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The investigators of these abstracts have stated in their submission letter that prospective studies where patients are involved have institutional or Ethics Committee approval and informed patient consent, and that the studies using experimental animals have institutional approval.

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A-1

The effect of the medetomidine–ketamine combination on haemodynamic parameters during haemorrhagic shock

L. Hess, A. Brezina

Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction: Haemorrhagic shock continues to be a dramatic event in emergency medicine. The drug used most often for sedation, analgesia, or general anaesthesia is ketamine. Ketamine has central sympathomimetic effects thus raising blood pressure. It favours flow through the splanchnic bed. Because of its psychomimetic effects, it is often combined with midazolam, which, however, in the presence of hypovolaemia, may further decrease blood pressure [1]. Infusion of the α_2 agonist medetomidine increases blood pressure in the pig [3] while in man, it reduces the incidence of psychomimetic effects following ketamine administration [2]. It was for these reasons that we decided to test the medetomidine–ketamine combination in haemorrhagic shock in the pig.

Method: The study was conducted with a total of 20 Minnesota minipigs weighing 25–32 kg of either sex. The experiment was approved by the institute's ethics committee. In a randomized study, haemorrhagic shock (predetermined as a mean arterial pressure of 40 mmHg) was induced in two groups of pigs for 2 h. Anaesthesia was induced in each group using a combination of propofol at an infusion rate of 10 mg kg^{-1} hr^{-1} and remifentanil at a rate of 1 μg kg^{-1} min^{-1}. Following haemorrhagic shock induction, anaesthesia was changed, in the first group of pigs, to a combination of medetomidine at an infusion rate of 10 μg kg^{-1} h^{-1} and ketamine at an infusion rate of 5 mg kg^{-1} h^{-1}. All pigs were ventilated using a mixture of oxygen (50%) with air. Blood was collected every 30 min of haemorrhagic shock to reach a mean arterial pressure of 40 mmHg. After establishing baseline haemodynamic values, heart rate and arterial pressure were determined at 30-minute intervals as were central haemodynamic parameters obtained from a Swan-Ganz catheter. The values were used to calculate stroke volume, cardiac volume, and peripheral vascular resistance. Total blood losses were determined at the end of the experiment. Acid base balance and lactate were examined at the same time intervals. At the end of the trials the minipigs were sacrificed during general anaesthesia by T_{61}. The differences in haemodynamic parameters, blood losses and acid base balance were statistically evaluated using the *t*-test and Bonferroni significance level correction.

Results: The differences in starting values between the groups were statistically insignificant.

Table 1. shows statistically significant differences between the propofol–remifentanil combination and the medetomidine–ketamine combination.

	Propofol + remifentanil	Medetomidine + ketamine	*P*
MAP (mmHg)			
30 min	65 ± 6	97 ± 11	<0.001
60 min	60 ± 4	71.5 ± 4	<0.001
90 min	56 ± 4	68 ± 10	<0.05
HR (beat min^{-1})			
Starting values	85 ± 18	89 ± 19	n.s.
90 min	127 ± 17	86 ± 25	<0.01
120 min	147 ± 21	107 ± 26	<0.05
CVR (dyn s cm^{-5})			
Starting values	2050 ± 310	1930 ± 600	n.s.
30 min	1860 ± 525	2414 ± 354	<0.05
Blood losses (mL)			
30 min	230 ± 67	362 ± 90	<0.01
120 min	1110 ± 250	0320 ± 130	<0.05

The differences between the two groups in pulmonary artery pressure, stroke volume, cardiac volume, and acid base balance were not statistically significant.

Conclusion: The medetomidine–ketamine combination, increasing blood pressure and decreasing heart rate, could find a use in analgesia and sedation or TIVA in haemorrhagic shock.

References:

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3 Vainio OM, Bloor BC, Kim C. Cardiovascular effects of a ketamine-medetomidine combination that produces deep sedation in Yucatan mini swine. *Lab Anim Sci* 1992; **42:** 582–588.

A-2

Haemodynamics during skin incision and sternotomy in CABG surgery: remifentanil versus fentanyl

D. Mekiš, M. Kamenik, M. Pecan

Department of Anaesthesia, Intensive Care and Pain Therapy, Maribor Teaching Hospital, Maribor, Slovenia

Introduction: Haemodynamic response to surgical stimulation can cause perioperative myocardial ischaemia, especially in a patient with coronary artery disease [1]. In a prospective randomized trial we studied the haemodynamic stability during skin incision and sternotomy for CABG surgery in patients receiving remifentanil-propofol or fentanyl-propofol anaesthesia.

Method: After informed consent we studied 30 patients scheduled for elective CABG surgery. Anaesthesia was induced and continued with a continuous infusion of propofol and a single dose of pancuronium. With respect to the opioid used the patients were randomly assigned to two groups. The remifentanil group (R) received 0.5 μg kg^{-1} min^{-1} remifentanil and the fentanyl group (F) received fentanyl 10 μg kg^{-1} during the induction of anaesthesia. For 5 min. before and for 30 min after skin incision we continuously registered invasive blood pressure and heart rate using an online data transfer to a PC. We also registered the need for additional fentanyl and the incidence of use of phenylephrine and nitroglycerine for maintaining mean arterial pressure (MAP) between 65 and 85 mmHg**.** MAP outside this range for more than 1 min we defined as hypertension or hypotension and rescue medication was started. Statistical analysis was by using paired and unpaired *t*-test and chi-squared test where appropriate.

Results: There were no statistical significant differences between the groups with respect to age, gender, weight, height, ejection fraction and NYHA. After skin incision the MAP increased statistically significantly in the F but not in the R group. 7 out of 16 patients in the R group and 13 out of 14 patients in the F group developed hypertension. The incidence of hypertension ($P = 0.014$) and the need for nitroglycerine ($P = 0.03$) were significantly higher in the F than in the R group.

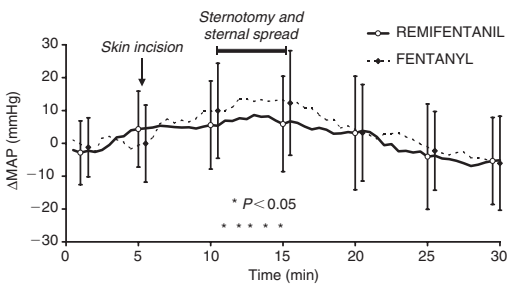

Figure. Time course of mean arterial pressure change (ΔMAP) in both groups of patients.

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Discussion: Our results show more stable haemodynamics after skin incision and sternotomy in patients receiving remifentanil–propofol than patients receiving fentanyl–propofol during the induction of anaesthesia.

Reference:

1 Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction? *Anesthesiology* 1985; **62:** 107–114.

A-3

Remifentanil versus alfentanil and target-controlled infusion of propofol for cardiac anaesthesia

J.H. Heijmans[1], J.G. Maessen[2], P.M. Roekaerts[1]

[1]Departments of Anesthesiology and [2]Cardio-Thoracic Surgery; University Hospital Maastricht, Maastricht, The Netherlands; and The Cardiovascular Research Institute of Maastricht (CARIM), Maastricht, The Netherlands

Introduction: This study compared the effects of two remifentanil infusion regimens on haemodynamic stability during coronary artery surgery and on recovery characteristics.

Method: In this double-blind, randomized, controlled study, 75 beta-blocked patients were enrolled and divided into three groups: higher dose remifentanil group, HDRG (0.5 $\mu g\,kg^{-1}\,min^{-1}$), low dose remifentanil group, LDRG (0.25 $\mu g\,kg^{-1}\,min^{-1}$) and an alfentanil group, AG (1 $\mu g\,kg^{-1}\,min^{-1}$) in combination with a target controlled infusion of propofol (1 $\mu g\,mL^{-1}$). Blood pressures and heart rate were registered at: T1, baseline; T2, four min after the start of induction; T3, three min after intubation; T4, three min after incision; T5, immediately before sternotomy; T6, three min after sternotomy; T7, immediately after heparinization. Signs of inadequate anaesthesia were treated with additional bolus doses of the opioid following strict criteria for administration. After arrival in the ICU, the sedative-analgesic infusions were continued for four hours. In the two remifentanil (remi) groups, patients received an infusion of remi 0.025 $\mu g\,kg^{-1}\,min^{-1}$ and in the alfentanil (alfent) group an infusion of alfent 0.1 $\mu g\,kg^{-1}\,min^{-1}$. Fifteen min before cessation of the sedative-analgesic infusion, piritramide 0.3 mg kg^{-1} iv. was administered in the remi groups and placebo in the alfent group. Statistics: Kruskal-Wallis, Fisher's exact test, mixed-model ANOVA with one common baseline value.

Results: *Haemodynamic stability*. Significant time-by-treatment interactions were seen for systolic arterial pressure ($P = 0.001$), for mean arterial pressure ($P = 0.009$) and for diastolic arterial pressure ($P = 0.006$). No significant interaction was seen for heart rate ($P = 0.489$). In the HDRG, blood pressures remained more stable and fewer extra bolus doses of the opioid sedative drugs ($P = 0.015$) had to be given, indicating better suppression of noxious stimuli (Table 1). *Extubation time*. Strict extubation criteria were described by the protocol. No differences were observed between median extubation times in the 3 groups after stopping the iv. administration of sedative-opioid drugs: 300 min in the HDRG, 270 min in the LDRG and 270 min in the AG ($P = 0.606$).

Table 1. Mean systolic arterial pressure (mmHg).

	T1	T2	T3	T4	T5	T6	T7
HDRG	147	103	116	110	114	121	107
LDRG	150	101	121	126	134	141	126
AG	146	108	119	137	138	145	122

HDRG: high dose remi; LDRG: low dose remi; AG: alfentanil.

Discussion: No differences were found in extubation times between the 3 groups. A higher doses of remifentanil was associated with superior suppression of intra-operative responses to noxious stimuli and resulted in superior haemodynamic stability.

References:

1 Burkle H, Dunbar S, Van Haken H. Remifentanil: a novel, short-acting, mu-opioid. *Anesth Analg* 1996; **83:** 646–651.
2 Roekaerts PMHJ, Gerrits HJ, Timmerman BE, et al. Continuous infusions of alfentanil and propofol for coronary artery surgery. *J Cardiothorac Vasc Anesth* 1995; **9:** 362–367.
3 Albrecht S, Schuttler J, Yarmush J. Postoperative pain management after intraoperative remifentanil. *Anesth Analg* 1999; **89** (Suppl 4)**:** S40–45.

A-4

Pre-bypass cardiovascular stability with target controlled infusions of remifentanil and propofol during heart valve surgery for aortic stenosis

I. Larmuseau, W. Nagels, R. Demeyere, E. Vandermeersch, P. Herijgers, W. Flameng

University Hospitals Leuven, Leuven, Belgium

Introduction: It has been demonstrated that remifentanil (REMI) can have detrimental haemodynamic effects during cardiac surgery when it is used with a conventional infusion technique [1]. This could be particularly the case for patients with severe aortic stenosis. A plasma-target controlled infusion (TCI) may lead to a more stable procedure.

Method: Ten consenting patients scheduled for aortic valve replacement for stenosis were enrolled for this total intravenous technique. At induction TCI of REMI and propofol (PROP) using the RUGLOOP program [2] were started and intubation was performed 5 min later. The plasma levels of REMI and PROP were calculated targeted plasma concentrations. The target concentrations could be altered between 6 and 14 ng mL^{-1} REMI and 1 to 4 $\mu g\,mL^{-1}$ PROP. Cisatracurium 0.2 mg kg^{-1} was administered and one litre Ringer's lactate was infused. Heart rate (HR), systolic (SAP), mean (MAP) and diastolic (DAP) arterial pressure were recorded continuously. When the MAP dropped below 60 mmHg, a bolus of 100 μg phenylephrine or 5 mg ephedrine was administered.

Statistical analysis included the Friedman's test. Values are mean $\pm$ SD with $P < 0.05$ considered statistically significant.

Results: The patients had a mean age of 65 ($\pm$10) years and a gradient of 78 ($\pm$23) mmHg across the aortic valve. The results are presented in Table 1.

Table 1. Haemodynamic parameters and calculated plasma levels.

	REMI (ng mL^{-1})	PROP ($\mu g\,mL^{-1}$)	HR (bpm)	SAP (mmHg)	MAP (mmHg)	DAP (mmHg)
Induction	6.0 ± 0.0	1.9 ± 0.1	78 ± 19	133 ± 13	90 ± 9	63 ± 9
Pre-LAR	8.2 ± 1.2	2.1 ± 0.3	65 ± 12	114 ± 33	78 ± 24	57 ± 17
INTUB + 30 s	7.3 ± 1.1	1.9 ± 0.6	70 ± 16	143 ± 28	97 ± 20	69 ± 14
INTUB + 2 min	5.9 ± 0.4	1.6 ± 0.4	63 ± 12	105 ± 17	71 ± 12	50 ± 12
INTUB + 5 min	5.9 ± 0.4	1.6 ± 0.4	60 ± 11	90 ± 11*	63 ± 9*	48 ± 9*
INC + 30 s	8.0 ± 1.5	1.7 ± 0.5	51 ± 10*	108 ± 19	75 ± 15	57 ± 12
INC + 2 min	8.4 ± 1.6	2.0 ± 0.5	54 ± 9*	121 ± 19	82 ± 15	66 ± 13
STER + 30 s	10.5 ± 1.3	2.4 ± 0.5	67 ± 19	122 ± 13	85 ± 8	63 ± 7
STER + 2 min	9.9 ± 1.0	2.3 ± 0.4	69 ± 26	117 ± 9	81 ± 6	60 ± 6

LAR: laryngoscopy; INTUB: intubation; INC: incision; STER: sternotomy; *$P < 0.05$ values are mean $\pm$ SD.

Phenylephrine or ephedrine needed to be administered between intubation and incision in 6 patients. The mean dose was 190 ($\pm$91) μg and 5 ($\pm$3.6) mg respectively. All procedures had an uneventful course.

Conclusions: TCI of REMI and PROP can be a suitable technique during aortic valve surgery for stenosis. A low dose of vasopressor might be necessary during the phase without surgical stress.

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1 Elliott P, O'Hare R, Bill KM, *et al*. Severe cardiovascular depression with remifentanil. *Anesth Analg* 2000; **91:** 58–61.
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A-5

Closed-loop propofol in open-heart surgery

I.A. Kozlov, V.M. Magilevets, V.V. Firsov

Research Institute of Transplantology and Artificial Organs, Moscow, Russia.

Introduction: The purpose of our study was to design and investigate the closed-loop propofol system (CLPS) with a mean arterial pressure (MAP) controller in open-heart surgery.

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Method: CLPS of 386DX 40 MHz PC, blood pressure sensor and Graseby 3400 infusion pump. The computer language programme sets the propofol infusion rate based on an empirical algorithm including a proportional component to maintain the measured mean arterial pressure (MAP) more closely to the target MAP (85% of patient standard MAP). The propofol concentrations were calculated by PK/PD model differential equations solving with Marsh's microconstants [1] and Kazama's age dependant BIS effect site microconstant [2] every 30s. Fentanyl was infused by a Graseby 3400 pump controlled by STANPUMP software installed on a 386PC. CLPS was used in 115 NYHA II–IV patients (17–75 years old) undergoing valve replacement. Data is expressed as mean ± SEM.

Results: The measured and target MAP difference during operation did not exceed 20%. BIS was 44 ± 4.2. Mean arterial pressure (mmHg) and propofol concentrations ($\mu g\,mL^{-1}$) are shown in the table.

	MAP (mmHg)	Blood conc.	BIS: effect site conc.	BP: effect site conc.
Intubation	70.4 ± 0.1	3.2 ± 0.1	3.0 ± 0.1	1.7 ± 0.1
Pre-CPB	75.2 ± 0.2	2.7 ± 0.2	2.3 ± 0.2	2.1 ± 0.1
During CPB	62.4 ± 0.2	1.6 ± 0.1	1.6 ± 0.1	1.8 ± 0.1
After CPB	73.4 ± 0.1	1.4 ± 0.1	1.2 ± 0.2	1.2 ± 0.1
Awakening	78.5 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.9 ± 0.1

Recovery time was 17.4 ± 0.14 min. 95% of patients were extubated in the operating room.

Discussion: CLPS is as effective as closed-loop alfentanil with MAP controller [3]. Designed CLPS is useful for anaesthesia maintenance during open-heart surgery, especially for early extubation. CLPS is not commercially available.

References:

1 Marsh B, White M, Morton N, *et al*. Pharmacokinetic model driven infusion of propofol in children. *Br J Anaesth* 1991; **67:** 41–48.
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A-6

Opioid sparing and side effect profile of three different analgesic techniques for cardiac surgery

K.M. Fayaz, R. Abel, S. Pugh, J.E. Hall, J.S. Mecklenburgh

Anaesthetic Department, University Hospital of Wales, Cardiff, South Wales, United Kingdom.

Introduction: 'Fast-tracking' of patients is increasingly used after coronary artery bypass graft (CABG) [1]. To achieve this, low dose short acting opioids are used intra-operatively. Consequently patients need additional opioids postoperatively with potential side effects [2]. This study assessed the side effects of three analgesia types in CABG patients.

Method: With Ethical approval, 60 ASA grade 1–4 patients, undergoing CABG were recruited to this double-blind pilot study using diclofenac, paracetamol and placebo suppositories. At induction patients were randomly allocated to three groups to receive**:**

Group **A**: Diclofenac 100 mg PR and paracetamol 1 g PR postoperatively. Diclofenac was repeated after 18 h and paracetamol every 6 h for 24 h.

Group **B**: Diclofenac PR 100 mg postoperatively as in Group **A,** except that placebos were given to replace paracetamol.

Group **C**: Two placebo suppositories at the same time as in Group **A.**

All patients received morphine patient-controlled analgesia (PCA), initially nurse controlled, until able to use the PCA themselves. Number of episodes of nausea and vomiting (PONV) in 24 h, a 4-point sedation score (1 = awake, 4 = unconscious) at 6, 12 and 24 h, renal parameters and blood loss 24 h postop were recorded by the blinded nurse.

Results: Results are mean (SD), median [range] or number.

	Morphine in 24 h (mg)	Pain score at 24 h	Sedation score 6 h	12 h	24 h	PONV in 24 h
Group **A**	22 (11)	1 [1–1]	3 [1–4]	1 [1–3]	2* [1–4]	30
Group **B**	27 (12)	1 [1–1]	2 [1–4]	1 [1–3]	2 [1–3]	18*
Group **C**	37 (15)*	1* [1–2]	4 [1–4]	2 [1–3]	2 [1–4]	37*

* Significant difference between other two groups <0.05. (ANOVA or Kruskal Wallis or chi squared tests).

Blood loss and renal parameters were not different between the three groups.

Conclusion: Both diclofenac alone or with paracetamol, reduced morphine consumption and nausea and vomiting postoperatively. Sedation was less in the paracetamol and diclofenac groups. Diclofenac alone or diclofenac with paracetamol have a significant opioid sparing effect in patients undergoing CABG surgery.

References:

1 Cheng DC, Karski J, Peniston C, *et al*. Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. *Anesthesiology* 1996; **85:** 1300–1310.
2 Ralley FE, Day FJ, Cheng DCH. Nonsteroidal anti-inflammatory drugs should be routinely administered for postoperative analgesia after cardiac surgery. *J Cardiothorac Vasc Anesth* 2000; **14:** 731–714.

A-7

Intravenous remifentanil combined with intrathecal morphine in off-pump coronary artery bypass grafting

G. Turker, S. Goren, S. Sahin, G. Korfali, E. Sayan

Department of Anaesthesiology and Reanimation, Uludag University Medical Faculty, Bursa, Turkey

Introduction: An ideal anaesthetic technique for off-pump coronary artery bypass grafting (OPCABG) should provide intraoperative haemodynamic stability and a pain-free recovery [1]. The aim of the current observer-blinded study was to evaluate the efficacy and safety of intravenous (IV) remifentanil combined with intrathecal morphine (ITM) in OPCABG patients.

Method: After ethics approval, patients were randomized to receive either IV remifentanil alone (Group R; $n = 21$) or IV remifentanil plus 10 $\mu g\,kg^{-1}$ of ITM (Group R + ITM; $n = 22$). Anaesthesia was induced using a standardized anaesthetic technique and maintained with remifentanil (0.1–0.5 $\mu g\,kg^{-1}\,min^{-1}$) and isoflurane (0.4–1.2%) which were adjusted by haemodynamic parameters (baseline values ± 20%). In the intensive care unit, the nursing staff administered incremental doses of morphine, 1 mg IV, for acute pain control prior to extubation. After extubation, each patient received IV patient controlled analgesia (PCA) with morphine (1 mg boluses and 5 min lockout time). Postoperative evaluations, including Ramsay sedation score, visual analogue pain score (VAS 0–100 mm) at rest and with coughing, and cumulative morphine consumption were performed 1 h, 2 h, 4 h, 8 h, 12 h, 24 h, and 48 h after extubation by the nurses unaware of the patients' study groups. The frequency and severity of side effects and time to extubation were also recorded. Statistical analysis was done with Mann-Whitney-*U* or χ^2 test.

Results: The two groups did not differ demographically.

	1 h	2 h	4 h	8 h	12 h	24 h	48 h
VAS at rest							
R	28 ± 15*	20 ± 16*	18 ± 13†	18 ± 14*	18 ± 14†	14 ± 9*	12 ± 9*
R + ITM	17 ± 14	10 ± 7	7 ± 8	9 ± 9	7 ± 6	7 ± 6	5 ± 5
VAS with coughing							
R	45 ± 24*	39 ± 22*	36 ± 20†	35 ± 22*	36 ± 22*	36 ± 17†	28 ± 14†
R + ITM	28 ± 17	25 ± 12	17 ± 14	20 ± 15	22 ± 14	20 ± 12	16 ± 12
PCA morphine use (mg)							
R	9 ± 2*	15 ± 4‡	19 ± 7‡	23 ± 10‡	28 ± 11‡	38 ± 12‡	53 ± 15†
R + ITM	6 ± 3	8 ± 4	9 ± 4	10 ± 5	13 ± 7	20 ± 10	34 ± 15

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	Group R ($n = 21$)	Group R + ITM ($n = 22$)
Time to extubation (min)	331 ± 82	363 ± 86
Total remifentanil dosage (μg)	2128 ± 851¶	1246 ± 411
Morphine pre-extubation (mg)	11 ± 5*	5 ± 3
Nausea (*n*) (grade 0/1/2/3)	7 (14/5/2/0)	9 (13/4/4/1)
Pruritus (*n*) (grade 0/1/2/3)	2 (19/2/0/0)	5 (17/4/1/0)

Mean ± SD; *$P < 0.05$, †$P < 0.01$, ¶$P < 0.001$, ‡$P < 0.0001$; Group R vs. Group R + ITM.

Discussion: Since adequate postoperative pain relief is a major concern, IV remifentanil combined with ITM is an effective and safe technique for controlling pain in OPCABG patients.

Reference:

1 Heames RM, Gill RS, Ohri SK, *et al*. Off-pump coronary artery surgery. *Anaesthesia* 2002; **57:** 676–685.

A-8

Is bispectral EEG analysis a target for hypnosis during cardiac anaesthesia?

R. Bonato, D. Pittarello, A. Marcassa, L. Pasini, G. Falasco, M.Gasparetto

Department of Anaesthesia and Intensive Care, University of Padua, Padua, Italy

Introduction: In spite of big progress in the pharmacology of anaesthetic drugs, there are still reports of intra-operative awareness [1]. Nowadays we find in the market place a new monitor, the bispectral index (BIS), to assess the depth of anaesthesia [2]. This prospective, randomized study aimed to test whether BIS-guided anaesthetic drug administration (propofol) would reduce the incidence of explicit and implicit memory.

Method: After approval by the Ethics Committee of Padua University Hospital, 73 patients (experimental group) plus 20 patients (control group) provided written informed consent and underwent general anaesthesia and cardiopulmonary bypass for cardiac surgery. During the operation patients of the control group received TIVA anaesthesia of propofol 4 mg $kg^{-1}h^{-1}$ and remifentanil titrated to a target value of arterial blood pressure. Patients of the experimental group were randomized to group A or group B. Both of these groups received remifentanil titrated to arterial blood pressure and propofol titrated to level 60 of BIS (group A) or level 40 (group B). A list of words was played via headphones to the experimental group during surgery. Postoperatively a standardized interview was conducted to determine the extent of intra-operative explicit memory and a Word Stem Completion Test (WSCT) [3] to detect implicit memory. Data were analysed with ANOVA test. $P > 0.05$ was considered significant.

Results: Demographic data were similar between groups. With the use of WSCT, overall significant intra-operative implicit memory was found ($P < 0.005$), but no patient had spontaneous or direct recall of intra-operative events. There were differences, but not significant, in the incidence of implicit memory between groups (BIS 60 group had a higher incidence than BIS 40 group: 7.6% vs. 7.0%).

Discussion: This study indicates that, with anaesthesia titrated on BIS value there is not explicit memory but patients are still capable of processing intra-operative auditory information, even at a BIS value of 40. A large randomized controlled trial of effectiveness is required before a widespread use of BIS monitoring can be recommended to prevent awareness.

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Sevoflurane decreases bispectral index more than halothane at equipotent MAC levels

H. Schwab, M.D. Seeberger, K. Skarvan, C. Kindler, M. Filipovic

Department of Anaesthesia, Kantonsspital, University of Basel, Basel, Switzerland

Introduction: The Minimum Alveolar Concentration (MAC) is used traditionally to quantitate depth of anaesthesia induced by inhalational anaesthetics and is based on the lack of movement after a painful stimulus [1]. The Bispectral Index (BIS) has been introduced more recently to measure the hypnotic effect of anaesthetics [2].

We examined whether sevoflurane (SEVO) and halothane (HALO) at equipotent MAC levels induce the same BIS scores.

Method: After institutional review board approval and informed written consent, 40 otherwise healthy patients (14 female, 26 male; median age 27 yr, range 18–47 yr) were randomized to receive either HALO or SEVO anaesthesia prior to minor surgery. No premedication was given. After inhalation induction of anaesthesia, orotracheal intubation was facilitated by fentanyl 2 μg kg^{-1} and rocuronium 0.6 mg kg^{-1}. Study measurements were performed at steady-state conditions 1 MAC and 1.5 MAC of the inhalational anaesthetic prior to surgical stimulation. Parameters measured were BIS, mean arterial pressure (MAP), heart rate (HR), and end-tidal concentrations of CO_2 (ET CO_2) and of the inhalational anaesthetic (Vol. %).

Results: Data are mean ± SD; *$P < 0.001$ (ANOVA for repeated measurements, post-hoc test: Scheffé's method)

	BIS	MAP [mmHg]	HR [1 min^{-1}]	ET CO_2 [kPa]	Vol. %
HALO awake	96 ± 2	83 ± 10	65 ± 11	–	–
SEVO awake	96 ± 2	83 ± 8	63 ± 10	–	–
HALO 1 MAC	55 ± 7	69 ± 10	62 ± 8	4.7 ± 0.1	0.8 ± 0.1
SEVO 1 MAC	34 ± 6*	71 ± 6	66 ± 8	4.6 ± 0.1	2.0 ± 0.0
HALO 1.5 MAC	49 ± 7	64 ± 8	63 ± 8	4.7 ± 0.1	1.1 ± 0.1
SEVO 1.5 MAC	29 ± 5*	68 ± 7	68 ± 8	4.7 ± 0.2	3.0 ± 0.0

Discussion: At equipotent MAC levels, SEVO induced lower BIS scores than HALO, indicating a stronger hypnotic effect of SEVO. This finding may support the thesis that immobility and hypnosis during anaesthesia arise from different sites of action [3].

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A-10

TCI propofol attenuates the inflammatory response in intermediate-risk elective CABG

T.B. Corcoran, A. Engel, A. O'Shea, H. Sakamoto, S. O'Callaghan-Enright, G.D. Shorten

Department of Anaesthesia and Intensive Care Medicine, Cork University Hospital and University College, Cork, Cork City, Republic of Ireland

Introduction: After CPB the systemic inflammatory response (SIR) is the result of complex interactions. Blood contact with a foreign surface, ischaemia/reperfusion injury and endotoxaemia all contribute to varying degrees, to the elaboration of the cellular and humoral processes that culminate in the SIR post CPB [1]. Propofol has been shown to have antioxidant properties [2]. We sought to determine whether the use of propofol would influence this inflammatory response in moderate risk elective CABG surgery.

Method: Twenty seven adult patients, with impaired myocardial function (EF < 0.4) undergoing elective coronary artery bypass grafting with cardiopulmonary bypass were randomly assigned to

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receive a standardized anaesthetic technique, and either a fixed-rate infusion of saline ($n = 13$) or Target Controlled Infusion of propofol ($n = 14$), 15 min before aortic cross-clamp release until 4 h after reperfusion. Patients in both groups received anaesthetic doses of isoflurane throughout. Serum concentrations of IL-6 and IL-8 were measured 15 min before reperfusion, and one, four and 24 h after reperfusion. Serum concentrations of IL-10 were measured 15 min before reperfusion, four and 24 h after reperfusion. Troponin I concentrations were measured at anaesthesa-induction and 24 h post reperfusion. Data was analysed using unpaired Student's *t*-tests.

Results: There was no difference between the groups in terms of lethal reperfusion injury (myocardial necrosis) as measured by Troponin I concentrations nor in IL-8 and IL-10 concentrations. 24 h after reperfusion, serum concentrations of interleukin-6 were significantly lower in the propofol treated group than in the saline-treated group: 227 (105) pmoles L^{-1} vs. 1118 (1334) pmoles L^{-1}, $P = 0.02$.

Table: IL-6 concentrations (pmoles L^{-1})

		After reperfusion		
	Before reperfusion	1 h	4 h	24 h
Control	53 (68)	217 (119)	1118 (1334)	656 (104.7)
Propofol	47.2 (71)	191 (128)	227 (105)	1070 (1311)

Conclusion: The serum concentrations of both Il-6 and Il-8 have been shown to correlate with aortic cross-clamp time and postoperative ventricular dysfunction [3]. Il-6 concentration is a marker of myocardial injury. These results suggest that propofol may have a role in attenuating the perioperative inflammatory response and reperfusion injury in intermediate-risk patients undergoing elective CABG.

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A-11

Monitoring spectral frequency index (SFx) reveals high inter-individual variation in propofol concentrations with TCI

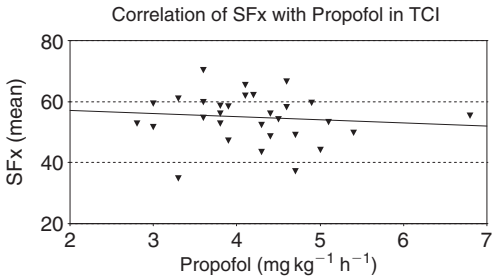
A. Fiehn, Th. Mohler, E. Lautsch[1]

Klinikum Kassel, Dep. of Cardiothoracic Anaesthesiology, University Kassel, [1]Dep. Applied Statistics, Kassel, Germany

Introduction: Target controlled infusions (TCI) propose a safe technique in anaesthesia [2]. An algorithm for calculating plasma concentration claims to predict depth of anaesthesia. In contradiction numerous reports showed the risk of intraoperative awareness.

Method: At random 30 CABG patients, out of a pool of 100, were retrospectively studied. Spectral frequency index (SFx) for depth of anaesthesia was obtained by using 16 channel computer aided encephalometry (CATEEM®) [1]. Dose of propofol (mg $kg^{-1}mL^{-1}$), TCI plasma concentration ($\mu g\,ml^{-1}$) obtained from Diprifusor® as well as demographics, left ventricular function (LVF), time of anaesthesia and place of extubation were noted. SPSS © Version 11 (SPSS Inc.) with Fisher's *t*-test for correlation and regression analysis (Pearson) was used for statistical analysis.

Results: No correlation between SFx and propofol dose was found ($r = -0.104$; $r^2 = 0.011$; $P = 0.291$). Individual patients adjusted for age, bodyweight, height and time of anaesthesia showed different dosage of propofol to maintain SFx in the targeted range (<70; >30). Regression analysis (b = −1.027) showed high inter individual variation between propofol dose (range = 2.8–6.8 mg $kg^{-1}h^{-1}$) and SFx (mean = 59.13) No intra-operative awareness event was reported.



Discussion: Especially in CABG patients with compromised ventricular function, there is a tendency to reduce anaesthetics. Since adequate depth of anaesthesia cannot be predicted for the individual patient, dosage of propofol by mg $kg^{-1}h^{-1}$ or target propofol plasma concentration might be unsafe in regard to intra-operative awareness. By the use of the SFx this problem could be prevented.

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A-12

Is Bispectral Index monitoring useful to detect severe injury to the brain ?

A. Flo, E. Massó, C. Cubells, E. Moret, X. Ruyra, J. Canet

Department of Anaesthesia, Hospital Germans Trias i Pujol, Badalona, Spain

Introduction: The Bispectral Index (BIS) is an EEG-based system for measuring the hypnotic effect of anaesthesia on the central nervous system. A global slowing or suppression of the EEG can be found in deep anaesthesia, hypothermia, low brain perfusion due to low cardiac output, or brain ischaemia resulting from vascular accidents [1]. The aim of this study was to evaluate the usefulness of BIS monitoring in detecting the early signs of inadequate perfusion of the brain.

Method: We followed up prospectively 485 patients undergoing emergency and elective cardiac surgery for a period of 1 year. We monitored all the patients and recorded all the changes in their BIS monitoring (degree of EEG suppression or an unexplained decrease in the BIS index). We classified these changes in the BIS monitoring as permanent (persisting continuously up to the end of the operation) or transient (lasting for few minutes during the induction of anaesthesia, aortic cannulation or aortic crossclamp; or reverting back to normal after rewarming in case of deep hypothermia and circulatory arrest).

We followed up all the patients postoperatively until discharge, to detect any neurological complications, which were classified into type I (transient or permanent ischaemic attack, coma or death) and type II (epileptic fits, delirium or agitation).

Results: We observed 27 neurological complications in 20 patients: 16 type I complications in 11 patients and 11 type II complications in 9 patients. Transient or permanent changes in the BIS monitoring were observed in 39 cases, of whom 4 with permanent changes died in the operating theatre. The remaining 35 cases were followed up.

	Neurological complications				
	Type I		Type II	None	
BIS Changes	Stroke, coma	TIA			
Transitory	0	0	1	28	29
Permanent	5	1	0	0	6
No changes	0	5	8	433	446
			20	461	481

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Transient changes in the BIS were observed in 29 patients. 7 of them had undergone deep hypothermia and circulatory arrest, of whom only 1 developed a type II complication (delirium) without any serious consequences. The other 22 patients, who had undergone normothermic cardiopulmonary bypass or off-pump surgery, did not show any neurological deficit postoperatively. Permanent changes in the BIS were observed in 6 patients. Four of them had undergone deep hypothermia and circulatory arrest, and the other 2 had undergone normothermic cardiopulmonary bypass. All of them developed type I neurological complications.

Discussion: All the patients with permanent changes in the BIS developed neurological complications. All the patients with severe neurological deficits showed changes in the BIS. BIS monitoring is a useful tool to detect severe injury to the brain during anaesthesia.

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A-13

Does bispectral index-guided sedation with clonidine affect the neuroendocrine and inflammatory response after cardiac surgery?

M. Moshirzadeh, W. J. Kox, W. Konertz, C. Spies

Department of Anaesthesiology, Charité University Hospital, Berlin, Germany

Introduction: The perioperative stress response can activate the hypothalamic-pituitary-adrenal-axis (HPA). This can cause a shift in the type 1/type 2 T-helper (Th1/Th2) cell balance toward a Th2-type humoral immune response. The down-regulation of the cell-mediated Th1-type immune response can increase the patient's susceptibility to infection [1]. Clonidine, an α_2-agonist, may reduce the postoperative infection rate by attenuating the perioperative stress response [2].

Method: After ethical approval and written informed consent 40 patients scheduled for elective coronary artery bypass grafting (CABG) were randomly assigned to either clonidine ($1.0\,\mu g\,kg^{-1}\,h^{-1}$) or placebo in a prospective, double-blind design. The infusion of the study medication began immediately after induction of balanced anaesthesia and was continued until 6 h after extubation. Sedation was assessed continuously by the bispectral index (BIS) on arrival to the ICU. The level of sedation was kept within the following BIS ranges: 55–75 before weaning, 65–85 during weaning and 85–95 after extubation. 5 blood samples were taken from each patient according to the study design. The measured parameters were ACTH, Cortisol, TNF-α, IL-6, IL-8, IL-10 and Th1/Th2-Ratio. Statistics: Mann-Whitney *U*-test, $P < 0.05$.

Results: The basic characteristics did not differ between the groups. There was no significant difference in the endocrine hormones or the cytokines measured between the two groups. The Th1/Th2-Ratio showed a significant difference 6 h postoperatively.

Table.

	Clonidine ($n = 20$)	Placebo ($n = 20$)	*P*
Th1/Th2-Ratio Median			
1. preoperative	12.58 ± 18.2	18.26 ± 12.5	ns
2. ICU arrival	9.72 ± 3.5	8.91 ± 3.8	ns
3. 6 h postoperative	11.04 ± 10	40.3 ± 60.06	0.03
4. 1 d postoperative	11.28 ± 5.2	7.6 ± 3.1	ns
5. 2 d postoperative	6.75 ± 1.5	11.14 ± 4.8	ns

Conclusion: α_2-agonists such as clonidine may have beneficial effects on reducing the pro-inflammatory reaction and attenuating the systemic inflammatory response usually observed after cardiac surgery.

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A-14

Biochemical markers of cerebrospinal ischaemia after repair of aneurysms of the descending and thoraco-abdominal aorta

R.E. Anderson[1], A. Winnerkvist[2], L-O. Hansson[3], O. Nilsson[4], L. Rosengren[5], G. Settergren[1], J. Vaage[2]

[1]Dept Cardiothoracic Anaesthetics and Intensive Care, [2]Dept Surgery, [3]Dept Clinical Chemistry, Karolinska Hospital, Stockholm, Sweden; [4]CanAg Diagnostics AB and [5]Dept Neurology, Sahlgrenska Hospital, Gothenburg, Sweden

Introduction: Clinical applications of a bio-marker for brain ischaemia are as numerous as for troponin for the heart [1]. Serum markers are normally validated according to clinical outcome, as cerebrospinal fluid (CSF) tapping is generally contraindicated. An indwelling intrathecal catheter is usually indicated during repair of descending aortic aneurysms with CSF drainage to facilitate spinal cord perfusion. The relatively high incidence of CNS damage provides both an opportunity and need for studying potential markers of ischaemic injury. This pilot study investigated the clinical potential of several markers of cerebral and spinal cord ischaemia in CSF and serum during aneurysm repair of the descending thoracic or thoraco-abdominal aorta.

Method: An observational study with 11 patients undergoing elective surgery with distal extracorporeal circulation and maintenance of CSF pressure <10 mmHg. Blood and CSF were sampled from before surgery until intrathecal catheter removal (1–4 days postoperatively). CSF and serum levels of S100B and its isoforms S100A1B and S100BB), neuronal specific enolase (NSE), and the CSF levels of glial fibrillary acidic protein (GFAP) and lactate were determined.

Results: Two patients had postoperative neurological deficit. One patient with stroke showed in CSF a 540-fold increased GFAP, a 6-fold NSE and S100B increase. One patient with paraplegia had in CSF a 270-fold increase in GFAP, a 2-fold increase in NSE and 5-fold increased S100B. One patient without deficit increased GFAP 10-fold, NSE 4-fold and S100B 23-fold in CSF. CSF-lactate increased $>50\%$ for 6/9 patients without neurological deficit. Serum S100B increased within 1 hr of surgery in all patients without any concomitant increase in CSF. There was a delayed increase of S100B and NSE with stroke and paraplegia. S100A1B was about 70% of total S100B in both serum and CSF in patients with or without neurological defects. S100B in CSF increased 3-fold in 3/9 asymptomatic patients.

Discussion: In patients with neurological deficit GFAP in CSF showed the most pronounced increase. Biochemical markers in CSF may increase without neurological symptoms. There is a significant increase in serum S100B from surgical trauma alone from non-cerebral sources, without any increase in CSF S100B.

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A-15

Normality range of cardiac troponin I after different cardiac surgery operations

V. Cedrati, G. Crescenzi, A.M. Scandroglio, E. Bignami, G. Aletti[1], F. Pappalardo, A. Zangrillo

Vita-Salute University San Raffaele Hospital and [1]Università degli Studi di Milano, Milan, Italy

Introduction: Cardiac surgery releases troponins even in the absence of ischaemic myocardial damage, depending on the type of surgery and the subsequent degree of direct surgical trauma. We assumed that different types of surgery determine dissimilar release of troponin I as a result of different tissue damage.

Method: With the local Ethics Committee approval 267 consecutive patients (F = 30%, age 61 ± 12.3 yr) who underwent either CABG, valve surgery or both between April to June 2002 were studied.

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Emergent operations were excluded. Standard premedication, monitoring (ECG, arterial and pulmonary pressure) and middle dose opiate anaesthesia were performed in all patients. Cardiopulmonary bypass was conducted during mild hypothermia (above 33°C). Myocardial protection was achieved by intermittent antegrade and retrograde cold blood cardioplegia and warm reperfusion just before removal of the aortic cross clamp. Blood samples for troponin I measurement were collected before surgery, at arrival in ICU, 4 and 18 h after the end of the procedure. cTnI was measured on a Dimension Xpand (Dade-Behring diagnostic) according to the manufacturer's instructions. Peak cTnI values are expressed as mean ± SD, median and range, 95th, 90th, 75th percentiles and compared with Anova test for inequality of population means.

Result: Table 1 shows peak troponin I concentrations after different cardiac interventions.

Table 1. Troponin I peak (ng mL^{-1}) and different surgical procedures (mean ± SD, median, 95°, 90°, 75° th percentile.

Surgery	No	Mean ± SD	Median	75°	90°	95°
OPCABG	32	2.5 ± 2.4	2.20 (0.5–13.4)	3.4	4.6	6.5
CABG (CPB)	59	10.2 ± 9.0	6.70 (1.9–48.9)	13.4	21.8	28.9
MVR	16	19.7 ± 18.1	12.30 (3.5–60)	19.9	42.8	60
AVR	25	8.6 ± 5.44	6.88 (24.3–0.02)	4.62	14.6	21.51
Mitral repair	52	9.5 ± 5.24	8.04 (25.8–0.36)	5.51	16	22.5

OPCABG: off pump coronary artery bypass; CPB: cardiopulmonary bypass; MVR: mitral valve replacement; AVR: aortic valve replacement.

Troponin peak level were statistically different among groups ($P < 0.001$). Off pump CABG and mitral valve replacement troponin showed respectively the lowest and the highest values and were significantly different from every other procedure ($P < 0.001$). We report 12 perioperative myocardial infarctions (4.5%).

Discussion: We found that peak cTnI after cardiac surgery depended on the type of surgery. Every hospital should determine its own normality range for the release of cardiac markers after each surgical procedures. This would better differentiate patients with a regular postoperative course from those at high postoperative risk of complications who could benefit from intensive monitorig and follow up.

A-16

Desflurane–sufentanil reduce troponin-I production after CABG

L. Tritapepe, C. Giorni, C. Di Giovanni, F. Pompei, E. Cuscianna, P. Pietropaoli

Dpt. of Anaesthesia and Critical Care, University 'La Sapienza' – Rome, Italy

Introduction: Volatile anaesthetics have been shown to improve myocardial recovery after brief or more prolonged ischaemic periods. Their cardiac effects have been related to membrane or intracellular mechanisms that enhance the recovery after ischaemia and reperfusion [1]. However, whereas many studies were made on atrial and ventricular myocytes of animals or humans in vitro, few studies were conducted in vivo analysing myocardial clinical responses after ischaemic insults. The aim of our study was to verify the safety utility of desflurane in a population of patients undergoing coronary bypass grafting and to measure the serum level of troponin I during and after surgery.

Method: After obtaining informed written consent from each patient, we have enrolled 107 pts, mean age 63 ± 11, who underwent coronary artery bypass with the use of extracorporeal circulation (ECC). Cardiac protection during aortic cross clamping was provided by blood cardioplegia. All pts had EF > 35%. Patients with valve pathology, COPD or insulin-dependent diabetes, were excluded from the protocol. All pts were premedicated with midazolam 2 mg iv. Venous and arterial lines and a pulmonary catheter when placed, were introduced after local anaesthesia. Pts were randomly divided in two groups: group DS (desflurane–sufentanil) of 52 pts and group PR (propofol–remifentanil) of 55 pts. The two groups were similar in respect to the demographic data and preoperative medicaments. Anaesthesia was induced with propofol 1.5 mg kg^{-1} (all pts) and sufentanil (1 μg kg^{-1}) in group DS and remifentanil (0.5 μg kg^{-1}) in group PR. Neuromuscular block was obtained with rocuronium in both groups. Anaesthesia was maintained with desflurane (0.8–1 MAC) and sufentanil (0.35 μg kg^{-1} h^{-1}) in group DS and propofol (3–5 mg kg^{-1} h^{-1}) and remifentanil (0.25–0.75 μg kg^{-1} h^{-1}) in group PR. The level of hypnosis was detected by BIS values and the concentration of desflurane or the dose of propofol was modified to maintain a value of BIS between 40–50. The same anaesthetic regimen was continued during ECC, and in group DS desflurane was directly given into the membrane oxygenator. During anaesthesia ST changes were noted and blood samples to measure troponin I and CK-MB values were taken at T0 (baseline), T1 (5 min after intubation), T2 (at the end of ECC), T3 (6 h after surgery), T4 (12 h after surgery) and T5 (24 h after surgery). Data were statistically analysed by one-way analysis of variance and post-hoc *t*-test with Bonferroni correction when appropriated. A value of $P < 0.05$ was considered significant.

Results: Haemodynamic data were quite good in both groups who had similar intubation time and length of stay in ICU. ST segment changes were detected in pts of group PR but were time-limited and without any clinical significance. These ST-changes were associated with blood elevation of troponin I in the same group of pts (Table 1). One patient of group DS and 5 pts of group PR suffered from perioperative myocardial infarction. All pts were discharged from ICU, and survived except 3 of group PR.

Table 1. Enzymes elevation during the study.

	CK PR	CK DS	CKMB PR	CKMB DS	cnT-I PR	cnT-I DS
T0	47 ± 11	58 ± 12	1.64 ± 0.42	3.87 ± 1.24	0.04 ± 0.02	0.35 ± 0.12
T1	119 ± 31*	172 ± 26*	2.38 ± 1.26	4.03 ± 2.76	0.22 ± 0.09	0.41 ± 0.22
T2	208 ± 56*	189 ± 36*	10.27 ± 4.32*	10.37 ± 4.21*	1.21 ± 0.44*	0.51 ± 0.34
T3	372 ± 46*	414 ± 58*	17.08 ± 6.31*	10.35 ± 5.78*	3.14 ± 1.15*	1.13 ± 0.65
T4	441 ± 55*	671 ± 69*	18.85 ± 4.76*	14.87 ± 6.43*	4.14 ± 1.25*	1.21 ± 0.29
T5	590 ± 86*	705 ± 103*	16.60 ± 3.59*	16.37 ± 8.29*	3.58 ± 0.71*	0.81 ± 0.25

*$P < 0.05$ within group.

Discussion: Several studies have reported the cardioprotective effects of halogenated anaesthetics against ischaemia and reperfusion injury [1]. Most are related to in-vitro study. Our investigation, despite a restricted number of pts enrolled and some methodological limitations, shows some interesting points. The first is related to the safe use of desflurane in cardiac surgery without any significant side effects. The second, the most important issue, is that the pts anaesthetized with desflurane had preserved cardiac function after weaning from ECC and had lower blood concentrations of troponin I than pts of group PR. The higher value of cardiac enzymes in group PR remains close to the range of temporary myocardial dysfunction [2,3], associated or not with ST modifications. Our data suggest that desflurane may have positive clinical implications due to its cardiac effects as were shown by a lower incidence of perioperative myocardial infarction.

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A-17

Glucose–insulin–potassium (GIK) solution improves recovery of left ventricular function in coronary surgery

M. Jovic, S. Gradinac, M. Vukovic, D. Nezic, B. Calija, B. Djukanovic, Z. Popovic

Dedinje Cardiovascular Institute-Belgrade, Belgrade, Yugoslavia

Introduction: Some studies strongly supported the evidence that glucose–insulin–potassium (GIK) therapy improves the recovery of the myocardium after myocardial infarction as well as after coronary

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surgery [1,2]. An open, prospective, randomized study was performed to evaluate the difference, if any, in concentration of the glucose and insulin on the functional recovery of the left ventricle (LV) after CABG surgery.

Method: 49 pts for coronary surgery with poor left ventricular function (EF <40%) were divided into three groups. In the pilot study Group C, 15 pts received the solution GIK0 (500 ml 10% glucose, insulin 0.25 IU kg^{-1}, K^+ 40 mM). After a dobutamine stress test on myocardial viability the remaining 34 pts were divided into two groups. Group A, 17 pts received a GIK1 infusion (500 ml, 30% glucose, insulin 1 IU kg^{-1}, K^+ 40 mM), while Group B, 17 pts received Ringer's solution. The rate of all infusions was 1 ml kg^{-1} h^{-1} after the induction of anaesthesia until aortic cross-clamping and after the aorta was unclamped. Haemodynamic parameters were measured at four time points. T1 – after induction of anaesthesia; T2 – after the operation (post.OP); T3 – 6 h post. OP and T4 – 24 h post. OP. ANOVA for repeated measures followed by Newman-Keuls test were used. Data are expressed as mean ± SD. $P < 0.05$ considered significant.

Results: LV function deteriorated during the first 6 h in all pts, extremely so in Group B pts. Significant LV functional recovery was evident in Group A and C pts after 24 h.

Table 1. Haemodynamic results.

	Group A		Group B		Group C	
	T1	T4	T1	T4	T1	T4
a	2.14 ± 0.3	3.05 ± 0.5*	2.47 ± 0.4	2.48 ± 0.5*	2.24 ± 0.5	3.16 ± 0.4##
b	31.2 ± 8	33.0 ± 11	33.2 ± 6	27.5 ± 9	29.7 ± 5.9	35.6 ± 9.4
c	14 ± 5	14 ± 3	13 ± 3	14 ± 3	10 ± 3	13 ± 2
d	411 ± 126	493 ± 179*	402 ± 113	348 ± 149*#	396 ± 112	463 ± 139#
e	103 ± 21	164 ± 30**	98 ± 22	136 ± 41**	110 ± 20	156 ± 30##

a: CI (L min^{-1} m^{-2}); b: LVSWI (g-m m^2); c: PCWP (mmHg); d: DO_2 (mL min^{-1} m^{-2}); e: VO_2 (mL min^{-1} m^{-2}).

*$P < 0.05$ A_4 vs. B_4; **$P < 0.001$ A_4 vs. B_4; #C_4 vs. B_4 $P < 0.05$; ##C_4 vs. B_4 $P < 0.001$

The main results are: CI in Groups A and C improved significantly postoperatively ($P = 0.0002$) with significant difference between the GIK and control groups ($P = 0.005$). LVSWI covariated with PCWP, improved significantly during the time in Groups A and C ($P = 0.0016$), differing from Group B ($P = 0.014$). Inotropic drug support was used in 5.5% pts group A and 13% pts group C vs. 31% pts group B.

Discussion: Results of our study indicate that GIK may have a role in protection and improvement of depressed myocardial function during the postoperative period after CABG surgery, while the difference in concentrations of glucose and insulin were not of significant importance.

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A-18

Continuous cervico-thoracic epidural anaesthesia for cardiac surgery: experience in more than 1500 patients

B. Muellejans

Karlsburg, Germany

Introduction: As sympathetic stimulation is one of the most important factors influencing perioperative morbidity and mortality in cardiac surgery, effective methods of sympathetic blockade may protect patients from events of myocardial ischaemia. Epidural anaesthesia is proven to be an effective anti-anginal and anti-ischaemic procedure in cardiac patients [1].

Despite the results of these studies many anaesthesiologists are reluctant to use this technique because of the potential risk of epidural haematoma in the context of anticoagulant medication. In our institution administration of epidural as an adjunct to general anaesthesia is presented to all patients scheduled for elective cardiac surgery following the guidelines for neuro-axial blockade in the presence of anticoagulant medication of the German Society of Anaesthesiology and Intensive Care Medicine [2].

Method: Between 1998 and 2002 we performed more than 1,500 cervico-thoracic epidural anaesthesias (CTEA) inserted at C7/T1 or T1/T2 intervertebral space in patients for coronary as well as non-coronary cardiac surgery. All epidural catheters (18G) were placed 1–2 h prior to surgery in the anaesthesia holding area.

Patients undergoing extracorporeal circulation (85%) received heparin 400 IU kg^{-1} BW pre bypass. Patients scheduled for off pump surgery (15%) received 100 IU kg^{-1} BW. 30% of our patients were preoperatively treated with acetylsalicylic acid, last administered the day before surgery. 5% had a co-medication of clopidogrel during the last 5 days prior to surgery. Bloody puncture led to postponement of surgery for 1–2 h.

Results: The rate of accidental dura perforation was 0.3% without any permanent adverse events. We did not observe signs of epidural haematoma, infection or any neurological damage. As an incidental finding we identified 1 patient with a syringomyelia showing signs of an accidential spinal anaesthesia following the administration of 2 ml bupivacaine 0.5% with epinephrine 1 : 200,000 (test dose). 80% of our patients were extubated during the first hour after surgery in the post anaesthetic care area. Patient controlled CTEA was continued until postoperative day 3. Acute pain management and analgesic satisfaction were discribed as excellent by 95% of all patients.

Discussion: We conclude that CTEA in the context of cardiac surgery is safe, comfortable and might be beneficial for cardiac patients if it is performed by a well experienced team observing appropriate precautions.

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A-19

High thoracic visceral epidural analgesia for epicardial mapping and radio frequency ablation of cardiac arrhythmias

P. Michálek, M. Stern, J. Šoupal[1], P. Neužil[2], R. Vivek[3]

[1,2]Na Homolce Hospital, [3]Massachussets Hospital,
[1]Dept of Cardiovascular Anaesthesia, [2,3]Dept of Cardiology,
[1,2]Prague, Czech Republic,
[3]Boston, U.S.

Introduction: The aim of this study was to evaluate the possibility of performing epicardial mapping and radiofrequency ablation (RFA) under a regional anaesthesia technique.

The location of arrhythmogenic substrate is mostly in the endocardium. The catheter mapping is hence performed by an endocardial (intravenous) approach. Some arrhythmias have an epicardial location (e.g. pre-excitation , focal triggers for ectopic atrial or ventricular tachycardias). These conditions require epicardial electrophysiological mapping and RFA [1]. The procedure is very painful by reason of catheter manipulation in the pericardial space.

Method: The total of 20 patients who underwent epicardial mapping and RFA in the period December 2001–December 2002 was studied. The mean age was 56.5 ± 8.7 years.

We have supposed that blocking visceral nocioceptive pathways would provide quality analgesia for the painful procedure. High thoracic epidural analgesia with a low concentration of

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local anaesthetic was chosen as the method of first choice [2]. Exclusion criteria (anticoagulant therapy) were standard [3]. An epidural catheter at the T2–T3 intervertebral space was inserted 5 cm cranially. A test dose of 3 ml 1% lidocaine was followed by 8 ml of local anaesthetic mixture (10 ml 1% lidocaine + 10 ml 1% levobupivacaine + 30 ml saline). Continuous epidural analgesia at 4 ml per hour was then continued. ECG, oximetry, invasive blood pressure and CVP were observed. The guidewires for mapping catheters were inserted from a subxiphoideal puncture after 30 min. We evaluated the following variables: quality of analgesia (VAS), cardiovascular stability, consumption of sedatives and narcotics and subjective satisfaction of the patients with the whole procedure.

Results: The procedure was successfully performed in all 20 patients (SE = 1.0). Mean time of its duration was 5.7 ± 2.2 h. Success rate of RFA was 64.5%. 4 patients required analgesia and sedation (sufentanil and midazolam). 19 patients were haemodynamically stable. One patient with LVEF 15% had hypotension treated by catecholamines. All the patients evaluated the analgesia as satisfactory. No complications associated with this kind of anaesthesia (e.g. unsuccessful puncture, spinal block, pneumothorax, bleeding) were noted.

Discussion: The high epidural thoracic analgesia with low concentrations of local anaesthetic solution is a very usable choice for this painful procedure. The success rate was high and complications minimal.

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A-20

Thoracic epidural analgesia reduces the perioperative stress response and troponin-I release in off-pump coronary artery bypass grafting patients

S. Goren, S. Sahin, F.N. Kaya, G. Korfali, D. Köse

Dept of Anaesthesiology and Reanimation, Uludag University School of Medicine, Bursa, Turkey

Introduction: Thoracic epidural analgesia (TEA) faces growing interest as an adjuvant and postoperative analgesic regimen, because of a decrease in myocardial ischaemia, perioperative stress and postoperative pain [1,2]. We performed a prospective, randomized, controlled trial to study the effects of TEA when combined with general anaesthesia (GA) on myocardial damage and stress response in off-pump coronary artery bypass grafting (OPCABG) patients.

Method: After ethics approval and written informed consent, 28 patients (45–70 yr, NHYA II–III, LVEF > 40%) scheduled for elective OPCABG were randomly assigned to one of 2 groups. Both groups received a standardized GA technique (ketamine, fentanyl, midazolam, rocuronium, sevoflurane). In group II (GA + TEA), TEA from T_{2-5} interspaces was used intra-operatively (5–7 ml 0.25% bupivacaine + 5 μg ml^{-1} fentanyl bolus, 5–7 ml h^{-1} infusion) and postoperatively (bupivacaine 0.125% + 3 μg ml^{-1} fentanyl infusion, 5 ml h^{-1} and 4–5 ml boluses as needed). In group I, postoperative analgesia was achieved with i.m. morphine and NSAIDS. Blood samples were obtained before and after induction (T0, T1), after sternotomy (T2), before and after bypass (T3, T4), and at 1, 4, 8, 12, and 24 h after surgery (T5–T9) for epinephrine, norepinephrine, ACTH, prolactin, troponin-I and creatine kinase-MB levels. Data were analysed using Mann-Whitney-*U* or Wilcoxon's tests as appropriate. Significance was set at $P < 0.05$.

Results: Both groups were comparable for demographic data and preoperative properties.

Table. Some data are summarized.

	T0	T4	T5	T7	T9
Epinephrine					
GA (n = 8)	40 ± 20	75 ± 34*	192 ± 63*	191 ± 54*	118 ± 25*
GA + TEA (n = 9)	52 ± 14	23 ± 8	63 ± 23	61 ± 11	54 ± 11
Norepinephrine					
GA (n = 8)	123 ± 55	231 ± 50†	368 ± 85*	607 ± 168*	586 ± 177
GA + TEA (n = 9)	111 ± 24	71 ± 31	184 ± 55	266 ± 52	360 ± 76
Troponin-I					
GA (n = 14)	0.2 ± 0.1	2.0 ± 1.5	4.3 ± 2.4	8.8 ± 3.1*	10.0 ± 1.1†
GA + *TEA* (n = 14)	0.2 ± 0.1	0.3 ± 0.1	0.9 ± 0.2	1.3 ± 0.4	0.6 ± 0.1
CK-MB					
GA (n = 14)	9.7 ± 0.9	16.1 ± 2.7	19.1 ± 2.4	23.5 ± 3.7	27.9 ± 3.6
GA + *TEA* (n = 14)	11.3 ± 1.1	14.8 ± 1.0	14.6 ± 1.4*	18.8 ± 1.1	21.5 ± 2.3

Epinephrine, norepinephrine: pg mL^{-1}; Troponin-I, CK-MB: ng mL^{-1}.
Mean ± SEM; *$P < 0.05$, †$P < 0.01$; Group GA vs. Group GA + TEA.

The changes in ACTH and prolactin were not significant between the groups.

Discussion: The results shown that TEA did not affect the increase in ACTH and prolactin levels, but attenuated the release of catecholamines and troponin-I. In conclusion, GA when combined with TEA provides better attenuation of stress response and myocardial damage then GA alone in patients undergoing OPCABG.

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A-21

Incidence and predictive factors for difficult laryngoscopy in cardiac surgery patients

E. Massó, A. Flo, E. Moret, C. Cubells, X. Ruyra, J. Canet

Department of Anaesthesia, Hospital Germans Trias i Pujol Badalona, Spain

Introduction: Obesity, age, male sex and diabetes mellitus are risk factors common to difficult laryngoscopy (DL) and coronary artery disease [1]. Angiotensin-converting enzyme (ACE) inhibitors have been related to DL [2]. The goal of our study was to find out the incidence of DL and to define its risk factors in the population of patients undergoing cardiac surgery.

Method: For a period of 20 months, we prospectively studied 593 patients undergoing cardiac surgery: 368 (62.1%) underwent coronary bypass and 224 (37.8%) non-coronary surgery . During the preoperative visit the anaesthesiologist recorded: age, sex, weight, height, body mass index (BMI), Mallampati class, thyromental distance, mouth opening, range of head extension, presence of teeth, long term treatment with ACE inhibitors; and history of snoring, insulin dependent diabetes mellitus and coronary artery disease. DL was defined as a Cormack-Lehane grade of 3 or 4 on direct laryngoscopy with a Macintosh blade of size 3. Univariate analysis was done to identify the factors that may predict DL; subsequently a multivariate analysis using logistic regression (P of entry <0.05) and odds ratio (95% confidence interval (CI)) were calculated.

Results: Thirty one patients (5.2%) had a DL. Male sex, Mallampati class 3 or 4, restricted head extension, presence of teeth, snoring, treatment with ACE-inhibitors, weight and obesity (BMI > 30 kg m^{-2}) were identified in the univariate analysis as potential risk factors for DL. In the multivariate analysis four factors were recognized as independent factors for DL.

Criteria	Odds ratio (CI 95%)	P
Presence of teeth	5.80 (1.69–19.90)	0.005
Restricted head extension	3.90 (1.76–8.67)	0.001
BMI > 30 kg m^{-2}	3.72 (1.66–8.30)	0.001
Male sex	3.53 (1.25–9.92)	0.017
ACE inhibitors	2.18 (1.00–4.79)	0.051

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Discussion: DL was reported in 5.2% of the patients undergoing cardiac surgery. Male sex and obesity are risk factors common to DL and coronary artery disease. More studies are needed to clarify the relation between DL and treatment with ACE inhibitors.

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A-22

Can the depth of insertion of a left-side double lumen endobronchial tube be predicted?

R. Alvarez-Rementería, A. Ventas, A. Sanchez, B. Balmisa, M. Arnzubía, A. De La Rotta

Fundación Jiménez Díaz, Madrid, Spain

Introduction: The aim of the study was to evaluate diverse parameters to predict the depth of insertion of an endobronchial left side double lumen tube (LDLT).

Method: Twenty six patients were selected in whom LDLT was indicated (Broncho-Cath; Mallinckrodt). The size of the LDLT was 39 F in men and 37 F in women. The correct position of the LDLT (CP) was verified using fibreoptic bronchoscopy, then the correct depth of the LDLT was defined by a mark on the LDLT, corresponding with the upper incisors. The correlation of the correct depth of the LDLT to height (H), to the length from the cricoid cartilage to the lower end of xiphoid (Xf) and to the length of the trachea from the C7 spinous process to the carina in the postero-anterior view of the chest radiograph (Rx) was analysed by means of multiple linear regression analysis. Agreement was tested using the statistical method of Bland and Altman (the mean value of the difference between predicted and measured value ± 2SD) [1].

Results: The study group had 25 patients (19 men and 6 women) mean height = 160 ± 9.6 cm and age 58.5 ± 18.5 years. The mean of the correct depth of the LDLT was CP = 25.7 ± 2.2 cm and the values of Xf and Rx were respectively Xf = 23.3 ± 2.9 cm and Rx = 12 ± 0.8 cm. The table shows the values of multiple linear regression analysis and agreements (95% confidence limits (95% C.L.))

	R^2	Regression line equation	95% C.L.
H	0.794	CP (cm) = (H × 0.20) − 5.48	−0.80 ± 1.97
Xf	0.662	CP (cm) = (Xf × 0.56) + 12.13	−0.32 ± 2.52
Rx	0.424	CP (cm) = (Rx × 1.69) + 6.78	−1.35 ± 3.29

Discussions: The height, the length from the cricoid cartilage to the xiphoid, and in minor degree the length of the trachea from the C7 spinous process to the carina in the chest radiograph, are measurements that are useful to predict the proper depth necessary to introduce a LDLT. The utilization of fibreoptic bronchoscopy is necessary to assure an acceptable position of the LDLT.

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A-23

Effects of PEEP on ventilatory and oxygenation parameters during pressure controlled one-lung ventilation

M. Şentürk, A. Dilek, E. Camci, E. Şentürk, M. Orhan, M. Tuğrul, K. Pembeci

Istanbul University, Medical Faculty of Istanbul, Dep. of Anaesthesiology, Istanbul, Turkey

Introduction: The positive effects of pressure controlled ventilation (PCV) during one-lung ventilation (OLV) have been shown [1]. The effects of PEEP during conventional OLV with volume controlled ventilation (VCV) are controversial [2]. The aim of this study was to investigate the effects of PEEP during PCV-OLV.

Method: After Ethics Committee approval and informed patient consent, 25 patients undergoing thoracotomy were studied (14 left, 11 right thoracotomy). During the first 5 min of OLV, all patients were ventilated with VCV (FiO_2: 1.0; f: 12 min^{-1}; appropriate tidal volume to achieve $ETCO_2$ of 4–4.6 kPa; PEEP: 0). After recording of ventilatory pressure values (Ppeak, Pplat, Pmean, Ppause and PEEPi) (PaO_2 and Qs/Qt were not measured because the OLV-time was (5 min) too short to obtain reliable measurements), ventilation was turned to PCV (FiO_2: 1.0; f: 12 min^{-1}; appropriate tidal volume to achieve $ETCO_2$ of 4–4.6 kPa) with PEEP: 0 (PCV-ZEEP:12 patients) or PEEP: 4 cmH_2O (PCV-PEEP:13 patients). After 20 min ventilatory pressures and PaO_2 (blood-gas analysis) were recorded, and pulmonary shunt (Qs/Qt) was calculated. In the next 20 min PCV-PEEP and PCV-ZEEP were applied in reverse sequence, followed by the same measurements. PEEPi was measured by pushing the 'expiratory hold' knob of the ventilator. ANOVA and Student's *t*-tests were used for statistics (significant if $P < 0.05$)

Results:

	VCV	PCV-ZEEP	PCV-PEEP
Ppeak (cmH_2O)	33.4 ± 4.2	28.3 ± 4.1*	28.9 ± 3.7*
Pplat (cmH_2O)	17.8 ± 3.2	16 ± 3*	16.7 ± 3*#
Pmean (cmH_2O)	9.5 ± 1.3	9 ± 1.3	10.5 ± 1.5*#
Ppause (cmH_2O)	19.8 ± 3.7	17.9 ± 1.3*	18.9 ± 3
PaO_2 (kPa)		25.2 ± 7.3*	30.7 ± 9.3
Qs/Qt (%)		38.4 ± 5.7*	33.4 ± 7.3

*$P < 0.05$ vs. VCV; #$P < 0.05$ vs. PCV-ZEEP.

Patients with PEEPi at VCV ($n = 14$ of 25) have benefited more from PCV-PEEP with no significant changes in ventilatory pressures compared to PCV-ZEEP (PaO_2: 32.5 ± 9.2 kPa vs. 26.2 ± 7.7 kPa; Qs/Qt: 32.7 ± 7.8% vs. 39.8 ± 5.5%; $P < 0.05$; respectively). In patients without PEEPi, there was no statistically significant increase in either respiratory pressures and gas exchange parameters with PCV-PEEP.

Discussion: In patients with PEEPi during OLV, PCV-PEEP is preferable vs. VCV and PCV-ZEEP according to the ventilatory and oxygenation parameters. In patients without PEEPi, the effects of external PEEP have to be evaluated individually.

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A-24

Effect of different recumbent positions on arterial oxygenation in valvular heart disease patients with cardiomegaly

G.D. Puri, A. Dutta, S.K. Nevin, S.S.K. Thingnam, P. Chari

Post Graduate Institution of Medical Education and Research, Chandigarh, India

Introduction: Chamber enlargement of the heart can affect lung functions by direct compression of lung or airways with attendant decreased ventilation [1] and also by altering the pulmonary vascular system such as reducing the calibre of left lower lobe vessels in the supine posture [2].

Method: Following institutional ethical committee approval, thirty premedicated valvular heart disease patients planned for cardiac surgery were studied. They were of either sex, having cardiothoracic (CT) ratio of. 0.5 or more on chest x-ray. Arterial blood-gas analysis was performed in supine (S), left lateral (LL) and right lateral (RL) postures in random sequence after keeping the patient in each posture for 15 min. Patients received oxygen supplementation at FiO_2 of 0.35 during the whole study period. PaO_2 and saturations in three different positions were compared and the difference related to left ventricular end diastolic diameter (LVEDD) obtained by echocardiography preoperatively and the CT ratio.

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Results: Arterial oxygen tension and saturations were highest in RL posture (Table 1). These were significantly higher in RL posture as compared to LL posture [$P < 0.01$, paired t test]. These were also significantly higher in RL as compared to S posture [$P < 0.01$, paired t test]. The difference between LL and S posture was not significant ($P > 0.05$). The difference in oxygen saturations between RL and LL postures was significantly related to LVEDD ($r = 0.55$ Pearson's correlation coefficient) but the relation was not significant with CT ratio ($r = 0.35$).

Table 1.

	Supine	Left Lateral	Right Lateral
$PaO_2 \pm$ SD kPa	13.5 ± 3.9	13.3 ± 3.9	14.9 ± 3.9*
$SpO_2 \pm$ SD %	97.2 ± 2.3	97.1 ± 1.7	97.7 ± 1.5*

*$P < 0.01$ as compared to Supine and Left Lateral.

Discussion: The decrease in saturation in the LL posture may be due to lung volume and airway compression of the left lung by the enlarged heart. This compression decreases ventilation of the left lung when this dependent lung is being perfused maximally in the LL position. The enlarged left ventricle expands in the left hemithorax resulting in predominant left lung compression. In the RL posture the effect of left ventricular enlargement on lung volumes is less. Absence of relation of change in saturation from right to left lateral position with CT ratio, may be because some of the patients had cardiomegaly on x-ray due to enlargement of cardiac chambers other than the left ventricle. Thus there was no improvement on attaining the RL posture**.** In conclusion, oxygenation in valvular heart disease with cardiomegaly due to left ventricular enlargement is best in RL posture when lying down in bed. Patients with left ventricular enlargements should be encouraged to lie in right lateral posture when in bed.

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A-25

Carnitine derivatives reduce endothelin generation during cardiopulmonary bypass in patients with diabetes

R. Lango, J. Siebert, J. Rogowski, R.T. Smolenski, P. Siondalski, M. Wujtewicz, W. Łysiak-Szydłowska

Chair and Department of Anesthesiology and Intensive Therapy, Medical University of Gdansk, Gdansk, Poland

Introduction: Carnitine deficiency is a recognized metabolic derangement resulting in the impairment of myocardial contractility, particularly in patients with diabetes undergoing coronary surgery. An exogenous supply of carnitine metabolites is known to exert cardio-protective effects, but its exact mechanism has not been established. Endothelin (ET) is a potent vasoactive peptide that has been identified in lung, kidney, brain and cardiomyocytes. Although ET is considered to be associated with vascular dysfunction it is also known to affect myocardial contractility. The purpose of the present study was to define whether preoperative administration of carnitine compounds can reduce myocardial ET release.

Method: Fifty-five patients with diabetes mellitus, undergoing CABG operation were given either 20 mg kg^{-1} b.w. L-carnitine (group C), propionyl-L-carnitine (group P), or placebo (group O) i.v. in a 12-hour infusion during the night preceding the operation, in a double-blind, randomized manner. Samples of arterial and coronary sinus blood were collected before the aortic cross-clamp (X-C) and 10 minutes after aortic X-C removal. ET concentration was determined with enzyme immunoassay and is expressed in arbitrary units ± SD. Data were compared among the groups with Student's t-test for independent samples.

Results: Lower pulmonary vascular resistance in groups P and C and higher mixed venous haemoglobin saturation with oxygen in group P compared to O was accompanied by attenuation of cardiac endothelin release.

Table. Endothelin concentration in coronary sinus.

	Group C	Group P	Group O
Before X-C	1.02 ± 2.67	1.28 ± 0.83	1.06 ± 2.34
10 min after X-C removal	0.71 ± 1.78	1.09 ± 0.79	1.84 ± 2.97

ET concentration 10 min after X-C removal increased by 0.78 ± 1.58 in O, while it decreased in C and P by −0.56 ± 1.31 and −0.19 ± 0.82 respectively ($P = 0.012$ for C vs. O and $P = 0.024$ for P vs. O). Aortic X-C time did not differ significantly among the groups (C: 42 ± 9.4 min, P: 47.1 ± 14.9 min, O: 46.2 ± 14.8 min.).

Discussion: ET has been suggested to be a marker for coronary endothelial dysfunction. High plasma levels of ET have been reported in different types of ischaemia. Reduction of biological effects of ET has been demonstrated to decrease myocardial ischaemia-reperfusion injury [1]. L-Carnitine and propionyl-L-carnitine administration reduces cardiac endothelin generation during CABG operation, which may play a significant role in cardio-protective effect of carnitine compounds administration.

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A-26

Acute renal dysfunction after cardiopulmonary bypass is related to a high pre-operative serum ferritin

G. Gueret, B. Rossignol, T. Aderrab, M.P. Moineau[1], J.P. Wargnier, A. Miossec, O. Corre, C.C. Arvieux

Département d'anesthésie-réanimation, [1]Service de médecine nucléaire, CHU la Cavale Blanche, Brest, France

Introduction: Postoperative acute renal failure (ARF) is not infrequent after cardiac surgery. This ARF is an independent risk factor of postoperative mortality. Pathophysiology of ARF is complex. Oxidation of cell membranes by iron catalysed reactive oxygen species has been proposed [1]. A prospective study showed that a decreased serum ferritin is a risk factor for acute renal dysfunction (ARD) [2]. On the other hand, ferritin levels are increased in ARF patients in non cardiac surgery [3]. The aim of this study was to confirm that a decreased serum ferritin was a risk factor of ARD in cardiac surgery.

Method: After ethical committee agreement and informed consent, 60 consecutive patients for cardiac surgery were prospectively included. Demographic data and risk factors of ARD were noted. ARD was defined as a 25% increase of serum creatinine [2]. Data were compared using chi-squared, t test or non-parametric tests when necessary. $P < 0.05$ was chosen as significant threshold.

Results: ARD occurred in 30 patients. Demographics data and surgery, CPB and aortic cross-clamping times were similar in both groups. Preoperative creatinine were comparable between both groups (75 ± 15 vs. 77 ± 17 mmol L^{-1}, $P = 0.47$). Pre-operative serum ferritin was higher in ARD group (241 ± 209 vs. 139 ± 110 μmol L, $P = 0.04$). Patients with a ferritin level higher than 215 μmol L^{-1} had a 2.16 fold risk of ARD (Table 1). Volume of hetastarch 6% administered during the operation was not a risk factor of ARD either (698 ± 496 ml vs. 621 ± 457, $P = 0.39$). Beta blocker therapy was also a risk factor of ARD (Table 1). Diuresis per hour during CPB was lower in ARD patients (56 ± 64 vs 105 ± 84 mLh^{-1}, $P = 0.013$).

Table 1. ARD probability and patients data.

	ARD+	ARD−	P
Ferritin >215 μmol L^{-1} (Y/N)	15/15	4/26	0.002
Diuresis per ECC <150 mL (Y/N)	27/3	13/17	0.004
Beta blocker therapy (Y/N)	21/9	13/17	0.037
Per operative catecholamine (Y/N)	19/11	16/14	0.43

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Conclusion: The high frequency of ARD in our study may be related to the relatively higher number of patients with valvular disease than in other studies. An increased serum ferritin is a risk factor of ARD in cardiac surgery. An increased inflammatory response may be an explanation for the high blood ferritin [3].

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A-27

Is the Cockcroft method reliable for the evaluation of creatinine clearance in cardiac surgery patients?

G. Gueret, B. Rossignol, T. Aderrabt, J.P. Wargnier, A. Miossec, O. Corre, C.C. Arvieux

Departement d'anesthesie-reanimation, Brest, France

Introduction: Evaluation of renal function is classically done using creatinine clearance. Creatinine clearance is not usually measured in the preoperative period. In 1976, Cockcroft proposed a new method to estimate the creatinine clearance [1]. This calculated clearance is commonly used but has not been evaluated in cardiac surgery. The aim of this study was to compare the creatinine clearance measured and calculated in cardiac surgery patients.

Method: After ethical committee agreement and informed consent, 60 patients of the cardiac department were included. Anaesthesia was with propofol, remifentanil and cisatracurium. After tracheal intubation, a Foley catheter was inserted in the bladder for collection of urine from induction until the start of CBP. Urinary and blood analyses were then realized in order (1) to measure the true creatinine clearance and (2) to estimate it using the Cockcroft's method [1]. Data were compared using paired *t*-test. $P < 0.05$ was chosen as significant threshold.

Results: 60 consecutive patients were prospectively included. No significant relation was found between the two methods (Figure 1, $P = 0.25$).

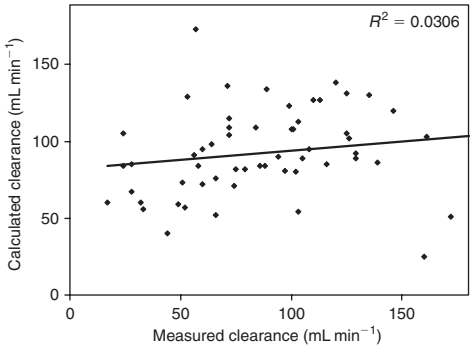

Figure 1. Relationship between measured and estimated creatinine clearance in cardiac surgery patients.

Conclusion: The Cockcroft method is not reliable enough to evaluate the creatinine clearance in cardiac surgery patients.

Reference:

1 Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16:** 31–41.

A-28

Low dose dopexamine does not alter subclinical renal indices following cardiac surgery

S.J. Allen, S.P. Penugonda, R.C. Baker, I. Young, T.J. McMurray, M.A. Armstrong, W.T. McBride

Departments of Anaesthesia, Immunobiology, Clinical Chemistry and Surgery, Queens University Belfast, Belfast, Northern Ireland, UK

Introduction: Subclinical renal injury (as measured by N acetyl β D Glucosaminidase, β-NAG) and dysfunction (α-1-microglobulin, α1 m, and microalbuminuria, MA) has been well documented following cardiopulmonary bypass. Typically this follows a biphasic pattern with an early (6–24 h) and a late (48–72 h) peak [1]. Dopexamine has been reported as improving renal function in both animal and human studies. The objective of this single blind randomized, controlled trial was to investigate whether dopexamine administered perioperatively during cardiac surgery reduces subclinical renal indices of injury and dysfunction up to 72 hours after surgery.

Method: 38 ASA III to IV patients undergoing elective cardiac surgery requiring cardiopulmonary bypass were randomly allocated to one of two groups. Group DP received dopexamine, at 0.5 mcg kg^{-1} min^{-1}, from induction of anaesthesia until 24 h after termination of cardiopulmonary bypass. Group C received placebo.Urine samples were obtained for α1 m, β-NAG, MA and creatinine measurement as follows: baseline (samples A,B), after cross-clamp release (sample C), and 2, 6, 24, 48 and 72 h post-CPB (samples D, E, F, G and H respectively). Results were analysed using Mann-Whitney *U* test or Wilcoxon's signed rank test as appropriate. 17 patients per group provided 90% power to detect one standard deviation actual difference between groups.

Results: Urinary NAG/creatinine, α1 m/creatinine ratios and MA/creatinine ratios increased significantly in both groups over the study period ($P < 0.01$) compared to baseline (see Table 1). However there were no significant differences between the control and treatment groups at any time.

Table 1. Selected urinary biochemistry results in groups C (control) and DP (dopexamine). Results are mean ± SEM.

	Baseline		24 h		72 h	
	C	DP	C	DP	C	DP
β-NAG/creatinine (μmol mmol^{-1})	16.8 (±3.5)	14.76 (±2.1)	86.45 (±23.9)	52.06 (±6.07)	103.62 (±23.2)	68.02 (±11.7)
α1 m/creatinine (mg mmol^{-1})	1.34 (±0.3)	0.91 (±0.2)	6.54 (±0.9)	7.34 (±0.7)	7.4 (±1.4)	6.62 (±1.5)
MA/creatinine (mg mmol^{-1})	0.44 (±0.4)	0.73 (±0.1)	2.28 (±0.4)	2.25 (±0.5)	2.47 (±0.4)	3.17 (±0.6)

Discussion: These results are in agreement with those of Dehne [2] et al who showed no effect of dopexamine on renal injury or function up to 24 h after bypass. Our results demonstrate that in this low risk population low dose dopexamine did not influence the subclinical renal dysfunction seen in the first 72 h following CPB. More work is needed to evaluate the drug in high risk patients.

References:

1 Gormley SM, McBride WT, Armstrong MA, *et al*. Plasma and urinary cytokine homeostasis and renal dysfunction during cardiac surgery. *Anesthesiology* 2000; **93:** 1210–1216.

2 Dehne MG, Klein TF, Muhling J, *et al*. Impairment of renal function after cardiopulmonary bypass is not influenced by dopexamine. *Ren Fail* 2001; **23:** 217–230.

A-29

Methylprednisolone reduces urinary transforming growth factor beta-1 concentration at aortic surgery

R.C. Baker[1], M.A. Armstrong[2], S.J. Allen[3], A.A.B. Barros D'Sa[1], W.T. McBride[3]

[1]Departments of Surgery, [2]Immunobiology [3]Clinical Anaesthesia, Queen's University of Belfast, Belfast, N. Ireland.

Introduction: Urinary transforming growth factor-beta 1 (uTGF-β1) potentiates renal scarring and is often elevated in progressive chronic renal diseases [1]. Recently we showed, for the first time, that acute increases in uTGF-β1 at cardiac surgery are significantly reduced by preoperative administration of methylprednisolone

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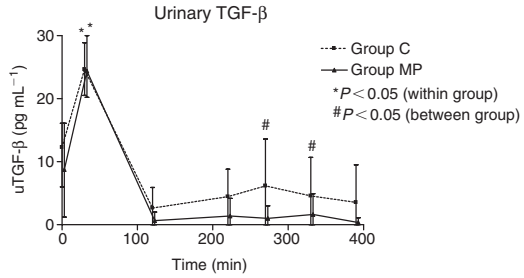
(MP) [2]. However the pathophysiological significance of this perioperative uTGF-β1 response remains unclear. We therefore developed an animal model of aortic ischaemia-reperfusion, to simulate the perioperative uTGF-β1 response and attempt to modulate this with MP.

Method: Forty-two pigs underwent laparotomy, fluid resuscitation for 60 min and then 150 min of infra-renal aortic cross-clamping followed by 180 min reperfusion. Samples were obtained for uTGF-β1 measurement as follows: preoperative baseline (PB) and 30, 120, 220, 270, 330 and 390 min after induction of anaesthesia. Pigs were randomized to 2 groups. Group C received placebo and group M received methylprednisolone 30 mg kg^{-1}, after obtaining the 30 min sample. Analysis between groups – Mann-Whitney *U* test; within groups – Wilcoxon matched pairs.

Results: There were no haemodynamic differences between groups. Compared to the PB sample there was a significant rise, in both groups, in the uTGF-β1 concentration following transfer, anaesthesia and laparotomy alone (group C; $P = 0.001$, group MP; $P = 0.006$). uTGF-β1 was significantly lower in group M compared to group C in the reperfusion period at time points 270 and 330 min ($P = 0.04$ and 0.05 respectively).



Discussion: Our model successfully simulated the changes in perioperative uTGF-β1 concentrations observed in patients. It allows further elucidation of the pathophysiological role of this response and its potential modulation in acute renal dysfunction.

References:

1 Chen S, Hong SW, Iglesias-de la Cruz MC, *et al*. The key role of the transforming growth factor-beta system in the pathogenesis of diabetic nephropathy. *Ren Fail* 2001; **23:** 471–481.

2 Allen SJ, Gormley SMC, Elliott P, *et al*. Urinary TGF-β is elevated following cardiac surgery and is reduced following methylprednisolone administration. *Br J Anaesth* 2002; **89:** 195.

Cardiac Function

A-30

Echocardiographic evaluation of effects of anaesthetics on diastolic function in healthy young humans

M. Filipovic, J. Wang, I. Michaux, C. Werner, E. Seeberger, K. Skarvan, M.D. Seeberger

University of Basel/Kantonsspital; Department of Anaesthesia, CH 4031 Basel, Switzerland

Introduction: Global left ventricular (LV) performance is critically determined by diastolic function. Nevertheless, the knowledge on effects of anaesthetics on diastolic function is limited and mainly based on animal and laboratory findings [1].

Method: After IRB approval and informed written consent, 60 patients (22 women; mean age 30 ± 8, range 18–47 yr) who were scheduled for minor surgical procedures were equally randomized to general anaesthesia with halothane (H), sevoflurane (S), or propofol (P). Two transthoracic (TTE) and 2 transoesophageal (TOE) echocardiographies were performed: TTE 1 before induction of anaesthesia; TTE 2 during spontaneous breathing under 1 MAC of H or S, or 4 μg mL^{-1} P delivered by a target controlled infusion system, respectively; TOE 1 after orotracheal intubation (facilitated by 2 μg kg^{-1} fentanyl and 0.6 mg kg^{-1} rocuronimum) and positive pressure ventilation under 1 MAC of H or S, or 4 μg mL^{-1} P; TOE 2 under 1.5 MAC of H or S, or 6 μg mL^{-1} P, respectively.

Results:

		TTE 1	TTE 2	TOE 1	TOE 2
SAP [mmHg]	H	116 ± 11	102 ± 9*	92 ± 10	84 ± 8**†
	S	120 ± 12	102 ± 9*	94 ± 7	90 ± 8‡
	P	116 ± 15	98 ± 10*	98 ± 10	99 ± 11†‡
HR [min^{-1}]	H	65 ± 11	63 ± 9†	62 ± 8†	63 ± 8
	S	63 ± 10	62 ± 10‡	66 ± 8	68 ± 8
	P	66 ± 9	76 ± 11*†‡	70 ± 10†	67 ± 10
E [cm sec^{-1}]	H	83 ± 12	81 ± 11†	66 ± 13	63 ± 14
	S	84 ± 12	84 ± 10‡	57 ± 11	57 ± 12
	P	80 ± 16	62 ± 15*†‡	56 ± 16	55 ± 14
A [cm sec^{-1}]	H	50 ± 12	41 ± 9*	26 ± 9†	23 ± 7†
	S	47 ± 13	37 ± 8*‡	25 ± 5‡	23 ± 9‡
	P	47 ± 9	46 ± 11‡	35 ± 10†‡	34 ± 15†‡
E/A	H	1.7 ± 0.3	2.1 ± 0.5†	2.9 ± 1.1†	3.1 ± 1.1†
	S	1.9 ± 0.4	2.4 ± 0.5‡	2.4 ± 0.7‡	2.8 ± 1.0‡
	P	1.7 ± 0.4	1.4 ± 0.5†‡	1.7 ± 0.5†‡	1.9 ± 0.8†‡
E [cm sec^{-1}]	H	18.9 ± 4.8	18.4 ± 3.5	14.4 ± 3.1	15.0 ± 2.6
	S	20.5 ± 4.2	19.4 ± 3.1‡	15.3 ± 2.6	15.7 ± 2.7
	P	18.8 ± 4.5	16.0 ± 3.8*‡	13.5 ± 3.7	13.7 ± 3.2

(*Continued*)

		TTE 1	TTE 2	TOE 1	TOE 2
FAC [%]	H	57 ± 7	50 ± 7*	41 ± 8†	35 ± 8**†
	S	55 ± 4	49 ± 7*	43 ± 10	37 ± 10**‡
	P	57 ± 5	55 ± 6	52 ± 10†	46 ± 8**†‡

Data are mean ± SD. SAP = systolic arterial pressure; HR = heart rate; E = peak early transmitral filling velocity; A = peak late transmitral filling velocity; E = early diastolic peak velocity of lateral mitral annulus; FAC = fractional area change. *$P < 0.05$ TTE 1 vs. TTE 2, **$P < 0.05$ TOE 1 vs. TOE 2; †$P < 0.05$, H vs. P, ‡$P < 0.05$ S vs. P (ANOVA followed by Scheffé's test).

Discussion: The results indicate that H and S do not impair LV relaxation but impair systolic function in healthy humans. Whether the changes in indices of diastolic function in the P group represent impairment of LV relaxation or whether they reflect changes in HR and preload requires further evaluation.

Reference:

1 Pagel PS, Grossman W, Haering JM, *et al*. Left ventricular diastolic function in the normal and diseased heart. Perspectives for the anesthesiologist (2). Anesthesiology 1993; **79:** 1104–1120.

A-31

The systolic fraction of pulmonary venous flow as a reliable index of wedge pressure

D. Pittarello, G. Falasco, M. Gasparetto, A. Marcassa, L. Pasini, R. Bonato

Department of Pharmacology and Anaesthesiology, University of Padova, Padova, Italy

Introduction: In patients with heart disease, left ventricle diastolic performance is often clinically evaluated by using a catheter to measure pulmonary capillary wedge pressure (PCWP). In an attempt to find a non-invasive method of assessing left ventricular diastolic performance, pulsed Doppler echocardiography of mitral inflow has been largely investigated and used. However, the dependence of mitral inflow patterns on multiple factors has greatly limited the clinical value of this measurement. In recent years it has become possible to record the pulmonary venous flow (PVF) velocity patterns clearly, using transoesophageal pulsed Doppler echocardiography (TOE). The aim of the present study was to investigate whether the pulmonary venous flow variables as recorded by TOE can be used to measure PCWP and supplement mitral flow studies in detecting left ventricular diastolic pressures in patients undergoing cardiovascular surgery.

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Method: To correlate Doppler variables of PVF and mitral flow with simultaneously measured PCWP, we studied prospectively 17 patients undergoing cardiovascular surgery for coronary artery disease. We measured the peak waves velocities of mitral flow and PVF, with the corresponding velocity time integrals and the systolic fraction of PVF (systolic velocity–time integral expressed as a fraction of total anterograde velocity–time integral of pulmonary flow). The PCWP, PVF and mitral flow were obtained in all patients after induction of anaesthesia, prior to sternotomy. For statistical tests we used a multiple stepwise linear regression analysis.
Result: While mitral inflow variables were not correlated with PCWP, Doppler variables of pulmonary venous flow correlated more strongly with PCWP and in particular the systolic fraction of pulmonary venous flow (Fig. 1).

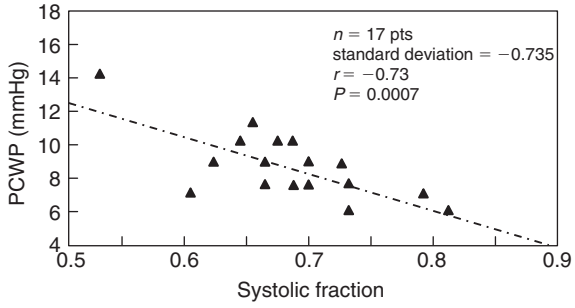


Fig. 1

Discussion: This study provides evidence that in the surgical setting observed, the systolic fraction of PVF measured by TOE is a safe, relatively non-invasive, and simple method to estimate PCWP sufficiently well to be used as a possible index of left ventricular diastolic performance.
Reference:
1 Poelzl G, Gattermeier M, Kratzer H, *et al*. Feasibility and accuracy of transthoracic Doppler echocardiographic estimation of pulmonary capillary wedge pressure applying different methods. *Eur J Heart Fail* 2001; **3:** 553–560.

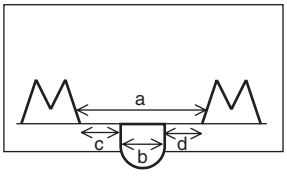
A-32

Right ventricular function during coronary surgery: feasibility of the Tei index

I. Michaux, M. Filipovic, J. Wang, K. Skarvan, M. Seeberger

Department of Anaesthesia, University of Basel, Basel, Switzerland

Introduction: Ischaemia during cardiopulmonary bypass (CPB) can provoke deterioration of right ventricular (RV) function. Echocardiographic evaluation of RV function is limited by the complex RV geometric form. In transthoracic echocardiography, the Tei index (the sum of isovolumetric contraction [IVCT = c] and relaxation [IVRT = d] times divided by the ejection time [b]) has been proposed for evaluation of systolic and diastolic RV function [1].



IVCT + IVRT = c + d = a – b
Tei = (a – b) / b

However, its feasibility by transoesophageal echocardiography (TOE) is unknown, and its usefulness during cardiac surgery has never been demonstrated. Accordingly, the aim of this pilot study was to evaluate the feasibility of the Tei index during coronary artery bypass graft surgery with CPB (on-pump CABG), and without CPB (OPCAB).

Method: Tei index was obtained in 39 patients after opening and before closure of the sternum for surgical revascularization. Twenty-six patients underwent on-pump CABG (in 13, cardiac arrest was obtained with antegrade crystalloid cardioplegia and for the others with antegrade blood cardioplegia), and 13 patients underwent OPCAB.

Results: Tei index could be obtained by TOE and measured off-line in all 39 patients at both time points. The Tei index was unchanged after OPCAB, whereas it markedly increased during on-pump CABG, without any difference between the 2 on-pump groups.

	Crystalloid Cardioplegia	Blood Cardioplegia	OPCAB
Number of patients	13	13	13
Preoperative Tei index	0.26 (0.12–0.32)*	0.13 (0.05–0.24)*	0.16 (0.04–0.25)
Postoperative Tei index	0.44 (0.21–0.58)*†	0.28 (0.15–0.52)*†	0.15 (0.06–0.28)†

Data are median (95% confidence interval).; *$P < 0.01$: postop. vs. preop. comparison (Wilcoxon signed rank test); †$P < 0.05$ postop. intergroup comparison (Kruskal-Wallis, followed by Mann-Whitney: crystalloid vs. OPCAB and blood vs. OPCAB).

Conclusion: The pilot data show that evaluation of the RV function using the Tei index is feasible by TOE during cardiac surgery. Furthermore, they suggest that CABG and OPCAB might differently affect RV function.
Reference:
1 Tei C, Dujardin KS, Hodge DO, *et al*. Doppler echocardiographic index for assessment of global right ventricular function. *J Am Soc Echocardiogr* 1996; **9:** 838–847.

A-33

Perioperative transoesophageal echocardiography is important during valve replacement

M. Hansen, G. Wagner, R. Dummler, M. Emmerich, O. Maisch, G. Klein

Department of Anaesthesiology, Robert-Bosch-Krankenhaus, Stuttgart, Germany

Introduction: Perioperative transoesophageal echocardiography (TOE) is an important and well known indication during surgical repair of valvular lesions. TOE during valve replacement is not routinely performed and only a category II indication in the practice guidelines [1].
Method: Retrospective analysis of the clinical impact after one year of TOE examinations with a multiplane probe perioperatively performed during valve replacement.
Results: From 10/2001 to 09/2002 we surveyed a total of 201 patients with echocardiographic examinations (done by two anaesthesiologists), 51 of them during valve replacement. 21 TOE examinations were done in mitral valve replacement, 25 in aortic valve procedures and 5 in double valve (mitral and aortic) replacements. In 16 of these cases valve procedures were combined with aorto-coronary bypasses. TOE examinations demonstrated in 8 patients (16%) clinically significant new information during the valve replacement procedure. 2 cases were pre-cardiopulmonary bypass (CPB) and 6 post-CPB findings:

TOE findings /number of cases	Pre- CPB	Post-CPB
Paravalvular leak		2
LVOT obstruction		2
Ruptured papillary muscle		1
Unknown perivalvular abscess	1	
Guiding venous cannulation, Eustachian valve	1	
Tamponade during minimal invasive aortic replacement		1

In 5 patients the operative procedure was changed because of the new diagnosis by TOE. In 2 cases with left ventricular outflow tract obstruction (LVOT, peak dp 25/29 mmHg) we changed the haemodynamic management.
Discussion: The risk of complications associated with TOE application is reported to be 0.2% [2]. Because of our new diagnosis detected by perioperative TOE, there were clear benefits for our patients. The new findings were entirely due to the TOE examination. They could neither be detected intra-operatively by the surgeon nor by routinely used anaesthetic monitoring, such as by pulmonary artery catheter.

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Conclusion: TOE examination during valve replacement procedures is useful for detection of clinically significant problems. These data support the routine use of TOE examinations during valve replacement in our institution.

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1 ASA and SCA Task Force on transesophageal echocardiography. Practice guidelines for perioperative transesophageal echocardiography. *Anesthesiology* 1996; **84:** 986–1006.

2 Kallmeyer IJ, Collard CD, Fox JA, *et al*. The safety of intraoperative transesophageal echocardiography: a case series of 7200 cardiac surgical patients. *Anesth Analg* 2001; **92:** 1126–1130.

A-34

Quantitative analysis of mitral annulus motion by Doppler tissue imaging indicates myocardial ischaemia

J. Wang, M. Filipovic, I. Michaux, E. Seeberger, C. Werner, K. Skarvan, M.D. Seeberger

Department of Anaesthesia, University Hospital of Basel, Basel, Switzerland

Introduction: Doppler tissue imaging (DTI) of mitral annulus motion is a novel technique to assess diastolic left ventricular function [1]. This study evaluated the usefulness of DTI for detection of myocardial ischaemia in anaesthetized patients.

Method: The study was performed in 32 patients during off-pump revascularization of the left anterior descending coronary artery (LAD). Pulsed wave DTI studies of peak early diastolic velocity of septal mitral annulus motion (Ea) and 2-dimensional images of 3 mid-oesophageal views (4 chamber, 2 chamber and long axis views) were obtained by transoesophageal echocardiography (2D-TOE) simultaneously with 7 lead ECGs and haemodynamic measurements at 3 time points: (1) after repositioning of the heart for LAD revascularization and fixation of the Octopus device (OCTO); (2) immediately after LAD occlusion (OCCL); (3) after insertion of an intracoronary shunt (SHUNT). Ischaemia was diagnosed if A) TOE showed marked deterioration of segmental wall motion (⩾2 grades on the 5 grade scale) in ⩾2 segments (16 segment model) in the LAD supplied territory and/or a ⩾1 mm ST segment shift in ⩾1 ECG lead.

Results: During LAD occlusion, evidence of ischaemia was found in 21 patients (ischaemia group), but not in 11 patients (non ischaemia group). Ea was significantly more decreased during OCCL in the ischaemia than in the non ischaemia group. A decrease in Ea of 0.75 cm s^{-1} provided a sensitivity of 85% and a specificity of 75% for detection of ischaemia (ROC analysis; area under the curve = 0.83; 95% CI 0.68–0.98). TOE/ECG evidence of ischaemia disappeared in 7/20 patients of the ischaemia group after placement of an intracoronary shunt. Ea increased in these 7 patients whereas it remained unchanged in the 13 patients with persistence of ischaemia.

Group	Time point	HR (min^{-1})	MAP (mmHg)	Ea (cm s^{-1})
Ischaemia (n = 21)	OCTO	72 ± 8	80 ± 19	5.7 ± 1.5
	OCCL	71 ± 7	74 ± 14	4.5 ± 1.2*
	SHUNT (n = 20)	71 ± 9	73 ± 17	4.6 ± 1.4
	Persisting ischaemia			
	NO (n = 7)			
	OCCL	69 ± 7	81 ± 8	4.5 ± 1.6
	SHUNT	70 ± 9	79 ± 6	5.2 ± 1.5*
	YES (n = 13)			
	OCCL	72 ± 9	68 ± 14	4.5 ± 1.1
	SHUNT	71 ± 9	68 ± 24	4.2 ± 1.3*
Non-ischaemia (n = 11)	OCTO	65 ± 25	80 ± 12	5.9 ± 1.7
	OCCL	68 ± 14	74 ± 14	5.5 ± 1.7*
	SHUNT(n = 6)	69 ± 11	73 ± 8	5.3 ± 1.9

Data are mean ± SD. *P < 0.01 ischaemia vs. non ischaemia group, and persistence vs. non-persistence of ischemia, respectively (ANOVA).

Discussion: Quantitative analysis of mitral annulus motion by DTI is sensitive for detection of intraoperative myocardial ischaemia and may become a useful clinical tool in the future.

Reference:

1 Sohn DW, Chai IH, Lee DJ, *et al*. Assessment of mitral annulus velocity by DTI in the evaluation of left ventricular diastolic function. *J Am Coll Cardiol* 1997; **30:** 474–480.

A-35

Myocardial strain and strain rate during aortic valve replacement: Evaluation by transoesophageal myocardial tissue velocity imaging

E. Sloth, T.F. Pedersen, C. Lindskov, I.K. Severinsen, M.B. Jensen

Dept. of Cardiothoracic Anaesthesiology, Skejby Sygehus, Aarhus University Hospital, Aarhus, Denmark

Introduction: During cardiac surgery procedures it is of paramount importance to monitor cardiac function. For example, in aortic valve replacement, changes in preload, afterload, contractility and diastolic function can be highly unpredictable. Tissue velocity imaging (TVI) and derived parameters such as strain (ε) and strain rate (SRI) have recently been proved to provide quantitative measures on myocardial contractility [1]. We hypothesized that changes in LV contractility due to altered loading conditions could be assessed by ε and strain rate. The aim of this study was to assess radial myocardial ε and SRI during weaning from cardiopulmonary bypass (CPB) in patients undergoing aortic valve replacement.

Method: Eight patients were studied using a Vivid 7 echo machine and dedicated software (GE-Ultrasound, Horten, Norway). From the transgastric short axis view TVI raw-data from three consecutive sinus beats was obtained and digitally stored for off-line analysis. TVI data was collected at five different times: (1) before (CPB), (2) on full CPB just before weaning, (3) on CPB with flow reduced to half of full flow, (4) immediately coming of CPB and (5) approximately 1 h later in the ICU. Radial anterior wall ε and SRI were determined from TVI colour maps by one experienced observer blinded to the time of data collection.

Student's t-test was used for comparison of data from different times and $P < 0.05$ was considered statistically significant.

Results:

Table 1. Pooled data for the five different times (1–5).

	1	2	3	4	5
Strain (%)	23	6	12	15	23
Strain rate (1/s)	1.03	0.16	1.00	1.17	1.3

There was an almost linear increase in ε and SRI during weaning from CPB. With (1) as reference value, ε was significantly reduced at time (2), (3) and (4) whereas SRI was only significantly reduced at time (2). ε and SRI reached the reference value in the ICU at time (5) one hour after coming off CPB, corresponding to time (5).

Discussion: Differentiating between volume load and contractility based on quantitative measures is essential for correct treatment of the haemodynamically unstable patient. Both ε and SRI showed a marked increase during loading of the LV. This study, although with a limited number of patients, shows that myocardial ε and SRI can be assessed from TOE and TVI colour maps. Volume loading seems to improve contractility in terms of increasing values of e and SRI. Further studies should be undertaken to assess the full merit of TVI and derived parameters as objective measures of myocardial contractility.

Reference:

1 D'hooge J, Heimdal A, Jamal F, *et al*. Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. *Eur J Echocardiogr* 2000; **1:** 154–170.

A-36

Substernal epicardial echocardiography imaging technology (SEE IT™): clinical evaluation of a new imaging technique in the postoperative cardiac surgical patient

J. Lai, M. Veltman, A. Kumar, L. Cope

Department of Anaesthesia, Westmead Hospital, Sydney, New South Wales, Australia

Introduction: A recent advance in the postoperative monitoring of the cardiac surgical patient has been the development of a

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mediastinal drain that incorporates a portal for substernal epicardial echocardiography. The SEE IT™ provides superior images when compared to transthoracic echocardiography (TTE) but with more convenience than transoesophageal echocardiography (TOE) [1,2]. The safety and utility of the technique was assessed in terms of its ability to examine ventricular function and measure haemodynamic variables.

Method: The SEE IT™ cannula was inserted in 25 consecutive adult cardiac surgical patients after obtaining ethics committee approval and written informed consent. An epicardial echocardiogram was performed postoperatively in the intensive care unit in the first 24 h. An adult Hewlett Packard Agilent 5 MHz multiplane TOE probe was inserted via the SEE IT™ sleeve. 2-D echocardiographic views were standardized into 4 positions and graded according to image quality. Ventricular function was assessed and fractional shortening calculated. Haemodynamic data were compared to pulmonary artery (PA) catheter and thermodilution cardiac output.

Results: Good 2-D echocardiographic views were obtained with the 4 standard views graded as sufficient for diagnosis in 23/25 patients (92%). Ventricular function was able to be assessed in 23/25 patients (92%) and found to be subnormal in 10/23 patients (43%). Estimated PA pressure by Doppler ultrasound correlated well with PA catheter recordings. No major complications occurred. Patients required minimal sedation with 65 mg being the average propofol dose for the procedure

Figure 1. Substernal 2D short axis view of the left ventricle.

Conclusions: Substernal epicardial echocardiography can be easily used in a standardized, reproducible manner to assess the postoperative ventricular function of cardiac surgical patients. We agree with previous studies [1,2] that the SEE IT™ combines the ease and safety of TTE with the excellent image quality of TOE.

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1 Furnary AP, Siqueria CJr, Lowe RI, *et al*. Initial clinical trial of substernal epicardial echocardiography: SEEing a new window to the postoperative heart. *Ann Thorac Surg* 2001; **72:** S1077–1082.

2 Hanlon JT, Lowe RI, Funary A. Substernal epicardial echocardiography: a new ultrasonic window to the postoperative heart. *J Am Soc Echocardiogr* 2000; **13:** 1335–1338.

A-37

Cardiac output measurement by pulse dye densitometry in cardiac surgery: validation against a reference technique of known accuracy

W. Baulig, E.O. Bernhard, D. Bettex, D. Schmidlin, E.R. Schmid

Division of Cardiovascular Anaesthesia, University Hospital of Zurich, Zurich, Switzerland

Introduction: Controversial results have been published regarding accuracy of cardiac output (CO) determination with pulse dye densitometry (CO-PDD). It was the aim of this study to validate CO-PDD in patients prior to and after coronary artery bypass grafting (CABG) against a reference method of known accuracy [2].

Method: Twenty-eight patients, age 47 to 81 (mean 62) years, male/female 24/4, scheduled for CABG surgery were included. After induction of anaesthesia, CO was assessed by bolus thermodilution (BCO), using 3 to 5 bolus injections of iced saline, and CO-PDD was measured in duplicate immediately thereafter, using a finger clip and 5 mg of indocyanine green. Measurements were repeated 3 to 24 h after admission to the intensive care unit (ICU). Agreement between mean BCO and CO-PDD values was assessed by Bland Altman analysis.

Results: One patient was excluded because of low preoperative pulsation amplitude for CO-PDD. Preoperative mean CO was 3.79 (range 2.37 to 6) $L\,min^{-1}$ for BCO and 3.38 (range 1.69 to 5.45) $L\,min^{-1}$ for CO-PDD. Mean bias was -0.42, limits of agreement ($\pm$2SD) were $\pm 1.91\,L\,min^{-1}$, and 2SD/mean BCO was 50.3%. CO data obtained in the ICU were not analysed because CO-PDD signals were low or absent in $>$40% of the patients.

Conclusion: CO-PDD is inaccurate in anaesthetized patients prior to CABG surgery. The observed underestimation in the low CO range is in accordance with other investigators [1,3] who evaluated agreement between BCO and CO-PDD in a cardiac surgical [3] or mixed ICU [1] patient population. Furthermore, a high incidence of low or missing CO-PDD signal amplitude was observed by us and others [3] in cardiac surgical ICU patients.

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A-38

Myocardial electrical impedance is correlated to coronary artery blood flow in humans

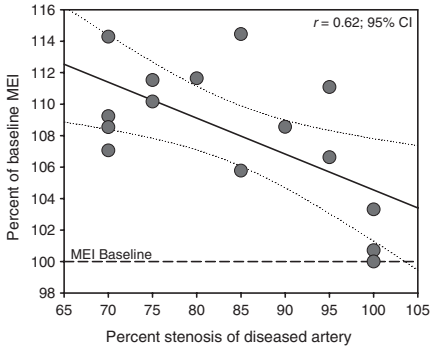
M.B. Howie, R. Dzwonczyk, C.L. del Rio

The Ohio State University, Columbus, OH, USA

Introduction: Myocardial electrical impedance (MEI) has been correlated to ischaemia and reperfusion of the heart muscle [1]. However, the mechanism behind the MEI changes under ischaemia is not clear. We studied the relationship between MEI and the degree of pre-operative coronary stenosis in patients undergoing off-pump coronary artery bypass (OPCAB) surgery, with the objective of shedding light on the subject.

Method: With institutional/FDA approval and informed consent, MEI was measured using a monitor previously described [1] on fifteen patients undergoing the OPCAB procedure. MEI readings were obtained from the distribution region of the targeted vessel (14 LAD, 1 RCA) during its occlusion/reperfusion, and were normalized by its baseline value (per patient). The normalized MEI change resulting from occlusion and the reported pre-operative stenosis were correlated. Significance was tested by two-tailed *t*-test and $P < 0.05$ was considered significant.

Results: As expected, MEI increased with occlusion of the targeted vessel, and decreased with its reperfusion. According to preoperative angiographic records, the degree of stenosis on the coronary artery targeted for bypass ranged between 70% and 100%. We discovered a significant ($P < 0.05$) relationship between the MEI increase and these values (see figure).



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Discussion: Our results suggest not only that the volume of conductive tissue, namely blood, in the myocardium plays an important role on the MEI changes observed during ischaemia, but also that MEI may be a predictor of myocardial damage occurring during surgical revascularization. We observed no MEI change in patients with total coronary stenosis, suggesting that in these patients, the myocardium was being perfused by collateral circulation and therefore, was not affected by surgical occlusion.

Reference:

1 Howie MB, Dzwonczyk R, McSweeney TD. An evaluation of a new two-electrode myocardial electrical impedance monitor for detecting myocardial ischemia. *Anesth Analg* 2001; **92:** 12–18.

A-39

Clinical significance of a new Q wave after cardiac surgery

G. Crescenzi, T. Bove, M.G. Calabrò, F. Pappalardo, C. Rosica, D. Mamo, G. Aletti, A. Zangrillo

Department of cardiac anesthesia and intensive care, San Raffaele Hospital – Vita e Salute University, Via Olgettina 60, Milan. Italy

Introduction: The recent findings in both the BARI and EAST trials showed a higher rate of Q-waves after CABG than after PTCA [1,2]. It has been questioned whether Q-waves after CABG and after PTCA represent a similar cardiac event. The aim of this study was to assess the clinical significance and the prognostic value of a new Q-wave after cardiac surgery, correlating the appearance of a Q-wave with the release of myocardial necrosis biochemical markers and with patient postoperative outcome.

Method: From April to June 2002 we prospectively evaluated 218 consecutive patients who underwent cardiac surgery. A twelve-lead ECG was performed preoperatively, immediately on admission to the intensive care unit, after 4 h, and every day until discharge. ECGs were read by cardiologists without knowledge of the patients' cardiac enzyme levels. A new Q-wave was defined as the appearance of a Q-wave $\geqslant$40 ms in at least two adjacent leads. The loss of R amplitude in precordial leads is considered equivalent to a Q wave. Blood samples were drawn at the same time and levels of troponin I (cTnI) and creatine kinase-MB (CK-MB) were assayed. We defined a cardiac event as a myocardial infarction or a ventricular dysfunction that required intra-aortic balloon pumping or inotropes for $>$12 hours in patients considered to be not at high risk preoperatively.

Results: Among 218 patients 15 (6.8%) presented with a new Q-wave after CABG. Within this group 7 patients (3.2%) had a raised biochemical marker (CK-MB and cTnI) and 8 patients did not. Six of these 8 patients had an old myocardial infarction before surgery without electrocardiographic evidence of Q-waves on the preoperative ECG. The distribution of new Q-waves in these patients was always in the inferior leads (D2, D3, aVF). A new Q-wave alone was not associated with postoperative cardiac events. The stratification of patients by peak cTnI was highly predictive of cardiac events (Table 1). Multivariate analysis confirmed that this effect was independent of ECG Q wave criteria for myocardial infarction.

Table. Troponin I (ng mL^{-1}) and Q waves as predictors of postoperative cardiac events.

Troponin I $\leqslant$ 11		Troponin I $>$ 11	
No Q wave (n = 134)	Q wave (n = 8)	No Q wave (n = 69)	Q wave (n = 7)
8.2	0.0	21.7	85.7

Discussion: The appearance of new Q-wave after cardiac surgery has little influence on short term clinical outcome [3]. Several authors reported the resolution or disappearance of perioperative Q-waves. These findings may be due to the recovery of stunned myocardium or the resolution of oedema. In addition, revascularization of ischaemic myocardium may 'unmask' a pre-existing MI in the vectorially opposite myocardium.

References:

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A-40

Which patients should undergo duplex carotid screening prior to coronary artery surgery?

V. Aboyans, P. Lacroix, C. Chauvreau M. Sellami, S. Karoutsos, V. Vrba, E. Cornu, M. Laskar

Department of Thoracic and Cardiovascular Surgery, Dupuytren University Hospital, Limoges, France

Introduction: Despite surgical techniques and medical care improvements, the rate of stroke after coronary bypass artery grafting (CABG) remains stable, mainly due to the ageing of the candidates and a growing prevalence of patients with multifocal atherosclerosis. Around half of these postoperative events are due to the high incidence of cerebrovascular disease in these patients [1,2]. We aimed to detect the risk factors for the presence of significant carotid lesions in these patients in order to optimize the screening.

Method: We prospectively studied 1043 consecutive patients undergoing CABG. A first subgroup of 825 patients was studied to establish the predictive model. In addition to their clinical and coronary angiography data, the results of physical examination and ankle-brachial index (ABI) measurements were noted. Next they benefited from a systematic Duplex study. Those with an artery stenosis $>$50% were considered as having a significant lesion. A multivariate analysis by logistic multiple regression was then performed to determine significant risk factors. The following 218 patients benefited from the same assessment protocol, and the ability of the model to predict $>$50% stenosis of the neck arteries has been assessed, compared to Duplex data.

Results: Among the first 825 patients, 108 (13.1%) had at least one significant lesion in their neck arteries. The independent risk factors were: past history of stroke or transient ischaemic attack, neck bruit, patent peripheral arterial disease (PAD), subclinical PAD (ABI $<$ 0.85), and age $>$70 yr. Neck auscultation alone had a poor sensitivity (23%). Among the subsequent 218 patients, the presence of at least one of these factors was able to detect 24 out of 26 (92.3%) patients with a significant stenosis, and could rule out 41% of them from a systematic Duplex screening. The overall sensitivity of this approach is 90%, with a negative predictive value of 96%, permitting a dramatic reduction in the number of Duplex assessments, by excluding low-risk patients.

Discussion: The excellent sensitivity of this risk assessment approach, enhanced by the use of a bedside ankle-brachial index measurement, is able to perform a cost-effective screening for cerebrovascular disease in CABG patients.

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2 Birincioglu CL, Bayazit M, Ulus AT, *et al*. Carotid disease is a risk factor for stroke in coronary bypass operations. *J Card Surg* 1999; **14:** 417–423.

A-41

Age related difference in effect of phenylephrine on femoral and radial artery systolic and pulse pressures

Y.L. Kwak, Y.J. Oh, J.H. Lee, H.K. Shinn, M.O. Kim, Y.W. Hong

College of Medicine, Yonsei University, Seoul, Korea

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Introduction: The radial artery is the most commonly used monitoring site for arterial pressure. However, it has been known that radial artery pressure (RAP) sometimes underestimates the central pressure [1] and femoral artery pressure (FAP) is known to more accurately reflect ascending aorta pressure in those circumstances. In many studies, FAP and RAP have been considered as central and peripheral artery pressures, respectively and there might be a possibility that age and peripheral vasoconstriction exert different effects on FAP and RAP. This study evaluated the effect of phenylephrine (Phe) on FAP and RAP and the change of pulse pressure (PP) in different age groups.

Method: With IRB approval, 51 patients without cardiovascular diseases, 26 patients younger than 25 yr (Y) and 25 patients older than 50 yr (O) were enrolled in this study. Radial and femoral arteries were cannulated with the same size 4.8 cm, 20 gauge angiocatheters. When FAP decreased by 30% below pre-anaesthetic values (Pre-A) after induction of anaesthesia, Phe was infused to raise FAP by 20% above values before Phe infusion. Heart rates, FAP and RAP were recorded before anaesthesia, before and after Phe infusion. Statistical analysis was performed by using Student's *t*-test. *P* values less than 0.05 were considered as statistically significant.

Results:

	Group Y			Group O		
		Phe			Phe	
	Pre-A	Before	After	Pre-A	Before	After
Systole-FAP	131 ± 11†	101 ± 13	127 ± 4†	150 ± 20	113 ± 14†	144 ± 19†
Systole-RAP	137 ± 16	100 ± 13	122 ± 16	146 ± 91	107 ± 11	137 ± 19
Diastole-FAP	71 ± 6	59 ± 7	80 ± 9†	76 ± 10	67 ± 10†	85 ± 4†
Diastole-RAP	70 ± 6	59 ± 8	78 ± 9	76 ± 10	66 ± 9	84 ± 13
Mean-FAP	93 ± 8†	75 ± 9†	97 ± 10†	103 ± 12	85 ± 11†	108 ± 15†
Mean-RAP	91 ± 7	72 ± 9	94 ± 11	101 ± 12	82 ± 10	104 ± 15
PP-FAP	60 ± 9†	42 ± 8	47 ± 8†‡	74 ± 13*	47 ± 7	59 ± 9*†‡
PP-RAP	67 ± 15	41 ± 10	44 ± 10‡	70 ± 13	4 ± 8	53 ± 10*‡

*$P < 0.05$ compared with Group Y, †$P < 0.05$ compared with RAP, ‡$P < 0.05$ compared with before-Phe.

Conclusions: Pressures and PP of FAP and RAP did not reveal a theoretical relationship of a central and peripheral arterial pressure in adult patients without cardiovascular diseases [2], though FAP has been known to reflect aortic pressure more accurately than RAP. RAP seemed to be accurately reflecting the change of FAP in the use of Phe.

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Cardiopulmonary Bypass and OPCAB

A-42

Mannitol in the bypass prime does not modify renal tubular function

K. Yallop, S. Twyman[1], A. Tang, D. Smith

Wessex Cardiothoracic Centre and [1]Dept of Biochemistry, Southampton General Hospital, Southampton, England

Introduction: Renal dysfunction occurs in 2–5% of adult patients following cardiopulmonary bypass (CPB), causing significant morbidity and mortality of 10–20% [1]. Mannitol is often added to the CPB prime to reduce renal damage, but previous studies using mannitol have produced conflicting results.

Method: In a double-blind, randomized, controlled trial in 40 cardiac surgical patients with normal renal function, 20 patients had 5 mL kg^{-1} of 10% mannitol in the CPB prime, while 20 had an equivalent volume of Hartmann's solution. Standard CPB prime was with Hartmann's solution 1000 ml, gelofusine 500 mL and 5000 iu heparin. Blood and urine samples were taken on admission (baseline), on arrival in the ITU and for 5 postoperative days for measurement of plasma urea and creatinine, urinary creatinine, microalbumin and retinol binding protein (RBP) [2]. Urinary microalbumin and RBP were indexed to urine creatinine, to indicate renal glomerular and tubular damage respectively.

Results: The two groups were similar in terms of pre-operative variables. There were no significant differences between mannitol and control patients for urine output, fluid balance, plasma creatinine or urea, or urinary microalbumin or RBP indexed to creatinine.

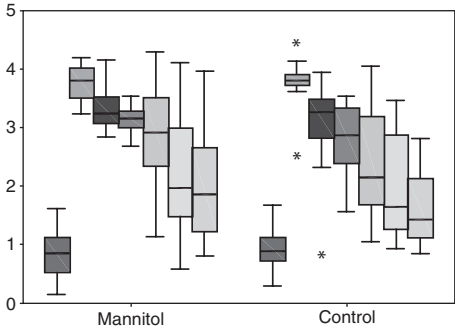

Figure: Log_{10} urinary RBP:creatinine index from baseline to post-operative day five in the two study groups.

Discussion: Mannitol has little impact on indices of renal function in patients with normal pre-operative plasma creatinine, and its routine use should therefore be reconsidered.

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A-43

Effectiveness of fenoldopam for patients undergoing cardiac surgery on cardiopulmonary bypass

L. Piaia., B. Persi., A.M. Camata., V. Salandin

Treviso Regional Hospital, Treviso, Italy

Introduction: Patients undergoing cardiac surgery on cardiopulmonary bypass (CPB) are prone to renal impairment from a period of uneven perfusion. The consequence is fluid retention leading to poor pulmonary postoperative function. Fenoldopam, a selective agonist at DA_1 receptors, acts on the smooth muscles of peripheral arteries (splanchnic, coronary and renal) causing their relaxation and subsequent vasodilatation. The aim of our study was to verify the usefulness of fenoldopam in preserving renal function and enhancing urine output after CPB in patients with normal renal function. The study was blinded with a placebo control group.

Method: Patients with normal serum creatinine undergoing CPB were randomly divided in two groups: 15 (group F) were treated with fenoldopam 0.03–0.08 μg kg^{-1} min^{-1} from the induction of anaesthesia, 13 (group C) were not treated. Infusion lasted for 24 h. Exclusion criteria were impaired renal function and low output syndrome before or after surgery. Creatinine clearance, serum creatinine, BUN, serum and urine electrolyte levels were measured before surgery and after 24 h. During surgery and the following 24 h the mean arterial pressure was maintained at 60–80 mmHg with fluid administration and/or inotropic support if necessary, right atrial pressure was maintained at 8–10 mmHg and haemoglobin level was maintained at 9–10 gm dL^{-1}. After CPB, at the end of the operation and after 24 h, blood losses, urine output and fluid infusions were recorded. Demographic and haemodynamic data, data regarding the total fluids balance and renal function indices were analysed using Student's *t*-test.

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Results: The main results are shown in the table. The total urine output after 24 h was statistically higher for group C ($P < 0.05$). Fluid administration during and after surgery and total fluid balance were similar in both groups.

	Group F	Group C	*P*
Preoperative creatinine (μmol L^{-1})	84.9 ± 10.6	82.2 ± 30.0	ns
Postoperative creatinine (μmol L^{-1})	98.1 ± 21.1	79.6 ± 29.2	ns
Preop BUN (mmol L^{-1})	6.3 ± 1.9	6.89 ± 2.6	ns
Postop BUN (mmol L^{-1})	6.76 ± 3.1	6.94 ± 2.3	ns
Preop creatinine clearance (mL min^{-1})	73.6 ± 18.6	74.8 ± 24.2	ns
Postop creatinine clearance (mL min^{-1})	76.4 ± 45.3	75.4 ± 29.1	ns
Diuresis during CPB (mL)	601 ± 317	523 ± 479	ns
24 h fluids given (mL)	9837 ± 1661	9693 ± 1644	ns
24 h diuresis (mL)	2633 ± 669	3609 ± 1523	<0.05

Discussion: Our hypothesis on the ability of fenoldopam to promote a negative fluids balance after cardiac surgery was not confirmed. The renal function parameters and total urine output did not show substantial differences between the two groups. Small differences in favour of group F during CPB and group C after surgery could be simply due to the restricted number of patients. The similarity of fluids balance and haemodynamic data in the two groups shows that the employment of fenoldopam at renal concentrations did not lower arterial blood pressure. The results cannot be extrapolated for patients with impaired renal function.

Reference:

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A-44

To which extend is anaemia tolerated on cardiopulmonary bypass?

F. Toraman, H. Karabulut, B. San, E. Demiray, S. Tarcan, C. Alhan

Acibadem Kadikoy Hospital, Istanbul and Mustafa Kemal University, Hatay, Turkey

Introduction: Most cardiac surgery is conducted on cardiopulmonary bypass (CPB) with a haematocrit of 0.20 to 0.25. However under special conditions, haematocrit values as low as 0.15 may be experienced. The purpose of this study was to compare the outcome of the patients with low and normal haematocrit levels on CPB.

Method: Of the 1280 consecutive patients undergoing isolated on pump (moderate hypothermia) coronary artery bypass grafting, 67 experienced a haematocrit of 0.20 or less (0.13–0.20) during CPB. These patients were compared for outcome with 1213 patients with a haematocrit of more than 0.20.

Results: Risk factors for low haematocrit on CPB were preoperative low haematocrit ($P = 0.001$), female gender ($P = 0.001$), age >70 ($P = 0.007$), insulin dependent diabetes ($P = 0.009$), and preoperative use of diuretic agents ($P = 0.003$). The incidence of postoperative complications (eg. stroke, renal failure, infection, pulmonary complications) were similar in the two groups.

	Low Hct ($n = 67$)	High Hct ($n = 1213$)	*P* value
Preoperative mean Hct (%)	35.9 ± 4.7	40.9 ± 5.2	0.0001
Mean lowest Hct during CPB (%)	18.3 ± 1.8	27 ± 3.9	0.0001
Postoperative mean Hct (%)	24.9 ± 3.2	31.5 ± 4.4	0.0001
Fluid balance end of operation (mL)	167 ± 579	46 ± 565	0.02
ICU stay (h)	22.5 ± 17	21.8 ± 13.5	ns
Length of hospital stay (d)	5.7 ± 1.6	5.4 ± 2.2	ns
RBC transfusion (IU/pt)	0.4 ± 0.8	0.4 ± 0.8	ns
Mortality (%)	0	0.98	ns

Conclusions: Low haematocrit (0.15–0.20) on CPB is usually transient and well tolerated in patients undergoing CABG. Aggressive transfusion should be avoided in case the pump flow is adequate

A-45

Propionyl-L-carnitine reduces pulmonary artery pressure after CABG in diabetic patients

R. Lango[1] J. Rogowski[2], R. T. Smolenski[3], J. Siebert[2], M. Wujtewicz[1], W. Łysiak-Szydłowska[4]

[1]Department of Anaesthesiology, [2]Department of Cardiac Surgery [3]Department of Biochemistry, [4]Department of Clinical Nutrition, Gdansk, Poland

Introduction: L-carnitine (LC) and its derivatives protect cardiac metabolism and function in myocardial ischaemia by increasing glucose metabolism and reducing the toxic effects of long-chain acyl-CoA. Propionyl-L-carnitine (PLC) inhibits production of free hydroxyl radicals, protects endothelial cellular membranes, and possibly limits endothelin action.

Method: 70 diabetic patients with ejection fraction not exceeding 50%, scheduled for CABG with the use of CPB, were included in the randomised double-blind study. 12 patients with perioperative myocardial infarction or IABP were excluded from further analysis. Patients were administered intravenously either 20 mg kg^{-1} b.w. of LC (group A), PLC (group B), or placebo (group C) within 12 h before the operation. Cardiac output was measured by thermodilution after opening the sternum, 45 min after weaning from CPB, and at 6, 12, and 24 h after finishing the operation. Haemodynamic parameters after CPB were analysed with two-way ANOVA (time, group).

Results: We observed significant difference in mean pulmonary artery pressure (MPAP; $P = 0.035$) and cardiac index (CI; $P = 0.036$) between the groups, with lower MPAP and higher CI observed in B. MPAP increased in time ($P = 0.001$). CI, MPAP, stroke index (SI), mean arterial pressure (MAP) systemic vascular resistance index (SVRI) are presented in the table (Mean (SD)).

Time		Baseline	45 min	6 h	12 h	24 h
CI (L/m^2)	A	2.8 (0.6)	3.2 (0.6)	3.0 (0.6)	3.1 (0.7)	3.1 (0.6)
	B	2.9 (0.4)	3.2 (0.6)	3.4 (0.7)	3.7 (0.8)	3.2 (0.7)
	C	2.7 (0.6)	2.8 (0.7)	3.0 (0.6)	2.9 (0.7)	3.1 (0.7)
MPAP (mmHg)	A	18.3 (5.8)	20.4 (3.5)	22.0 (4.4)	22.6 (4.4)	24.3 (5.2)
	B	16.7 (2.8)	18.7 (2.4)	19.9 (2.7)	20.6 (3.8)	21.8 (4.0)
	C	16.6 (4.3)	19.6 (2.9)	23.4 (3.9)	22.8 (4.2)	24.0 (5.1)
SI (mL/m^2)	A	38.0 (9.9)	35.0 (5.8)	34.4 (7.2)	35.4 (9.4)	36.1 (6.5)
	B	37.4 (5.2)	36.1 (7.9)	36.7 (6.2)	39.8 (7.6)	37.0 (5.2)
	C	34.5 (8.3)	31.4 (8.6)	33.7 (7.8)	33.8 (8.9)	34,2 (5.8)
MAP (mmHg)	A	80.8 (11.2)	79.0 (10.1)	78.9 (12.4)	80.0 (8.2)	81.7 (11.9)
	B	79.1 (8.8)	81.4 (8.9)	75.5 (7.7)	80.6 (9.0)	75.1 (8.8)
	C	79.5 (9.2)	76.9 (10.2)	75.8 (11.2)	77.8 (10.1)	80.0 (10.5)
SVRI (dyn·s cm^{-5}m^{-2})	A	2201 (526)	1859 (526)	1877 (456)	1858 (390)	1845 (481)
	B	2087 (375)	1852 (402)	1571 (354)	1604 (301)	1665 (286)
	C	2354 (534)	2050 (607)	1796 (405)	1973 (634)	1849 (455)

Discussion: Limiting the increase of PAP by PLC administration may offer an attractive supplementation to the treatment of pulmonary hypertension and right ventricular failure after cardiac-surgery. Its mechanism may include reduced neutrophil activation observed during PLC treatment of peripheral ischaemia [1].

Reference:

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A-46

SMA treated bypass circuits improve perfusion pressure following initiation of cardiopulmonary bypass

S.J Allen, S.P. Penugonda, S.W. MacGowan, M.A. Armstrong, T.J. McMurray, W.T. McBride

Departments of Anaesthesia and Immunobiology, Queens University, Cardiac Surgical Unit, Royal Victoria Hospital, Belfast, Northern Ireland, UK

Introduction: Falls in blood pressure following initiation of cardiopulmonary bypass (CPB) have been attributed to expression of

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bradykinins [1]. The introduction of biomaterials incorporating a copolymer into the bypass surface (Surface Modifying Additives SMA) reduces platelet adhesion and preserves blood pressure on CPB [2]. Since then, patients increasingly present for surgery on vasodilators such as ACE Inhibitors. We wished to see whether the use of SMA treated circuits in a randomly recruited population of patients, would preserve blood pressure on CPB.

Method: Forty ASA grade III–IV patients undergoing elective coronary artery bypass grafting were randomly allocated to SMA or non-SMA CPB circuits. Baseline mean arterial pressure (MAP) and MAP at 1–10 min following institution of CPB were measured via the radial artery. Phenylephrine was administered according to a local protocol and the total dose recorded. Results were assayed using *t* test between groups, $P < 0.05$ was considered significant. Subgroup analysis was performed on the basis of preoperative ACE inhibition (ACEI or non-ACEI).

Results: Twenty-one patients used ACEI (11 SMA: 10 control) Mean arterial pressure varied as in Figure 1. MAP was significantly higher in the SMA group at 6 and 9 min following institution of CPB. In the subgroup of patients using ACEI preoperatively ($n = 21$) those patients in the SMA group ($n = 11$) demonstrated significantly higher BP at 6, 7 and 9 minutes after CPB compared with control ($n = 10$).

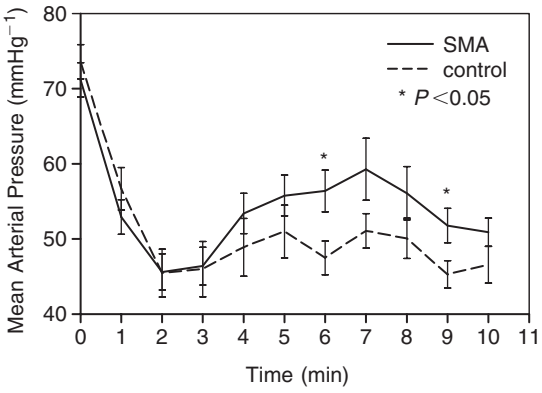

Figure 1. Bar graph showing alteration in mean arterial pressure over time in SMA and control groups ($n = 40$ i.e all patients irrespective of ACEI status). Bars show mean and standard deviation.

Discussion: SMA treated circuits resulted in amelioration of the drop in perfusion pressure after institution of CPB. This phenomenon was particularly important in the subgroup of patients receiving ACE inhibitors. Our work suggests that in the modern patient population where preoperative therapy renders CPB hypotension common, SMA circuits may be beneficial.

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A-47

The effect of methylene blue on cortisol levels in treatment of hypotension at the initiation of and after cardiopulmonary bypass in dogs

N. Yapici, A. Tarhan, T. Coruh, F. Yapici, Y. Aslan, A. Özler, Z. Aykac

Siyami Ersek Cardiovascular and Thoracic Surgery Center, Haydarpasa, Istanbul, Turkey

Introduction: Initiation of CPB is usually accompanied by a fall in mean arterial pressure and an increase in catecholamines, which combined with haemodilution, affect peripheral perfusion. We hypothesized in this experimental study that methylene blue (M), a cGMP inhibitor, can be an alternative to phenylephrine for treatment of this hypotensive situation [1].

Method: After ethics committee approval 12 dogs were divided into two groups: Group M, methylene blue and group P, phenylephrine. After sedation of the dogs with ketamine they were anaesthetized (sodium pentobarbital, 30 mg kg^{-1} intravenously), intubated, and mechanically ventilated with oxygen in air. A femoral artery and vein were cannulated. After a median sternotomy, a pulmonary artery catheter was inserted via the jugular vein. All dogs were anticoagulated with heparin. After cardiac cannulation CPB was initiated. When blood pressure fell below 40 mmHg we gave the Group M 2 mg kg^{-1} methylene blue, and group P 10 μg kg^{-1} phenylephrine. Blood samples were withdrawn at the times: T0, before CPB, T1, at the initiation of CPB (before the drug) and T2 15 min after CPB. Statistical analysis were made with ANOVA and Student's t-test.

Results:

	T0	T1	T2
Blood Pressure (mmHg)			
Group M	85 ± 12	30 ± 9°	80 ± 14°
Group P	90 ± 22	32 ± 6°	60 ± 12*°
Cortisol level (mic dL^{-1})			
Group M	1.49 ± 0.21	0.46 ± 0.03°	1.17 ± 0.24°
Group P	1.34 ± 0.18	0.39 ± 0.02°	3.27 ± 1.06°*

Data expressed mean ± SEM; °$P < 0.05$ in group; *$P < 0.05$ between groups.

Discussion: Hypotension is a major systemic side effect during cardiopulmonary bypass (CPB), especially at normothermia. The cause of the observed hypotension may be due to an initial haemodilution of the circulating catecholamines by the pump-priming solution. Methylene blue was used by Yiu to reverse refractory hypotension after CPB [2]. As shown in the table methylene blue did not increase the cortisol levels as much as phenylephrine. In accordance with these data we concluded that methylene blue can be used as an alternative drug to treat hypotension.

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A-48

Endothelial dysfunction and acute lung injury during cardiopulmonary bypass in pigs is prevented by inhaled nitric oxide

A. Ruiz, I. Rovira, J. Martínez, C. Ayats[1], S. Acero[1]

Departament d´Anestesiologia i Reanimació i [1]IMCV, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain

Introduction: Cardiopulmonary bypass (CPB), mandatory in many cases of cardiac surgery, activates a multifactor systemic inflammatory response leading to endothelial dysfunction. In the lung, one of the most important target organs, endothelial dysfunction increases vascular permeability and induces alveolar oedema, hypoxaemia and pulmonary hypertension (PHT) [1]. Inhaled nitric oxide (iNO) a selective pulmonary vasodilator, ameliorates hypoxaemia and reduces PHT in many clinical settings [2]. Endogenous NO is reduced after CPB [3]. We investigated the effects of iNO on endothelial dysfunction and acute lung injury in an acute experimental model of CPB.

Method: Twelve anaesthetized and mechanically ventilated pigs were studied in two groups of six: Group 1 (control) and group 2 (iNO). All animals were on CPB for 2 h. Group 1 received no treatment and group 2 received 5–8 ppm of iNO before, during (NO gas flow was added to the gases of the oxygenator) and after CPB.

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Endothelial function was assessed by measuring the change in pulmonary vascular resistance induced by acetylcholine (endothelial-dependent relaxation) and by sodium nitroprusside (endothelial-independent relaxation). Acute lung injury was assessed by measuring arterial blood-gases and pulmonary haemodynamics. All measurements were performed before and after 2 h of CPB.

Results: Endothelial-dependent and independent relaxation, PaO_2, and mean pulmonary artery pressure are shown in the table.

	Group 1		Group 2	
PVR change	Before	After CPB	Before	After CPB
ACH (%)	−31 ± 27	$^{+}$8 ± 7*	−34 ± 21	−20 ± 31#
SNP (%)	−33 ± 3	−26 ± 9	−26 ± 30	−36 ± 16*
PaO_2 (kPa)	28.5 ± 3.1	12.5 ± 1.5*	30.3 ± 5.1	28.8 ± 4.4#
mPAP (mmHg)	18 ± 2	23 ± 2*	16 ± 3	15 ± 3#

Mean ± SD, ANOVA & Bonferroni, *$P < 0.05$ vs before, # vs. group 1; ACH (acetylcholine), SNP (sodium nitroprusside)

Discussion: Two hours of CPB induced a lack of response of endothelium to acetylcholine, a profound decrease in PaO_2 and an increase in mean PAP. These effects were totally avoided by iNO. Therefore, short-term iNO administration in this experimental model of CPB prevented endothelial dysfunction and the subsequent PHT and hypoxaemia.

References:

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A-49

Nitric oxide during CPB

L. Mantovani, C. Gerli, G. Aletti[1], F. Pappalardo, G. Marino, A. Zangrillo

Department of Anesthesiology, Vita-Salute University of Milan, IRCCS San Raffaele Hospital; [1]Dpt. of Mathematics, University of Milan, Italy

Introduction: Nitric oxide (NO) is released by many human tissues, especially by the endothelium where it is synthesized from vascular wall receptors in response to pulse and shear stress. Minimal amounts of NO released in the bloodstream regulate the vascular tone. The aim of this study was to investigate the production of NO (through spectrophotometry) and its relation with hypotension during cardiopulmonary bypass (CPB).

Method: We studied 30 consecutive patients, EF > 30%, undergoing cardiac surgery with CPB. Data are expressed as mean ± SD. Exclusion criteria were represented by a low ejection fraction.

Results: Patients characteristics: age (63 ± 13 years), male/female ratio 2.75, weight (70 ± 10.8 Kg), β-blockers (10%), ACEI (36%), need of vasoconstrictor during CPB (40%), aortic cross-clamp duration (53 ± 14.2 min), CPB (73 ± 20.2 min). Values for NO and invasive mean arterial pressure (MAP) at time 1, 2, 3, 4 are shown in Table 1.

Table 1. showing NO and MAP values during surgery.

Time	NO (mmol L^{-1})	MAP (mm Hg)
OR arrival	1497 ± 1224	94 ± 15.5
Post-anaesthesia induction	1457 ± 1189	74 ± 13.2
Start CPB	905 ± 695	54 ± 15.9
15 min CPB	953 ± 761	71 ± 12.4
30 min CPB	1116 ± 684	57 ± 14.9
45 min CPB	1203 ± 718	73 ± 11.2
Weaning from CPB	1372 ± 623	70 ± 11.4
ITU arrival	742 ± 1117	80 ± 11.3

Internal temperature was 36.4 ± 0.5°C preop. and was lowered to 35.4 ± 0.9°C after 30 min of CPB and 36.9 ± 0.9°C at ICU arrival.

All patients had an uneventful outcome. Univariate analysis showed no relationship between NO and other preoperative variables with the exception of patient weight and NO ($P < 0.01$).

Discussion: Many factors are known to regulate the blood pressure during CPB. The hypothesis that intra-operative hypotension is mediated by incremental NO synthesis is not supported by the results of our study. Even so NO may still have an intracellular effect in smooth muscle though not reflected in extracellular concentration Our data showed no relationship between MAP and NO changes. The physio-pathologic mechanisms controlling arterial blood pressure during CPB remain indeterminate. Other vasoconstrictor agents (i.e. endothelin) could vary during this phase of the operation. MAP depends on an equilibrium between vasoconstrictors and vasodilator agents. More patients and the study of other mediators are probably needed to better understand this mechanism.

Reference:

1 Katz SD. Mechanisms and implications of endothelial dysfunction in congestive heart failure. *Curr Opin Cardiol* 1997; **12:** 259–264.

A-50

The effect of flow type during cardiopulmonary bypass on endotoxin core antibodies during and after cardiac surgery

T.J. Ridgway, D.J. Turfrey, N.P. Sutcliffe

HCI International Medical Centre, Glasgow, UK

Introduction: Pulsatile flow during cardiopulmonary bypass (CPB) has been shown to improve intestinal perfusion. Studies have shown lower levels of endotoxin in patients who receive pulsatile flow rather than continuous flow on CPB [1,2]. During endotoxaemia, levels of endotoxin antibodies fall. Low levels have been shown to correlate with a poor outcome [3]. This study aimed to assess the effect of different types of flow during CPB on the levels of IgM and IgG endotoxin core antibodies (EndoCAb) during and after cardiac surgery.

Method: Thirty one patients for elective coronary artery bypass grafting (CABG) were studied prospectively. Patients with a history of gastrointestinal disease were excluded. The patients were randomly allocated to receive either pulsatile ($n = 15$) or continuous ($n = 16$) flow during CPB. Anaesthesia for both groups was standardized using target controlled infusions of propofol and alfentanil. Blood samples were taken from the arterial line at 7 time points pre-operatively and within the first 24 h post ICU admission and assayed for levels of IgM and IgG EndoCAb. Statistical analysis was conducted using the Mann-Whitney rank sum test to compare the data from the two groups.

Results: There was no statistically significant difference in IgM or IgG EndoCAb levels at any time point between the two groups.

Table. IgM and IgG (mean values)

		Post CPB			
	Pre-op	30 min	*P*	24 h	*P*
IgM pulsatile	74.07	31.04	0.005	37.47	0.012
IgM continuous	54.66	25.17	0.003	28.23	0.005
IgG pulsatile	103.89	43.68	0.015	56.83	0.012
IgG continuous	125.27	70.61	0.003	80.25	0.005

These results show levels of both IgM and IgG EndoCAb fell significantly from baseline with the lowest levels occurring 30 min after the onset of CPB and not returning to pre-operative levels even 24 h post ICU admission.

Discussion: This study would suggest that pulsatile flow does not decrease the degree of endotoxaemia during CPB, as measured by a fall in the levels of EndoCAb. Levels fell in both groups in the first 24 h, probably due to endotoxaemia. However, other factors such as haemodilution on CPB may have contributed to the decrease. A prime of 1.5 l was used in the CPB pump which should lead to a fall in EndoCAb levels of approximately 25–30%. The reduction in levels that we measured were significantly reduced even taking this haemodilution into account.

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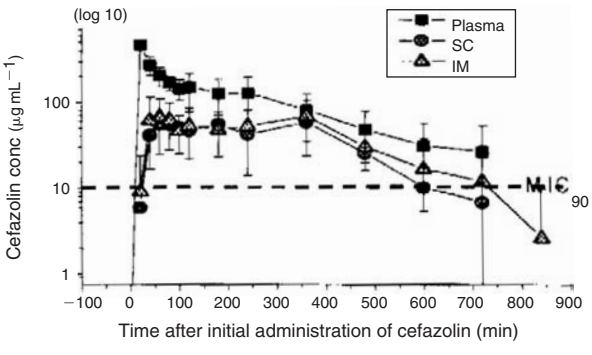
A-51

Plasma and interstitial concentrations of cefazolin during and after cardiopulmonary bypass

D. Hutschala[1], K. Skhirtladze[1], B. Mayer[2], M. Petsch[2], E. Gruber[1], M. Müller[2], E. Tschernko[1]

[1]Dept. of Cardiothoracic and Vascular Anaesthesia & Intensive Care; [2]Dept. of Clinical Pharmacology, Univ. of Vienna, General Hospital, Vienna, Austria

Introduction: Despite prophylactic antibiotic treatment, wound infections remain a severe problem after cardiac surgery (CS). This might be due to several reasons: (1) the antibiotic could be adherent to the tubing of the cardiopulmonary circuit, (2) changes in micro- and macrocirculatory blood flow, (3) increased volume of drug distribution due to intraoperative fluid resuscitation, and (4) capillary leak due to activated inflammatory mechanisms. This prospective, descriptive study aimed at gaining information on plasma and target site concentrations of cefazolin in patients undergoing CS.
Method: Cefazolin was administered for standard antibiotic prophylaxis in 12 patients undergoing elective CS, before skin incision (4 g), before start of extracorporeal circuit (2 g), and at the end of surgery (2 g). Unbound, i.e. microbiologically active concentrations of cefazolin were measured in the interstitial space of subcutaneous tissue (microdialysis probe #1) and muscular tissue (microdialysis probe #2) at regular intervals during and after surgery. Plasma concentration was evaluated simultaneously. Microdialysis is based on sampling of analytes from the extracellular space by means of a semi-permeable membrane of a microdialysis probe [1]. Data are mean ± SD.
Results: The average age of patients was 60 ± 12 years. Patients presented with a weight of 82 ± 12.6 kg and a height of 171.8 ± 7.8 cm. The interstitial concentration of cefazolin exceeded the MIC_{90} (minimal inhibitory concentration) for 550 min after administration of the initial dose (Figure). However, the maximum plasma concentration was about ten times higher compared to the highest interstitial concentration (467 ± 20.2 $\mu g\,mL^{-1}$ versus 57.4 ± 34.0 $\mu g\,mL^{-1}$) of cefazolin.



Conclusion: If cefazolin is administered in the above mentioned dose, prevention against wound infection should be sufficient during cardiac surgery for susceptible pathogens.
Reference:
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A-52

Systemic vascular resistance during rewarming from cardiopulmonary bypass determines post-operative hypothermia

C.D. Deakin, P. Picton

Shackleton Department of Anaesthetics, Southampton University Hospital, Southampton, UK

Introduction: Rewarming from the hypothermic phase of cardiopulmonary bypass requires delivery of thermal energy to both core and peripheral compartments [1]. Peripheral rewarming is slower than core because vasoconstriction limits peripheral blood flow and heat transfer. Systemic vascular resistance (SVR) is a marker of peripheral vasoconstriction and might be expected to be related to the efficiency of peripheral rewarming [2]. We examined the relation between SVR and the adequacy of rewarming in patients following pharmacological manipulation of the SVR.
Method: Patients were randomly assigned to receive sodium nitroprusside (SNP) during rewarming to maintain a mean arterial pressure (MAP) of 40 mmHg. In the remaining patients MAP was not altered pharmacologically during rewarming. SVR was calculated from the MAP and pump flow. Patients in the control group were subdivided into those administered ACE inhibitor (ACEI) therapy within 5 days of surgery. Post-operative hypothermia was assessed by measuring the coldest post-operative core temperature (tympanic) after seperation from CPB and time to passively rewarm to 37.0°C. Results are given as mean (± standard deviation).
Results: 120 patients were entered into the study, of whom 58 were administered SNP. Of the 62 remaining patients, 21 had received ACE inhibitors in the perioperative period (ACEI group) and the remainder formed the control group. Results were analysed using ANOVA. There was no significant difference in patient characteristics or thermal state prior to rewarming between groups. There was no difference in core temperature between groups on separation from CPB.

Table 1. SVR and temperature data: mean (±1SD).

	Control	ACEI group	SNP group	*P*
Mean SVR during rewarming (dyn s cm^{-5})	1194 (±329)	978 (±168)	768 (±81)	<0.001
Coldest post-operative temperature (°C)	35.0 (±0.8)	35.3 (±0.8)	35.6 (±0.6)	<0.0001
Time to rewarm to 37.0°C (min)	440 (±165)	312 (±133)	299 (±111)	<0.001

Discussion: SVR during rewarming was lowest in the SNP group, intermediate in the ACEI group and highest in the control group. Post-operative hypothermia was related to SVR, being greatest in the control group and least in the SNP group. Vasodilation is believed to improve peripheral rewarming and minimise the post-operative afterdrop in core temperature.
References:
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A-53

Minimally invasive cardiac surgery: a 5-year experience with 170 patients

G. Fita, I. Rovira, P. Matute, E. Greco, C. Barriuso, C. Gomar, C. Roux, J.L. Pomar

Departments of Anaesthesia and Cardiac Surgery, Hospital Clínic, Barcelona, Spain

Introduction: Port-Access™ system (Heartport Inc, Redwood City, CA) affords the convenience of cardiopulmonary bypass (CPB) and hypothermic cardiac arrest without requiring sternotomy. The aim of the present study was to describe our experience and to

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emphasize the usefulness of transoesophageal echocardiography (TOE).

Method: Between September 1997 and October 2002, 170 patients underwent cardiac surgery using Port-Access™ for mitral valve surgery. Both an 'endocoronary-sinus' catheter and an 'endopulmonary vent' catheter were inserted from the right jugular vein into the coronary sinus and pulmonary artery for retrograde cardioplegia and venting. A minimal (4–6 cm) anterior right thoracotomy was employed in all cases. We compared the total and anaesthetic time and the post-operative complications with 87 unselected patients undergoing standard sternotomy for mitral valve surgery (control group) during the same period. The paired Student's *t* test and Wilcoxon's test were used. $P < 0.05$ was considered statistically significant.

Results: CPB and endoaortic clamp times were 86.3 ± 51.2 (20–457) and 53.3 ± 21.9 (10–190) minutes, respectively. 4% of cases (6 patients) required conversion to standard sternotomy because of: uncontrolled atrial haemorrhage (1 patient), aortic dissection (1 patient), iliac venous laceration (1 patient), poor visualization of target lesions (2 patient) and impossibility to introduce the TOE probe (1 patient). TOE was used in 100% of cases and fluoroscopy only in 20%. Catheter and cannulae positioning was always done under TOE guidance .Mean postoperative extubation time and ICU stay were 5 ± 6 h (2–312) and 12 ± 11.8 h (5–1200), respectively. Overall hospital mortality and at 30 days after discharge was 1.7% (3 patients) and 0.6% (1 patient) respectively. Overall mean hospital stay was 7.5 ± 7.03 days (1–72).

Table 1. present postoperative complications.

	P-A Group	Control Group
Atrial fibrillation	12.5%	26.7%*
Redo for bleeding	4.7%	5.0%
Permanent stroke	0.7%	2.0%
Renal failure	1.5%	5.0%*
Intubation >12 h	5.5%	8.6%

P-A: Port-Access. *$P < 0.05$.

Anaesthetic induction and monitoring time was longer in the P-A Group than in Control Group ($P = 0.026$; $R^2 = 0.07$); however in the P-A Group there was a significant decrease in the anaesthetic time (18.2% less, 20.06 min.).

Conclusions: In our opinion, the minimally invasive port-access surgery is reproducible with low perioperative mortality and with an outcome similar to conventional operations. TOE is an essential monitor for this surgery.

References:

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A-54

The effect of intraluminal shunt use on myocardial damage during MIDCAB

W. Kruczak[1], M. Cisowski[2], D. Szurlej[1], L. Machej[1], A. Bochenek[2]

[1]Department of Anaesthesia, [2]Department of Cardiac Surgery, Silesian Heart Centre, Katowice, Poland

Introduction: Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) is a method of surgical treatment in patients with LAD (left anterior descending artery) lesions. The use of a trans-luminal shunt during MIDCAB procedures reduces acute ischaemia and wall motion abnormalities [1]. The aim of this study was to evaluate the effect of the intraluminal shunt use on myocardial damage during MIDCAB by measuring postoperative troponin I level (Tn I).

Method: Forty patients undergoing MIDCAB were divided into two groups. In group A ($n = 20$) anastomosis was performed by intraluminal shunt use and in group B ($n = 20$) by use of tourniquets. Blood samples were taken before operation and 12, 24 h postoperatively for troponin I levels. Other data recorded included demographic data, duration of surgery, time to perform the anastomosis and incidence of perioperative myocardial infarction. *T*-test was used for statistical analysis.

Results: Patients in both groups were comparable statistically for: demographic data, duration of surgery, time to perform the anastomosis and troponin I level before operation. In group A we observed statistically lower levels of troponin I at 12 and 24 h postoperatively ($P < 0.05$).

Group	A ($n = 20$)	B ($n = 20$)
Age [y]	58.91	55.54
Sex M/F	16/4	17/3
Surgery time [min]	176.3	182.5
Anastomosis time [min]	16.3	15.2
Perioperative MI [n]	0	0
Tn I 0 [ng mL^{-1}]	<0.1	<0.1
Tn I 12 h [ng mL^{-1}]	0.2*	0.384
Tn I 24 h [ng mL^{-1}]	0.206*	0.365

Tn I norm < 0.1 ng mL^{-1}; *$P < 0.05$

Discussion: Results of this study indicate that intraluminal shunt use during MIDCAB reduced myocardial damage measured by postoperative troponin I level.

Reference:

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A-55

Haemodynamic changes during off-pump coronary artery bypass surgery

A. Yavorovsky, N. Trekova, B. Shabalkin, I. Zhbanov, V. Morozan, I. Zhidkov, E. Sokolova, A. Bunatian.

Russian Research Centre of Surgery, RAMS, Moscow, Russia

Introduction: Haemodynamic changes occur during off-pump coronary artery bypass surgery (OPCAB) when the heart is displaced. We therefore aimed to evaluate haemodynamic consequences of the OPCAB procedure.

Method: In 15 patients undergoing OPCAB surgery mean arterial pressure (MAP), heart rate (HR), cardiac output (CO), right and left atrial pressures (RAP and LAP), mean pulmonary artery pressure (MPAP), right ventricular end-diastolic pressure (REVDP), right ventricular end-diastolic volume (REDV) were measured before (T0) and after tilting (T1) the heart for anastomosis of left anterior descending (LAD), circumflex (CX) and posterior descending artery (PDA).

All data are expressed as mean values and standard deviation. Statistical analysis was with Student's *t*-test (M ± SD; *$P < 0.05$).

Results: Compared to baseline data (To) displacement of the heart led to a decrease of MAP during performance of all anastomoses. Significant reduction of CO was found only during anastomosis of CX and PDA. At these times RAP, RVEDP increased and MPAP and LAP decreased. Positioning for the circumflex artery caused a decrease of RVEDV.

The haemodynamic compromise was larger for CX anastomosis than PDA.

Table 1. Haemodynamic changes with positioning (the results are presented as mean ± standard error in T0 and changes for percentage in T1).

	LAD		CX		PDA	
	T0	T1	T0	T1	T0	T1
MAP	79 ± 13	−19%*	89 ± 17	−31%*	83 ± 15	−27%*
CO	5.1 ± 1.2	−12%	4.7 ± 1.3	−36%*	5.3 ± 1.1	−31%*
RAP	7 ± 2.7	+11%	5.5 ± 2.5	+65%*	6.2 ± 2.3	+33%*
RVEDP	3.8 ± 0.9	+9%	4.3 ± 1.3	+40%*	2.9 ± 1.1	+31%*
MPAP	17 ± 5.6	+9%	19 ± 6.1	−25%*	15 ± 4.7	−20%
RVEDV	171 ± 57	−12%	182 ± 65	−30%*	193 ± 53	−23%
LAP	9 ± 3.9	+10%	8.2 ± 3.1	−30%*	10.1 ± 3.5	−22%

Conclusion: The increased RAP, RVEDP and decreased LAP, MPAP, RVEDV in positioning for CX and PDA suggests that the main cause

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of haemodynamic changes is impairment of outflow from the right ventricle into the pulmonary artery and disturbed filling of the RV.

Reference:

1 Mathison M, Edgerton JR, Horswell J, *et al*. Analysis of hemodynamic changes during beating heart surgical procedures. *Ann Thorac Surg* 2000; **70:** 1355–1361.

A-56

Comparison of haemodynamic changes between different coronary artery anastomoses during off-pump coronary artery bypass graft surgery

Y.L. Kwak, H.K. Shinn, Y.W. Hong,

College of Medicine, Yonsei University, Seoul, Korea

Introduction: Haemodynamic deterioration during anastomosis is a main problem for off-pump coronary artery bypass graft surgery (OPCAB) [1]. This study was designed to compare haemodynamic changes in the course of time during coronary artery anastomosis between three coronary territories with continuous cardiac output and mixed venous oxygen saturation (SVO_2) monitoring.

Method: With IRB approval, thirty patients undergoing OPCAB were studied. A pulmonary artery catheter for continuous cardiac output and SVO_2 monitoring was inserted before anaesthesia. Haemodynamic measurements were recorded after pericardiotomy (baseline), 1, 3, 5, 10, and 15 min after the application of a tissue stabilizer and after removal of the stabilizer during each coronary artery anastomosis. Norepinephrine were used to maintain mean arterial pressure (MAP) more than 60 mmHg. Statistical analysis was performed with repeated measures of ANOVA and one-way ANOVA. *P* value less than 0.05 was considered statistically significant.

Results:

		1 min	3 min	5 min	10 min
MAP	LAD	84 ± 15*	84 ± 12	81 ± 11	81 ± 10
	LCX	77 ± 13	83 ± 10	81 ± 11	81 ± 10*
	RCA	76 ± 19	84 ± 14	80 ± 10	80 ± 10
CI (%)	LAD	−3 ± 22	−12 ± 23*	−16 ± 20*	−17 ± 21*
	LCX	−21 ± 18*†	−28 ± 18*†	−31 ± 23*†	−31 ± 19*†
	RCA	−13 ± 25*	−19 ± 21*	−24 ± 21*	−26 ± 22*
SVO_2 (%)	LAD	−7 ± 7*	−9 ± 7*	−11 ± 9*	−10 ± 8*
	LCX	−15 ± 9*†	−17 ± 10*†	−18 ± 10* †	−18 ± 11*†
	RCA	−11 ± 12*	−15 ± 12*	−15 ± 13*	−16 ± 11*

%: percent change from baseline,*$P < 0.05$ compared to baseline, †$P < 0.05$ compared with the other groups.

Mean pulmonary artery pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) significantly increased only in left anterior descending artery territory but increased insignificantly during other artery anastomoses. There was no statistically significant difference in MPAP and PCWP between all coronary artery anastomoses. CVP significantly increased in all territories without any significant difference between coronary artery territories. The amount of norepinephrine used was most in LCX territories.

Discussion: CI and SVO_2 decreased significantly during all coronary artery anastomoses immediately after the stabilizer application. The degree of reduction in CI and SVO_2 increased with time, though MAP was maintained constantly. CI and SVO_2 during LCX were consistently below normal values. Therefore close monitoring and interventions are needed during graft anastomoses.

Reference:

1 Do QB, Goyer C, Chavanon O, *et al*. Hemodynamic changes during off-pump CABG surgery. *Eur J Cardiothorac Surg* 2002; **21:** 385–390.

A-57

Haemodynamics during exposure of the back wall of the heart during OPCAB surgery: Xpose® versus pericardial stitches

J. Raumanns[1], J.F. Gummert[2], A. Petry[1]

[1]Dept. of Anaesthesiology; [2]Clinic for Cardiac Surgery; Heartcenter University of Leipzig, Leipzig, Germany

Introduction: Stabilizing systems like the Xpose® (Guidant: Menlo Park, CA; USA) suction device promise to offer better haemodynamic conditions and less mitral valve regurgitation during exposure of the inferior and lateral walls of the heart in beating heart surgery. Haemodynamics in this setting can be impaired [1] and were investigated in this study comparing the Xpose® suction device (XS) vs. simple pericardial stitches (PS).

Method: Twenty seven patients were evaluated after informed consent. Haemodynamic parameters included: heart rate (HR), mean arterial blood pressure (MAP), central venous pressure (CVP) and cardiac index (CI). Baseline measurements were made in a head-down position before the heart was tilted for inferior vessel anastomosis (T0-inf.) or lateral vessel anastomosis (T0-lat.). Measurements were repeated after displacement of the heart, exposing the inferior wall (T1-inf.) 18 times (in 18 patients) and exposing the lateral wall (T1-lat.) 21 times (in 19 patients). Displacement of the heart was started using alternately XS or PS as the first technique. After completion of measurments the heart was returned to normal position so haemodynamics could recover to baseline values (T0). Then again the heart was displaced in the same position in the same patient for the second measurement using the alternative exposing technique. Transoesophageal echocardiography was used to detect mitral valve regurgitation (MR).

Results: HR showed no significant changes at any time point of measurement. Exposure of the inferior and lateral wall (T1-inf./T1-lat.) went along with a significant decrease of MAP without differences between XS and PS. CVP showed no significant changes at any time point or between XS and PS. CI decreased significantly during heart displacement (T1-values) without significant differences regarding the inferior or lateral wall or the exposing technique. There was no increase of MR during displacement of the heart except in 3 patients (1 in XS; 2 in PS). Data are expressed in the table as mean values and standard deviation (statistical analysis: Student's *t*-test including Bonferroni correction; significance value *$P < 0.05$).

	HR (bt min^{-1})	MAP (mmHg)	CVP (mmHg)	CI (L min^{-1} m^{-2})
T0-inf/XS	68.2 ± 15.6	87.6 ± 12.4	10.3 ± 4.4	2.79 ± 0.4
T0-inf/PS	67.4 ± 13.7	88.1 ± 10.2	10.8 ± 3.9	2.71 ± 0.3
T1-inf/XS	69.6 ± 14.5	69.2 ± 12.1*	12.5 ± 4.0	2.08 ± 0.4*
T1-inf/PS	70.8 ± 14.3	68.0 ± 12.6*	13.4 ± 4.9	1.94 ± 0.4*
T0-lat/XS	67.4 ± 14.2	93.4 ± 9.8	11.3 ± 3.5	2.69 ± 0.3
T0-lat/PS	68.1 ± 12.8	92.1 ± 11.4	10.9 ± 4.1	2.74 ± 0.3
T1-lat/XS	69.9 ± 14.1	66.1 ± 11.4*	15.1 ± 4.1	1.93 ± 0.5*
T1-lat/PS	70.8 ± 15.6	67.7 ± 11.7*	15.1 ± 4.1	1.93 ± 0.5*

Discussion: As haemodynamic parameters and degree of mitral valve regurgitation showed no significant differences, the use of Xpose® did not offer any additional benefit.

Reference:

1 Raumanns J, Diegeler A, Gummert J, *et al*. Haemodynamic changes in OPCAB procedures regarding different coronary artery anastomoses. *Eur J Anaesth* 2001; **18** (Suppl 22): A55.

A-58

The effect of pre-operative propranolol or atenolol on dobutamine infusion in off-pump coronary artery bypass grafting

Y.J. Oh, J.H. Lee, H.K. Shinn, Y.L. Kwak, Y.W. Hong

College of Medicine, Yonsei University, Seoul, Korea

Introduction: Preoperative β-adrenoceptor (β-AR) antagonist administration is known to improve ventricular function by decreasing the myocardial oxygen demand and by preventing agonist-induced β-AR desensitization in coronary artery obstructive disease [1]. This study evaluated the effect of pre-operative propranolol or atenolol medication on the response to dobutamine in patients undergoing off-pump coronary artery bypass graft surgery (OPCAB).

Method: With IRB approval, 35 patients undergoing OPCAB treated with propranolol (P-group, $n = 22$, 73 ± 23 mg d^{-1}) or atenolol (A-group, $n = 13$, 41 ± 20 mg d^{-1}) pre-operatively were

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enrolled. Patients with ejection fraction less than 40% or heart failure were excluded. The infusion of dobutamine was started at 2 $\mu g\,kg^{-1}\,min^{-1}$ (D2) for 5 min and the dosage was increased to 4 $\mu g\,kg^{-1}\,min^{-1}$ (D4) then 8 $\mu g\,kg^{-1}\,min^{-1}$ (D8) every 5 min in both groups. The same protocol was performed twice before and after coronary artery anastomosis (pre-graft and post-graft). Repeated measures of ANOVA and unpaired *t*-test was used for statistical analysis. *P* values <0.05 were considered significant.

Results:

		D0		D4		D8	
		P	A	P	A	P	A
CI	PreG	2.3	2.4	2.4	2.3	2.4	2.5
	PostG	2.6	2.6	2.9†	2.8	2.8	3.0†
MAP	PreG	81	89	98*	96*	107*	98*
	PostG	82	81	83	80	88	80
MPAP	PreG	18	18	20*	20	23*	23*
	PostG	20	18	19	18	19	19
HR	PreG	56	52	53*	51	52	55
	PostG	66	66	69†	70†	75†	75†
SVRI	PreG	2538	2924	3106*	3154	3407*	3112
	PostG	2259	2360	2184	2176	2397	2008

Values are mean, CI: cardiac index ($L\,min^{-1}\,m^{-2}$), MAP: mean arterial pressure (mmHg), MPAP: mean pulmonary arterial pressure (mmHg), HR: heart rate ($beat\,min^{-1}$), SVRI: systemic vascular resistance index ($dyn\,s\,cm^{-5}\,m^{-2}$), * $P < 0.05$ compared with the value of the baseline in pregraft, † $P < 0.05$ compared with the value of the baseline in postgraft.

During the pre-graft period, the % changes of MAP from D0 were significantly greater in P-group than in A-group at all doses and the % change of SVRI from D0 was also significantly higher in P-group than in A-group at D8. There was no significant statistical difference in the % changes of variables from D0 between both groups at all doses during post-graft period.

Discussion: The activation of α-agonistic effect of dobutamine seems to be associated with the increase in SVRI in P-group during the pre-graft period. β-AR desensitization does not seem to be developing during post-graft period in patients undergoing OPCAB treated with β-AR antagonist. Decrease in the plasma concentration of propranolol and atenolol may cause the different haemodynamic effect between the pre- and post-graft periods.

Reference:

1 Sill JC, Nugent M, Moyer TP, *et al*. Influence of propranolol plasma levels on hemodynamics during coronary artery bypass surgery. *Anesthesiology* 1984; **60:** 455–463.

A-59

Redo CABG is not a contraindication for off-pump cardiac surgery: our experience

C. Gerli, L. Mantovani, G. Aletti[1], A. Romano, A. Zangrillo

Department of Cardiac Anesthesia and Intensive Care, "Vita e Salute" University of Milan, [1]Department of Mathematics, University of Milan, Via Olgettina 60, Milano, Italy

Introduction: Redo CABG surgery is associated with a more difficult perioperative management. Since 1998 our institution has performed beating heart CABG surgery with increasing enthusiasm through the years. Redo CABG is particularly at risk of complications because it is associated with significant morbidity related to the re-opening of the sternum, manipulation of the heart and lesions or embolism from the old grafts. The extensive mediastinal dissection, necessary to isolate and control the grafts (particularly the LIMA) and the epicardial coronaries, expose the patient to a high risk of bleeding. This phenomenon is further worsened by the pathological impact of altered coagulation after a long CPB. The consolidated knowledge from the literature of the beneficial effects of OP-CABG surgery on postoperative bleeding and blood products requirements makes the OP-technique particularly attractive in this population.

Method: Between January 1998 and July 2002, 132 patients (mean age 65 ± 8 yr) underwent reoperative coronary artery bypass grafting: 41 pt. (31.1%) without cardiopulmonary bypass, 91 pt (68.9%) with CPB. A midsternotomy approach was used to dissect out the left internal mammary artery (LIMA) and to obtain an optimal exposure of the heart. Total intravenous anaesthesia (propofol and fentanyl at standard doses) and a careful attention to preload were targets of our anaesthesiological technique. During the off-pump procedure a mechanical stabilizer and intracoronary shunts were always used. All patients received tranexamic acid as antifibrinolysis prophylaxis. According to our experience, in OP-CABG surgery there are multiple sources of activation of fibrinolysis such as sternotomy, pericardiotomy and use of suction.

The results of the OP-REDO CABG population were compared to those where CPB was used. Multivariate analysis was performed.

Results: Overall mortality rate was 8.8% (8 pts.) in the CPB population vs. 4.9% (2 pts.) in off-pump ($P < 0.05$). 22 (24.4%) CPB pts needed major inotropic support for unstable haemodynamics due to ischaemia or arrhythmias vs. 4 pts (9.8%) ($P < 0.09$).

Table 1. shows the major events.

	CPB	OP-CABG	*P*
ICU stay (days)	2.8	1.5	0.02
Intubation (hours)	37	10	0.0001
Grafts (number)	2.5	1.4	<0.001
Transfusion (patients)	43 (47%)	8 (19%)	0.004
Ischaemic event (pts)	22	4	0.09
Re-opening (pts)	8 (8.8%)	0	0.1
Stroke (pts)	2	1	ns

Discussion: In our institution we always try to perform OP revascularization if possible. Redo CABG can be performed safely without cardiopulmonary bypass with a low perioperative morbidity and mortality [1]. The OP-CABG approach in our population has significantly reduced the need for prolonged mechanical ventilation, re-exploration and use of blood products.

Reference:

1 Trehan N, Mishra YK, Malhotra R, *et al*. Off pump redo coronary artery bypass grafting. *Ann Thorac Surg* 2000; **70:** 1026–1029.

A-60

Off-pump revascularization in patients with left ventricular dysfunction: haemodynamic evaluation

E. Conti, M. Ferrante, G. Finamore, V. Pede, V. Praštalo, R. La Monica, R. Martinez Escobar, G. Rodella, B. Amari

Department of Cardiac Anaesthesia and Intensive Care, Poliambulanza Hospital, Brescia, Italy

Introduction: Coronary artery bypass (CAB) in patients (pts) with left ventricular dysfunction (LVD) is still a high-risk procedure. Many authors demonstrate not only safety and feasibility of off-pump CAB (OPCAB) in this group of high-risk pts, but also improvement in clinical outcome [1]. Only a few papers investigated haemodynamic changes in these pts during surgery. The aim of this study is to describe haemodynamic parameters and clinical outcome of pts with LVD undergoing OPCAB.

Method: Ten consecutive pts with ejection fraction (EF) <35% were submitted to OPCAB in a 6 months period in our institution, where systematic use of beating heart surgery is pursued. After informed consent, a Swan Ganz catheter was positioned to record all haemodynamic parameters. Time points of measurements were: T_0 = baseline (pre-induction); T_1 = during anterior wall CAB; T_2 = at release of compression; T_3 = lateral wall CAB; T_4 = release; T_5 = inferior wall CAB; T_6 = release; T_7 = end of surgery. Inotropes (dopamine or epinephrine) were given if cardiac index remained $<2\,L\,min^{-1}\,m^{-2}$ despite fluid loading. Metaraminol was given to keep MAP >70 mmHg. Results were analysed using paired *t*-test.

Results: Mean EF was 27 ± 6%, mean EuroSCORE was 5.2 (range 3–9). An average of 2.3 ± 0.8 graft/pt were performed. 1 pt was dropped out for conversion to on-pump CAB. 12, 6 and 3 grafts respectively were performed on anterior, lateral and inferior walls.

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7 of 9 pts needed inotropic support intra-operatively. Mean intubation time was 19.6 h (range 3–63), 5/9 pts had intubation time <12 h, mean ICU stay was 2.2 ± 1.3 days. There was no hospital mortality, no neurological complication and no myocardial infarction. Post-operative complications were: 1 acute renal failure, 2 respiratory failures, 2 haemodynamic instabilities. Main results are listed in Table (mean ± SD).

	CI ($L\,min^{-1}\,m^{-2}$)	SvO_2 (%)	HR ($beats\,min^{-1}$)	MAP (mmHg)	DO_2 ($mL\,min^{-1}\,m^{-2}$)	VO_2 ($mL\,min^{-1}\,m^{-2}$)
T_0	2.4 ± 0.7	71 ± 8	90 ± 15	88 ± 15	416 ± 131	106 ± 32
T_1	2.4 ± 0.5	76 ± 7*	103 ± 25*	78 ± 11	387 ± 126	85 ± 29*
T_2	2.7 ± 0.7	79 ± 5#	103 ± 27	81 ± 9	432 ± 136	83 ± 29#
T_3	1.5 ± 0.3#	63 ± 13*	110 ± 18#	74 ± 6*	253 ± 81#	87 ± 39#
T_4	2.2 ± 0.4	74 ± 8	104 ± 19*	83 ± 17	337 ± 62*	79 ± 25#
T_5	1.9 ± 0.8	77 ± 1*	104 ± 8	86 ± 15	365 ± 168	81 ± 40
T_6	1.9 ± 0.6	77 ± 4*	101 ± 19	82 ± 12	368 ± 158	77 ± 18
T_7	2.7 ± 0.6	75 ± 5*	103 ± 21*	76 ± 7*	431 ± 101	101 ± 34*

*$P < 0.05$, #$P < 0.01$ compared to T_0. CI: cardiac index; SvO_2: central venous saturation; HR: heart rate; MAP: mean arterial pressure; DO_2: oxygen delivery; VO_2: oxygen consumption.

Discussion: CI, MAP, SvO_2 and DO_2 showed their largest drop during lateral wall CAB (−35%, −16%, −10% and −39% respectively if compared to T_0). This severe haemodynamic derangement was transient and recovered after release of compression, so that the procedure was well tolerated. We conclude that invasive monitoring is mandatory in pts with LVD undergoing OPCAB. DO_2 appear to be the most useful parameter in describing the adequacy of haemodynamic status. Two pts who showed a prolonged subcritical level of DO_2 had the most severe post-operative morbidity.

Reference:

1 Shennib H, Endo M, Benhamed O, *et al*. Surgical revascularization in patients with poor left ventricular function: On- or Off-Pump? *Ann Thorac Surg* 2002; **74:** S1 344–347.

A-61

Change in cerebral oxygenation during off-pump coronary artery bypass grafting

Sung Hee Han[1], Jae-Hyon Bahk[2], Byung Moon Ham[2], Young Tak Lee[3]

[1]Dept of Anesthesiology, College of Medicine, Hallym University, [2]Dept.of Anesthesiology, Seoul National Univ. Hosp, [3]Dept. Cardiothorac Surg. Samsung Medical Center, Seoul, Korea (ROK)

Introduction: Neurologic dysfunction is now recognized as a major cause of morbidity after cardiac surgery. During off pump coronary artery bypass graft (OPCAB), haemodynamic instability asssociated with heart displacement is often unavoidable [1]. In relation to cerebral oxygenation, the haemodynamic instability during the period of posterior vessel anastomoses can be a concern. With near-infrared spectroscopy, we examined the change in regional cerebral oxygen saturation (rSO2) during OPCAB

Method: Twenty patients undergoing OPCAB were included in this prospective study (male/female; 12/8, age; 66.5 ± 4.2). Patients with known neurologic problems were excluded. Anaesthesia was maintained with end-tidal isoflurane 0.7–1.2% and a mixture of oxygen–nitrous oxide 50%. Cardiac index (CI), heart rate (HR), mean arterial pressure (MAP), and rSO2 were measured. CI was measured with a thermodilution technique and rSO2 with near-infrared spectroscopy (INVOS 3100, Somanetics). Parameters were measured 30 min after induction of general anaesthesia (baseline), 10 min after exposure and stabilization of each target artery (left anterior descending artery (LAD), posterior descending artery (PDA) and circumflex branch of left coronary artery (LCx)) and 30 min after completion of anastomoses (End). Values for each period were compared by repeated measures ANOVA. Data are expressed as mean ± SD. Significance was defined as $P < 0.05$.

Results: Parameters at LAD and End were all the same as the values at baseline, except increased HR (79.9 ± 9.1, 78.7 ± 11.2, each $P < 0.05$).

	Baseline	PDA	LCx
rSO2 (%)	71.7 ± 6.1	70.6 ± 7.6*	67.9 ± 8.5*
CI ($L\,min^{-1}\,m^{-2}$)	3.68 ± 0.7	3.16 ± 0.8*	2.54 ± 0.5*
MAP (mmHg)	89.9 ± 8.1	73.7 ± 6.3*	72.1 ± 8.8*
HR ($beat\,min^{-1}$)	75.2 ± 10	80.5 ± 10.7*	77.8 ± 10.4*

Discussion: Although over neurologic complications such as stroke and coma are uncommon, subtle neurologic abnormalities are often observed after CABG [2]. In this study, during PDA and LCx anastomoses, as a consequence of heart displacement, CI and MAP were reduced, as was cerebral perfusion pressure. As a result, rSO2 decreased. Since inadequate cerebral oxygenation is known to be related to impaired postoperative cognitive function [3], monitoring of rSO2 wold be helpful during OPCAB.

References:

1 Grundeman PF, Borst C, van Herwaarden JA, *et al*. Hemodynamic changes during displacement of the beating heart by the Utrecht Octopus method. *Ann Thorac Surg* 1997; **63** (Suppl.6): S88–92.

2 McKhann GM, Goldsborough MA, Borowicz LM Jr, *et al*. Cognitive outcome after coronary artery bypass: a one-year prospective study. *Ann Thorac Surg* 1997; **63:** 510–515.

3 Croughwell ND, Newman MF, Blumenthal JA, *et al*. Jugular bulb saturation and cognitive dysfunction after cardiopulmonary bypass. *Ann Thorac Surg* 1994; **58:** 1702–1708.

A-62

Off-pump CABG may reduce the risk of complications in elderly patients

L. Villa, C. Savi, C. Erimia, V. Mazzanti, A. Condemi

'L.SACCO' Hospital, Milan – Italy

Introduction: The advent of off-pump myocardial revascularization (OPCABG) has markedly contributed in lowering complications linked with cardiac surgery in older people. The aim of our study is to verify that OPCABG may lead to a safer postoperative course in elderly patients (pts).

Method: After ethical committee approval, we performed a comparative study between 49 pts operated upon for CABG with cardiopulmonary bypass (CPB) and 31 pts with the off-pump technique (OPCABG) from January 1999 to September 2002 at our Institution. All pts had an age above 80 years.

Preoperative physiologic data included: Canadian Cardiovascular Society Score (CCS), Clinical Risk Score (CRS) of Higgins, ejection fraction, serum creatinine $>130\,\mu mol\,L^{-1}$ (CRF). Due to a CCS >2 surgeons shifted to the OPCABG. Both groups underwent the same anaesthesia regimen. Among postoperative complications: bleeding, a new myocardial infarction (MI), mechanical ventilation (Mech vent), stroke and an increase of serum creatinine above $175\,\mu mol\,L^{-1}$ (ARF), were considered. ICU stay, days of hospitalization and mortality were compared between the 2 groups. Data, mean and SD, were analysed by Student's *t*-test and chi-squared test, where appropriate.

Results: The OPCABG group with a significant difference in CCS score predetermine a high-risk surgical approach. The remaining preoperative variables investigated did not differ significantly among the 2 groups of pts. The postoperative course was characterized by a reduced time of mechanical ventilation required by pts in the OPCABG group. Regarding the other variables, the complication rate was comparable in both groups. Although ARF developed in 13% of pts in the OPCABG group, this was not significantly different from the CPB group (Table 1). ICU stay, hospitalization and mortality did not show any significant difference between the groups.

Table 1. Results are summarized in following table.

	CPB ($n = 49$)	OPCABG ($n = 31$)	P value
Bleeding (mL)	660 ± 348.41	645 ± 399.6	ns
MI (pts)	5 (10.2%)	4 (12.9%)	ns
ARF (pts)	4 (8.1%)	4 (12.9%)	ns
Stroke (pts)	2 (4.1%)	1 (3.2%)	ns
Mech Vent (h)	24.85 ± 6.47	12.93 ± 5.86	<0.05
ICU (days)	2.79 ± 2.78	2.16 ± 1.37	ns
Hospital (days)	12.1 ± 5.96	10 ± 5.74	ns
Deaths (pts)	3 (6.1%)	3 (9.6%)	ns

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Discussion: OPCABG surgery is nowadays an affordable tool and can be performed with a reasonably low morbidity and mortality in selected groups of high-risk pts. Our study shows that this surgical option in an elderly population may be the preferable way in order to reduce the time of mechanical ventilation required postoperatively and so lowering the risk of pulmonary complications.

A-63

Hypermetabolic response after coronary surgery performed on or off-pump

E. Sisillo, G. Juliano, S. Salis, N. Rondello, S. Gregu

IRCCS Centro Cardiologico Monzino Dept of Anaesthesia and ICU, Milano, Italy

Introduction: It is well known that a hypermetabolic status ensues after cardiac surgery and this is reflected by an increased VO_2 that persists for several hours or a few days after the procedure. To investigate the role of cardiopulmonary bypass (CPB), we studied oxygen metabolism in coronary artery bypass procedures performed on (CABG) and off-pump (OPCAB).

Method: After informed consent and approval by the Ethic Committee, 25 patients (19 male, 6 female) who underwent coronary surgery were enrolled in the study and randomized to CABG ($n = 14$) and OPCAB ($n = 11$). All patients received the same anaesthetic management. Oxygen metabolism variables were assessed before anaesthesia induction, 5 min after anaesthesia induction, 5 min after protamine administration, at skin closure then 9 h and 18 h after the end of surgery. VO_2 was measured by a blood sample obtained from a Swan-Ganz catheter with a standard formula: $VO_2 = Qp * 10 * (CaO_2–CvO_2)$. Data were analysed with analysis of covariance. A P value less than 0.05 was considered statistically significant.

Results: All patients had an uneventful postoperative course and no major complications were recorded. No patient required inotropic drug support either during surgery or in the Intensive Care Unit. The table shows the levels of VO_2, DO_2 and oxygen extraction (ExO_2) at baseline before anaesthesia induction (Base), and at 9 and 18 hours after surgery pooled together (Post) in CABG and OPCAB.

	CABG		OPCAB	
	Base	Post	Base	Post
VO_2 (mL min^{-1} m^{-2})	121 ± 11	168 ± 8	98 ± 13	156 ± 8
DO_2 (mL min^{-1} m^{-2})	613 ± 33	475 ± 24	581 ± 39	452 ± 24
ExO_2 (%)	21 ± 1.7	35 ± 1.1*	18 ± 1.9	35 ± 1.1*

*$P < 0.05$: post vs. base.

No differences were found at baseline and in postoperative period between CABG and OPCAB in VO_2, DO_2 and ExO_2 levels.

Discussion: The occurrence of a hypermetabolic status ensuing after cardiac surgery was previously widely documented. CPB was regarded as a major factor of the derangement in oxygen metabolism occurring during and after cardiac surgery. Our data show that there are no significant differences between CABG and OPCAB in postoperative VO_2, DO_2 and ExO_2 levels. Other factors, such as general surgical trauma, are likely to be the main contributors to this phenomenon.

Reference:

1 Tulla H, Takala J, Alhava E, *et al*.: Hypermetabolism after coronary artery bypass. *J Thorac Cardiovasc Surg* 1991; **101:** 598–600.

A-64

No thermogenic effect of an amino acid infusion in heart surgery with cardiopulmonary bypass

E. Selldén[1], G. Settergren[2], D. Rimeika[2], S. Lindah[1]

Department of Surgical Sciences, Karolinska Institute, [1]Divisions of Anesthesia and Intensive Care; [2]Cardiothoracic Anaesthetics and Intensive Care, Karolinska Hospital, Stockholm, Sweden.

Introduction: Persistent hypothermia after heart surgery may preclude early extubation. Infusing amino acids increased body temperature in abdominal surgery and in healthy volunteers [1,2]. The current study tested the hypothesis that a similar effect would be observed during and after heart surgery.

Method: Patients undergoing coronary artery bypass grafting (CABG) or aortic valve replacement (AVR) were studied with ethical committee approval and informed patient consent. The study was placebo-controlled, prospective and double-blinded. Randomized patients received 500 ml of either Vamin 18^R ($n = 17$) or Ringer actetate^R ($n = 17$) in 4 h. Infusion start ≈30 min before the end of cardiopulmonary bypass (CPB), which was performed at ≈34°C with rewarming to 36–37°C. The lowest pulmonary artery temperature after CPB was noted as was the time when it reached 37°C. The pulmonary oxygen uptake was calculated from the oxygen concentration in the systemic and pulmonary artery and thermodilution cardiac output. Statistics: analysis of variance.

Results: Demographic data, medication including β-blockers, CPB-data and case mix were comparable. The lowest mean PA temperature (°C) after CPB was 35.9 (0.1 SEM) for Vamin and 35.6 (0.2) for Ringer and the increase per hour was 0.6 (0.1) and 0.6 (0.0), respectively, with no difference between the groups. Figure 1 shows the oxygen data. The infusions were well tolerated.

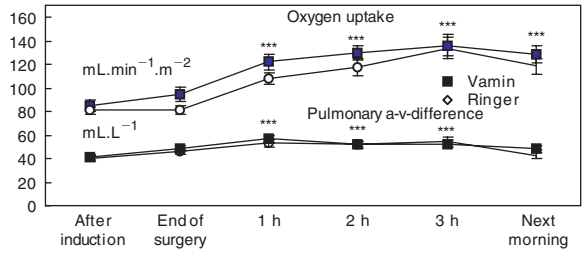

Figure 1.

Both the pulmonary uptake and the a-v-difference of oxygen increased after surgery compared to before but with no difference between the groups.

Discussion: The exact mechanism for the thermogenic effect of nutrients is not known. The observed lack of effect was most probably due to temperature gradients between different body compartments caused by hypothermic CPB and maybe also to a general depression of metabolism by medication with β-blockers.

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A-65

Subcutaneous tissue oxygen tension measurements in wound tissue after off-pump or conventional coronary revascularization

D.J. Buggy, C. Cody, B. Marsh.

Department of Anaesthesia & Intensive Care Medicine, Mater, Misericordiae Hospital, Dublin, Ireland

Introduction: Directly-measured subcutaneous tissue oxygen tension ($PsqO_2$) reflects the adequacy of tissue oxygenation and directly influences surgical-wound healing [1]. Cardiopulmonary bypass (CPB) elicits a profound systemic inflammatory response, which contributes to postoperative microcirculatory abnormalities [2]. Off-Pump coronary artery bypass (OPCAB) reduces the systemic inflammatory response induced by CPB [3]. We tested the hypothesis that OPCAB would increase $PsqO_2$ measurements in wound tissue by minimising CPB-induced systemic inflammation.

Method: Twenty patients undergoing coronary revascularization were enrolled in this non-randomized, prospective, cohort study. Ten consecutive patients scheduled for OPCAB were compared with ten having conventional CPB. All patients had a tissue oxygen

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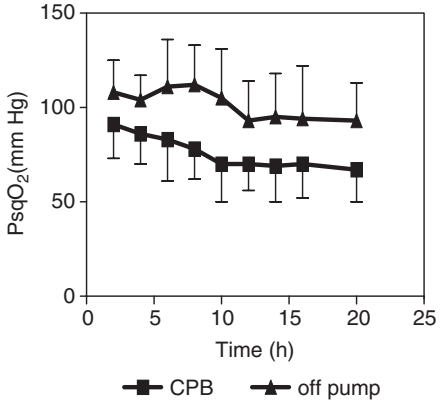
sensor (Licox, Hamps, UK) implanted longitudinally into the subcutaneous tissue of the leg in the saphenous vein harvest wound. The oxygen sensor was located within a subcutaneous, saline-filled tonometer, on a single-use probe and displayed on a digital bedside monitor. Data was downloaded for 20 h postoperatively, commencing with closure of the saphenous wound.

Results: $PsqO_2$ was significantly higher in OPCAB patients (Fig). Arterial PaO_2, plasma pH, lactate, postoperative core and peripheral temperatures, intra-operative and postoperative fluids administered were similar in both groups.



Conclusion: Postoperative $PsqO_2$ measurements in wound tissue were higher for 20 h after OPCAB compared with CPB, which could reduce the risk of surgical-wound infection. Reduction in CPB-induced inflammatory response is probably the major explanatory factor.

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A-66

A case series of implantation of a new cardiac support device for treatment of cardiac failure: haemodynamic and echocardiographic data

J. Grosse, U.R. Döpfmer, S. Dushe, J. Braun, W.J. Kox, C. Spies

Department of Anaesthesiology, Charité Hospital of the Humboldt University, Berlin, Germany

Introduction: Twenty seven patients underwent implantation of a new passive cardiac support device (CSD; Acorn Inc, St Paul, USA) in our institution. This preliminary report presents haemodynamic data and the end diastolic area of the left ventricle as measured in the mid-papillary short transgastric axis view (LVEDA) by TOE of the first 10 patients undergoing this procedure. More details about this new therapeutic concept and intermediate outcome results are published by Konertz and coworkers [1]. In short, after a median sternotomy patients are placed on cardiopulmonary bypass (CPB). An aortic cross-clamp is only used if an additional procedure is carried out. In this series one patient underwent aortic valve replacement and three other patients mitral valve reconstruction. With the patient on bypass a textile polyester mesh device is fitted snugly around the right and left ventricle and fixed with about 10 sutures close to the atrioventricular groove.

Method: After induction of anaesthesia with fentanyl and etomidate and maintenance with fentanyl, pancuronium and isoflurane we measured central venous pressure (CVP), pulmonary artery wedged pressure (PCWP), the LVEDA and cardiac index (CI). The same measurements were taken one hour after weaning off CPB i.e. shortly after sternal closure. Differences in mean values at these points in time were compared using Wilcoxon´s rank sum test.

Results are given in Table 1

Table 1. Data are given as means ± standard deviations.

	T1	T2	*P*
CVP (mmHg)	8.1 ± 3.2	12.0 ± 2.4	0.017*
PCWP (mmHg)	13.9 ± 4.3	15.3 ± 4.7	0.416
CI ($L\,min^{-1}m^{-2}$)	2.3 ± 0.9	2.3 ± 0.5	0.87
LVEDA (cm^2)	36.1 ± 11	29.0 ± 10	0.006*

T1: after induction of anaesthesia; T2: one hour after weaning off CPB.

Discussion: We could not detect a change in the PCWP despite the mechanically induced decrease in LVEDA of roughly 20%. However the right ventricular compliance seems to be reduced by the device which is reflected by an increased CVP. Cardiac index was unchanged. At T1 only 3 patients received low dose dobutamine, at T2 all patients received inotropes in a standardized manner, the most potent being epinephrine up to a dose of $0.1\,\mu g\,kg^{-1}min^{-1}$. Obviously filling pressures and LVEDA are not only influenced by the CSD but also by fluid and inotropic management.

Reference:

1 Konertz WF, Shapland JE, Hotz H, *et al*. Passive containment and reverse remodeling by a novel textile cardiac support device. *Circulation* 2001; **104** (Suppl 1): 1270–1275.

Transfusion and Coagulation

A-67

Prediction of blood use in a cardiac surgical unit

L. Anderson, G. Weir, M. Steven, A. Macfie, S. Buchanan, I. Quasim

Department of Anaesthesia, Western Infirmary, Glasgow G11 6NT, Scotland

Introduction: There is increasing evidence that transfusion of red cells and platelets or fresh frozen plasma (FFP) may be detrimental to patient outcomes [1]. A prospective audit was performed in our unit to assess our current transfusion practice and to analyse data for possible preoperative predictive factors.

Method: A prospective audit was performed including all patients admitted to our cardiac intensive care unit. Demographic details were noted as were details of the operation performed, surgeon, preoperative haemoglobin (Hb), preoperative medication, common risk indices, red cell and blood product use. We also noted mediastinal drain losses and hospital discharge haemoglobin.

Results: Data from 433 patients were analysed using Minitab statistical software version 10.5. Mean age was 62 yr and most patients were male (71%). 75% had CABG and 14% had valve surgery. 49% were transfused during their hospital stay and 7% received FFP or platelets. Mean hospital admission and discharge Hb were 13.6 and $9.8\,g\,d\,L^{-1}$ respectively, mean drain losses were 857 mL, mean weight was 78.4 kg and mean Parsonnet 89, Parsonnet 95 and EuroSCORE were 9, 5.6 and 4 respectively.

Multiple regression analysis was performed on potential predictor variables using the best subsets procedure, and it was found that the best independent preoperative predictors of blood use were low admission Hb, low weight and high EuroSCORE. Surprisingly preoperative medication and procedure performed were not predictive. The best combination of 2 factors was weight and preoperative Hb.

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The best combination of 3 was weight, Hb and EuroSCORE, and of 4 was weight, Hb, EuroSCORE and surgeon.

There were no predictive factors for FFP or platelet use.

Discussion: While some factors were expected, it is surprising that others e.g. preoperative medication, were not useful. If mediastinal drain losses were included in the analyses, predictability was naturally increased. However, our aim was to be able to predict blood use better preoperatively that we may target pharmacologically (e.g. with aprotinin which is not routinely used in our unit) the most at risk of requiring transfusion. It is our intention to continue the audit and to attempt to devise a simple preoperative risk index for our patients so that at risk patients may be identified at the preadmission clinic.

Reference:

1 Spiess BD, Ley C, Body SC, *et al*. Hematocrit value on intensive care unit entry influences the frequency of Q-wave myocardial infarction after coronary artery bypass grafting. McSPI Research Group. *J Thorac Cardiovasc Surg* 1998; **116:** 460–467.

A-68

The effect of heparin on vascular endothelial function by monitoring intracellular accumulation of cGMP

J. Gal, B. Riedel, N. Marczin, D. Royston

Dept. of Anaesth., Royal Brompton & Harefield NHS Trust, London, United Kingdom

Introduction: Endothelial dysfunction has been proposed as an important element in the low cardiac output state that may complicate the postoperative period following cardiac surgery. The endothelial L-arginine-NO-cGMP pathway is one of the critical determinants of vascular regulation [1]. We hypothesized that heparin, routinely used during cardiac surgery, could influence this pathway [2]. Our group tested this hypothesis by monitoring intracellular accumulation of cGMP in heparin-treated saphenous vein.

Method: Following IRB approval, saphenous vein was obtained from patients undergoing routine CABG surgery, prior to systemic heparinization. Veins were dissected clean, cut into rings (4 mm width). Rings were then incubated in the absence of (control) or in the presence of unfractionated porcine heparin ($5\,IU\,mL^{-1} \times 4\,h$). Ongoing NO production and associated cGMP formation were assessed from the influence of the NO synthase inhibitor L-NAME ($10\,M^{-4} \times 30\,min$). Intracellular cGMP was extracted by HCl (200 μL, 0.1 M, 60 min) and quantified by radioimmunassay using murine polyclonal cGMP antibody. Experiments ($n = 10$) were performed in triplicate and results corrected for wet tissue weight. Wilcoxon's matched pairs rank signed sum test was used for statistics (UNISTAT®). Statistical significance is defined as $P < 0.05$.

Results: Mean absolute values of cGMP fell in the heparin and L-NAME treated rings. Simultaneous administration of protamine sulphate completely eliminated the heparin response.

	Control	Heparin	L-NAME
Levels of cGMP (pmol/g-wet tissue) (mean ± sem)	78.8 ± 24.3 (mean ± sem)	53.3 ± 13.5 (mean ± sem)	45.0 ± 9.7
Reduction in GMP accumulation (% of control values)		67.6 ± 11.8 ($P < 0.05$)	57.1 ± 9.3 ($P < 0.05$)

Discussion: The effect of L-NAME on cGMP levels suggests ongoing NO production contributes significantly to cGMP accumulation in human saphenous vein. This is the first observation that heparin exerts a negative influence on intracellular cGMP accumulation. This observation might have important implications regarding the pathogenesis of endothelial dysfunction, especially in patients with already compromised function associated with a wide variety of disease states that receive heparin therapy.

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1 Moncada S, Palmer RM, Higgs EA. Nitric oxide physiology, pathophysiology and pharmacology. *Pharmacol Rev* 1991; **43:** 109–142.

2 Upchurch GR Jr, Welch GN, Freedman JE, *et al*. High-dose heparin decreases nitric oxide production by cultured bovine endothelial cells. *Circulation* 1997; **95:** 2115–2121.

A-69

Bedside aPTT measurement after cardiopulmonary bypass: impact on protamine treatment

H. Kirkegaard, C. Lindskov

Department of Anaesthesia and Intensive Care, Skejby Sygehus, Aarhus University Hospital, Aarhus, Denmark

Introduction: Activated clotting time (ACT) is used to test for residual heparin effect following cardiac surgery. Based on information about bleeding tendency and ACT the anaesthesiologist decides if further protamine treatment is needed. Activated partial thromboplastin time (aPTT) can now be measured at the bedside using portable monitoring equipment, the CoagueCheck Pro® (Roche Diagnostic, Mannheim, Germany) [1]. The aim of the present study was to investigate whether the use of aPTT instead of ACT had any influence on protamine treatment in the recovery room.

Method: The study was approved by the regional ethical committee. 30 cardiac patients operated on during cardiopulmonary bypass were investigated. At arrival at the recovery room ACT (Hemochron® using celite as activator) (ACThem), and aPTT (CoagueCheck Pro®)(aPTTcc) were measured, simultaneously; aPTTcc was measured twice. The bleeding tendency was estimated as mediastinal chest tube drainage. Within ½ h after arrival blood samples for laboratory aPTTlab measurements were drawn and simultaneously another aPTTcc measurement performed. Correlation, bias ± 2SD (limits of agreement (LA)) analyses were performed. Indications for protamine treatment based on ACThem, aPTTcc and bleeding tendency were evaluated retrospectively by one of the staff anaesthesiologists.

Results: There was a good correlation between replicated aPTTcc, measurements, $r^2 = 0.98$, bias 0.39 s, LA 5.57 to −4.79 s. Bias and LA between aPTTlab (49 ± 20 s, reference interval 24–35 s) and aPTTcc (54 ± 16 s, reference interval 20–41 s) measurements were 1.62 s and 27.1 to −23.9 s, respectively, $r^2 = 0.62$. At the time of arrival at the recovery room bleeding tendency was $112 \pm 101\,mL\,h^{-1}$ (mean ± SD). Based on ACThem measurement and bleeding tendency, 7 patients with ACThem values ranging from 144 to 178 s would have received extra protamine 50 mg. With aPTTcc 22 patients with aPTTcc values ranging from 46.8 to 105.3 s would have received extra protamine.

Discussion: When evaluation of the residual heparin effect was based on aPTTcc measurements 73% of patients were treated with extra protamine compared to 23% with ACThem. Using lower ACT values as indicators for protamine treatment would increase the number of patients treated. However, the ACT is probably not the most appropriate test for diagnosing residual heparin, because it is relatively insensitive to heparin concentrations $<0.06\,U\,mL^{-1}$ [2]. LA between aPTTlab and aPTTcc measurements is acceptable and aPTTcc precision is good, and we propose to use bedside aPTT measurements for diagnosing residual heparin effect.

References:

1 Boldt J, Walz G, Triem J, *et al*. Point-of-care (POC) measurement of coagulation after cardiac surgery. *Intensive Care Med* 1998; **24:** 1187–1193.

2 Murray DJ, Brosnahan WJ, Pennell B, *et al*. Heparin detection by the activated coagulation time: a comparison of the sensitivity of coagulation tests and heparin assays. *J Cardiothorac Vasc Anesth* 1997; **11:** 24–28.

A-70

The effect of anti-fibrinolytic agents on exhaled nitric oxide during cardiac surgery: a double blind placebo controlled trial

P. Diprose, S. Dawkins, C.D. Deakin, R. Gill, M.J. Herbertson, D.C. Smith.

Southampton University Hospitals, Southampton, UK

Introduction: It is common for patients to develop impaired gas exchange after cardiopulmonary bypass (CPB). Previous studies have demonstrated that in patients undergoing coronary artery

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bypass grafting (CABG), nitric oxide (NO) levels decrease as the alveolar-arterial difference increases [1,2]. This is presumed to occur as a result of worsening ventilation-perfusion mismatch [3]. We hypothesized that exhaled NO levels in patients undergoing cardiopulmonary bypass may be altered by the use of anti-fibrinolytic agents, in particular aprotinin, since this has been shown to exhibit some anti-inflammatory actions.

Method: Patients about to undergo CPB procedures were recruited as part of a randomized double-blind placebo controlled trial in blood conservation. There were three groups of patients. APR group received 2 million units (MU) of aprotinin prior to skin incision with 2 MU into the pump and an infusion of 0.5 MU per hour. TXA group received 5 g of tranexamic acid prior to skin incision with equivalent volume saline infusions. P group were given saline placebo throughout. The rate of production of nitric oxide was measured with the chemiluminescence method resulting from the gas phase reaction of NO with ozone using the LR2500 analyser (Logan Research Limited, Rochester, UK). Measurements were taken prior to CPB and after CPB had been discontinued and the sternum closed. Data analysis was with paired or independent samples *t* test, as appropriate.

Results: 78 patients were recruited and randomized (26 in each arm), 2 patients from each of the APR and TXA groups were subsequently excluded as a result of protocol violation. No patients received intravenous nitrates. The median age of patients, the Parsonnet score, EuroSCORE, cross-clamp and bypass times were comparable between groups. The change in the rate of nitric oxide production for the three groups between the two time points showed no significant difference (mean change in NO production (in parts per billion per second): $P = 0.704$, APR $= -0.857$, TXA $= 0.335$). No significant differences were detected between the drug groups for CPB effect (differences in the means between groups: PvAPR $= 0.787$, PvTXA $= -0.405$, APRvTXA $= -1.192$).

Discussion: We have been unable to show any difference in the rate of production of nitric oxide before and after CPB. Aprotinin does not appear to exert any detectable effect on nitric oxide production.

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1 Cuthbertson BH, Stott SA, Webster NR. Exhaled nitric oxide as a marker of lung injury in coronary artery bypass surgery. *Br J Anaesth* 2002; **89:** 247–250.

2 Ishibe Y, Liu R, Hirosawa J, *et al*. Exhaled nitric oxide level decreases after cardiopulmonary bypass in adult patients. *Crit Care Med* 2000; **28:** 3823–3827.

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A-71

Inotropic support and early outcome in patients undergoing cardiac surgery: high dose versus low dose aprotinin

M. Balanika, M. Tsitsika, K. Bare, A. Samothrakis, K. Sotiriou
E. Karamichali

Department of Anesthesiology, Evangelismos General Hospital, Athens, Greece

Introduction: Aprotinin, a serine protease inhibitor, possesses anti-inflammatory properties and reduces patient exposure to blood and blood products. The aim of this study was to evaluate the influence of aprotinin dosage on the inotropic support and the outcome in a high risk group of patients undergoing cardiac surgery.

Method: After institutional approval and informed consent, 36 patients undergoing elective coronary artery bypass grafting cardiac surgery with a preoperative ejection fraction $<35\%$ were included in the study. Exclusion criteria were antiplatelet agents preoperatively or a prolonged coagulation times. After induction of anaesthesia and an aprotinin test dose, patients were randomized in a double-blind fashion (anaesthetists and ICU personnel were unaware of the study). Group H: high-dose aprotinin (2×10^6 KIU loading dose, $5 \times 10^5\,h^{-1}$ KIU infusion rate, and 2×10^6 KIU in the pump prime). Group L: low-dose aprotinin (1×10^6 KIU loading dose, 25×10^4 KIU infusion rate and 2×10^6 KIU in the pump prime. Group C: normal saline at the respective time points.

Requirements for inotropic support were defined as epinephrine, norepinephrine, or intra-aortic balloon pump (IABP) commencing intra-operatively or within 12 h post-operatively. Blood and platelets transfusions, and Intensive Care Unit (ICU) length of stay were also recorded.

Statistical analysis was performed using Student's *t*-test ($P < 0.05$ was considered significant).

Results: There were no significant differences between groups as regards demographic data and preoperative ejection fraction. Compared to Group C, inotropic support was significantly lower in groups H and L. Furthermore, ICU length of stay , blood and platelets transfusions were significantly reduced in groups H and L. Nevertheless, no statistically significant differences were observed between Groups H and L as regards inotropic support, ICU length of stay, blood and platelets transfusions (see Table).

Table 1.

	Group H ($n = 12$)	Group L ($n = 12$)	Group C ($n = 12$)
Epinephrine ($\mu g\,kg^{-1}\,min^{-1}$) (mean ± SD)	0.04 ± 0.0187**	0.042 ± 0.026**	0.076 ± 0.028
Norepinephrine ($\mu g\,kg^{-1}\,min^{-1}$) (mean ± SD)	0.08 ± 0.042*	0.086 ± 0.044*	0.136 ± 0.07
IABP (n)	–	1	3
Blood units (mean ± SD)	1.16 ± 1.21**	1.91 ± 1.03*	3.16 ± 1.06
Platelets units (mean ± SD)	0.75 ± 1.36**	1.5 ± 1.79*	4.16 ± 2.40
ICU length of stay (days) (mean ± SD)	2.58 ± 0.75***	3.08 ± 0.95**	4.16 ± 0.68
Re-exploration (*n*)	–	1	2

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ compared to control group C.

Discussion: Our data suggest that high-dose aprotinin does not reduce inotropic support and does not improve early outcome in high risk patients undergoing CABG surgery in comparison with low-dose aprotinin. Further studies are needed to confirm our results.

Reference:

1 Davis R, Whittington R. Aprotinin. A review of it's pharmacology and therapeutic efficacy in reducing blood loss associated with cardiac surgery. *Drugs* 1995; **49:** 954–983.

A-72

Excessive activation of haemostasis takes place in the early postoperative period after routine CABG surgery

R. Busley, S. Braun[1], W. Dietrich

Departments of Anaesthesiology and [1]Laboratory Medicine, German Heart Center Munich, Munich, Germany

Introduction: Although it is well recognised that the extracorporeal circulation (ECC) is associated with major enhancement of coagulation [1], little is known about haemostatic progression in the early postoperative period after CABG [2]. The aim of this prospective clinical pilot study was to characterize the course of postoperative thrombin generation and to identify factors which might induce increased postoperative coagulation, elevating the risk for thrombotic complications.

Method: Ten male patients (ASA physical status 2–3, NYHA 2–3, age 53–75 yr) participated in this trial after informed consent and ethics committee approval. All patients had elective CABG with total arterial or combined arterial and venous grafts and were not pre-treated with iv. heparin. All patients received 375 IU kg^{-1} of heparin before ECC and 5–7 million KIU of aprotinin during ECC. The effect of heparin was reversed by protamine chloride after ECC (ACT $\leqslant$ 160 s). Antithrombin (AT) and protein C levels as well as parameters of coagulation activation (prothrombin fragment $F_{1.2}$; thrombin–antithrombin-complex) and fibrinolytic activity (D-dimers) were recorded before and during operation and until the fifth postoperative day. Data are presented by mean values.

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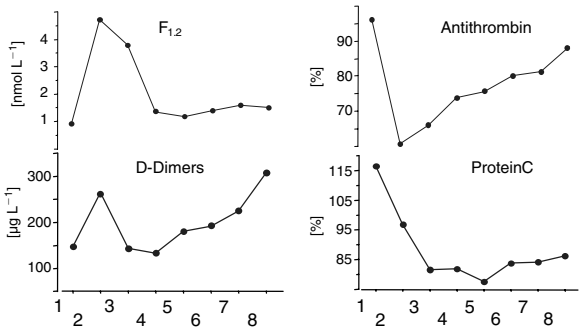
Results: Antithrombin and protein C were significantly reduced during the first five postoperative days. Major enhancement of coagulation activation and excessive fibrinolytic activity takes place in this period, as demonstrated by increased prothrombin fragments $F_{1.2}$, thrombin–antithrombin-complexes (data not shown) and D-dimers.



1: PreOP, 2: OP-End 3: 4 h POP, 4: POD1, 5: POD2, 6: POD3, 7: POD4, 8: POD5.

Discussion: The observed major activation of coagulation in the first five postoperative days after routine CABG may eventually result in thrombotic complications. Surprisingly, fibrinolytic activity was extremely pronounced in the postoperative period, exceeding post-ECC values at POD5. Physiologic antithrombotic agents like AT and protein C remained low, indicating increased consumption in the postoperative period. Attenuation of haemostatic activation reduces postoperative complications [3]. Maintenance of physiologic AT and protein C levels by substitution could possibly support that objective.

References:

1 Slaughter TF, LeBleu TH, Douglas JM Jr, *et al*. Characterization of prothrombin activation during cardiac surgery by hemostatic molecular markers. *Anesthesiology* 1994; **80:** 520–526.

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3 Mangano DT. Aspirin and mortality from coronary bypass surgery. *N Engl J Med* 2002; **347:** 1309–1317.

A-73

Post cardiopulmonary bypass bleeding: comparison of two cardiopulmonary bypass circuits

S. Casella, M.A. Calò, A. Giacomin, F. Manente, G. Cascio, C. La Valle, P. Michielon

Department of Anaesthesia and Intensive Care, Mirano's Hospital, Mirano (Venice), Italy

Introduction: We have compared the effects on postoperative bleeding of two oxygenators, uncoated and coated with phosphorylcholine (PC) (Dideco Avant 903 and Dideco Avant 903 Phisio) during elective adult cardiac surgical operations.

Method: 187 adult patients (pts) were prospectively randomized into 2 groups. Group 1 (98 pts) used the Avant 903 circuit; group 2 (89 pts) used the Avant 903 Phisio circuit. Operative and anaesthesiological techniques were the same for both groups. Patients were heparinized with 300 UI kg^{-1} body weight. Activated clotting time (ACT, Hemocron Junior) was maintained above 450 s during the extracorporeal circulation (ECC). After ECC, residual blood prime was returned to the patient after centrifugation and washing. Chest tube drainage was measured at the end of the day of the operation and then every 24 h until chest tubes removal. At the same times prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT) and platelet (plt) count were measured. Packed red blood cells (PRBC) were transfused for a haemoglobin (Hb) <8 g dL^{-1}; fresh frozen plasma (FFP) was administered for a PT (INR) >1.5 coupled with bleeding of >150 mL h^{-1} for 2 consecutive hours; tranexamic acid (TA) was administered by continuous infusion with bleeding >100 mL h^{-1} for 2 consecutive hours.

Result: Data were expressed as mean ± SD. Comparison of patient data was done using Student's *t*-test. No differences between the two groups were found for ACT, haematological and coagulation profile during ECC, before and after the operation. Significant differences were found in the postoperative period (p.o.) for platelet count, blood loss; there were different blood transfusion requirements (see Table).

	AVANT (n = 98)	A.PHISIO (n = 89)	P
Total blood loss (mL)	1066 ± 557	865 ± 572	<0.0001
Platelet count (mL)			
After operation	136 ± 47	171 ± 52	<0.0001
1st p.o.day	150 ± 52	173 ± 49	<0.0001
2nd p.o.day	137 ± 50	158 ± 52	<0.0001
3rd p.o.day	138 ± 37	155 ± 62	<0.0001
Transfusion (pts)			
PRBC	52 U: 16	30 U: 15	
FFP	29 U: 12	13 U: 6	
Plt	4 U: 1	0	
TA infusion (pts)	18	7	

Discussion: Coated oxygenators and circuits reduce blood loss and blood transfusions requirements in the postoperative period in elective cardiac operations. PC coating appears to have a favourable effect on blood platelets, which is more obvious after studying the changes during CPB [1]. Moreover we found an interesting reduction in PRBC and FFP requirements using coated circuits. We are studying again this part of results.

Reference:

1 De Somer F, Francois K, van Oeveren W, *et al*. Phosphorylcholine coating of extracorporeal circuits provides natural protection against blood activation by the material surface. *Eur J Cardiothorac Surg* 2000; **18:** 602–606.

A-74

Intraoperative autohaemotransfusion during CABG

N. Trekova, A. Javorovsky, A. Bunatian

Russian Research Center of Surgery, Moscow, Russia

Introduction: Intraoperative autohaemotransfusion (acute haemodilution) is an available method of saving patient blood [1]. Routinely autologous blood is collected from the main veins after induction of anaesthesia. We use autologous blood collection from the right atrium after heparin administration and aorta cannulation. The aim of this study was to compare clinical and laboratory evaluation of a routine and modified method of autologous blood collection.

Method: After approval by the local ethical committee 40 patients undergoing CABG with cardiopulmonary bypass (CPB) were randomly divided into 2 equal groups. In group 1, 6–10 mL kg^{-1} of patient's blood was collected from the internal jugular vein after induction. In group 2 the same volume of patient's blood was collected from the right atrium after heparinization before the start of CPB. Colloid infusion to correct fluid deficiency was used in group 1. In group 2 perfusate from the CPB circuit through the arterial cannulae was used if necessary. Collected blood was reinfused in both groups after protamine administration. Statistical analysis was done using *t*-test.

Results: There were no significant differences between the groups in the volume of collected autologous blood and haemodynamic data. The duration of blood collection and time between collection and reinfusion of blood were less in patients of group 2. Microscopic analysis and laboratory assessment showed that platelet count and function were higher and microclots were rare in the autologous blood collected from right atrium (mean ± SD).

	Group 1	Group 2
Volume of collected blood (mL)	495 ± 151	578 ± 120
Duration of blood collection (min)	23 ± 6.0	4.0 ± 1.2*
Time between blood collection and re-infusion (min)	174 ± 19	133 ± 25*
Collected blood platelet count	68.5 ± 18.9 × 10^9	124.8 ± 22 × 10^9*
Collected blood microclots (% pts)	90	10
Amplitude of platelet aggregation (mm)	14.2 ± 9.7	24.3 ± 12.6*
Rate of platelet aggregation (mm min^{-1})	2.6 ± 0.2	4.6 ± 0.6*

*$P < 0.05$

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Conclusion: Autologous blood collection from the right atrium has advantages over routine collection from the internal jugular vein. There is better preservation of platelet count and function, prevention of microclots formation, and shortening of the time between collection and re-infusion of blood. These factors may be useful for prophylaxis against post CPB bleeding.

Reference:

1 Cooley DA. Conservation of blood during cardiovascular surgery. *Am J Surg* 1995; **170** (Suppl 6A): 53S–59S.

A-75

The efficiency of high volume autologous blood donation and the use of a cell saver in reducing donor blood requirements in on-pump CABG

S.E. Naumenko, M.G. Pokrovsky, A.V. Danilenko, S.F. Kim

Regional outpatient of cardiology, Novosibirsk, Russia

Introduction: A previous study has demonstrated that autologous blood donation during on-pump CABG with the use of a cell saver did not reduce the need for donor blood transfusions [1]. Perhaps the reason for this ineffectiveness was the low volume of autologous blood reserved. The present study was performed to assess the effectiveness of intraoperative high volume blood donation for reducing the exposure to allogeneic blood or blood products in patients with on-pump CABG with the use of a cell saver.

Method: In a prospective, randomized clinical trial 61 patients undergoing elective coronary bypass grafting with cardiopulmonary bypass were randomly assigned to one of two groups: group I ($n = 31$) – autologous high volume blood donation ($16.4 \pm 1.9\,mL\,kg^{-1}$ – about 24% of estimated circulating blood volume) and group II ($n = 30$) – autologous blood donation $8.8 \pm 0.5\,mL\,kg^{-1}$ (about 12% of estimated circulating blood volume). Autologous blood was collected at the beginning of surgery after pre-heparinization with 20 mg of heparin but before systemic heparinization and transfused after the end of cardiopulmonary bypass. In all patients of both groups the cell saver (Cell Saver5, Hemonetics®) was used intraoperatively. Haemoglobin concentration (gL^{-1}), haematocrit level (%), and erythrocyte count ($\times 10^{12}$) were measured at day 1, 2 and 3 after surgery and by the time of discharge from hospital. Obtained results were statistically analysed using appropriate t-test and chi-squared test for categorical variables using "Statistica-5" for Windows. Results are expressed as mean ± SD.

Results: Groups did not differ significantly with respect to preoperative premedication and surgical data, blood loss, and no patient needed re-exploration for bleeding. Fresh frozen plasma was transfused in 1 patient in group I (410 mL) and in 1 patient in group II (280 mL), $P > 0.05$. Bank blood was transfused in 1 patient (500 mL) in group II, $P > 0.05$.

Table 1. summarizes haemoglobin changes (gL^{-1}).

Hb gL^{-1}	Group I (M ± SD)	Group II (M ± SD)
Preop.	147.8 ± 9.4	147.7 ± 8.7
1 day	122.1 ± 12.0*	126.6 ± 14.7*
2 day	118.3 ± 15.2*	116.4 ± 16.0*
3 day	114.9 ± 12.5*	119.0 ± 17.5*
Discharge	120.9 ± 15.9*	125.3 ± 14.5*

*$P < 0.01$ vs. Preop.; $P > 0.05$ between groups.

Conclusion: In our study intraoperative high volume autologous blood donation ($16.4 \pm 1.9\,mL\,kg^{-1}$) did not reduce the exposure to allogeneic blood, blood products, and was not associated with higher haemoglobin concentration, haematocrit level, and erythrocyte count in the postoperative period.

Reference:

1 Naumenko SE, Pokrovskiy MG, Belavin AS, *et al*. The efficiency of autologous blood donation in reducing donor blood requirements in on-pump CABG with the use of cell saver. *Eur J Anaesthesiol* 2001; **18** (Suppl 22): A65.

A-76

Effect of acute normovolaemic haemodilution on coagulation status

M. Krupa, D. Moskowitz, J. Klein, H. Bennett, A. Shander

Englewood Hospital and Medical Center, Englewood, NJ, USA

Introduction: Acute normovolaemic haemodilution (ANH) is effective in reducing allogeneic transfusions [1]. During the process of ANH, coagulation abnormalities may be a concern. Thromboelastography (TEG) has been used to guide and reduce transfusions in cardiac surgery by using point-of-care coagulation monitoring [2]. In two studies of ANH, we assessed coagulation in patients undergoing general surgery and thromboelastography (TEG) in cardiac surgery patients.

Method: We examined coagulation measures from arterial samples at baseline and following ANH during general surgery (Study 1: $n = 28$, standard laboratory: PT, aPTT, Hct., fibrinogen), and during cardiac surgery (Study 2: $n = 300$, TEG: R, K, ANG (α angle), MA) to determine if these measures were altered by ANH and if they predicted coagulopathy.

Results: *Study 1*: ANH averaged 1,571 ± 364 mL of whole blood withdrawn. To achieve normovolaemia, an average volume of 1531 mL and 2684 mL of crystalloids and colloid (Hextend) were replaced at 1 and 1.5 L of ANH respectively. The mean Hb dropped from 12.3 ± 1.5 of pre ANH baseline to $9.2 \pm 1.3\,g\,dL^{-1}$ after 1.5 L ANH ($P < 0.001$). There was no difference in aPTT (29 ± 4 s vs. 29 ± 7 s, $P = 0.37$) between pre ANH baseline and post-1.5 L ANH. Platelet counts (202 ± 50 K vs. 161 ± 43 K, $P < 0.005$) and fibrinogen levels ($345 \pm 83\,mg\,L^{-1}$ vs. $236 \pm 71\,mg\,L^{-1}$, $P < 0.005$) decreased. PT increased from 13.1 ± 0.9 s to 14.3 ± 1.4 s ($P < 0.001$) as did INR from 1.2 ± 0.2 to 1.4 ± 0.3 ($P < 0.005$). There was no associated abnormal or excessive bleeding reported by the surgical teams on any of the trial patients.

Study 2: An average of 1,288 ± 597 mL of ANH was performed in each patient. Euvolaemia was maintained by infusion of crystalloids and colloid (Hextend, 612 ± 224 mL). TEG values below were all in millimetres (mm).

	Baseline	Post ANH	Paired *t*-test	*P* value
R	9.0 ± 2.8	7.7 ± 2.5	8.47	<0.001
K	2.7 ± 1.1	3.1 ± 1.4	−4.26	<0.001
MA	70.1 ± 5.7	64.7 ± 6.8	17.84	<0.001
ANG	71.2 ± 6.2	69.6 ± 6.6	4.00	<0.001

While statistically highly significant, the post-ANH TEG values remained within the limits of normal and no coagulopathies were observed clinically. The peri-operative transfusion rate for these 300 patients was 7%.

Discussion: Thromboelastography (TEG) has been used to guide and reduce transfusions in cardiac surgery by using point-of-care monitoring [2]. ANH is safe and may help to avoid allogeneic transfusions. Moreover, ANH alters TEG values from the high-normal range towards the mid-normal range of coagulability. Point-of-care monitoring of TEG values can guide the use of more specific component therapy rather than allogeneic transfusions.

References:

1 Matot I, Scheinin O, Jurim O, *et al*. Effectiveness of acute normovolemic hemodilution to minimize allogenic blood transfusion in major liver resection. *Anesthesiology* 2002; **97:** 794–800.

2 Shore-Lesserson L, Manspiezer HE, DePerio M, *et al*. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg* 1999; **88:** 312–319.

A-77

Clopidogrel does not increase bleeding and allogenic blood transfusion in coronary artery surgery

H. Karabulut, F. Toraman, S. Evrenkaya, S. Tarcan, C. Alhan

Acibadem Kadikoy Hospital, Istanbul, Turkey

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Introduction: Platelet dysfunction is one of the major reasons of postoperative bleeding following coronary artery surgery [1,2]. The aim of this study was to evaluate the effects of clopidogrel, a specific and potent irreversible inhibitor of platelet aggregation, on bleeding and use of blood and blood products after coronary artery bypass grafting (CABG) surgery.
Method: Preoperative patient characteristics and perioperative and postoperative data were collected prospectively in 1628 consecutive patients undergoing isolated CABG performed by the same surgical and anaesthesia team. Of these, 48 were receiving clopidogrel preoperatively. Baseline characteristics, chest tube output, and the need for re-exploration or for blood and blood product transfusion of clopidogrel recipients and non-recipients were compared. Continuous variables were analysed with Student's *t*-test. The χ^2 test and Fisher's exact test were used to compare categorical variables. All data were expressed with mean ± SD.
Results: The need for re-exploration or for blood and blood product transfusion, chest tube output, ICU length of stay (20.1 ± 2.9 vs. 21.9 ± 13.5 h; P = ns), and hospital length of stay (5.5 ± 1.7 vs. 5.4 ± 2.1 days; P = ns) were similar in clopidogrel recipients and nonrecipients, respectively.

	Clopidogrel Group (n = 48)	Control Group (n = 1580)	P value
PT (s)	12.6 ± 1.6	11.5 ± 1.7	0.013
APTT (s)	32.6 ± 4.5	21.4 ± 14.5	0.007
Platelets (K mL^{-1})	275 ± 98	280 ± 72	ns
No. of distal anastomoses	2.6 ± 1.1	2.8 ± 1.1	ns
CPB time (min)	55 ± 26	63 ± 25	ns
Total chest tube output (mL)	719 ± 265	612 ± 350	ns
Re-exploration (%)	0	1	ns
RBC transfusion (U/pt)	0.5 ± 0.9	0.4 ± 0.9	ns
Fresh frozen plasma (U/pt)	1.1 ± 1.2	0.9 ± 1.1	ns
Platelet transfusion	0	0	ns

PT: Prothrombin time; APTT: activated partial thromboplastin time; CPB: cardiopulmonary bypass; RBC: red blood cells

Discussion: The results of this study suggest that preoperative use of clopidrogel is not associated with increased bleeding and need for surgical exploration as well as risk of blood and blood product transfusions after CABG.
References:
1 Yende S, Wunderink RG. Effect of clopidogrel on bleeding after coronary bypass surgery. *Crit Care Med* 2002; **29:** 2271–2275.
2 Woodman RC, Harker LA. Bleeding complications associated with cardiopulmonary bypass. *Blood* 1990; **76:** 1680–1697.

A-78

The effect of gelatin versus starch on postoperative bleeding in adult CABG patients (COCOT – colloid versus colloid trial)

T. Drabek, H. Riha

Institute for Clinical and Experimental Medicine, Postgraduate Medical School, Prague, Czech Republic

Introduction: The use of starches for volume substitution in cardiac surgery has been repeatedly reported to carry a significant risk for possible excessive bleeding [1]. However, gelatins are considered to be relatively safe.

To evaluate the effect of gelatin versus starch on postoperative bleeding and the rate of pharmacological and/or surgical interventions, we designed a double-blind prospective randomized study comparing gelatin (Gelofusine) to hydroxyethyl starch (Elohaest 6%, 200,000/0.60-0.66) for volume substitution during the coronary artery bypass grafting procedure (CABG) using cardiopulmonary bypass (CPB) in adult patients (COCOT – Colloid versus Colloid Trial).
Method: Adult patients scheduled for CABG with an ejection fraction >40% were studied. The patients had no prior open-heart procedure, and no other cardiac procedure except CABG was performed during this setting. In all patients, the pre-procedure haemocoagulation parameters were within normal limits.

Twenty-one patients were randomized to receive gelatin, and twenty-four were randomized to receive starch. Every patient in each group received an infusion of 500 mL of colloid prior to initiation of CPB, and 500 mL of the same type of colloid after weaning from CPB.

We monitored the amount of chest tube drainage at three time points: 3 h, 6 h and 12 h postoperatively, and we recorded the need for pharmacological intervention. Chest tube drainage within 150 mL in each of the first two hours postoperatively or 100 mL in each of the first 3 h postoperatively did not receive pharmacological intervention. We used Student's *t*-test to evaluate the results, which are given as mean ± SD.
Results: The results are summarized in the Table. We were not able to document that administration of starch is associated with more extensive blood loss. There was no difference in the use of pharmacological intervention (4/21 gelatin group vs. 6/24 starch group).

Table

Postop. time (h)	Gelofusine, mL (n = 21)	Elohaest, mL (n = 24)	P
3	361 ± 122	394 ± 170	<0.5
6	508 ± 163	510 ± 193	<1.0
12	656 ± 205	661 ± 221	<0.95

Discussion: Hydroxyethyl starch infusion in adult cardiac surgery patients undergoing coronary artery bypass grafting using cardiopulmonary bypass is as safe as administration of gelatin in the same volume.
Reference:
1 Cope JT, Banks D, Mauney MC, *et al*. Intraoperative hetastarch infusion impairs hemostasis after cardiac operations. *Ann Thor Surg* 1997; **63:** 78–83.

A-79

Increased need of fluid during cardiopulmonary bypass increases blood transfusion and length of hospital stay

F. Toraman, H. Karabulut, S. Evrenkaya, E. Demiray, B. Sarı, S. Tarcan, C. Alhan

Acibadem Kadikoy Hospital, Istanbul and Mustafa Kemal University, Hatay Istanbul, Turkey

Introduction: Haemodilution and an increase in capillary permeability occurring with cardiopulmonary bypass (CPB) impose a risk for tissue oedema and blood transfusion that may result in an increased complication rate after coronary artery bypass grafting (CABG) [1].
Method: Of the 1280 consecutive patients undergoing isolated on-pump CABG, total fluid balance at the end of the operation was less than 500 mL in 1155 (group 1) and more than or equal to 500 mL in 125 (group 2). During CPB, blood was added to the reservoir only when haematocrit fell to 17% or less and crystalloid solution only when the pump flow fell below 2.0 L min^{-1} m^{-2}. Anaesthetic, surgical, and postoperative management and indications were the same in all patients as a single surgical and anaesthesia team performed all operations. Patients younger than 70 yr had transfusion of homologous blood if their haematocrit levels were less than 21% and haemoglobin levels were less than 7 mg dL^{-1}, whereas patients older than 70 yr were transfused if their haematocrit and haemoglobin levels were less than 24% and 8 mg dL^{-1}, respectively. No patients were excluded from the study. All data were expressed as mean ± SD.
Results: Hypertension, diabetes, chronic obstructive pulmonary disease, NYHA Class III–IV, use of ACE inhibitors, chronic renal failure, and female gender were the significant preoperative risk factors for inreased volume replacement during CPB. The groups

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were similar in body mass index, preoperative haematocrit values, total fluid balance in the intensive care unit (ICU), and total chest tube output. However, red blood cells transfusion rate, re-admission rate to the ICU and length of hospital stay were significantly higher in group 2 patients. Multiple logistic regression revealed that age >70 yr ($P < 0.001$, OR: 2.0, 95% CI: 1.4–2.8), and total fluid balance >500 mL at the end of the operation ($P < 0.01$, OR: 2.2, 95% CI: 1.5–3.2) were predictors of increased length of stay. For transfusion of red blood cells, age >70 yr ($P < 0.0001$, OR: 2.3, 95% CI: 1.6–3.3), and total fluid balance >500 mL at the end of the operation ($P < 0.001$, OR: 2.0, 95% CI: 1.3–2.9) were the only significant risk factors.

	Group 1 ($n = 1155$)	Group 2 ($n = 125$)	P value
Preoperative Hct (%)	40.2 ± 4.7	39.9 ± 5.3	ns
Hct after CPB (%)	26 ± 4.4	24.8 ± 5.0	0.002
Total balance after CPB (mL)	−113 ± 388	985 ± 467	0.0001
Chest tube output (mL)	612 ± 347	623 ± 370	ns
Transfused RBC (U/pt)	0.36 ± 0.85	0.69 ± 1.39	0.01
ICU stay (h)	22 ± 14	22 ± 8	ns
ICU readmission (%)	1.8	5.6	0.015
Hospital LOS (d)	5.3 ± 1.8	6.3 ± 4	0.0001
Mortality (%)	0.9	1.6	ns

Discussion: This study suggest that inreased need of fluid during CPB increases blood transfusion and length of hospital stay.

Reference:

1 Hachenberg T, Tenling A, Rothen HU, *et al*. Thoracic intravascular and extravascular fluid volumes in cardiac surgical patients. *Anesthesiology* 1993; **79:** 976–984.

A-80

OPCAB reduces transfusion requirements: a retrospective analysis of 1170 patients

E. Sisillo, L. Salvi, C. Brambillasca, G. Merli, C. Beverini, F. Biolcati

IRCCS Centro Cardiologico Monzino. Dept. of Anaesthesia and ICU, Milano, Italy

Introduction: Reduction in transfusion of blood products has been previously reported in patients submitted to off-pump coronary artery bypass (OPCAB), although in small groups of patients [1,2].

Method: To determine whether and to what extent, OPCAB surgery reduces transfusion requirements, a retrospective data base review of all the 1170 patients undergoing isolated coronary surgery at this institution from January 2001 to October 2002 was performed. 695 patients underwent traditional CABG and 475 underwent OPCAB. Data analysis included demographic, preoperative risk factors, operative details, rate of transfusion requirements, number of transfused blood units/patient (at the clinical discretion of the attending anaesthetist), and number of re-operations for bleeding. Fisher's exact test, chi-squared test and Mann-Whitney *U* test were utilized as appropriate. Significance was set at $P < 0.05$.

Results: There was no statistical difference in the age, sex, or underlying co-morbidities between patients undergoing CABG and OPCAB.

Table shows the reviewed data.

	CABG	OPCAB	P
Redo (%)	0.5	8.8	0.0001
Urgent/emergency (%)	4.6	1.7	0.008
Hospital deaths (%)	0.7	0.6	ns
Perioperative MI (%)	2.0	0.4	0.02
IABP (%)	1.7	0.2	0.02
Bleeding (mL)	650 (333)	578 (395)	0.001
Transfusion Pts. (%)	33	16.8	0.0001
Re-opening (%)	1.7	0.2	0.02

Discussion: OPCAB surgery, in this study, was shown to carry the same risk for hospital death and to a slightly reduced incidence of peri-operative MI and utilization of IABP. OPCAB patients had less bleeding despite the higher number of redo operations. A significant decrease in transfusion requirement and frequency of re-operation for bleeding was demonstrated. Due to the high costs of blood products in our country (both economic and social), OPCAB surgery could contribute to a strategy of cost containment.

References:

1 Yokoyama T, Baumgartner FJ, Gheissari A, *et al*. Off-pump versus on-pump coronary bypass in high-risk subgroups. *Ann Thorac Surg* 2000; **70:** 1546–1550.

2 Angelini GD, Taylor FC, Reeves BC, *et al*. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. *Lancet* 2002; **360:** 1194–1199.

A-81

Metabolic acidosis in cardiac surgery with CPB: role of the Stewart approach and the chloride

G. Gueret, B. Rossignol, M. Moquery, J.P. Wargnier, O. Corre, C.C. Arvieux

Département d'anesthésie reanimation, CHU la Cavale Blanche, Brest, France

Introduction: Metabolic acidosis is common after cardiac surgery but the exact mechanism is discussed. Recently, Liskaser [1] and Hayhoe [2] found that CPB-induced metabolic acidosis appears to be iatrogenic, derived from the effect of pump prime fluid and was mostly due to increases in serum chloride concentration and strong ion difference (SID).

Method: After informed consent and ethical committee agreement, cardiac surgery patients were prospectively included. Anaesthesia was with etomidate, propofol (TCI), remifentanil and cisatracurium. The CPB priming (1400 mL) contained 107 mmol L^{-1} of chloride and 7.9 mmol L^{-1} of lactate. Biochemistry (Na, K, Ca, Mg, P, Cl, lactate, base excess BE, pH, $PaCO_2$, albumin) was performed before (T1) and after (T2) CPB, and at ICU arrival (T3). Strong ion difference (SID) was calculated as (Na + K + Mg + Ca) − Cl. Values were compared with linear regression.

Results: 30 patients were included. Catecholamines were administered to 19 patients (norepinephrine 14, epinephrine 5 and dobutamine 3). No significant variation of BE occurred during the study, but we found a significant decrease of SID and a significant increase of the chloride between T1 and T2. No correlation was found between delta BE and delta SID ($r^2 = 0.00003$) or delta chloride (Figure 1).

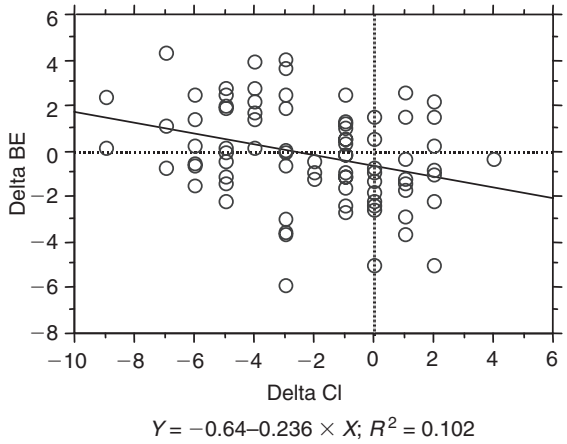

Figure 1. Correlation between delta Chloride and delta BE.

Conclusion: SID and chloride variations were not correlated with BE variations in our study. This may be due to: 1-BE was calculated and not measured. 2-delta BE is independent of the variations of SID. 3-delta BE is dependent of the variations of many variables including SID. Chloride concentration of the priming was lower than in Liskaser's study (150 mmol L^{-1}). This may explain the difference of results on BE and SID between the two studies.

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References:
1 Liskaser FJ, Bellomo R, Hayhoe M, *et al*. Role of pump prime in the etiology and pathogenesis of cardiopulmonary bypass-associated acidosis. *Anesthesiology* 2000; **93:** 1170–1173.
2 Hayhoe M, Bellomo R, Liu G, *et al*. The aetiology and pathogenesis of cardiopulmonary bypass-associated metabolic acidosis using polygeline pump prime. *Intensive Care Med* 1999; **25:** 680–685.

Paediatrics

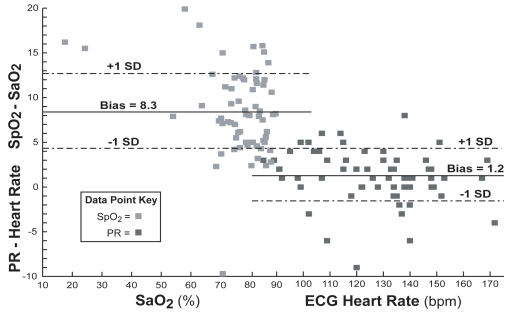
A-82

Accuracy of the Imagyn PRO_2 reflectance pulse oximeter in cyanotic infants requiring cardiac surgery

B.F. Keogh, A.A. Kelleher, S.I. Jaggar, R.J. Kightley, C.J. Morgan
Department of Anaesthesia, Royal Brompton Hospital, London, England, United Kingdom

Introduction: A study was undertaken to determine the SpO_2 and pulse rate (PR) accuracy in a pre-release version of the PRO_2 Reflectance Pulse Oximeter from Imagyn Medical Technologies (Irvine, CA, USA) [1]. This has a distinctive reflectance design, whereby three central light sources and two photodetector rings are located on the same flat, disc-shaped sensor. Perceived advantages include enhanced signal capture in low perfusion states, utility of placement at central sites and accurate calibration to very low SpO_2 values ($SpO_2 < 30\%$).
Method: Ten infants (5 neonates) were studied (wt. 4.9 $\pm$ 2.5 kg). Diagnoses were pulmonary atresia (5), tetralogy of Fallot (2) and transposition (3). Entry criteria were $SpO_2 < 90\%$, ECG monitored for heart rate and an indwelling arterial line. The PRO_2 PR values were referenced against the ECG heart rate and SpO_2 values were referenced against SaO_2 values from blood CO-oximetry (ABL 725, Radiometer, Brønshøj, Denmark).
Results: Sixty six matched data sets (27 intraoperative, 39 PICU) were obtained over a broad range of SaO_2 (18–89%), heart rate (85–172 beat min^{-1}) and total Hb (8.8–19.5 g dL^{-1}). PRO_2 sensor sites included: abdomen, axilla, back, chest, flank, forehead, and thigh. When adjusted for a positive bias, the SpO_2 to SaO_2 correlated within the ISO standard, as did the PRO_2 PR to ECG heart rate.

	Bias (range), see plot	Precision
PR (beat min^{-1})	+1.2 (−9.0 to +8.0)	±2.9
SpO_2 (%)	+8.3 (+0.1 to +19.9)	±4.2



Discussion: A pre-release version of the Imagyn oximeter was tested without adverse effects on 10 infants with cardiac disease. PR values were highly accurate and the SpO_2 bias plot exhibited a simple linear bias, requiring adjustment to the interpretative algorithm. The utility of central sensor positioning was striking, particularly when surgical manoeuvres resulted in signal loss from peripherally sited transmission oximeters. We observed the ability to easily obtain reliable information from a range of central sensor sites to be an extremely valuable feature of the PRO_2 device.

Reference:
1 Mendelson Y, Lewinsky RM, Wasserman Y. Multi-wavelength reflectance pulse oximetry. *Anesth Analg* 2002; **94:** S26–S30.

A-83

Haemodynamic effects of ketamine and propofol in children during cardiac catheterization

E.Öklü[1], F.S.Bulutcu[1], U.Özbek[1], Y.Yalçın[2], E.Cakalı[1], O.Bayındır[1]
Kadir Has University, Florence Nightingale Hospital, [1]Anaesthesiology and Reanimation, [2]Pediatric Cardiology, Istanbul, Turkey

Introduction: A wide variety of anaesthetic agents or combinations have been used for sedating children with congenital heart disease during cardiac catheterization. But studies that have examined the effects of agents on the cardiovascular stability mostly focused on the changes in heart rate and blood pressure. In fact, especially during diagnostic cardiac catheterization, maintenance of the airway without requiring added oxygen and the effects of anaesthetic agents on the magnitude and direction of intracardiac shunt were expected to be minimal [1]. Therefore in this prospective, randomized and blind (cardiologist) study, we aimed to compare the effects of propofol to ketamine on pulmonary and systemic haemodynamic status.
Method: After approval of the Ethics Committee and informed concent from the parent, 41 patients, aged 1 month to 13 years, ASA II–III, scheduled for preoperative diagnosis or evaluation of postoperative results were included in the study. Patients were separated into three groups based on the shunt (diagnosed by transthoracic echocardiography before the catheterization): those without cardiac shunt (Group I, $n = 11$), left-to-right shunt (Group II, $n = 12$), right-to-left shunt (Group III, $n = 18$). Groups were randomly allocated to receive propofol infusion (6 mg kg^{-1} h^{-1}) or ketamine infusion (4 mg kg^{-1} h^{-1}) during the procedure. Following the insertion of a femoral catheter under local anaesthesia, two sets of data were collected, the first before administration of infusion and the second after discontinuation of infusions at the end of the procedure. The superior venae cava, left and right atrium, aorta and pulmonary artery pressures were measured and blood for gas analysis was taken at the same time. Oxygen consumption (Vo_2), mean systemic arterial pressure (mSAP), mean pulmonary artery pressure (mPAP), pulmonary and systemic vascular resistance (PVR, SVR), the ratio between PVR/SVR and pulmonary blood flow (Qp), systemic blood flow (Qs) and pulmonary to systemic blood flow ratio (Qp/Qs) were measured according to the Fick method and standard formulae. Haemodynamic data were compared by using Mann-Whitney *U* and Wilcoxon's test, $P < 0.05$ was considered significant.
Results: Groups with shunt (Group II and III), had a significant decrease in SVR and significant increase in Qs ($P < 0.05$), whereas PVR and Qp did not change significantly. These changes resulted in a significant increase in PVR/SVR and significant decrease in Qp/Qs ($P < 0.05$). In all groups, ketamine infusion was associated with a significant increase in mSAP ($P < 0.05$) but no statistical difference was found in SVR, PVR, SVR/PVR, Qp, Qs, or Qp/Qs.
Discussion: During congenital cardiac catheterization, propofol infusion may decrease the Qp/Qs ratio. Especially in children with cardiac shunts, this may change the direction of intracardiac shunt flow so we may need to pay attention to the cardiac pathophysiology while choosing the anaesthetic agent.

Reference:
1 Morray JP, Lynn AM, Stamm SJ, *et al*. Hemodynamic effects of ketamine in children with congenital heart disease. *Anesth Analg* 1984; **63:** 895–899.

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A-84

End-tidal CO_2 monitoring in perioperative pulmonary blood flow evaluation

Z. Sungur, E. Çamcı, M. Tuğrul, E. Tireli[1]

Department of Anesthesiology and [1]Cardiac Surgery of Istanbul Medical Faculty, Istanbul, Turkey

Introduction: The gradient between arterial and end tidal CO_2 (DCO_2) is a reliable indicator to assess pulmonary blood flow when cardiac output, ventilation parameters and metabolic rate remain constant [1]. The aim of the study was to determine the value of DCO_2 during systemic to pulmonary shunt creation in cyanotic children.

Method: After ethical approval, children with cyanotic heart disease undergoing palliative surgery were included in the study. Haemodynamic and respiratory parameters, end tidal-CO_2 and blood-gases were noted: after intubation (t_1), with open thorax before intervention (t_2), with open thorax after intervention (t_3), at the end of surgery (t_4) and in the postoperative follow-up (t_5). The pulmonary artery blood flow was not measured. Wilcoxon's test was performed to compare the gradient between arterial and end tidal CO_2 at the indicated times.

Results: Eighteen children whose mean age was 17.5 ± 14.7 months, mean weight 8.7 ± 2.8 kg and mean initial oxygen saturation 57.6 ± 14%, were included. A Blalock-Taussig shunt was performed in 13 patients, central shunt in 3 patients and a shunt between main pulmonary artery and a branch of the aorta in 2 children. 5 of the patients were extubated in the operating room. Average postoperative mechanical ventilation time was 3.6 ± 1.9 h. DCO_2 is shown in Figure 1. The gradient at t_3 and t_4 was significantly lower than the gradient at t_2.

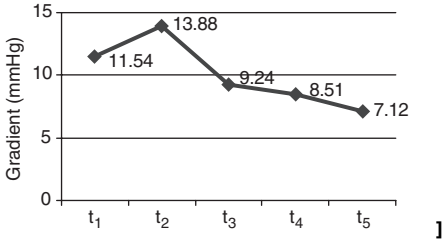

Figure 1. Change in DCO_2 gradient.

Discussion: Arterial to end tidal CO_2 gradient decreased significantly with increased pulmonary blood flow. $EtCO_2$, which is a part of routine monitoring, may be used to assess the efficacy of palliative surgery that aims to increase pulmonary blood flow.

Reference:

1 Smolinsky AK, Shinfeld A, Paret G, *et al*. End-tidal CO_2 levels are a reliable indicator of band tightness in pulmonary artery banding. *Ann Thorac Surg* 1995; **60** (Suppl 6): 523–524.

A-85

Comparison of sevoflurane and isoflurane anaesthesia in paediatric open heart surgery

E. Székely[1], A. Székely[1], E. Sápi[1], Z. Sikos[2], L. Király[3], A. Szatmári[4]

[1]Dpt of Ped. Anaesthesia and Intensive Care, [2]Dpt. of Laboratory, [3]Dpt of Ped. Card. Surgery, [4]Dpt. of Ped. Cardiology, Gottsegen National Institute of Cardiology, Budapest, Hungary

Introduction: Sevoflurane is associated with less tachycardia and coronary vasodilatation than isoflurane and thus might be associated with less myocardial ischaemia. We evaluated paediatric patients in this respect [1].

Method: Following Ethic Committee approval the data of 95 infants and children undergoing open heart surgery were retrospectively and consecutively investigated. Sevoflurane (S) and isoflurane (I) were administered during operation (included CPB) in conjunction with fentanyl boluses (total 3–7 $\mu g\,kg^{-1}$) and pancuronium (total 0.3–0.5 $mg\,kg^{-1}$). The following data was collected: demographics, diagnosis, intraoperative parameters (operation time, time of aorta cross clamp and cardiopulmonary bypass (CPB), haemodynamics, inotropic support, fluid balance, transfusion and ST changes). Blood samples were drawn at the end of operation and on the first postoperative day (POD1). Creatine kinase and MB isoenzyme {CK, CKMB} [2], lactate-dehydrogenase {LDH} and its heart isoenzyme {aHBDH} and renal function were measured. We investigated the warm up time of patients (reaching 34.5°C skin temperature). Statistical analysis consisted of Mann-Whitney *U* test and ANOVA. $P < 0.05$ was considered significant. Data are mean ± SD, or number of cases.

Results: There was no death in the investigated groups. Distribution of diagnosis was comparable in the two groups. There were no differences between the two groups in respect of intraoperative parameters and postoperative laboratory values. However patients received isoflurane had a shorter warm up time.

	Isoflurane	Sevoflurane	*P*
N	50	45	
Age (yr)	6.1 ± 5.6	4.1 ± 4.1	0.06
CKMB arrival ($IU\,L^{-1}$)	109 ± 68	111 ± 69	0.35
CKMB POD1 ($IU\,L^{-1}$)	77 ± 81	60 ± 31	0.21
Norepinephrine (*n*)	8	10	0.44
Fluid balance ($mL\,kg^{-1}$)	17.1 ± 16.9	17.8 ± 19.2	0.82
Warm up time (h)	2.6 ± 1.7	6.2 ± 8.1*	0.02

Discussion: Our results indicate that sevoflurane and isoflurane were comparable with respect to incidence and severity of intra- and postoperative myocardial ischaemia during paediatric cardiac surgery. However, analgesia and sedation after sevoflurane anaesthesia must be started in the operation theatre to prevent postoperative vasoconstriction because of its short elimination time.

References:

1 Ebert TJ, Harkin CP, Muzi M. Cardiovascular responses to sevoflurane: a review *Anesth Analg* 1995; **81** (Suppl 6): S11–22. Review.

2 Taggart DP, Hadjinikolas L, Wong K, *et al*. Vulnerability of paediatric myocardium to cardiac surgery. *Heart* 1996; **76:** 214–217.

A-86

Remifentanil use in pulmonary hypertension associated with congenital heart disease

E.A. Akpek, Ç. Erkaya, A. Donmez, Ş. Mercan[1], A. Esen, G. Arslan

Baskent University Faculty of Medicine, Departments of Anesthesiology and [1]Cardiovascular Surgery, Ankara, Turkey

Introduction: In paediatric cardiac surgery, the effect of anaesthetic agents on the systemic and pulmonary vascular dynamics is one of the determinants of outcome. In this study, we investigated the effect of remifentanil on pulmonary artery and airway pressures in children with pre-existing pulmonary hypertension and compared it with fentanyl.

Method: Children with pre-existing pulmonary hypertension (PA/Ao > 0.5) and aged between 6 months and 6 yr were studied in a prospective randomized and controlled design. Hospital Ethical committee approval and consents from children's parents were obtained. Fentanyl was given as 20 $\mu g\,kg^{-1}$ IV bolus + 20 $\mu g\,kg^{-1}\,h^{-1}$ infusion in Group 1 (control, $n = 9$) and remifentanil was given as 2 $\mu g\,kg^{-1}$ IV bolus + 2 $\mu g\,kg^{-1}\,m^{-1}$ infusion in Group 2 ($n = 11$). In addition, anaesthesia induction and maintenance were provided with midazolam (bolus at induction and continuous infusion for maintenance), pancuronium and air/O_2. Systemic and pulmonary haemodynamic variables and airway pressures were recorded intra- and postoperatively. Data were analysed with Mann Whitney *U* and Wilcoxon tests.

Results: Demographic data, time to extubation, ICU and hospital stay were similar between groups. After protamine administration, peripheral oxygen desaturation without haemodynamic deterioration was observed in six children (50%) with remifentanil use. Pulmonary artery pressures after CPB and during the first 4 h of ICU were similar ($P > 0.05$). Peak and mean airway pressures before and after CPB, and during the first 4 h of ICU were also similar ($P > 0.05$). Systemic arterial pressures in the first 4 h post-surgery were significantly higher in the remifentanil group ($P < 0.05$). Oxygen saturation before and after CPB, and during the first 4

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hours of ICU were lower in the remifentanil group but the differences were not significant ($P > 0.05$).

Conclusion: The effects of remifentanil on pulmonary artery and airway pressures were similar to fentanyl in children with preoperative pulmonary hypertension undergoing surgery for congenital heart disease. Low oxygen saturation values observed with remifentanil use require further investigation.

Reference:

1 Duncan HP, Cloote A, Weir PM *et al*. Reducing stress responses in the pre-bypass phase of open heart surgery in infants and young children: a comparison of different fentanyl doses. *Br J Anaesth* 2000; **84:** 556–564.

A-87

Comparison of conventional and combined ultrafiltration for paediatric cardiac surgery

Z. Sungur, E. Çamcı, K.Sever[1], E. Tireli[1], M Tuğrul

Department of Anesthesiology and [1]Cardiac Surgery of Istanbul Medical Faculty, Istanbul, Turkey

Introduction: The increase in total body water is one of the major side effects of cardiopulmonary bypass (CPB) that can cause more severe problems in paediatric patients in the postoperative period. In this study modified ultrafiltration combined with a conventional method was used to overcome these undesired result of CPB [1].

Method: After ethical approval, thirty children undergoing open-heart surgery were randomized in two groups. In group I (G1) conventional ultrafiltration was performed during the rewarming period of CPB. In group 2 (G2) conventional and modified ultrafiltration were combined during and at the end of CPB respectively. Haemodynamic and ventilatory data, transfusion requirements and IL-8 levels were noted in the 24-hour follow-up. Tracheal extubation and ICU discharge were according to a protocol. The statistic analysis was performed with Mann-Whitney *U* test.

Results: Two groups were comparable for age (12.9 ± 12.9 vs. 9.4 ± 1.9 months) and body weight (7.31 ± 1 vs. 7.27 ± 0.74 kg) in GI and GII respectively. CPB or aortic cross-clamp times were also similar in the two groups. Patients' diagnosis were transposition of great arteries, ventricular septal defect, atrioventricular canal, tetralogy of Fallot or total anomalous pulmonary venous drainage.

Table 1

	Group 1	Group 2
Bleeding (mL/24 h)	154.3 ± 44.5	79.2 ± 24.2***
Transfusion (mL/24 h)	142 ± 41	78.4 ± 29.9***
Mech.Ventilation time (h)	50.6 ± 51	19.7 ± 19.7*
ICU stay (h)	82.1 ± 61.5	38.7 ± 22.5*

*$P < 0.05$; ***$P < 0.001$.

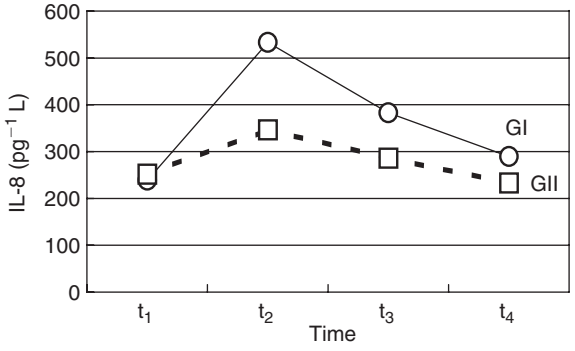

Figure: IL-8 levels; t_1 before; t_2 end; t_3 6 h after; t_4 24 h after CPB.

Discussion: Combined ultrafiltration reduced bleeding and transfusion requirements significantly. In the early postoperative follow-up, haemodynamic and respiratory parameters as well as the inflammatory mediator response were better in the combined group, but the difference disappeared at 24th hour. However the mechanical ventilation period and ICU stay were both lower in the combined ultrafiltration group. In paediatric cardiac surgery, combining two methods of ultrafiltration is recommended to reduce side effects of CPB more effectively when compared to the conventional method.

Reference:

1 Bando K, Turrentine MW, Vijay P, *et al*. Effect of modified ultrafiltration in high-risk patients undergoing operations for congenital heart disease. *Ann Thorac Surg* 1998; **66:** 821–827.

A-88

The effect of caudal morphine analgesia on extubation time in paediatric cardiac surgery

N. Hagau, I. Vlad, S. Negrutiu, F. Steiu, A. Muresan

Department of Anesthesiology and Intensive Care, Heart Institute 'N. Stancioiu' Cluj – Napoca, Romania

Introduction: The aim of this study was to evaluate the effect of morphine caudal analgesia on extubation time in the group of paediatric cardiac surgery patients who are usually extubated in the early postoperative period.

Method: After written informed consent and ethical approval, we included 116 paediatric cardiac surgery patients between 5 months and 10 yr of age undergoing uncomplicated surgical repair. The study was blinded to ICU personnel. The patients were randomly allocated to two groups of 58 each: Group I, caudal morphine analgesia (CMA), received morphine 100 $\mu g\,kg^{-1}$ in saline (0.5 $ml\,kg^{-1}$) caudally, after anaesthesia induction and before surgical incision. Group II (no CMA) did not receive caudal morphine. Premedication and induction were similar in both groups. For anaesthetic maintenance both groups received isoflurane (0.5–1%) and fentanyl. The fentanyl dose was variable, as required to block autonomic reactions during surgical intervention. The amount of intra-operative fentanyl ($\mu g\,kg^{-1}\,h^{-1}$) and extubation time (h) were recorded.

Statistical data is expressed as mean ± standard deviation. Statistical significance was detected by paired Student's *t*-test and nonparametric test (Wilcoxon's test) for evaluation. $P < 0.05$ was considered as statistically significant.

Results: The mean intraoperative iv. fentanyl was significantly less in patients who received caudal morphine (2.45 ± 1.65 $\mu g\,kg^{-1}\,h^{-1}$) compared with those who received iv. fentanyl alone (8.9 ± 3.46 $\mu g\,kg^{-1}\,h^{-1}$) $P < 0.0005$. The time to extubation was significantly less in patients who received caudal morphine (2.56 ± 2.69 h) compared with those who received iv. fentanyl alone (5.65. ± 3.48 h). $P < 0.005$. Three patient in the caudal group (all of them more than 15 kg weight) were extubated late because of morphine respiratory depression.

Discussion: (1) A significant difference was observed between the groups in terms of intra-operative fentanyl need. We have shown that caudal morphine (100 $\mu g\,kg^{-1}$) reduces the need for intra-operative fentanyl for an adequate anaesthesia level in children undergoing cardiac surgery. (2) Extubation time was also significantly reduced in the group with caudal morphine analgesia.

References:

1 Lee TWR, Jacobsohn E. Tracheal extubation should occur routinely in the operating room after cardiac surgery. *J Cardiothorac Vasc Anesth* 2000; **14:** 603–610.

2 Özcengiz D, Gűndűz M, Özbek H. The effect of perioperative caudal tramadol on sevoflurane requirements of children. *Eur J Anaesth* 2000; **17** (Suppl 19): A342.

A-89

Sedation with propofol after paediatric open heart surgery: is it safe?

A. Székely[1], E. Székely[1], E. Sápi[1], Z. Sikos[2], L. Király[3], A.Szatmári[4]

[1]Dpt of Ped. Anaesthesia and Intensive Care, [2]Dpt. of Laboratory, [3]Dpt of Ped. Card. Surgery, [4]Dpt. of Ped. Cardiology, Gottsegen National Institute of Cardiology, Budapest, Hungary

Introduction: The pharmacokinetic profile of propofol makes it an attractive agent for sedation of mechanically ventilated children. Recently, more papers reported unexpected development of

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bradyarrhythmias, metabolic acidosis, even rhabdomyolysis and fatal outcomes after propofol administration [1].

Method: Following Ethic Committee approval the data of 77 children were retrospectively and consecutively investigated. We excluded patients who were younger than one year of age and those who needed muscle relaxants in the postoperative period. Midazolam group (M) were sedated with 2–2.5 $\mu g\,kg^{-1}\,min^{-1}$ continuous infusion and in the other group propofol (P) was given as a 35–40 $\mu g\,kg^{-1}\,min^{-1}$ infusion (only above 3 yr of age). Both sedatives were combined with fentanyl 1 $\mu g\,kg^{-1}\,h^{-1}$ infusion. The following variables were analysed: demographics, diagnosis, intraoperative parameters: operation time, time of aorta cross-clamp and cardiopulmonary bypass (CPB), fluid balance, transfusion; postoperative factors: haemodynamics, time of extubation, inotropic support and laboratory values, such as creatine kinase and MB isoenzyme (CK, CKMB) [2], lactate-dehydrogenase (LDH) and its heart isoenzyme (aHBDH), blood sugar max, base excess max (BE) and renal function. The blood samples were drawn after arrival in the ICU and on the first postoperative day (POD1). Statistical analysis consisted of Mann-Whitney *U* test and ANOVA.

Results: There was no death in the investigated groups. The midazolam group was younger and had shorter CPB and operation times. Distribution of diagnosis was comparable between the two groups. The propofol group showed an increase in triglyceride values, but no lipidaemia occurred. CK activity but not CKMB was significantly higher in the P patients at POD1, without signs of metabolic acidosis. Haemodynamically, M had higher peak heart rates, than P (152 ± 19 vs. 137 ± 22).

Table:

	Midazolam (n = 40)	Propofol (n = 37)	P value
Age (yr)	4.5 ± 4.9	7.7 ± 4.9	0.006
CK arrival ($IU\,L^{-1}$)	799 ± 593	812 ± 614	0.93
CK POD1 ($IU\,L^{-1}$)	547 ± 323	1019 ± 950*	0.01
CKMB arrival ($IU\,L^{-1}$)	109 ± 68	111 ± 69	0.93
CKMB POD1 ($IU\,L^{-1}$)	53 ± 27	69 ± 55	0.15
BE max ($mmol\,L^{-1}$)	−6.4 ± 1.8	−5.8 ± 2.3	0.25
Triglyceride ($mmol\,L^{-1}$)	0.49 ± 0.16	0.66 ± 0.45*	0.05

Discussion: Our results indicate that propofol infusion in the paediatric ICU had no adverse effects on metabolic and haemodynamic postoperative conditions. However, CK must be frequently measured since CK activity may increase even during low-dose and mid-term administration.

References:

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Postoperative Topics

A-90

Postoperative analgesia with remifentanil in patients undergoing cardiac surgery

B. Steinlechner, M. Ponschab, S. Eislmeir, H. Koinig, A. Rajek

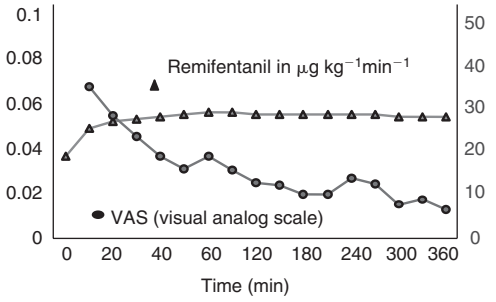
Department of Cardio-Thoracic and Vascular Anaesthesia and Intensive Care Medicine, University of Vienna, Vienna, Austria

Introduction: Postoperative pain induced stress response increases levels of catecholamines, causing hypertension, tachycardia and increased myocardial oxygen consumption. Therefore, an excellent pain management after cardiac surgery increases patient comfort while reducing postoperative complications. Remifentanil, a new and potent opioid with a very short elimination half-time, may be the ideal drug for intense postoperative analgesia and predictable recovery [1,2].

The object of this study was to define the ideal dose for continuous postoperative administration of remifentanil.

Method: After approval of the local ethics committee 28 patients were studied after cardiac surgery. General anaesthesia was performed using a continuous infusion of remifentanil and propofol. Before extubation 8 mg of lornoxicam was administered and remifentanil was reduced to a dose of 0.035 $\mu g\,kg^{-1}\,min^{-1}$ in every patient. After extubation, every 10 min during the first hour a visual analogue scale (VAS) for pain, a pain intensity score (PIS) and the level of consciousness (LOS) were recorded. During the following five hours the evaluation was performed every 30 min. Heart rate, respiratory rate, mean arterial pressure and oxygen saturation were documented at all time points. At a VAS higher than 30, remifentanil dose was increased by 0.005 $\mu g\,kg^{-1}\,min^{-1}$.

Results: Twenty-two men and 6 women with a mean age of 64 ± 10 yr undergoing cardiac surgery were included in this study. The time to extubation was 191 ± 88 min. The remifentanil dose was increased up to a maximum of 0.053 $\mu g\,kg^{-1}\,min^{-1}$ during the first 30 min whereas VAS and PIS decreased. There was no significant change in heart rate, mean arterial pressure, oxygen saturation and respiratory rate during the study period. Data are presented as mean ± SD.



Discussion: Remifentanil at a dose of 0.05 $\mu g\,kg^{-1}\,min^{-1}$ is highly effective for pain treatment in extubated patients. This short acting opioid is easily titratable and provides haemodynamic stability, increases patient comfort without causing any respiratory problems.

References:

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A-91

Similar pain scores after early and late extubation in heart surgery with cardiopulmonary bypass

P. Holmér Pettersson, G. Settergren, A. Öwall

Department of Surgical Sciences, Karolinska Institute, Division of Cardiothoracic Anaesthetics and Intensive Care, Karolinska Hospital, Stockholm, Sweden

Introduction: The tradition of using long-acting agents in cardiac anaesthesia often resulted in prolonged ventilation. Today many patients are extubated early. In selected groups of patients, fast track has been shown to be safe and cost-effective [1]. The current study addressed the question if early extubation results in more pain or in an increased use of analgesics.

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Method: Sixty patients, after ethical committee approval and informed consent, were randomized to extubation at about 2 (early) or 6 (late) hours (h) after heart surgery. Anaesthesia was based on propofol and remifentanil. Ketobemidone iv. was administered before the remifentanil infusion was stopped. In the intensive care unit analgesia and sedation were based on infusions of ketobemidone and propofol. Pain during coughing or deep-breathing was evaluated after extubation and hourly thereafter in awake patients using a visual analogue scale (VAS) range from 0 = no pain to 10 = most severe pain. The aim was to avoid VAS scores >3 and if it occurred, the infusion rate of ketobemidone was increased and a bolus dose was given. Blood levels of ketobemidone were measured at 4, 8 and 16 h after surgery. Analysis of variance, Kruskal-Wallis, *t*-test and χ^2 were used when appropriate.
Results: Three patients in the late group were excluded due to incomplete data. The groups were comparable with respect to demographics and case mix. Time to extubation was 3 h 19 min (early) and 6 h 44 min (late). Duration of surgery was somewhat shorter in the early group 2 h 41 min vs. 3 h 13 min ($P < 0.05$). Pain scores ranged from 0–10 but did not differ between the early and late group. Twenty-one patients never scored higher than 3, while 11 patients scored >3 once and 25 scored >3 more than once. Neither the accumulated dose kg^{-1} (median) of ketobemidone, 37 (early) vs. 31 mg (late) nor the blood concentrations of ketobemidone differed between the groups. There was a weak positive correlation between the accumulated doses of ketobemidone and the corresponding blood concentrations.
Discussion: Pain assessment and opioid consumption did not differ between patients randomized to either early or late extubation. In more than half of the patients pain treatment was at times inadequate during the postoperative period. The aim was to avoid pain scores >3, but such scores were noted rather frequently. Similar results have been reported with a morphine-based regimen for postoperative pain control [2]. Future protocols for postoperative analgesia must aim at avoiding the occurrence of high VAS-scores, irrespective of time of extubation.
References:
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A-92

Analgesic effects of interpleural bupivacaine with fentanyl for post-thoracotomy pain

D. Karakaya, S. Baris, F. Özkan, S. Demircan, U. Gök, E. Üstün, A.Tür,

Ondokuzmayis University, Departments of Anaesthesiology and Thoracic Surgery, Samsun, Turkey

Introduction: The choice of analgesic technique and drug for post-thoracotomy pain is controversial [1]. The aim of this study was to investigate the analgesic effect of bupivacaine/fentanyl with epinephrine combination given interpleurally after thoracotomy in a randomized placebo and intravenous controlled manner.
Method: Sixty ASA physical status I and III patients scheduled for posterolateral thoracotomy were included in the study. Patients were randomly divided into four groups to receive either 0.5% bupivacaine/1.5 $\mu g\,kg^{-1}$ fentanyl with 5 $\mu g\,mL^{-1}$ epinephrine ($n = 15$, group IPBF), or 0.5% bupivacaine with 5 $\mu g\,mL^{-1}$ epinephrine ($n = 15$, group IPB), or saline ($n = 15$, group IPS) in a total volume of 15–20 mL in 60 s by an interpleural catheter placed at the end of surgery by direct vision. The same volume of bupivacaine 0.25% and 1.5 $\mu g\,kg^{-1}$ fentanyl with 5 $\mu g\,mL^{-1}$ epinephrine to group IPBF, bupivacaine 0.25% with 5 $\mu g\,mL^{-1}$ epinephrine to Group IPB or saline to group IPS was injected through the interpleural catheter every 6 h for 48 h postoperatively. Intravenous fentanyl ($n = 15$, group IVF) and interpleural saline group (IPS) received a 1.5 $\mu g\,kg^{-1}$ fentanyl intravenous bolus at the first complaint of pain. All patients also received patient-controlled analgesia (PCA) with fentanyl for 48 h postoperatively. Adequacy of pain relief was evaluated with the 'Prince Henry Pain Scale' [2] (0 = no pain on coughing and 4 = severe pain at rest) and visual analogue pain scale. Fentanyl consumption and complications were evaluated for 48 h. Kruskal-Wallis analysis of variance, Mann-Whitney *U*, Kolmogorov Smirnov and chi-squared tests were used when appropriate for statistical analysis.
Results: Visual analogue scale scores were significantly higher in interpleural saline group at 4 and 12 h postoperatively (6.6 ± 0.4 and 5.0 ± 0.5 respectively) ($P < 0.05$). Significantly more patients in interpleural bupivacaine with fentanyl group had lower pain score during coughing and deep breathing (Table). Total fentanyl consumption via PCA device was significantly higher in intravenous fentanyl group (1069.3 ± 96 μg) than interpleural groups (577.3 ± 72.2 μg, 651.1 ± 61.9 μg, 601.0 ± 62.6 μg in IPBF, IPB and IPS groups respectively) ($P < 0.005$).

Table 1. Number of patients having 'Prince Henry pain scale' ⩽1/⩾2.

	Group IPBF	Group IPB	Group IPS	Group IVF
4 h	6/9*	4/11	1/14	3/12
8 h	11/4$^{\delta}$	4/11	4/11	3/12
12 h	10/5$^{\#}$	5/10	5/10	4/11
24 h	11/4*	7/8	5/10	6/9
48 h	12/3*	7/8	3/12	10/5

*$P < 0.05$ versus group IPS, $^{\delta}P < 0.05$ versus groups IPB, IPS and IVF; $^{\#}P < 0.05$ versus group IVF.

Conclusion: We conclude that although total fentanyl consumption decreased in the interpleural groups, pain during coughing and deep breathing was significantly reduced in only the interpleural bupivacaine/fentanyl with epinephrine group.
Reference:
1 VadeBoncouer TR. Interpleural regional analgesia. In: Ferrante FM, VadeBoncouer TR eds. *Postoperative pain management.* New York: Churchill Livingstone, 1993; 383–402.

A-93

Epidural analgesia for thoracic surgery comparing two analgesic profiles: continuous ropivacaine plus fentanyl vs. boluses of methadone

M.J. Jiménez, J. Pérez, F.J. Tercero, I. Rovira, G. Fita, M. Rubio, C. Gomar

Departments of Anaesthesia and Thoracic Surgery, Hospital Clinic, Universitat de Barcelona, Barcelone, Spain

Introduction: Management of post-thoracotomy pain becomes a challenge for anaesthesiologists because of the combination of underlying pulmonary disease and the severity of surgical pain. Epidural analgesia is considered one of the most efficient analgesic techniques for managing this kind of pain. Present tendencies recommend Patient Controlled Epidural Analgesia (PCEA) with local anaesthetic combined with low doses of opioids [1] but in our experience, single opioid epidural administration can achieve the same analgesic effects without blocking the sympathetic system and keeping muscular strength [2]. This study compares an epidural infusion of ropivacaine plus fentanyl versus boluses of epidural methadone in post-thoracotomy pain management.
Method: Patients undergoing thoracotomy for lung resection were randomly divided into two groups receiving epidural analgesia (T8–T9). Group P ($n = 25$) had PCEA (continuous infusion plus bolus) of 0.16% ropivacaine + fentanyl 3.5 $\mu g\,mL^{-1}$. Group M ($n = 23$) received epidural methadone (5–6 mg) every 8 h. Ketorolac was given in both groups (30 mg/8 h). Data analysis: analgesic level (VAS: 0–10) at rest and effort; pulmonary function (peak expiratory flow, gas exchange, respiratory rate); secondary effects (hypotension, motor block, sedation or vomiting) were recorded at 1, 2, 6, 12, 24 and 48 h postoperatively.
Results: No differences were found in VAS values between groups (Table 1). The statistically significant differences found were: (1) % of

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patients that needed rescue analgesia at 24 and 48 h (higher in group P); (2) hypotension events at the first hour (P group patients); (3) PaO_2 at 24 h (lower in M group patients) (Table 2). $PaCO_2$ values were similar between groups. After discharge from ICU (48 h stay), HR, BP and respiratory rate were controlled.

Table 1

	VAS rest (mean)						VAS effort (mean)					
Hours	1	2	6	12	24	48	1	2	6	12	24	48
Group P	3.3	2.4	1.2	0.9	0.9	0.6	4.7	4.1	2.6	2.5	3.1	2.5
Group M	2.7	2.1	1.3	1.1	0.9	0.7	3.8	3.3	3.0	2.7	3.2	1.5

Table 2

	Rescue (%)			Hypotension (%)			PaO_2 (kPa)		
Hours	1	24	48	1	24	48	1	24	48
Group P	44	32*	28*	28*	12	0	14.8	12	11
Group M	69.6	8.7	0	0	8.7	4.3	14.8	10.5*	10.3

Percentage (%) and mean values. Anova *t* test $*P < 0.05$.

Conclusions: In this study, methadone showed a better analgesic profile than PCEA because of its lower need for analgesic rescue and lack of hypotensive or vomiting events. Pulmonary function parameters were similar between groups and even though PaO_2 was lower in the methadone group values remained at a clinically safe level.

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A-94

Myocardial recovery after cardiac surgery: is the ECG an indicator of stunning? A comparison between beating heart and standard CPB CABG

G. Crescenzi, F. Pappalardo, A.M. Scandroglio, G. Landoni, V. Cedrati, E. Bignami, A. Zangrillo

Department of Cardiac Anesthesia and Intensive Care, San Raffaele Hospital – Vita e Salute University, Via Olgettina 60, 20100 Milano, Italy

Introduction: Some authors [1,2] have observed the prognostic relevance of QRS changes in lead V5 during cardiac surgery with CPB. We have compared the V4–V5 leads R wave amplitude in patients undergoing CABG with or without CPB on the hypothesis that these transient changes might reflect myocardial stunning secondary to aortic cross clamping, eliminating the confounding effects of CPB.

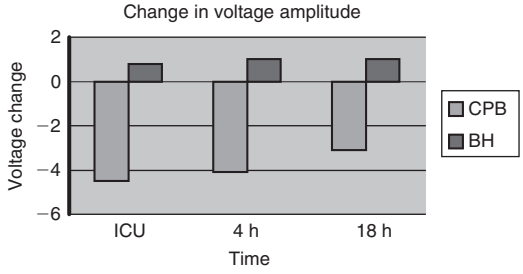
Method: Fifty four patients (19 beating heart (BH) off-pump, 35 CPB) undergoing isolated, multi-vessel revascularization were enrolled. A control group of 31 patients undergoing mitral valve repair was evaluated. 41 patients with an abnormal preoperative ECG or a perioperative MI were excluded. R wave amplitude in leads V4–V5 was measured at baseline, at arrival in ICU, 4 and 12 hours postoperatively. At the same time myocardial necrosis markers (CK-MB, cTnI) were measured.

Dichotomic variables were analysed with χ^2 and Fisher's test; stepwise multivariate logistic regression was performed to study the correlation between the perioperative variables and the loss of potentials. Only variables with a statistical significance ($P < 0.01$) at univariate analysis entered the regression.

Results: Patient population was homogeneous for preoperative characteristics and ECG data. ECG tracings recorded at ICU arrival and after 4 h showed a significant reduction of R wave amplitude in V4–V5 in the CPB group, whereas the BH population had an increase. Both absolute and delta (Δ) values are statistically significant ($P = 0.03$; $P = 0.0002$). The ECG returned to the preoperative amplitude 18 h after surgery.

CK-MB and cTnI were clearly higher in the CPB population, confirming the data in the literature, with a linear correlation between the release of troponin and R wave amplitude in V5.

At multivariate analysis the surgical technique (CPB vs. BH) was the only variable associated with the loss of amplitude of R wave in the precordial leads V4–V5 (OR 4.3, CI 95% 1.09–233, $P = 0.0002$).



Difference between preop and postop lead V5 amplitude (mm); BH = beating heart.

Discussion: Myocardial conductivity is a major determinant of R wave amplitude [3] in acute myocardial ischaemia. The slow recovery of R wave amplitude after CPB with aortic cross clamping suggests that ischaemia-reperfusion also delays its recovery. This electrophysiological disturbance might be related to stunning of the left ventricular myocardium. This phenomenon may not be seen after beating heart procedures because the utilization of an intra-coronary shunt protects against ischaemia reperfusion injury. The trend in R wave potentials in V4-V5 strictly reproduces the 'recovery pattern' of stunned myocardium after CPB. The nadir of amplitude reduction of R wave troughs at 5 h, with recovery within 24 h. Stunned myocardium is revealed also by the linear correlation between these ECG changes and the release of troponin.

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A-95

Long-term alterations of heart rate dynamics after CABG surgery

T. Laitio, H. Huikuri, J. Jalonen, E. Kentala, H. Scheinin

Turku University Hospital, Turku, Finland

Introduction: It has been suggested that fractal organization may be a central organizing principle of physiological structure and function [1]. Earlier studies have shown that the change of fractal heart rate (HR) dynamics toward more random behaviour, i.e. decrease of fractal scaling exponent α_1, is predictive for morbidity and mortality in a variety of life-threatening cardiac pathologies [1]. Similar alterations in nonlinear dynamics appear in the immediate postoperative phase of coronary artery bypass graft (CABG) surgery [2]. On the contrary, breakdown of fractal HR dynamics toward more predictable and less complex behaviour, i.e. increase of fractal scaling exponent α, is associated with physiological aging [1]. The purpose of this study was to determine whether alterations of HR dynamics recover during one year follow-up of CABG surgery.

Method: Continuous 24-hour electrocardiograph recordings were performed in 26 elective CABG surgery patients one week before surgery, during the first postoperative day, six weeks and six months postoperatively. In addition, recordings were performed in 17 patients one year postoperatively. Time and frequency domain measures of HRV were assessed along with measurement of short- and intermediate-term fractal scaling exponents (α_1 and α_2) of detrended fluctuation analysis (DFA), and approximate entropy (ApEn) [1].

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Results: Time and frequency domain measures decreased significantly after operation and stayed low during the follow-up period. Scaling exponent α_1 decreased postoperatively and recovered during the period of six weeks to six months. Scaling exponent α_2 increased (preoperative vs. one year postoperative values: 1.10 ± 0.09 vs. 1.18 ± 0.09, $P < 0.01$) and ApEn decreased significantly (0.94 ± 0.20 vs. 0.83 ± 0.20, $P < 0.01$, Wilcoxon test with Bonferroni correction) during the first postoperative year.

Discussion: Current results show a breakdown of fractal organization of HR dynamics toward less complex and predictable behavior after CABG surgery. These alterations are similar to those seen in physiological aging. However, the prognostic value of such alterations is not known but may result in a less adaptable system.

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A-96

Can intrapulmonary shunt after cardiopulmonary bypass be prevented by ventilatory manoeuvres?

A. Bambazek[1], W. Wisser[1], E. Gruber[1], K. Skhirdlatze[1], P. Keznickl[1], E. Tschernko[1]

[1]Dept. of Cardiothoracic and Vascular Anaesthesia & Intensive Care; [2]Dept. of Cardiothoracic Surgery, Univ. of Vienna, General Hospital, Vienna, Austria

Introduction: It has been proven in humans and animals that atelectasis is a major cause of intrapulmonary shunt and hypoxaemia after cardiopulmonary bypass (CPB) [1]. Animal studies suggest that shunt can be prevented entirely by a total vital capacity manoeuvre (TVCM) performed before termination of CPB. However, we could not confirm these findings in humans [2]. The aim of this study was to test whether inverse ratio ventilation after CPB could be beneficial in preventing postoperative pulmonary shunt.

Method: Thirty-six patients scheduled for coronary artery bypass grafting (CABG) were randomly assigned to receive no TVCM (Control group; $n = 12$), a standard TVCM (TVCM group; $n = 12$), or a standard TVCM with subsequent inverse ratio ventilation (Inverse group; $n = 12$). Additionally, 12 consecutive patients undergoing Off-pump coronary artery bypass grafting (Off-pump group) were studied. The ICU personnel was not aware of the group assignment. Systemic and central haemodynamics, the pattern of breathing, and ventilatory mechanics (pulmonary compliance = V_T/end-inspiratory pressure minus end-expiratory pressure) were evaluated after induction of anaesthesia, after sternotomy, after CPB and skin-closure, and four hours after extubation. Data are mean ± SD. ANOVA was used for statistical analysis.

Results: The use of TVCMs reduced ($P < 0.05$) intrapulmonary shunt after termination of CPB. However, shunting increased ($P < 0.05$) in all groups (table) although less pronounced inthe Off-pump group ($P < 0.05$). Pulmonary compliance decreased ($P < 0.05$) in all groups except the Off-pump group after extubation.

Table. Intrapulmonary shunts (%).

	Baseline (%)	After extubation (%)
Control	8.2 ± 3.3	25.6 ± 8.1*
TVCM	8.7 ± 3.4	24.4 ± 8.5*
Inverse	7.9 ± 1.9	24.5 ± 9.6*
Off-pump	7.8 ± 2.8	14.0 ± 5.3*†

*$P < 0.05$ vs. control; †$P < 0.05$ vs. TVCM and Inverse.

Conclusion: The development of intrapulmonary shunt and hypoxaemia after CABG can be reduced by performance of TVCMs in the early postoperative period. Inverse ratio ventilation shows no benefit. However, Off-pump surgery is superior in preventing shunt and hypoxaemia after CABG in the immediate and early postoperative period.

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A-97

Does apolipoprotein E ε4 allele affect neurobehavioral status after on-pump coronary artery bypass grafting?

Fatma Zekiye Aşkar[1], Hasan Yurday Çetin[1], Özgül Çetin[2], Ahmet Acarer[3], Emre Kumral[3], Buket Kosova[4], Tahir Yağdi

[1]Departments of Anaesthesiology and Intensive Care, [3]Neurology, [2]Psychiatry, [4]Medical Biology and Cardiovascular Surgery, Medical School, Ege University, Izmir, Turkey

Introduction: The presence of Apolipoprotein E ε4 (APOE4) allele is being considered as a risk factor for cognitive decline after cardiac surgery [1,2]. We studied the effect of APOE4 allele on neurobehavioural status after on-pump coronary artery bypass grafting (CABG).

Method: After ethics committee approval and informed consent, we enrolled 58 patients, 44 male and 14 female, who would undergo elective CABG surgery while on cardiopulmonary bypass (CPB). Patients with neurologic or psychiatric disorder and those who had restriction to complete neurobehavioural tests were excluded. Prior to the operation, neurologic examination and neurobehavioural cognitive status test-COGNISTAT (The Neurobehavioral Cognitive Status Examination, The Northern California Neurobehavioral Group, Inc.) – were performed by trained people (a neurologist and a psychologist). Both procedures were repeated on the day of discharge and 3 months after surgery. A standard anaesthesia protocol was used for all patients. The genotypes of the patients for APOE4 were identified by molecular DNA analysis with real-time online polymerase chain reaction and fluorescence resonance energy transfer technique on blood samples. The neuro/cognitive testers did not know the APOE4 results. APOE4 positive ($n = 14$; 24.1%) and APOE4 negative ($n = 44$; 75.9%) patients' performance on COGNISTAT and their neurologic status were compared. When analysing individual data, for each subtest of COGNISTAT, significant deterioration was defined as 20% deficit from baseline. The data were evaluated with Friedman test, Wilcoxon's signed ranks test, Mann-Whitney *U* test and Fisher's exact test. Bonferroni's correction was applied for repeated parameters. $P < 0.05$ was considered significant.

Results: There was no statistically significant difference between the two groups of patients' demographic data. No neurologic impairment was observed on examinations. CPB time and cross-clamp times were similar. According to individual data analysis statistically significant percentage of declining patients and the subtests they performed poor are shown in Table1.

Table 1. Statistically significant percentage of declining patients for given subtests of COGNISTAT.

	Day of discharge vs. Preop.	3 months later vs. preop.	3 months later vs. day of discharge
APOE4(−)'ve	*Construction* 22.7% ($P = 0.007$) *Judgement* 4.5% ($P = 0.022$)	*Orientation* 2.3% ($P = 0.043$)	No decline in any subtest
APOE4(+)'ve	*Orientation* 14.3% ($P = 0.001$) *Construction* 64.3% ($P = 0.007$) *Judgement* 28.6% ($P = 0.022$)	No decline in any subtest	No decline in any subtest

Discussion: According to this data, APOE4 allele does not seem to affect neurobehavioral status after CABG surgery.

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A-98

Acute renal failure after cardiac surgery: toward a common definition?

C. Solinas, M. Mazzoni, R. Ceriani, G.B. Villa, M. Deledda, G. Zarcone, M. Locati, E. Cremonesi, V. Arena[1] and F. Bortone

Anesthesia and ICU, [1]Cardiac Surgery, Humanitas Gavazzeni, Bergamo, Italy

Introduction: New criteria to define acute renal failure have been recently proposed by Bellomo [1]. This definition should adjust for degree of injury and renal dysfunction, for the presence of chronic renal failure and the need for renal replacement therapy (RRT). A serum creatinine and plasma urea above the normal reference values ($>120\,\mu mol\,L^{-1}$ and $>8\,mmol\,L^{-1}$ respectively) and/or urine output <800 mL/24 h, define acute renal injury (ARI) and the values that are twice the upper values for normal (creatinine $>240\,\mu mol\,L^{-1}$ and urea $>16\,mmol\,L^{-1}$ and and/or urine output <400 ml/24 h) define acute renal failure syndrome (ARFS). Finally, ARFS where the use of RRT becomes necessary is indicated by severe ARFS. The presence of chronic renal failure is indicated by an addendum like 'acute on chronic' (A/C). Therefore, we evaluated the epidemiology and the consequences of postoperative acute renal changes as defined by these newly proposed criteria in a cardiac population.

Method: All adult patients undergoing a cardiac operation between January 1, and December 5 2002 ($n = 645$) were stratified according to EuroSCORE risk categories.

Results:

EuroSCORE risk	Low (%)	Intermediate (%)	High (%)
Overall Population	23.4	38.5	38.0
No Renal Complication	31.6*	41.4*	27.0*
ARI + ARI A/C	9.7	40.2	51.8
ARFS + ARFS A/C	7.7	19.2	73.1
Severe ARFS	3.8	7.7	88.5

*$P < 0.01$ No Renal Complic. vs ARI, ARFS, and Severe ARFS χ^2 test.

	No renal complications	ARI + A/C	ARFS + A/C	Severe ARFS
Incidence (%)	64.2	26.7	4.2	4.2
ICU LOS (h) ± SD	32.6 ± 30.7	75.9* ± 84.5	141.9* ± 116.9	289.5* ± 126.5
Hospital mortality (%)	0.5	2.3	3.7	25.9†°

*$P < 0.01$ *t* test †$P < 0.01$ vs ARI and No Compl °$P = 0.05$ vs ARFS χ^2 test.

Discussion: Acute postoperative renal changes were more frequent for higher preoperative risk category. Increasing degrees of postoperative renal impairment were associated with prolongation of ICU stay without affecting mortality. Adverse outcome may be explained by more severe levels of multi organ impairment. These definitions seem applicable to this selected patient population and may be helpful to describe the impact of degrees of renal injury and failure on the use of ICU resources and on outcome. The adoption of common criteria to define acute renal failure should be encouraged to facilitate research in this field.

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A-99

Renal blood flow with and without intra-aortic counterpulsation

P. Sprogøe, C.L. Christiansen, A. Hørlyck, J. Solvig

Dept. of Cardiothoracic and Vascular Surgery, Dept. of Cardiothoracic Anaesthesia, Dept. of Radiology, Skejby Sygehus, Aarhus University Hospital, Denmark.

Introduction: The aim of this investigation was to monitor changes in renal blood flow due to intra-aortic balloon counterpulsation (IABP).

Method: Over a period of 21 months, 7 patients with an ejection fraction (EF) <25%, undergoing CABG surgery, were included.

The IAB was preoperatively inserted into the femoral artery by a percutaneous technique. The IABP counterpulsation supported the circulation during surgery except during aortic X-clamping, and postoperatively until the circulation was stable.

Spectral-Doppler ultrasound was used in order to estimate the interlobular blood flow velocity of the renal artery in all patients preoperatively (pre-IABP), after arrival in ICU (per-IABP) and after removal of the IABP (post-IABP).

The most representative spectral-curves from each patient were used to quantify the velocity profiles. The velocity profiles are described as Balloon Index (BI) = maximum systolic velocity/mean velocity.

Plasma creatinine was lower per-IABP and creatinine clearance were measured pre-IABP, per-IABP and post-IABP. Data are presented as mean values ± SD. Statistical analysis was made with Kruskal-Wallis test for one-way analysis of variance by ranks.

Results: The 7 patients had 12 pre-, 23 per- and 19 post-IABP representative Doppler-ultrasound BI calculated. BI-values (pre-, per- and post-IABP) did change over time ($P < 0.05$) (table), so that BI was less per-IABP than pre- and post-IABP ($P < 0.21$).

Plasma-creatinine was lower per-IABP, but the changes were not significant ($P < 0.21$). The same change was seen with creatinine clearance, which was higher per-IABP, but not significantly ($P < 0.44$).

	Pre-IABP	Per-IABP	Post-IABP
Balloon index ($m\,s^{-1}$)	2.2 ± 0.31	1.6 ± 0.06	1.98 ± 0.08
P Creatinine ($mmol\,L^{-1}$)	125 ± 16	105 ± 11	112 ± 16
Creatinine-Cl ($mL\,s^{-1}$)	62 ± 26	95 ± 19	75.7 ± 11

Conclusion: IABP counterpulsation increased renal blood flow measured by Doppler ultrasound without any significant changes in creatinine clearance values.

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A-100

Insulin resistance after cardiac surgery: maintaining euglycaemia with insulin and thoracic epidural analgesia

R.E. Anderson[1], J. Ehrenberg[1], G. Barr[1], T. Ivert[2]

[1]Dept Cardiothoracic Anaesthetics Intensive Care, [2]Dept Surgery, Karolinska Hospital, Stockholm, Sweden

Introduction: Normoglycaemia after cardiac surgery decreases mortality and morbidity markedly [1]. Hyperglycaemia depresses phagocytic function, while insulin increases neutrophil count and phagocytic capacity. Fasting and surgical stress contribute to insulin resistance and aggressive perioperative insulin treatment, feasible only in the ICU, is required to achieve euglycaemia (even in non-diabetics). Ward resources are often limited to serial blood glucose (B-Glu) testing for diabetics. Thoracic epidural analgesia (TEDA) improves per-op glucose tolerance [2]. The goal of this pilot study was to determine if TEDA, per- and 3 days post-op, would minimize the need for treating postoperative hyperglycaemia in non-diabetics.

Method: Non-diabetic patients with TEDA ($N = 6$; Th 1-4; per-op 10 mL + 5 mL bupivacaine 0.5%; post-op infusion bupivacaine $1\,mg\,mL^{-1}$ + sufentanil $0.5\,\mu g\,mL^{-1}$ + clonidine $1\,\mu g\,mL^{-1}$) for CABG surgery, were compared to controls ($N = 15$). B-Glu was measured frequently on day 0, and 4 times daily for day 1–3. No glucose was given before or during surgery, but patients received $100\,mg\,kg^{-1}h^{-1}$ postoperatively in ICU and insulin to maintain

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B-Glu < 6.1 mmol l^{-1} (ca 24 h). Patients returned to the ward on the morning after operation; B-Glu was measured 4 time/day for 3 days (fasting, 2–3 h postprandial); no insulin was given on the ward.

Results: All patients had normal fasting B-Glu and S-insulin preoperatively. Maintaining euglycaemia during the perioperative 24 h (mean 7 vs. 6.3 mmol L^{-1} for controls vs. TEDA) required 72 vs. 41 units insulin ($P < 0.002$). On the wards, all patients in both groups had repeated hyperglycaemia, both fasting and 3 h postprandial.

Table: shows percentage of B-glucose measurements in relation to a B-Glu (mmol/L) of 6.1 and 10 during 3 postoperative days.

	N	Fasting <6.1	3 h post-prandial <6.1	% >10
Controls	15	45%	8%	11%
TEDA	6	20%	6%	6%

Discussion: The insulin resistance arising in conjunction with cardiac surgery results in postoperative hyperglycaemia for at least 3 days. TEDA activated before surgery and maintained several days postoperatively decreases the amount of insulin required to maintain normoglycaemia during the peri-operative 24 h period, but does not measurably (preliminary data, on-going study) prevent hyperglycaemia during the 3 first postoperative days. This suggests that TEDA inhibits stress hormone-induced glycogenolysis but does not dampen postoperative insulin resistance. This study demonstrates that even for non-diabetics, hyperglycaemia is a common problem days after CABG surgery.

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A-101

A prospective study of postoperative hyperamylasaemia in cardiac surgical patients

M. Lips, M. Stritesky, J. Kunstyr, D. Rubes

Charles University Teaching Hospital, Prague, Czech Republic

Introduction: Incidence of hyperamylasaemia after cardiac surgery is reported in about 30–70% of patients [1]. The exact cause of elevated serum levels of amylase remains unclear. The goal of our study was to established the possible cause of its elevation and evaluate the influence of increased levels of serum amylase on the postoperative course and clinical outcome of cardiac surgical patients.

Method: The cohort of 110 randomly selected patients who underwent cardiac surgery at our institution was studied prospectively. There were 77 male and 33 female with mean age 69 (45–80) years. Serial blood and urine samples were obtained on the 1st and 2nd mornings after operation. Pancreatic isoamylase, creatinine, the fractional clearance of pancreatic isoamylase (relative to creatinine clearance) were measured. To establish the severity of pancreatic cellular injury we used the semi quantitative urinary trypsinogen-2 dipstick test. Postoperatively we observed clinical signs of acute pancreatitis, route of feeding and time to discharge from the postoperative intensive care unit.

Results: In 22 out of 110 patients (20%), at least one blood sample showed an increased level of serum pancreatic isoamylase. (Table 1). Trypsinogen-2 dipstick test was positive in only one patient (with hyperamylasaemia). No patient showed clinical signs of acute pancreatitis. Statistically significant independent predictors of postoperative hyperamylasaemia were preoperative elevated pancreatic isoamylase and a perioperative haemodynamic insult (sustained low cardiac output with mean blood pressure <50 mmHg).

Table 1.

Group	No. of Patients	P-isoamylase (μkat L^{-1}) mean (SD)
No amylasaemia	88	0.43 (0.15)
Hyperamylasaemia	22	2.18 (1.73)

Discussion: Elevated pancreatic isoamylase within 48 h after cardiac surgery probably does not represent serious pancreatic injury [2]. Its elevation is related to a preoperative elevated serum pancreatic isoamylase. Another possible cause seems to be a perioperative haemodynamic insult. According to other authors [2,3] and to our results, we can conclude that an isolated postoperative increase of pancreatic isoamylase without clinical signs of acute pancreatitis does not affect the operative results after cardiac surgery.

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A-102

Preoperative procalcitonin levels and the incidence of complications in the early postoperative period after heart transplantation

E. Urbańska, P. Knapik, P. Nadziakiewicz, W. Saucha, J. Puzio

Department of Cardiac Anesthesia, Silesian Center for Heart Diseases, Zabrze, Poland

Introduction: Procalcitonin (PCT) levels below 0.5 ng mL^{-1} are considered as normal [1]. Heart transplant recipients sometimes present increased PCT levels before heart transplantation. This is probably due to immune activation in patients with severe heart failure [2]. PCT level >2 ng mL^{-1} in a cardiac donor at the time of explantation appears to predict early graft failure-related mortality [3]. However the prognostic value of initial PCT levels in a heart transplant recipient remains unknown. The aim of this study was to find out whether preoperative PCT levels may be linked to complications in the early postoperative period after heart transplantation.

Method: PCT levels were measured in 50 patients before heart transplantation. Patients were divided into two groups according to initial PCT levels. Normal preoperative PCT levels (<0.5 ng mL^{-1}) were found in 32 patients, while increased PCT levels (⩾0.5 ng mL^{-1}) in 18 patients. Important data regarding patients have been compared between groups (see table below). *T*-test and Fisher's exact test were used for statistical analysis and $P < 0.05$ was considered significant.

Results: Mean preoperative PCT level was 0.7 ng mL^{-1} (from 0.07 ng mL^{-1} to 3.6 ng mL^{-1}). Results are presented in Table 1:

Initial PCT		<0.5 ng mL^{-1} ($n = 32$)	⩾0.5 ng mL^{-1} ($n = 18$)	*P*
Age (years)		47 ± 9	43 ± 13	NS
Gender	male	34 (89%)	11 (92%)	NS
	female	4 (11%)	1 (8%)	
Perfusion time (min)		170 ± 49	209 ± 88	NS
Cross-clamp time (min)		179.3 ± 59	235 ± 70	<0.01
Ventilation time (hours)		53 ± 70	44 ± 50	NS
Infection incidence		6 (18.7%)	3 (16.6%)	NS
Multi organ failure		1 (3.1%)	2 (11.1%)	NS
Haemofiltration		2 (6.2%)	0 (0%)	NS
Norepinephrine infusion		5 (15.6%)	3 (16.6%)	NS
Platelet supplementation		10 (31.2%)	4 (22.2%)	NS
Death		4 (12.5%)	3 (16.6%)	NS

Conclusion: Preoperative PCT levels were not linked to the incidence of postoperative complications after heart transplantation within the observed range of values.

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A-103

Postoperative course and economic impact of coronary surgery without cardiopulmonary bypass

I. Rätsep, V. Toome, K. Kalling, I. Karu, J. Narbekov, H. Erm, R. Loit, A. Kink

North Estonian Regional Hospital, Tallinn, Estonia

Introduction: Off-pump coronary artery surgery (OPCAB) is reported to have superior results in terms of recovery, early complications and hospital costs compared to conventional coronary artery bypass (CCAB) with extracorporeal circulation (ECC) [1]. The aim of this retrospective study was to specify differences between these two techniques in our institution.

Method: Ninety five consecutive patients having operations between September and December 2001 were included in an OPCAB group ($n = 48$) or CCAB group ($n = 43$). Decision about the technique used was based on organizational facilities but not on clinical indications. The groups were comparable in terms of demographics and preoperative risk scoring. All patients had similar anaesthetic management. Postoperative laboratory and clinical data were compared using one-way ANOVA and Chi-squared tests. $P < 0.05$ was considered statistically significant.

Results: The number of distal anastomoses was significantly higher in the CCAB group than in the OPCAB group (3.3 vs. 2.8). Three patients (1 in OPCAB group) were re-operated due to bleeding. One patient (CCAB) developed a myocardial infarction and no patient died in hospital. Statistically significant differences between the study groups are expressed in the table as mean ± SD. Total hospital cost per case was lower in the OPCAB group (5430 EUR vs. 6549 EUR).

Table:

	CCAB ($n = 43$)	OPCAB ($n = 50$)	P
PaO_2 at ICU arrival [kPa]	15.9 ± 5.2	18.9 ± 5.1	<0.05
Time on ventilator [h]	11.3 ± 4.9	8.9 ± 3.3	<0.05
LOS in ICU [h]	51.5	30.6	<0.05
LOS in hospital [d]	9.4 ± 6.6	7.8 ± 2.4	0.117
Inotropic support in ICU [n]	12	1	<0.001
Platelet count [$\times 10^9 L^{-1}$]	171.4 ± 56.4	205.1 ± 46.9	<0.05

Discussion: As the duration of surgery was comparable for both groups, the number of distal anastomoses is unlikely to have changed the postoperative course. We conclude that OPCAB patients had a more favourable ICU period regarding the need for ventilatory and inotropic support. Lower hospital cost is mainly due to shorter ICU stay and omission of ECC.

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A-104

Thoracic spinal cord stimulation for treatment of refractory angina pectoris

A. Dongas, S. Eckert[1], H. Güldner[2], D. Horstkotte[1], K. Inoue

Depts. of Anaesthesiology, [1]Cardiology and [2]Cardiovascular Surgery, Heart Centre NRW, University of Bochum, Bad Oeynhausen, Germany

Introduction: Spinal cord stimulation (SCS) as a treatment for refractory angina pectoris was first reported in 1987 [1]. With the development of modern electronic techniques, this modality became routinely used in some European centres. We evaluated this new method in 17 patients in whom neither coronary artery bypass grafting (CABG) nor percutaneous transluminal coronary angioplasty seemed to be suitable.

Method: All patients (16 male, 1 female, age 66 ± 8 yr) had angina in Canadian Cardiovascular Society (CCS) functional class III or IV and therefore their daily activities were restricted to a great extent. In prone position, a 4-polar stimulation electrode was placed with local anaesthesia through Th6 to Th8 into the epidural space under fluoroscopy. The correct placement was verified by location of paraesthesia which was provoked by an external stimulator. The location of paraesthesia corresponded to the area of anginal pain. An internal stimulator was implanted under general anaesthesia in the lateral position after stimulation trials of 3 to 6 days.

Results: In 15 of 17 patients, the SCS was highly effective. In a follow-up period of 1 to 23 months, 6 patients experienced no anginal pain at all. In 4 patients, the CCS functional class III reduced to CCS I and in 5 patients, CCS IV to CCS II. In 2 patients, a revision of the stimulation electrodes was necessary due to dislocations (3 weeks and 6 months after implantations).

Discussion: Mannheimer *et al*. [2] found in their randomized trial that mortality rate and cerebrovascular morbidity were lower in the SCS group than in the CABG group while the relief of symptom was similar in both groups. We consider also that the SCS is a reliable and effective treatment for refractory angina pectoris when other methods fail to alleviate pain. The correct implantation of the SCS system is easy to perform and well accepted by patients.

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