ELSEVIER

International Journal of Cardiology 143 (2010) 302–308

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Myocardial metabolism assessed by microdialysis: A prospective randomized study in on- and off-pump coronary bypass surgery ☆

Vittorio Mantovani [a,*], Charles Kennergren [b], Mogens Bugge [b], Andrea Sala [a], Peter Lönnroth [c], Eva Berglin [b]

[a] Dept. of Cardiac Surgery, University of Insubria, Ospedale di Circolo – Fondazione Macchi, I-21100 Varese, Italy
[b] Dept. of Cardiothoracic Surgery, Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden
[c] Dept. of Medicine, Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden

Received 9 March 2008; received in revised form 30 May 2008; accepted 4 March 2009
Available online 5 April 2009

Abstract

Objective: The aim of the study was to compare energetic metabolism in the myocardium during coronary surgery with and without cardiopulmonary bypass by means of microdialysis.
Methods: Twenty-six low-risk patients were prospectively randomized to off-pump versus on-pump surgery. Microdialysis was used to sample myocardial interstitial fluid during and for 23 hours after surgery.
Results: Preoperative characteristics and clinical outcome were similar in both groups. Blood glucose and lactate did not differ between groups throughout the observation time. During surgery, intramyocardial levels of glucose, pyruvate and urea were unaffected in off-pump patients, while the same substances significantly decreased ($p<0.05$) in on-pump patients during cardioplegic arrest, and increased during reperfusion. Interstitial lactate levels were higher during off-pump surgery ($p<0.05$). From 3 to 15 hours after surgery, intramyocardial concentrations of glucose, urea and lactate were higher in off-pump patients ($p<0.001$), while pyruvate was higher in on-pump patients ($p<0.01$). Intramyocardial lactate/pyruvate ratio never differed between groups. Postoperatively, cumulative blood release of troponin-T was significantly higher in the on-pump group ($p<0.005$).
Conclusions: Microdialysis could demonstrate significant differences in energetic metabolism between the two groups. Our data confirm and might help in explaining the lower release of myocardial ischemic markers after off-pump surgery.

Keywords: Coronary artery bypass graft; Myocardial metabolism; Off-pump; Microdialysis

1. Introduction

Since the early nineties, off-pump coronary artery bypass grafting (CABG) gained diffusion in the hope of avoiding the morbidity caused by cardio-pulmonary bypass (CPB) [1]. Retrospective studies of large databases showed significant advantages of off-pump technique regarding risk-adjusted mortality, renal failure, brain damage and lung function [2]. Small prospective randomized studies showed the superiority of off-pump technique regarding blood-products requirement, hospital stay and myocardial enzyme release [3].

However, it has been stated that avoiding CPB does not bring as many advantages as expected [4], especially in low-risk patients; literature reports are conflicting and the majority of CABGs are still performed on-pump. The American Heart Association stated that the superiority of either technique cannot be declared on the basis of data so far available and that a large randomized study is required [5]. A relevant issue is that the overall results of both techniques in the wide majority of patients are so good that a very high

☆ The research was carried out at Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden.

* Corresponding author. University of Insubria, Ospedale di Circolo – Fondazione Macchi, Viale Borri 57, 21100 Varese, Italy. Tel.: +39 347 464 2780; fax +39 0332 264 394.
E-mail address: vitmantovani@hotmail.com (V. Mantovani).

0167-5273/$ - see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijcard.2009.03.033

Table 1
Preoperative data.

Variable	Off-pump	On-pump	*p*
Number of cases	12	13	
Age, years	66±9	67±6	.67
Gender, M/F, %	75/25	62/38	.67
BSA, sqm	1.97±0.15	1.92±0.12	.41
LVEF, %	55±11	58±10	.46
Creatinine, μmol/L	81±11	84±14	.54
CCS	1.7 ±1.3	1.8±1.1	.71
NYHA	1.4±0.7	1.3±0.5	.64
Previous AMI, %	67	62	>.99
Higgin's score	1.1±0.8	1.2±0.9	.83
LAD system disease, %	100	100	ns
RCA system disease, %	42	31	.69
CVI, %	8	0	.48
Diabetes mellitus, %	8	8	>.99
Homa index	1.9±1.3	1.6±1.4	.67
Betablocker, %	92	100	.48
Statins, %	100	100	ns
Sinus rhythm, %	100	100	ns

BSA=body surface area; BMI= body mass index; LVEF=left ventricular ejection fraction; CCS=Canadian Cardiology Society angina pectoris class; NYHA=New York Heart Association class; AMI=acute myocardial infarction; LAD=left anterior descending coronary artery; RCA=right coronary artery; CVI=cerebrovascular incidents. Continuous variables are expressed as means±standard deviations.

number of patients should be enrolled in randomized studies in order to demonstrate differences in operative mortality or similar major end-points. The Veteran Administration started one in 2002, targeting 2200 cases. By 2005, more than 8800 patients were screened but only 1327 randomized [6]. Even this number might be too low to assess those end-points. Therefore, we chose myocardial metabolism as our end-point in the hope of demonstrating differences between techniques even in a small group of patients. By moving the sampling closer to the cellular level rather than analyzing peripheral blood only, we hoped to record findings which might otherwise be unidentifiable.

Microdialysis is a technique for metabolic monitoring of various tissues and organs at the level of extra-cellular fluid, through a thin probe which mimics a blood capillary.

Cardiac applications were mainly in animal models. Our group adopted it to detect sub-clinical metabolic differences during cardiac surgery [7–9]. Subsequently, we modified our technique to obtain real-time bedside monitoring [10].

The aim of this study was to record myocardial metabolism and ischemic markers by means of microdialysis in low-risk patients randomized to off-pump versus on-pump surgery.

2. Materials and methods

The study was approved by the Ethics Committee of the Sahlgrenska University Hospital in accordance with the Helsinki declaration. Twenty-six Caucasian patients, 17 men and 9 women, mean age 66±7 years, were, after signing an informed consent, randomized in a 1:1 ratio to off-pump or on-pump technique, by breaking a sealed envelope the day before surgery.

Table 1 shows relevant preoperative data. The patients were elective coronary cases with one or two-vessel disease. The left anterior descending coronary artery (LAD) had significant stenoses in all cases. Exclusion criteria were obtuse marginal vessel disease, previous cardiac surgery, associated cardiac pathologies, ejection fraction <35%, serum creatinine >150 micromol/L, steroid therapy and blood-transmitted disease. Glucose was not administered during the observation time.

2.1. Anaesthesia

After premedication with morphine 0.1 mg/kg, scopolamine 0.4 mg and flunitrazepam 1 mg, anaesthesia was induced with 3–5 mg/kg of thiopental and pancuronium 0.1 mg/kg and continued with fentanyl and sevoflurane.

2.2. Surgery

All operations were performed through median sternotomy. The pericardium was incised and a microdialysis probe was implanted in the left ventricle parallel to the LAD and distally to the planned site of anastomosis. The time needed to prepare the left internal thoracic artery (LITA) was used as equilibration time for microdialysis. Patients were heparinized with 150 IU/kg bw in the off-pump group and 300 IU/Kg bw in the on-pump group. In the on-pump group body temperature was kept above

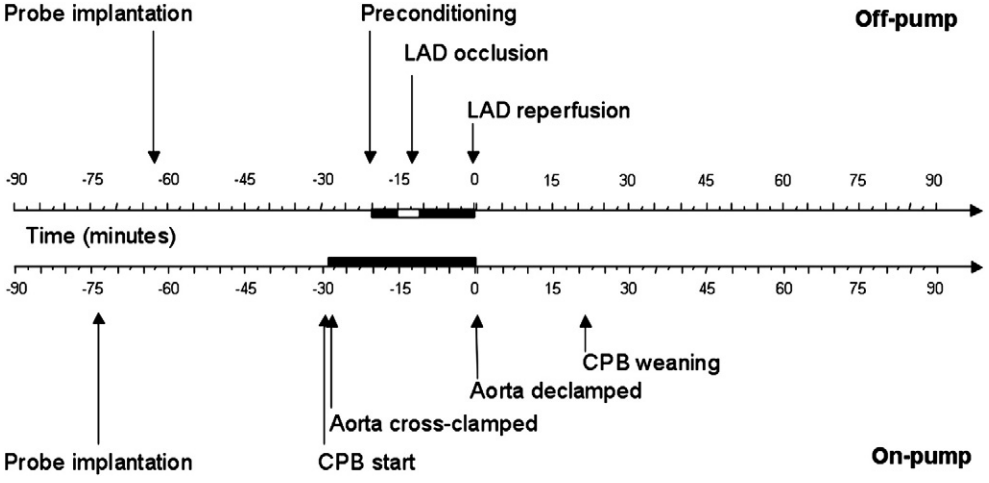

Fig. 1. Time table for events of importance during the surgical procedure. The dark bars represent the cardioplegic arrest for the on-pump group and the coronary occlusion preceded by ischemic preconditioning for the off-pump group. CPB=cardio-pulmonary bypass; LAD=left anterior descending coronary artery.