteries, an RHA was established in the RHA-OPCAB patients.

Results: A stable haemodynamic condition was achieved for 98% of the RHA-OPCAB patients. The study group had less postoperative chest drain bleeding \( P < 0.001 \), shorter ventilation time \( P = 0.001 \), and lower blood levels of creatine kinase (CK) and brain CK \( P < 0.001 \) compared to the control group.

Conclusion: The results indicate that RHA-OPCAB is a realistic alternative to cCABG. The procedure can be safely performed most likely resulting in reduced postoperative bleeding, myocardial damage, and ventilation time.

Keywords: Off pump coronary artery bypass; Coronary artery bypass surgery; Right heart assist

1. Introduction

The past decade has seen a considerable change in the patient population referred to coronary artery bypass treatment (CABG). The patients are older than before and co-morbidity therefore increases the perioperative risk. A trend towards less traumatic approaches in the treatment of the patients with ischaemic heart diseases is often advocated [1]. In the last two decades, myocardial protection, anaesthetic management, surgical techniques, and postoperative intensive care methods have been subject to continuous improvement. Still, mortality and, in particular, morbidity following cardiac surgical procedures is a problem [2–4].

Conventional coronary artery bypass surgery (cCABG) with cardiopulmonary bypass (CPB) has been regarded as the reference surgical technique for patients with coronary artery disease [5]. The use of a heart–lung machine, however, involves risk of neurological, renal, and respiratory postoperative dysfunction, mainly due to a diffuse inflammatory response, and dysfunction of the coagulation system. Consequently, since the mid 1990s off-pump coronary artery bypass grafting (OPCAB) has been considered as a beneficial approach for selected patients [6–8].

Nierich et al. [9] investigated the haemodynamic profile for the OPCAB patients with target vessels on the anterior and lateral aspects of the heart. No significant haemodynamic changes were observed during this procedure. However, accessing these marginal arteries is hampered by space limitations that may compromise the quality of the anastomoses and often causes haemodynamic instability following manipulations of the heart. Dislocation of the heart leads to biventricular dysfunction because of kinking of the low-pressure right atrium and ventricle, which impairs blood flow in the pulmonary circulation. Accordingly, the low left ventricular preload leads to systemic circulatory failure. To provide sufficient preload to the left
ventricle in such situations, a right-sided circulatory assist may be an alternative to the CPB.

Animal studies have verified that right heart assist (RHA) normalizes haemodynamics even with the heart maximally tilted [10–13]. The feasibility of RHA has not yet been demonstrated in major clinical studies [14,15]. Therefore, the aim of this study was to evaluate RHA-CABG on 50 patients and compare the data of a similar-sized control group operated on with cCABG.

2. Materials and methods

2.1. The RHA-CABG group

The study comprised 50 adult patients admitted to Aarhus University Hospital for a first-time elective CABG for three-vessel disease (3VD) including a marginal artery, and a left ventricular ejection fraction (EF) > 35%. Patients were included regardless of age, gender, EuroSCORE, or diabetic disease. Not included were patients suffering from unstable angina pectoris (continuous infusion of nitroglycerine at the day of operation), or an unstable preoperative haemodynamic condition (continuous infusion of inotropics at the day of operation), or an unstable left ventricular ejection fraction.

Informed consent was obtained from all patients. The study was approved by the local ethical committee and conducted in accordance with the Helsinki II Declaration. Before revascularization, the patients were included in the RHA-CABG group. All patients were examined 3 months later at an outpatient clinic.

2.2. Control group

Each RHA-CABG group patient was retrospectively matched to a control patient operated on by cCABG in the same period. Matching was performed on 50 patients according to, age, sex, 3VD, EuroSCORE [16], and EF by computer-aided selection from the local database. The operator was blinded to the patient outcome while selecting.

2.3. Management of anaesthesia and intensive care

After premedication with diazepam 0.10 mg/kg, the general anaesthesia was induced by propofol 1.5–2.5 mg/kg and sufentanil 3–5 µg/kg. Muscle relaxation was accomplished by pancuronium 0.1 mg/kg. Propofol 1.5–2.5 mg/kg per hour was given during surgery. Continuous mixed venous oxygen saturation (SvO₂) supplemented by pump flow, pressure monitoring of left atrial pressure (LAP), and pulmonary artery pressure (PAP) were applied to monitor the circulatory status. Intravascular lines for continuous pressure monitoring were applied to monitor mean blood pressures from the radial artery (MAP) and central venous pressure (CVP) from the right internal jugular vein. Cardiac output (CO) of ten patients was measured in the aorta with a PiCCO catheter (ViCare DK) inserted through the right femoral artery [17]. The ST segment in the ECG was monitored continuously to detect signs of myocardial ischaemia and cardiovascular instability during cardiac manipulations, target artery immobilization, and flow interruption. Dobutamine and nitroglycerine as perfusion were administered as necessary to normalize haemodynamics.

Postoperative ventilatory support continued until stable haemodynamic conditions were ensured. Chest drain blood was auto-transfused whenever necessary during the first 8 postoperative hours. In both groups criteria for transfusion of red blood cells were identical namely at a haematocrit < 25% during operation, or < 30% postoperatively.

2.4. Surgical technique in the RHA-CABG group

After midline sternotomy, the left internal mammary artery (LIMA) was harvested. When the pericardium was opened, the LIMA was anastomosed to the left descending artery (LAD). The venous grafts were anastomosed immediately afterwards. Generally, the distal anastomoses were completed before the proximal ones. The coronary arteries were snared proximally with a suture and a tourniquet to prevent bleeding during the distal anastomosis. An Octopus Stabilization System (Medtronic, Grand Rapids, MI) was used to immobilize the exposed target coronary artery. An RHA was established before performing the distal anastomosis to the marginal coronary arteries. A 28-F two-stage inlet catheter (Jostra, Germany) was placed in the right atrium. A 14-F outlet cannula (Jostra) was placed through a purse string suture directly in the pulmonary trunk. After completion of the last distal anastomosis and taking the heart back to its normal position, the perfusion cannulae were removed. All bypass grafts were immediately quality controlled by flow measuring by means of a Doppler transit time flow probe (CardioMed, Norway). During the procedure the patients were kept normothermic using a Bair Hugger Temperature Management System (Augustine Medical Inc., MN).

2.5. Right heart assist

A BioMedicus centrifugal pump head (80 ml) with 3/8-inch tubings was primed with 400 ml lactated Ringer solution and connected to the venous catheter and the arterial cannula. Initially, the pump was set at 2.5 l/min per 3000 rpm displacing the blood from the inlet to the outlet cannula (Fig. 1).
Heparin (Leo) was given before mammary takedown at a dose of 100 IU/kg body weight. A satisfactory anticoagulation level was defined as activated clotting time (ACT) > 200 s as measured at a Hemocron Jr (Vingmed, Denmark). Supplemental heparin was administered as necessary. After removal of the perfusion cannulae, heparin was neutralized with 50 mg protamine sulphate (Leo).

2.6. Surgical techniques for the control group

After cannulation of the aorta and right atrium, CPB was initiated to allow aortic cross-clamping and antegrade cold crystalloid cardioplegic (St. Thomas II). Central anastomoses were performed after distal by means of a side clamp. After completion of the distal anastomoses the patients were gradually weaned from CPB. The blood remaining in the heart–lungen machine was re-transfused.

2.7. Cardiopulmonary bypass (CPB)

The circuit comprised a membrane oxygenator (Quadrox, Jostra), a softbag venous reservoir (Safe II, Polystan, Denmark), cardiotomy reservoir (Gish, USA), silicone tubings (Polystan), and an arterial filter (Pall, UK). The HLM (Polystan) had occlusive roller pumps.

Prime consisted of 1800 ml of lactated Ringer solution with an addition of 5000 IU of heparin. CPB was conducted at 34 °C. During perfusion, the pump flow was maintained at a cardiac index at 2.4 l/m² per minute maintaining SvO₂ > 70% (CDI 100, 3M, USA). Acid–base balance followed an alpha-stat regime [18]. During CPB the haematocrit was kept between 0.25 and 0.30.

Anticoagulation was achieved by administering 300 IU heparin/kg body weight to an ACT level > 480 s. To neutralize the heparin after surgery 1 mg protamine sulphate (Leo) pr. 100 IU heparin was administered.

2.8. Outcome measures

We studied peri- and postoperative course and complications and also worked out a 3-month postoperative status for the RHA-CABG group. As for the control group, we studied peri- and postoperative course and complications during admission. The peri- and postoperative outcome measures were defined as mortality and cardiac, pulmonary, cerebral, renal, and bleeding complications according to these definitions: AMI (defined as Q-wave changes or loss of R-wave in the electrocardiogram and creatine kinase (CK)-MB release > 40 μg/l), atrial fibrillation, need for inotropic support > 1 day, ventilatory support > 24 h, major neurological deficit as coma, stupor or paresis, se-creatine > 200 μmol/l, need for haemofiltration, need for re-operation due to bleeding, need for allogenic transfusion of red blood cells. The 3-month follow-up consisted of data on survival, reappearance of angina, cardiac-related hospitalization and intervention, and the requirement anti-angina medication.

2.9. Statistical analysis

In the statistical analysis, haemodynamic changes between baseline values and values on RHA were analysed by means of a Mann–Whitney U-test or a paired Student t-test, depending on distribution. The clinical outcome data were compared with an unpaired Student’s t-test or a chi-square test. Statistically significant differences were defined as the level at which the P-value was less than 0.05. SPSS statistical software (SPSS Inc., Chicago) and Microsoft Excel 2000 was used for statistical analysis and graphical presentation.

3. Results

3.1. Patient characteristics

In the period February 2000 to March 2001, 55 patients were accepted to participate in the study. Five patients were excluded since MAP or SvO₂ did not decrease to < 50% within 1 min of elevation of the heart. On these patients,
an OPCAB was performed. Demographic data of the RHA-CABG group and controls appear in Table 1.

### 3.2. Descriptive perioperative data of the RHA-CABG group

The following data are presented as mean (range). Duration of the operations: 2.8 h (2.0–4.0). Planned number of grafts: 3.4 (2–6) and 3.3 (2–5) were actually performed. All patients received one or two grafts to the circumflex area, besides grafting on the LAD and the RCA. During the distal anastomotic procedure intravascular shunts were used in 3% of the procedures, 68% of the arteries were ligated, and 29% were performed without either of the two. During establishment of the distal anastomosis, changes in the ST-segment of the ECG was seen on 16 patients. The ECG was normalized in all patients shortly after the distal anastomosis was finished. After completion of the proximal anastomosis the blood flow in the grafts was 52 ml/min (10–190). In one case the blood flow in LIMA to LAD was 10 ml/min due to a poor graft material and a venous graft was established to the LAD segment. The intra-operative mean blood loss was 500 ml (200–900). No patients received allogenic blood products during surgery. Forty patients had no inotropic support during surgery. Nine patients required low-dose dobutamine (1–3 μg/kg/min) to support the haemodynamics aiming at a MAP above 60 mmHg. One patient developed refractory ventricular fibrillation and the RHA system had to be converted to a Cardio Pulmonary Support system; the operation was completed as a beating heart procedure and resulted in full recovery. Six patients developed atrial fibrillation during the procedure, three had short episodes of ventricular fibrillation and three had short episodes of both atrial and ventricular fibrillation; intra-pericardial defibrillation was successfully used to regain the sinus rhythm; no further medical or other kind of treatment was necessary.

The haemodynamic parameters during RHA support are shown in Figs. 2–6. The RHA procedure lasted 18 min (6–26), with a blood flow on the pump set at 2 l/min (1.6–2.4). The mean arterial pressure decreased significantly during the first 10 min of RHA from 78 mmHg (±11) (mean (SD)) to 69 mmHg (±13) and was restored hereafter to reference values (Fig. 2).

The venous oxygen saturation (SvO₂) decreased significantly after 2 min. The mean starting point value was 72% and the minimum during the RHA procedure was 62% (±5) and the minimum during the RHA procedure was 62% (±8). The SvO₂ did not recover to basic values during the RHA procedure (Fig. 3).

The CVP, LAP, and PAP increased significantly during RHA, and did not normalize until the heart was brought back to its normal position and the pump was stopped (Figs. 4–6).

The cardiac index was measured on the last ten patients and showed no significant change during the procedure, as there was no significant change in the heart rate during the procedure.

### 3.3. Postoperative outcome

The postoperative outcome measures are shown in Table 2. The patients in the RHA-CABG group had significantly less chest drain bleeding 14 h postoperatively than the control group (722 ml (200–2200) vs. 1214 ml (150–2725)). There was no significant difference in

![Fig. 2. Mean arterial pressure (MAP) ± SD, minimum and maximum during right heart assist (RHA) (n = 50). There is a significant decrease in MAP by initiation of RHA until 8 min after the start (marked *). The intervals shown here apply also to Figs. 3–6: 1, before cannulation; 2, initiation of RHA; 3, 2 min after start; 4, 4 min after start; 5, 6 min after start; 6, 8 min after start; 7, 10 min after start; 8, 12 min after start; 9, 14 min after start; 10, 16 min after start; 11, 18 min, end of RHA.](image)

![Fig. 3. Mean mixed venous oxygen saturation (SvO₂) ± SD, minimum and maximum during right heart assist (RHA) (n = 50). There is a significant decrease in SvO₂ during RHA (marked *).](image)
the frequency of re-operations in the two groups ($n = 2$ vs. 8) as there was no significant difference in the frequency of patients receiving allogenic red blood cells ($n = 25$ vs. 34). In the RHA-CABG group the patients were on ventilator significantly shorter time (5.7 h (0–18) vs. 7.9 (3–17)) (long-term ventilation not included), and the CK and brain CK (CKB) levels were significantly lower compared to those of the control group (CK = 455 (127–1245) µg/l; (CKB = 17.3 µg/l (6–52) vs. 29.2 (6–52)). No significant difference was found in the number of patients having a postoperative level of se-creatinine $> 200$ µmol/l ($n = 1$ vs. 4), as no difference was found between the groups in terms of length of hospitalization (5.7 days (3–12) vs. 6.2 (4–21)).

3.4. Major complications

In the RHA-CABG group two patients died. One patient suffered from postoperative complications in the form of gastrointestinal bleeding on day seven. Due to a perforated ventricular ulcer, a Billroth II operation was performed. The patient developed sepsis and died 18 days after the bypass operation. The other developed low MAP 2 h postoperatively. The patient underwent re-operation and a thrombus formation was found in one of the grafts. Despite intensive medical treatment the patient died 4 days after surgery from acute myocardial infarction and multi-organ failure. Forty-eight patients (96%) were discharged from hospital in good health.

In the control group, one patient died 7 days postoperatively from untreatable atrial fibrillation, universal intestinal ischaemia and sepsis. Three patients suffered from major cerebral complications after the operation. One patient had facial palsy and hemi weakness; one had severe cerebral damage and never regained consciousness. Additionally, one patient suffered from hemiparesis due to a hypotensive crisis 2 days after surgery. Forty-six patients (92%) were discharged from the hospital in good health.

3.5. Description of RHA-CABG group at 3-month follow up

Three months postoperatively one patient suffering from severe diabetes mellitus was admitted again due to re-angina. An angiography revealed an occluded graft and a stent was inserted. Preoperatively 20% of the patients were medicated with beta-blockers/ACE inhibitors, nitrates, and calcium antagonists. After 3 months, none of the patients received three-drug anti-anginal medication. Preoperatively 44% were medicated for anti-angina with two drugs; this number was reduced to 16% after 3 months.

Forty patients responded to a questionnaire. Out of these, 38 patients described their situation as ‘better/almost no symptoms’, and two reported ‘unchanged’. Two patients had died, and eight did not respond.

4. Discussion

The few clinical data published on RHA-CABG describe the use of the Enabler and the A-Med RHA systems [14,15]. Both systems use a single cannula technique with a right atrium approach, which is attractive, but may not counter-balance the uncertainty of correct positioning of the distal
end of the cannula, displacing itself over the pulmonary valve. None of the systems have heparin-coated disposals. In our study, the BioMedicus centrifugal pump was used giving the option of using a reduced amount of heparin, and a higher degree of biocompatibility due to a tip-to-tip heparin-coated disposal system [19]. Therefore, we found the double-cannula, heparin-coated approach more suitable for partially bypassing the right ventricle.

4.1. Postoperative outcome in terms of safety and complications

We found that MAP decreased significantly compared with baseline values 2 min after pump start, but normalized within 8 min. The CO and HR remained constant. The SvO₂ saw a significant decrease during pump time – but not to critically low values – and the SVO₂ normalized shortly after termination of RHA. PAP, CVP and LAP increased during RHA. This indicates that the left ventricle is not fully able to overcome the workload in a displaced position. Evidently, a pump flow of 2 l/min was not an inadequate support of the right ventricle, since CVP increased. However, an increase of the pump flow will cause the left atrium to overload and the LAP and PAP to further increase, thus straining the left ventricle. This might be due to mitral valve insufficiency caused by the kinking of the heart. Surgery was completed on the majority of the patients (80%) without inotropic support, and indicating that the circulatory system is able to adjust to the situation. For 18% of the patients it was necessary to use a slight stimulation with a beta-agonist to maintain acceptable values of MAP, Svo₂ and CO.

Twelve patients (24%) had short episodes (seconds) of atrial or ventricular fibrillation during surgery. This phenomenon may be related to the surgery on a non-occluded artery on which the snare is tightened around the vessel proximal to the stenoses. In this way, the myocardium suffers from ischaemia, which may give rise to arrhythmia. In all cases but one sinus rhythm was achieved either spontaneously or by a single defibrillation. Even though CABG with RHA on patients with 3VD entails short episodes of compromised haemodynamics, it does not seem to affect the overall postoperative outcome compared to the patients in the control group patients operated on with HLM.

4.2. Postoperative bleeding

The patients in the RHA-CABG group had significantly less chest drain bleeding, although there was no significant difference of frequency of re-operation for bleeding. There was no difference between the two groups regarding the need for allogenic blood transfusion, a confirmation of data from Nader et al. [20]. However, the use of RHA implicates less contact by blood to foreign surfaces, less haemodilution, no autotransfusion from suction from the operative field, and less heparinization. This approach is likely to retain the platelet function and coagulation ability of the blood postoperatively as compared to patients operated on using cCABG.

4.3. Cardiac complications

The control group had a significantly higher peak of plasma level of CK and CKB postoperatively than the RHA-CABG group, indicating a higher degree of diffuse myocardial damage. Three control group patients suffered from perioperative acute myocardial infarction compared to one patient in the RHA-CABG group (not significant). In the control group, 16 patients were medicated for postoperative atrial fibrillation compared to nine in the study group (not significant). These indicators seem to point in the same direction, that RHA-CABG is less traumatic to the myocardium than the cCABG procedure.

4.4. Complications to the CNS

To perform a cCABG, aortic cross-clamping and cannulation of the aorta is necessary. Patients with ischaemic heart disease tend to have some degree of atherosclerosis in the aorta. Manipulation of the aorta involves the risk of tear of the atherosclerotic debris, which may subsequently end up as an embolus in the brain or other vital organs [21]. In our study, three

<table>
<thead>
<tr>
<th>Variable</th>
<th>RHA-CABG (n = 50)</th>
<th>cCABG (n = 50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest drain bleeding 14 h postop. (ml)</td>
<td>722 ± 353 (200–2200)</td>
<td>1214 ± 616 (150–2725)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine kinase (µg/l)</td>
<td>455 ± 261 (127–1245)</td>
<td>909 ± 716 (179–3642)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine kinase MB (µg/l)</td>
<td>17.3 ± 12.9 (6–52)</td>
<td>29.2 ± 6 (6–52)</td>
<td>0.08</td>
</tr>
<tr>
<td>Ventilation (h)</td>
<td>5.68 ± 4.0 (0–18)</td>
<td>7.85 ± 3.42 (3–17)</td>
<td>0.001</td>
</tr>
<tr>
<td>No. of distal anastomoses</td>
<td>3.27 ± 0.69 (2–5)</td>
<td>3.29 ± 0.69 (2–5)</td>
<td>NS</td>
</tr>
</tbody>
</table>

The results show a significantly less chest drain bleeding in the RHA-CABG group, lower creatinine kinase in the RHA-CABG group, and ventilator hours are fewer in the RHA-CABG. There is no difference between the groups in the level of the creatinine kinase MB. NS, not significant.
control group patients had severe neurological damage while in hospital. None of the patients in the study group showed damage to the CNS (no significant difference). Svenmarker et al. [19] report cognitive dysfunction in 50% of the cCABG cases; some of this might be due to the anaesthesia and the general stress on the body. Diegeler et al. [22] proved in a randomized study \( (n = 40) \) between OPCAB/cCABG that, 1 week postoperatively, 90% of the cCABG had postoperative impairment of the cognitive function versus no impairment in the off-pump group. Their findings confirm the association between cerebral microembolism and impairment in postoperative cognitive tests.

CABG with RHA is not a completely pump-less approach but the cannulation sites are both on the right side. Accordingly, the risk of systemic embolization caused by the perfusion system is significantly reduced.

4.5. Limitations of the study

The study was a feasibility study including 50 patients. After closing the study, we formed a control group according to specific criteria. Had the groups been chosen by random, the question of a true difference of the surgical approach might have been answered. A discussion of any difference in the quality of the anastomosis between the two groups is only possible if angiographies are performed postoperatively. This, however, was not the perspective of this study. The same consultant operated on all patients in the RHA-CABG group. This gives a one-surgeon experience, which can be defended by the fact that this is a new technique, but more surgeons in the control group probably results in more scattered data making the comparison difficult.

Accordingly, this study can be considered as a valid justification for conduction of a large-scale prospective randomized clinical controlled study.

4.6. Conclusion

The present non-randomized study demonstrates a significant difference between the RHA-CABG group and the control group in terms of postoperative bleeding, myocardial enzyme release, and postoperative ventilation time. Other data might indicate a positive trend for the RHA approach as regards CNS protection, reduced frequency of perioperative AMI, and a reduced requirement for allogenic blood products transfusion. We conclude that revascularization on patients with 3VD by means of the beating heart procedure and RHA is a safe technique, which will provide high-quality results in comparison to what can be achieved by cCABG.

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References


