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Research Article

Study of perioperative extravascular lung water and intrathoracic blood volume in patients undergoing CABG surgery with or without cardiopulmonary bypass

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KEYWORDS

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OPCAB VS on-pump surgery

Abstract *Background:* Whether off-pump coronary artery bypass graft (OPCAB) surgery is superior to traditional on-pump coronary artery bypass graft (CABG) surgery still one of the most controversial areas of cardiac surgery and anesthesia. We hypothesized that OPCAB surgery may result in less accumulation of extra-vascular lung water (EVLW) and intra-thoracic blood volume (ITBV) in the peri-operative period.

Patients and Methods: Thirty patients underwent elective CABG surgery were randomized for this study, 15 OPCAB (group 1) and 15 on Pump (group 2). We measured EVLW and ITBV by PiCCO monitor in 8 times; before induction of anesthesia, after induction of anesthesia and before skin incision, before starting revascularization in group 1 or before cardiopulmonary bypass in group 2, at the end of revascularization in group 1 or at the end of CBP in group 2, at the end of surgery (after skin closure), two hours after the end of surgery, six hours after the end of surgery, twelve hours after the end of surgery and finally in the morning of first postoperative period.

Results: Demographic data and the preoperative characteristics were comparable in both patient groups. The intra-operative course was uneventful, and the intra-operative and postoperative characteristics were comparable in both patient groups. In all patients, complete revascularization was achieved. Extra-vascular lung water and intra-thoracic blood volume did not differ between groups in all times of measurements.

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Discussion and Conclusion: The clinical advantage of off-pump CABG surgery over standard extracorporeal circulation in regard to lung water content was not found in our study. In conclusion, the presumed superiority of off pump surgery for coronary artery bypass grafting could not be confirmed in our group of patients.

1. Introduction

In spite being initiated almost three decades ago [1], off-pump surgery still one of the most hotly debated issues in cardiac surgery and anesthesia. Off-pump surgery was initially proposed to allow coronary artery bypass grafting (CABG) surgery in developing countries without the need for cardiopulmonary bypass (CPB) machine to save cost that was beyond the economic reality of the majority of patients. Despite initial skepticism about its technical feasibility, off-pump CABG was gradually adopted by some surgeons who believed that the elimination of CPB machine could potentially and substantially eliminate the adverse clinical consequences of extracorporeal circulation (ECC) [2,3].

As the off-pump concept moved into the surgical arena, the hope was that it would decrease peri-operative morbidity and possibly mortality, and the fear was that revascularization would be more difficult, less complete, and less effective over the long term, and multiple studies have addressed these issues [4,5].

To our knowledge there is no study up till now compared the difference in extra-vascular lung water (EVLW) accumulation during both surgical techniques (off and on-pump). It is generally believed that pulmonary edema is a common complication after cardiopulmonary bypass (CPB) for cardiac surgery and extra-vascular lung water is increased in the edematous lungs [6]. One possible mechanism of impaired oxygenation in cardiac surgery with ECC is the accumulation of extra-vascular lung water. Intra-thoracic blood volume (ITBV) and pulmonary blood volume (PBV) also may increase after separation from ECC, which can influence both cardiac performance and pulmonary capillary fluid filtration [7].

The Pulse Contour Cardiac Output (PiCCO)® is an innovative technology that monitors the cardiac preload volume through the global end diastolic volume (GEDV) and gives an estimation of the intra-thoracic blood volume, an indicator of circulating volume and of the extra-vascular lung water (EVLWI), which is considered to be a good estimator of interstitial lung edema. Moreover PiCCO®, through a "beat to beat" analysis of the arterial pressure wave, measures continuous cardiac output.

We hypothesized that off-pump CABG may result in less accumulation of extra-vascular lung water in the peri-operative period. So we designed a prospective randomized study to compare the effects of off-pump and on pump CABG surgery on extra-vascular lung water and intra-thoracic blood volume.

2. Patients and methods

Thirty patients underwent elective CABG surgery were randomized for this study. The study was approved by the Hospital Ethical Committee and all patients gave written informed consents. Exclusion criteria were; severely impaired left ventricular function (ejection fraction $<40\%$), recent myocardial infarction (<6 weeks), pulmonary disease, severe systemic non-cardiac disease, renal or liver impairment, insulin dependent diabetes or any endocrine disorder, infectious disease before operation, chronic inflammatory disease, malignant disease or patients under diuretic treatment.

On the morning of the operation, patients were randomly selected to either group 1 or group 2. Group 1 (15 patients) for off-pump CABG and group 2 (15 patients) for conventional CABG with CPB. Cardiac medication including beta-adrenergic blocking agents, calcium-channel blocking agents and nitrates was continued until the morning of surgery. All patients were pre-medicated with lorazepam 40 $\mu g\ kg^{-1}$ orally the night of the operation and morphine sulfate 70 $\mu g\ kg^{-1}$ and scopolamine 8 $\mu g\ kg^{-1}$ intramuscularly one hour before the operation.

Anesthesia was induced with sufentanil 2 $\mu g\ kg^{-1}$ and midazolam 0.15 $mg\ kg^{-1}$ and maintained with sufentanil 1.0 $\mu g\ kg^{-1}\ h^{-1}$ and midazolam 0.12 $mg\ kg^{-1}\ h^{-1}$. In the two groups tracheal intubation was facilitated with pancuronium bromide 0.1 $mg\ kg^{-1}$. A bolus dose of sufentanil 0.5 $\mu g\ kg^{-1}$ was given before skin incision. No acute normovolemic hemodilution was allowed during this study. Patients were ventilated with oxygen/air ($FiO2 = 0.5$) with tidal volume of 5–8 ml/kg aiming to normocapnia.

Heparin 300 IU/kg, and additional heparin were be given until ACT > 400.

Protamine sulfate was given in the same dosage as the initially administered heparin dose to antagonize heparin effect. Before CPB patients received 500 ml gelofusine, followed by Ringer's lactate solution (RL) sufficient to maintain pulmonary artery wedge pressure (WP) 8–14 mmHg. Mild hypothermic CPB at a rectal temperature between 30 and 32 °C, a blood flow of 2.4 $L\ min^{-1}\ M^{-2}$, and a mean arterial pressure were maintained between 60 and 90 mmHg. The left ventricle was vented, and lungs were statically inflated (5 mmHg pressure) with oxygen during CPB. FC ZAfter weaning from CPB fluids (RL or "pump blood") was given to maintain WP between 8–16 mmHg depending on the patient's hemodynamics, If cardiac index is less than 2 L/m^{-2}/min.

2.1. Patient monitoring

Consists of five-lead ECG, pulse oximetry, capnography, body temperature (rectal and nasopharyngeal), end-tidal gas monitoring, invasive arterial pressure, central venous pressure, and pulmonary artery pressure. The PICCO device ®(Palsion Medical System, Munich, Germany) with a central venous injection and the use of an arterial thermo-dilution catheter were used to measure; intra-thoracic blood volume, extra-vascular lung water, stroke volume index, systemic vascular resistance index, cardiac index and cardiac function index, and global end-diastolic volume.

2.2. Off-pump technique (group 1)

A standard median sternotomy was performed. A retractor (CTS/Guidant Cupertino California) was placed and the pericardial edges were lifted. Three to four deep pericardial sutures were placed on the left sided pericardium posterior of the phrenic nerve to rotate and displace the heart anteriorly and to the right. As an additional measurement, when necessary for the hemodynamic status, the patient was tilted to the right and placed in Trendelenburg position. Traction on the right sided pericardial edge sutures was regulated according to surgical needs. The temperature of the patient was maintained above 36 °C by a warming mattress and by warming the intravenous fluid administration. The ultima access platform/stabilizer (CTS/guidant Cupertino California®) was used for presenting and stabilizing the coronary arteries. After dissecting the left internal mammary artery (LIMA) from its origin to below the bifurcation, the patient was heparinized with 200 IU kg^{-1} IV as a bolus followed by an infusion of 2000 IU h^{-1} to maintain the activated coagulation time (ACT) > 300 s (Hemochron 801®; International Technidyne Corp; Edison, NJ). Distal anastomoses were performed first. In all cases the LIMA anastomosis to the diagonal branch(s) and/or left anterior descending (LAD) were routinely performed first before the right internal mammary (RIMA) or vein graft anastomosis to the right coronary artery (RCA), inferior and posterior arteries. The proximal vein graft anastomoses were performed using a side-beating clamp while maintaining the systolic blood pressure < 100 mmHg. The distal anastomoses were made under local ligation of the coronary vessel with prolene 5-0, and a FloCal® shunt was used for all distal anastomoses. After the last proximal anastomosis the heparin was reversed by protamine sulfate. Inotropic support with dopamine and/or noradrenaline was used when indicated.

2.3. Cardiopulmonary bypass technique (group 2)

Routine median sternotomy was performed and the pericardial edges were lifted. After dissecting of the LIMA from its origin to below the bifurcation, the patient was heparinized with a bolus of 300 IU kg^{-1} IV to achieve an ACT > 450 s. Additional increments of heparin were administered during the procedure to maintain the ACT > 450 s. Cardiopulmonary bypass was instituted using a Cobe hollow fiber membrane oxygenator. The circuit was primed with 1100 ml (500 ml gelofusine + 500 ml Ringer's solution + 100 ml mannitol). The CPB flow was maintained at 2.4 L min^{-1} m^{-2}, and mild hypothermia of 32 °C was accomplished. Cold cardioplegic solution was given after cross-clamping for myocardial protection (800–1000 ml initially and 200–300 ml after every 30 min through the aortic root and 100 ml after every distal anastomosis through the vein graft). The distal vein graft anastomoses were performed first, while the distal LIMA anastomoses to the diagonal branches and or LAD were performed last. The proximal vein graft anastomosis was performed under side clamping of the aorta. After de-clamping, the heart was defibrillated, if needed, then the patient was re-warmed to a rectal temperature of at least 34 °C. After weaning of the CPB and de-cannulation the heparin was reversed with protamine sulfate. Inotropic support with dopamine and/or noradrenalin was used during weaning when indicated.

2.3.1. Postoperative management

All patients followed standard care and processes on the ICU and postoperative ward until discharge from the hospital. On arrival to the ICU, hemodynamic and ventilation criteria were recorded every 15 min before extubation and hourly until discharge from ICU. Patients were weaned from mechanical ventilation as soon as they were hemodynamically stable, responded to verbal stimulation, completely re-warmed and when blood loss did not exceed 100 ml/h. Postoperative pain management was achieved with doses of piritramide i.v. boluses of 5–10 mg. The time to extubation, postoperative fluid and blood transfusion requirement, the need for inotropic support, the presence of postoperative complications, the length of stay in the ICU were recorded. Patients were discharged from the ICU on the first morning, if they were hemodynamically stable, had normal blood gases under spontaneous respiration and acceptable cardiac enzymes.

2.4. Data collection

In addition to demographic data, preoperative, intra-operative and postoperative characteristics of patient groups, the extravascular lung water and intra-thoracic blood volume were derived by the PICCO device.

2.5. Time of measurement

Before induction of anesthesia (T0), after induction of anesthesia and before skin incision (T1), before starting revascularization in group 1 or before cardiopulmonary bypass in group 2 (T2), at the end of revascularization in group 1 or at the end of CBP in group 2 (T3), at the end of surgery (after skin closure) (T4), two hours after the end of surgery (T5), six hours after the end of surgery (T6), twelve hours after the end of surgery (T7) and finally in the morning of first postoperative period (T8).

2.6. Statistical analysis

Calculations were performed on a personal computer using SPSS version 16.0.

The groups were tested for differences with Student's *t*-test for continuous variables and Fisher's exact test for categorical variables. For comparing PiCCO parameters between the two groups at each time point Mann–Whitney U-test was used. Repeated measures analysis of variance together with Bonferroni adjustment was used for multiple within-group comparisons. In all cases p value less than 0.05 was considered to indicate statistical significance.

3. Results

One patient from group 2 was excluded from statistical analysis because of missed data. Demographic data and the preoperative clinical characteristics were comparable in both patient groups (Table 1). The intra-operative course was uneventful, and the intra-operative and postoperative characteristics were comparable in both patient groups (Table 2). In all patients complete revascularization was achieved. Extra-vascular lung water (Table 3) and Intra-thoracic blood volume (Table 4), did not differ between groups in all times of measurements.

Table 1 Demographic and preoperative characteristics of patient groups.

	Group 1(off-pump) 15 patients	Group 2 (on-pump) 14 patients	*P* value
Age (years)	56 ± 9	62 ± 9	0.21
Height (cm)	176 ± 9	179 ± 8	0.56
Weight (kg)	84 ± 14	79 ± 19	0.62
Sex (m/F)	9/6	8/6	0.96
NYHA(1) class (II/III/IV)	6/4/5	4/5/5	0.91
Smoking (N/Y)2	8/7	7/7	0.89
Diabetes (N/Y)2	10/5	8/6	0.93
Hypertension (N/Y)2	11/4	9/5	0.74
Number of affected vessels	3.2 ± 0.9	3.6 ± 0.7	0.69

The data are shown as mean ± SD for the continuous variables and as numbers for categorical variables, (1) NYHA = New York Heart Association, (2) N = no, Y = yes.

Table 2 Intra-operative & postoperative characteristics of patient groups.

	Group 1(off-pump) 15 patients	Group 2(on-pump) 14 patients	*P* value
Number of grafts	3.4.2 ± 1.1	4.1 ± 0.8	0.958
Intra-operative blood intake (ml/kg)	3.2 ± 3.6	2.5 ± 3.8	0.600
Intra-operative fluid intake (ml/kg)[1]	44.0 ± 13.0	60.0 ± 19.0	0.002
Intra-operative fluid output(ml/kg)[1]	20.1 ± 9.0	23.8 ± 12.8	0.042
Total surgical time (min)	266.0 ± 40.0	253.0 ± 39.0	0.216
CPB[2] time (min)	_	114.0 ± 19.0	_
Aorta cross-clamping time (min)	_	74.0 ± 13.0	_
Time to tracheal extubation (h)	11.6 ± 6.8	10.8 ± 3.9	0.770
ICU LOS[3] (h)	32.2 ± 15.1	23.9 ± 7.0	0.092

The data are shown as mean ± SD.
[1] There is difference between groups.
[2] CPB = cardio-pulmonary bypass.
[3] ICU LOS = intensive care unit length of stay.

Table 3 Extra-vascular lung water did not differ between groups in all times of measurements.

Measure	Group	Mean ± S.D	*P* Value
EVLWI.0	1	7.2 ± 1.2	.274
	2	7.7 ± 0.9	
EVLWI.1	1	7.3 ± 1.5	.328
	2	8.1 ± 2.0	
EVLWI.2	1	7.6 ± 2.0	.197
	2	8.7 ± 1.8	
EVLWI.3	1	7.4 ± 1.9	.342
	2	8.2 ± 1.8	
EVLWI.4	1	7.0 ± 3.3	.306
	2	8.5 ± 3.0	
EVLWI.5	1	7.1 ± 2.6	.640
	2	7.7 ± 2.8	
EVLWI.6	1	6.30 ±.9	.600
	2	6.8 ± 2.3	
EVLWI.7	1	5.5 ± 1.4	.289
	2	7.1 ± 3.4	
EVLWI.8	1	6.8 ± 1.9	.173
	2	8.3 ± 2.3	

The data are shown as mean ± SD.
EVLWI = Extra-vascular lung water index.

Table 4 Intra-thoracic blood volume did not differ between groups in all times of measurements.

Measure	Group	Mean ± S.D	*P* Value
ITBVI.0	1	757.2 ± 194.4	.054
	2	906.1 ± 174.1	
ITBVI.1	1	1001.2 ± 136.6	.438
	2	897.2 ± 391.9	
ITBVI.2	1	931.1 ± 150.0	.456
	2	882.0 ± 145.1	
ITBVI.3	1	849.4 ± 147.5	.216
	2	956.5 ± 223.9	
ITBVI.4	1	975.7 ± 260.2	.380
	2	1148.3 ± 548.1	
ITBVI.5	1	864.0 ± 84.0	.213
	2	948.4 ± 178.4	
ITBVI.6	1	954.8 ± 185.8	.311
	2	1091.1 ± 343.7	
ITBVI.7	1	972.8 ± 186.1	.432
	2	1109.0 ± 374.09	
ITBVI.8	1	956.8 ± 118.2	.373
	2	1050.3 ± 262.0	

The data are shown as mean ± SD.
ITBVI = Intra-thoracic blood volume Index.

4. Discussion

Performing coronary revascularization on cardiopulmonary bypass has been an effective, safe, and time-proven technique, furthermore it is the gold standard with which all other surgical revascularization methods have been compared. However, this technique can result in myocardial ischemic injury [8], neuro-cognitive deficits and strokes and activate inflammatory pathways that contribute to pulmonary, renal, and hematologic complications [8,9].

Whether off-pump coronary artery bypass graft (OPCAB) surgery is superior to traditional on-pump coronary artery bypass graft (CABG) surgery still one of the most controversial areas of cardiac surgery and anesthesia. OPCAB offered a promising alternative strategy that had the potential to decrease peri-operative morbidity, mortality, and cost by eliminating CPB. In North America, OPCAB procedures peaked at 25% in 2004 and have declined steadily since that time [10]. It is a more technically demanding procedure and results in less complete revascularization. There is growing concern that OPCAB is associated with reduced long-term graft patency and increased need for revascularization procedures and results in inferior long-term survival compared with traditional on-pump CABG surgery [11].

This study was undertaken mainly to investigate the changes of extra-vascular lung water and intra-thoracic blood volume during and after CABG surgery with and without CPB and the influence of both techniques on the early post-operative period. We hypothesized that the on pump group would have higher levels of EVLW and ITBV during and early after the operation. Our hypothesis was based on the previous finding of respiratory insufficiency after operations using CPB which is termed ‘‘post-perfusion lung’’ [12]. It is characterized by an increasing fluid accumulation in the pulmonary tissue with consecutive deterioration of the pulmonary gas exchange. One of the fundamental lesions in this disease is an abnormal increase in pulmonary endothelial permeability [12–14].

No wonder that patients in the CPB group received higher volumes of intra-operative i.v. fluids and infusion therapy, and produced more volumes of urine than the off-pump group and this is because of the priming solution of the ECC. However this was not affect the EVLW or ITBV in this group and there were no differences between groups in all times of measurement. The previously defined syndrome of severe pulmonary capillary leakage causing interstitial or alveolar pulmonary edema (‘‘pump lung’’) [15] was not observed in our patients. Furthermore, EVLW and ITBV have not increased in either group all through the study period.

We think that venting the ventricle and statically inflation of the lung with oxygen during ECC may explain our finding. As it was reported that over distention of the ventricle and damage of the pulmonary capillaries during CPB occur, due to increased blood flow from the bronchial circulation or inadequate venting of the left ventricle and pulmonary collapse during CPB may aggravate these problems [16].

Another explanation to the similarity of effect of both techniques on EVLW and ITBV is that we have added hyperoncotic solutions (gelofusine and mannitol) to prime of the CPB. During CPB with a hypooncotic prime, after an initial decrease in colloid osmotic pressure (COP), an incomplete compensatory increase in COP takes place due to both an efflux of water from the intravascular to extra-vascular space and to an influx of albumin from mobilizable peripheral albumin stores, and the decrease in COP caused by hemodilution increases trans-capillary fluid flux [17]. The clinical advantage of off-pump CABG surgery over standard extracorporeal circulation in regard to lung water content was not found in our study. In conclusion, the presumed superiority of off pump surgery for coronary artery bypass grafting in our group of patients could not be confirmed.

Conflict of interest

Authors certify that there is no conflict of interest with any financial organization regarding the material discussed in this manuscript.

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