

Comparison of haemodynamics and myocardial injury markers under desflurane vs. propofol anaesthesia for off-pump coronary surgery. A prospective randomised trial

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Abstract

Background: Several studies have highlighted that volatile anaesthetics improve myocardial protection in cardiopulmonary bypass coronary surgery. However, the haemodynamic effect of desflurane in off-pump coronary surgery has not been clarified yet. Our study hypothesis was that desflurane-fentanyl anaesthesia could decrease myocardial injury markers and improve haemodynamics compared to propofol-fentanyl in patients undergoing off-pump coronary surgery.

Methods: Design: Prospective, randomised open-label study. Sixty elective patients with left ventricular ejection fraction above 30% received either desflurane (group D, n = 32) or propofol (group P, n = 28), in addition to fentanyl and vecuronium bromide anaesthesia for off-pump coronary surgery. Assessment of haemodynamic function included thermodilution continuous cardiac output and right ventricular end diastolic volume.

Results: No significant differences in cardiac output, stroke volume and mean arterial pressure were noted between groups. The only observed difference in haemodynamic profile was that group D demonstrated improved stability, expressed as left ventricular stroke work index (LVSWI). Decrease in LVSWI after performing distal anastomoses was smaller in D compared to P (median value: –14.3 and –19.8 [g m⁻² beat⁻¹]), respectively ($P = 0.029$). Oxygen uptake index (VO₂I) and oxygen extraction ratio (OER) after skin incision were lower in D, while blood lactate concentration was slightly higher after surgery in D compared to P. The groups did not differ with respect to CK-MB and troponin I concentration.

Conclusions: This study demonstrated no difference between desflurane and propofol anaesthesia for off-pump coronary surgery in major haemodynamic parameters, as well as in myocardial injury markers and the long-term outcome. However, the study indicated that desflurane might accelerate recovery of myocardial contractility, as assessed by LVSWI. Lower oxygen uptake and elevated lactate under desflurane anaesthesia indicated a discrete shift towards anaerobic metabolism.

Clinical trial registration information: NCT00528515 (<http://www.clinicaltrials.gov/ct2/show/NCT00528515?term=NCT00528515&rank=1>)

Key words: anaesthetics, intravenous; anaesthetics, inhalation; haemodynamics; coronary artery bypass, off-pump; oxygen consumption

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The reduction of postoperative complications related to cardiopulmonary bypass is the major goal of developing less invasive techniques such as off-pump coronary surgery. This method, however, is not free from complications, including sequels of haemodynamic instability. Both propofol and volatile anaesthetics, in addition to opioids and muscle relaxants, are widely considered safe during coronary surgery, being free from significant haemodynamic compromise. Volatile anaesthetics have been reported to exert cardio-protective effects referred to as 'anaesthetic conditioning', exceeding propofol-related myocardial protection [1–5]. Similarly to sevoflurane and isoflurane, desflurane has also been demonstrated to reduce the serum concentration of myocardial necrosis biomarkers and improve heart function in patients undergoing cardiopulmonary bypass coronary surgery [1]. The negative effect of propofol on the left ventricular systolic function has been demonstrated to be similar to desflurane [6]. An experimental study in dogs submitted to myocardial ischaemia-reperfusion demonstrated that left ventricular wall thickening fraction recovered earlier under desflurane compared to propofol anaesthesia [7]. Yet the question as to whether volatile anaesthesia with desflurane for off-pump coronary surgery patients is superior to intravenous anaesthesia with propofol remains unresolved.

The primary aim of this study was to assess the influence of desflurane and propofol anaesthesia on cardiovascular function and serum concentrations of myocardial necrosis markers in patients submitted to off-pump coronary surgery. The secondary aim was to compare oxygen uptake and extraction ratio under desflurane and propofol anaesthesia.

METHODS

PATIENTS

The study protocol conformed to the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki. It was approved by the local institutional review board for scientific studies (NKEBN/364-A/2005) and registered in the Clinical Trials Protocol Registration System (NCT 00528515). Sixty two patients scheduled for off-pump coronary revascularisation in a tertiary care centre were randomly assigned either to group D (desflurane; $n = 32$) or group P (propofol; $n = 30$) by a simple randomisation method between March 2006 and December 2007. All patients signed written informed consent. The attending anaesthesiologist was responsible for patient enrollment and the generation of the random allocation sequence, thus the study was not blinded to evaluators. Two patients from P were excluded immediately before surgery due to the surgeon's decision to operate on-pump, leaving $n = 28$ in the analysis. The flow-chart of the studied patients is presented in Figure 1. Conversion to cardiopul-

monary bypass coronary surgery was not necessary in any patient during the procedure. Left ventricular ejection fraction below 30%, myocardial infarction less than two months before surgery, urgent surgery, atrial fibrillation, age over 80, preoperative serum creatinine above 1.9 mg dL^{-1} and moderate to severe mitral or tricuspid valve regurgitation were considered exclusion criteria.

ANAESTHETIC MANAGEMENT

All patients received lorazepam $50 \mu\text{g kg}^{-1}$, ranitidine 150 mg, and metoprolol 12.5 mg one hour before transport to the operating theatre. Both groups received the same intravenous anaesthesia induction, consisting of 0.2 mg fentanyl, 0.3 mg kg^{-1} etomidate and vecuronium bromide 0.1 mg kg^{-1} for muscle relaxation. The latter dose was followed by continuous infusion at the rate of $0.05 \text{ mg kg}^{-1} \text{ h}^{-1}$ until the sternum was closed. For intraoperative analgesia, both groups received fentanyl in fractions up to a total dose of $20\text{--}30 \mu\text{g kg}^{-1}$. After anaesthesia induction, triple lumen catheter and pulmonary artery catheter for continuous cardiac output measurement (CCO mbo V, 774HF75, Edwards Lifesciences, Irvine, CA, USA) were introduced via the right internal jugular vein. Maintenance of anaesthesia in group D was accomplished with inhaled desflurane by a vaporiser set to 3–9% throughout the procedure, oxygen flow set to 1 L min^{-1} , and air flow set to 2 L min^{-1} for an initial 5 min, and then reduced to 0.6 L min^{-1} and 0.8 L min^{-1} respectively. The attending anaesthesiologist aimed at maintaining 1 MAC of desflurane for at least 15 minutes before coronary artery clamping. Maintenance of anaesthesia in group P was accomplished using continuous intravenous infusion of propofol $2\text{--}4 \text{ mg kg}^{-1} \text{ h}^{-1}$. Desflurane concentration and propofol infusion rate were adjusted according to haemodynamic parameters and the depth of anaesthesia, as assessed with BIS, aiming at its range of 40–60. After positioning of the pulmonary artery catheter, it was connected to a Vigilance monitor (Edwards Lifesciences) for continuous measurement of cardiac output, right ventricular end-diastolic volume (RVEDV) and mixed venous haemoglobin saturation with oxygen (SvO_2). SvO_2 sensor was calibrated *in vivo* after the catheter insertion and again after patient admission to postoperative ICU. Mitral and tricuspid valves regurgitations were assessed during heart displacement with multi-plane transoesophageal echocardiography (TEE) transducer (GE Medical Systems 6Tc-RS; 5.0MHz) and Vivid q Cardiac Ultrasound System. Before anaesthesia induction, patients received 500 mL of Ringer lactate solution supplemented with 2 g of magnesium sulfate. Further intraoperative fluids infusion rate was administered at the discretion of the attending anaesthesiologist, including an additional 500 mL Ringer lactate solution

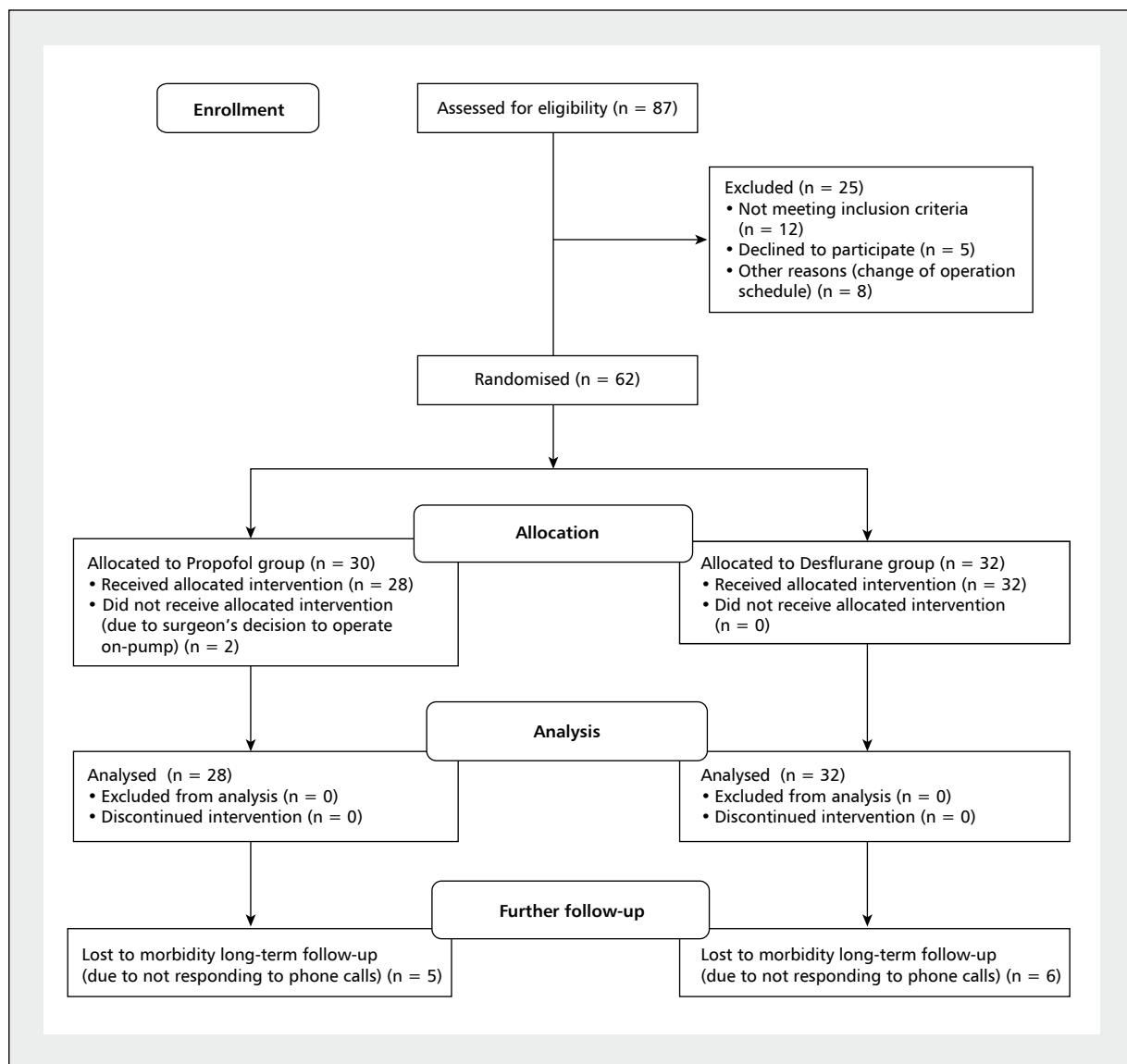


Figure 1. Flow chart of the patients assessed for the study enrollment

before sternum opening and further crystalloid or colloid infusion depending on central venous pressure (CVP) and fluid responsiveness. After administration of 2,000 mL of Ringer-lactate, patients were administered 0.5–1 L of oxypoligelatine solution. Red blood cell concentrate was transfused whenever haemoglobin concentration decreased below 8 g dL⁻¹. Continuous nitroglycerine infusion was administered at very low rate (50 µg h⁻¹) in all patients in order to enable rapid blood pressure control, by increasing the dose during aortic side-clamping. Its infusion rate was determined by the attending anaesthesiologist. 200 units kg⁻¹ of unfractionated heparin was administered four minutes before clamping of the internal thoracic artery, coronary artery or aorta (depending on the surgical technique). Whenever mean arterial blood pressure decreased below 65 mm Hg during the performance of anastomoses to coronary arter-

ies, the operating table was set to 5–15° head-down position. When mean arterial blood pressure remained below 65 mm Hg despite head-down positioning, catecholamines infusion should have been administered, at the discretion of the anaesthesiologist. Catecholamines infusion rates should be titrated in order to keep mean arterial blood pressure between 65 and 75 mm Hg. After finishing the last coronary anastomose, 100 mg of protamine sulfate was administered in a 5-minute infusion into a peripheral vein.

SURGICAL MANAGEMENT

All surgical procedures were performed via median sternotomy. Heart stabilisation for performing anastomoses to coronary vessels was achieved with the aid of a vacuum stabiliser (Octopus III Tissue Stabilizer System; Medtronic Inc., USA). Heart displacement was accomplished by pericardial sutures

and gauze cloth placement in the pericardium. No coronary shunts were used during clamping of coronary arteries.

HAEMODYNAMIC MONITORING AND DATA COLLECTION

The following haemodynamic parameters were registered: mean arterial blood pressure (MAP), heart rate (HR), mean pulmonary artery pressure (mPAP), central venous pressure (CVP), pulmonary artery wedge pressure (PAWP), as well as pulmonary artery haemoglobin saturation with oxygen (SvO₂). Haemodynamic parameters and SvO₂ were analysed in the following time points: before skin incision (1), three minutes after skin incision (2), after sternum opening (3), before heart positioning for performing the first distal anastomose (4), ten (5), 20 (6), 30 (7), and 40 minutes (8) after completion of the last distal anastomose, as well as after patient admission to the postoperative department (9). At the same time-points, doses of vasopressors and vasodilators as well as inotropic drugs were recorded. Based on thermodilution cardiac output, the following parameters were calculated: cardiac index (CI), stroke index (SI), left and right ventricular stroke work indices (LVSWI, RVSWI), systemic and pulmonary vascular resistance indices (SVRI, PVRI), as well as right ventricular end-diastolic volume index (RVEDVI) according to standard equations [8]. Oxygen delivery and uptake indices (DO₂I, VO₂I), as well as oxygen extraction ratio (OER) calculations, were performed before skin incision (time-point 1), immediately after opening the sternum (time-point 3), and after ICU admission (time-point 9). Blood gas analysis and haemoglobin concentration, as well as lactate concentration after ICU admission (time-point 9), were assessed with an ABL800 Flex 835 blood analyser (Radiometer, Copenhagen, Denmark). In order to avoid extensive measurement error of haemodynamic parameters, the degree of tricuspid valve regurgitation was assessed with TEE. Perioperative myocardial damage was assessed 18 hours after surgery, based on the analysis of phosphocreatine kinase MB fraction (CK-MB) and troponin I level with immunochemical method (Rxl-HM, Dade-Behring, Germany) and immunologic method (ARCHITECT, Abbott Park, IL, USA), respectively. ECG was obtained after patient admission to postoperative ICU and 18 hours after surgery.

FOLLOW-UP

Patients were followed-up with respect to survival, major adverse cardiac and cerebro-vascular events (MACCE), coronary re-intervention and hospital admission due to heart failure or suspected myocardial ischaemia.

STATISTICAL ANALYSIS

Categorical variables were compared between groups with chi² test. Data was tested for normal distribution with

Shapiro-Wilk test. Two-way analysis of variance (RM-ANOVA) examining group and time factors was performed to assess inter-group differences over time. Data with normal distribution was compared between groups with Student's *t*-test. Data with non-normal distribution was compared between groups with Mann-Whitney *U* test and is presented as median, quartiles and range. Data measured in several time-points and data with normal distribution is presented as mean ± SD.

Follow-up data was collected between 1 December 2011 and 15 June 2012 by phone call or, when this proved impossible, by checking the national health service database. Follow-up was performed by asking patients, or their close relatives, questions on the following items: if the patient was alive/date of death, major adverse cardiac and cerebrovascular events (MACCE) after discharge from cardiac surgical department, performing coronary angiography, need for coronary stenting or re-do coronary surgery, patient's hospital readmission due to heart failure or suspected myocardial ischaemia. Long-term survival of the patients from both groups was compared by Kaplan-Meier survival curves and Cox-Mantel test.

As there was no previous study on the left ventricular stroke work in off-pump CABG under desflurane and propofol anaesthesia, sample size calculation was based on results of the study on the difference in dp/dt change between desflurane and propofol after CABG surgery with the use of CPB [5]. Presuming standard deviation of the difference as 15% and difference in the change of LVSWI 12% between groups, a two-sample *t*-test would require a sample size of 25 patients per group to achieve 80% power with $\alpha = 0.05$. Because some data was not normally distributed, the authors planned to use the Mann-Whitney *U* test, which requires about a 5% larger sample size. To compensate for dropouts, the authors planned to include 62 patients in both groups. Statistica 8.0 (StatSoft, Tulsa, OK, USA) software was used for all statistical tests and a *P* value below 0.05 was considered significant.

RESULTS

Baseline characteristics and demographic parameters are presented in Table 1. There was no significant difference between the groups in terms of patient age, body mass index, number of patients with a history of myocardial infarction, diabetes mellitus, and arterial hypertension. Severity of heart failure according to New York Heart Association (NYHA) and coronary artery disease assessed with Canadian Coronary Surgery (CCS) score, as well as pre-operative left ventricular ejection fraction, were also not significantly different between the groups. No significant difference between the groups in the number of distal and proximal anastomoses, as well as the time of ischaemia resulting

Table 1. Baseline patient characteristics, as well as data regarding anaesthesia and surgery. Values presented as median (IQR; Range) or mean \pm SD

	Group D (n = 32)	Group P (n = 28)	P value
Age (years)	66 (IQR = 59–71; Range: 41–75)	59.5 (IQR = 53.5–68; Range: 37–75)	0.076
Weight (kg)	82.3 \pm 13.6	87.1 \pm 14.3	0.186
BMI	28.4 (IQR = 26.3–30.4; Range: 22.5–46.9)	29.2 (IQR = 26.7–32.7; Range: 23.8–40.5)	0.277
Gender (Male/Female)	21/11	22/6	0.435
LVEF	54.09 \pm 8.05	58.21 \pm 8.85	0.059
No of patients with NYHA I/ NYHA II	6/26	3/25	0.479
Number of patients with CCS2/CCS3	26/6	23/5	0.978
Number of patients with arterial hypertension	29	26	0.954
Number of patients with history of myocardial infarction	10	9	0.91
Number of patients with diabetes mellitus	10	6	0.944
Number of anastomoses to coronary artery	3 (IQR = 2–5, Range: 2–4)	3 (IQR = 3–4, Range: 1–6)	0.431
Number of anastomoses to aorta	2 (IQR = 1–2, Range: 1–3)	2 (IQR = 1–2, Range: 0–3)	0.846
Cumulative coronary arteries clamping time (min)	31 (IQR = 27–38, Range: 18–57)	34.5 (IQR = 28–40.5; Range: 6–78)	0.313
Cumulative dose of fentanyl ($\mu\text{g kg}^{-1}$)	28.78 \pm 4.288	30.15 \pm 5.18	0.26
Cumulative dose of vecuronium bromide ($\mu\text{g kg}^{-1}$)	270 \pm 44.04	278.7 \pm 52.86	0.502
Volume of transfused fluids (mL)	2,500 (IQR = 2,500–3,000; Range: 2,000–5,000)	2,825 (IQR = 2,500–3,125; Range: 1,700–6,250)	0.558
Intraoperative fluid balance (mL)	675 (IQR = –10 – +1,040; Range: –960 – +2,810)	435 (IQR = +240 – +835; Range: –1,000 – +1,260)	0.633

from clamping of coronary arteries, was observed (Table 1). Cumulative doses of fentanyl and vecuronium bromide did not significantly differ between the groups (Table 1). Depth of anaesthesia, as assessed by BIS index, was also not significantly different (Fig. 2).

HAEMODYNAMIC FUNCTION

No significant differences between the groups in terms of heart rate, MAP, CVP, PAWP, CI, SI, LVSWI, RVSWI, SVRI, PVRI, and RVEDVI were observed. Haemodynamic parameters during off-pump coronary surgery are presented in Figures 3 and 4. No significant differences in CI, SI and LVSWI were observed between the groups. However, changes of these parameters over time were different between the groups, as demonstrated by group and time effect in RM-ANOVA. Reduction of LVSWI ten minutes after performing the last distal anastomose in reference to its value before heart displacement was significantly smaller in group D (Median = -14.3 [$\text{g m m}^{-2} \text{ beat}^{-1}$], IQR: from -20.00 to -3.99) compared to P (Median = -19.8 [$\text{g m m}^{-2} \text{ beat}^{-1}$], IQR: from -26.56 to -12.08) respectively ($P = 0.029$). All analysed haemodynamic parameters, except PVRI, changed significantly over time. Mean ABP, mPAP, RVEDVI, CI and SI, LVSWI,

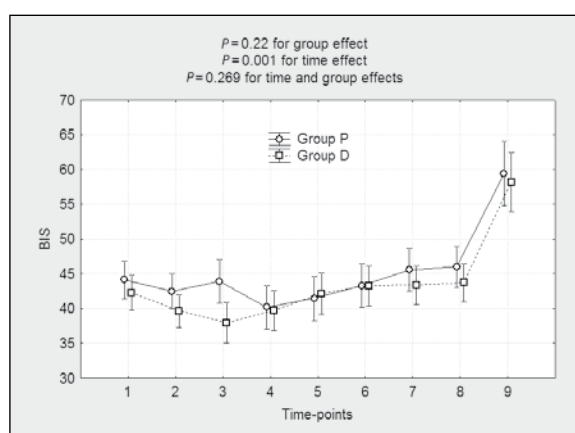


Figure 2. BIS index changes during study. Time-points: before skin incision (1), three minutes after skin incision (2), directly after opening the sternum (3), before heart displacement for coronary anastomoses (4), ten (5), 20 (6), 30 (7), and 40 minutes after finishing the last distal anastomoses (8), as well as directly after ICU admission (9)

and RVSWI decreased while HR and SVRI increased over time (Figs 3, 4).

DO_2I was not different between the groups. VO_2I was significantly lower in D compared to P after skin incision and tended to be lower after sternum opening, although

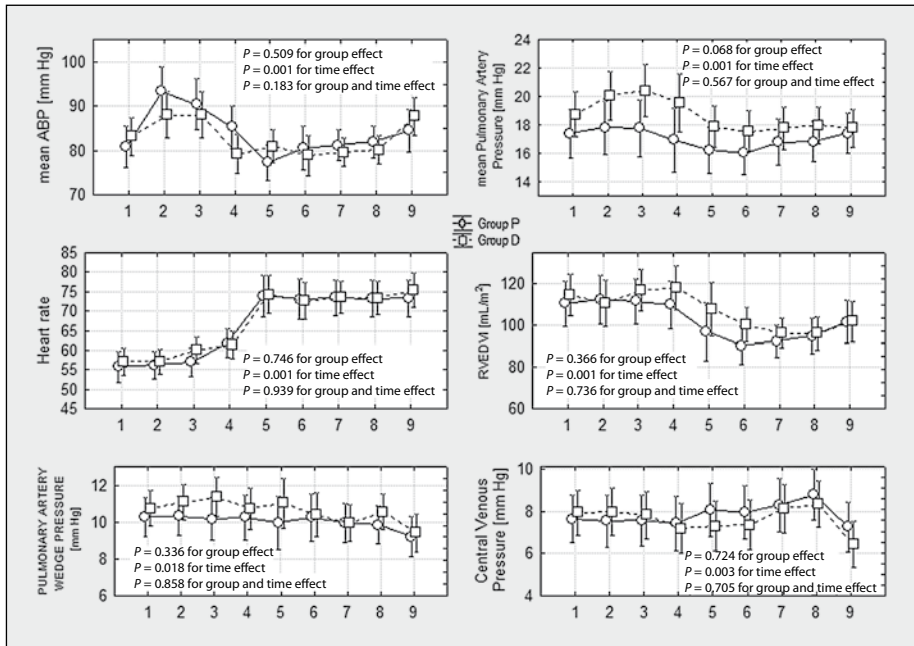


Figure 3. Changes of: mean arterial and pulmonary artery pressure, heart rate, right ventricular end-diastolic volume index, pulmonary artery wedge pressure, as well as central venous pressure. Time-points: before skin incision (1), three minutes after skin incision (2), directly after opening the sternum (3), before heart displacement for coronary anastomoses (4), ten (5), 20 (6), 30 (7), and 40 minutes after finishing the last distal anastomoses (8), as well as directly after ICU admission (9)

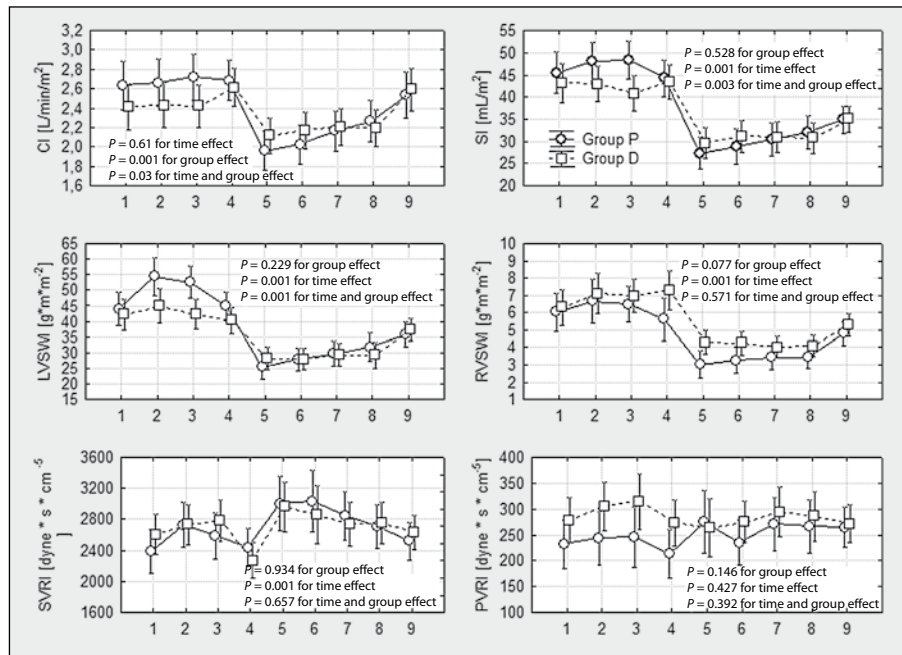


Figure 4. Cardiac index (CI), stroke volume index (SI), left and right ventricular stroke work indices (LVSWI and RVSWI), systemic. Time-points: before skin incision (1), three minutes after skin incision (2), directly after opening the sternum (3), before heart displacement for coronary anastomoses (4), ten (5), 20 (6), 30 (7), and 40 minutes after finishing the last distal anastomoses (8), as well as directly after ICU admission (9)

Table 2. Oxygen delivery index (DO₂I), oxygen uptake index (VO₂I) and oxygen extraction ratio (OER) after skin incision, after sternum opening and after ICU admission. Values presented as median (IQR; range)

	Group D (n = 32)	Group P (n = 28)	P value
DO ₂ I after skin incision (mL min ⁻¹ m ⁻²)	400 (IQR = 352–504; Range: 200–623)	433 (IQR = 343–575; Range: 248–772)	0.428
DO ₂ I after sternum opening (mL min ⁻¹ m ⁻²)	420 (IQR = 360–475; Range: 250–602)	433 (IQR = 355–565; Range: 242–782)	0.283
DO ₂ I after ICU admission (mL min ⁻¹ m ⁻²)	375 (IQR = 315–435; Range: 240–1,020)	372 (IQR = 340–415; Range: 245–625)	0.959
VO ₂ I after skin incision (mL min ⁻¹ m ⁻²)	87 (IQR = 70–113; Range: 50–167)	109 (IQR = 88–155; Range: 66–234)	0.013
VO ₂ I after sternum opening (mL min ⁻¹ m ⁻²)	92 (IQR = 68–118; Range: 48–207)	103 (IQR = 80–148; Range: 65–205)	0.084
VO ₂ I after ICU admission (mL min ⁻¹ m ⁻²)	95 (IQR = 88–113; Range: 46–181)	107 (IQR = 87–116; Range: 61–131)	0.491
OER after skin incision (mL min ⁻¹ m ⁻²)	0.218 (IQR = 0.192–0.251; Range: 0.12–0.342)	0.263 (IQR = 0.224–0.295; Range: 0.177–0.382)	0.011
OER after sternum opening (mL min ⁻¹ m ⁻²)	0.221 (IQR = 0.202–0.259; Range: 0.149–0.351)	0.246 (IQR = 0.209–0.289; Range: 0.158–0.320)	0.170
OER after ICU admission (mL min ⁻¹ m ⁻²)	0.256 (IQR 0.221–0.293; Range: 0.149–0.351)	0.265 (IQR = 0.245–0.302; Range: 0.158–0.356)	0.347

the difference in the latter did not reach statistical significance. Similarly, significantly lower OER was observed in D compared to P after skin incision. Oxygen delivery, uptake and extraction ratio are presented in Table 2.

Pulmonary artery haemoglobin saturation with oxygen (SvO₂), as assessed with oxymetric sensor of pulmonary artery catheter, tended to be higher in D, but the difference did not reach statistical significance. Time exerted a significant effect on SvO₂, which decreased after accomplishment of the last distal anastomose (Fig. 4). Lactate concentration after ICU admission was higher in D (median = 1.1 mmol L⁻¹, IQR: 0.9–1.4; Range: 0.8–2.6), compared to P (median = 0.9 mmol L⁻¹, IQR: 0.8 – 1.1; Range: 0.5 – 2.3, *P* = 0.001). No patient included in the study was administered catecholamine infusion during surgery. One patient from group D was administered 0.1 mg kg⁻¹ min⁻¹ norepinephrine and 5.1 mg kg⁻¹ min⁻¹ dobutamine after ICU admission. Mean dose of nitroglycerine did not differ significantly between the groups. No significant difference between the groups was observed in fluid balance and volume of fluids transfused during surgery, including crystalloids, colloids and blood products (Table 1).

MARKERS OF MYOCARDIAL NECROSIS AND SYMPTOMS OF ISCHAEMIA

Non ST-elevation perioperative myocardial infarction was recorded in one patient from group D and in one patient from group P. In one patient from group P, ST-elevation myocardial infarction developed on the 4th postoperative day, which led to urgent redo-CABG with

good clinical effects. Median of CK-MB was 3.0 mg L⁻¹ (IQR: 2.2–3.9; Range: 0.6–40) in D, which was not different from P (median = 4.2 mg L⁻¹, IQR: 2.5–6.2; Range: 1–15.9) (*P* = 0.2). Median troponin I concentration was 0.41 µg L⁻¹ (IQR: 0.21–0.68; Range: 0.01–15.56) in D and 0.5 µg L⁻¹ (IQR: 0.15–1.16; Range: 0.04–1.75) in P (*P* = 0.478).

FOLLOW-UP

All patients were followed up with respect to long-term mortality. The median follow-up time of survivors was 5.18 years (IQR: 4.78–5.66, Range: 3.21–6.21). Neither cerebral stroke nor a need for coronary re-do surgery was reported during follow-up. No significant differences between the groups in long-term mortality and MACCE were observed. However, due to a communication failure, 14 patients were lost to morbidity follow up. Kaplan-Meier curves of mortality comprising causes of death are presented in Figure 5. Time to hospital readmissions due to heart failure or myocardial ischaemia, and time to coronary angiography, as well as the need for coronary stenting, is presented in Table 3.

DISCUSSION

This study did not demonstrate a significant benefit of desflurane-fentanyl over propofol-fentanyl anaesthesia with respect to important haemodynamic parameters, including cardiac index, stroke index and mean arterial blood pressure. The only difference observed between groups regarded the decrease in left ventricular stroke work after suturing anastomoses to coronary arteries, which was smaller under

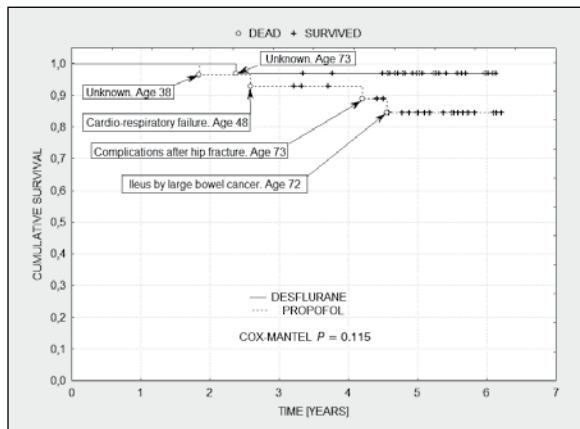


Figure 5. Cumulative survival curves with indicated causes of death

desflurane anaesthesia compared to propofol anaesthesia. Significant group and time effect on LVSWI and smaller reduction of LVSWI in group D compared to P indicated earlier recovery of left ventricular contractility under desflurane anaesthesia during reperfusion, which could be attributed to desflurane cardioprotective effect. However, it must be emphasised that accelerated recovery of LVSWI in group D was not accompanied by increased cardiac output and arterial blood pressure. Therefore it is not clear if this observation could represent any important clinical benefit.

Previous studies demonstrated earlier and more complete recovery of myocardial contractile function after CPB under volatile anaesthesia compared to intravenous anaesthesia [4, 9, 10]. We were unable to find papers which demonstrated earlier recovery of myocardial contractility under desflurane anaesthesia for off-pump coronary surgery.

Faster recovery from myocardial stunning, as assessed with left ventricular wall thickening fraction, has been observed in dogs treated with desflurane compared to propo-

fol [7]. Propofol, when compared to sevoflurane, in patients undergoing off-pump coronary surgery has been shown to be related to deeper left ventricular function compromise and delayed recovery of haemodynamic parameters [11]. Similarly, lower cardiac output after 15 min reperfusion and higher troponin I concentration was observed in off-pump coronary surgery under propofol anaesthesia when compared to sevoflurane [12]. Decreased cardiac output while performing coronary anastomoses and on early reperfusion was listed among risk factors of postoperative complications in off-pump coronary surgery patients [13].

The very similar values of PAWP, CVP and RVEDVI in both groups indicate that any potential difference in other haemodynamic parameters should not be attributed to different preload. As there were no significant differences in the number of coronary artery anastomoses, total clamping time of coronary arteries, and doses of opioids and BIS index, we assumed that neither the surgical procedure nor the depth of anaesthesia should significantly affect inter-group comparison of haemodynamic parameters.

The study protocol could enable detection of both pre- and post-conditioning effect of desflurane, albeit without distinguishing one from another. We did not observe a significant effect of desflurane on blood concentrations of markers of myocardial ischaemia: troponin I and CK-MB. Earlier studies demonstrated conflicting results: a decreased concentration after volatile anaesthesia [12, 14], or no effect [10, 15–18]. In two studies published recently, late postconditioning with sevoflurane used for sedation after coronary surgery also did not provide reduction of troponin release [19, 20]. In our patients, the time of ischaemia (median 11 min) was shorter than reported in studies demonstrating significant cardioprotective effect of volatile anaesthesia for off-pump coronary surgery (> 15 min) [11]. Thus, it is very likely that in our study, the time of ischaemia was not long enough to re-

Table 3. Morbidity follow-up for MACCE, comprising hospitalisation due to congestive heart failure, myocardial infarction, stroke, as well as for hospital readmission due to myocardial ischaemia, the need to perform coronary angiography, the need for coronary stenting

Patient's age	Group	Time to first hospital readmission due to heart failure	Time to first hospital readmission due to myocardial ischaemia	Time to coronary angiography	Need for coronary stenting
70	D		5 years	5 years	No
75	D	3 years			No
66	D		5 years	5 years	No
40	D	5 years (myocarditis)			
66	D		4 years	4 years	Yes
51	P		2 years	2 years 5 years	No Yes
60	P		6 months 1 year		No
54	P	4 years			
59	P		6 years	6 years	Yes

sult in myocardial damage and the cardioprotective effect of desflurane could not manifest itself explicitly. Other potential factors contributing to the lack of conditioning effect could be the use of β -blockers on the morning of surgery and oral anti-glycaemic agents administered in the evening before surgery to some of our patients.

Our study showed for the first time that under a similar depth of anaesthesia, as assessed by BIS, oxygen consumption and extraction ratio were lower after skin incision in patients anaesthetised with desflurane. This effect can be attributed to the decrease of overall metabolic rate, specific inhibition of oxidative metabolism or a shift towards glucose metabolism under desflurane anaesthesia.

However, these differences became insignificant after sternum opening and declined after ICU admission, when patients were sedated after surgical procedure. The slightly higher lactate concentration immediately after surgery in group D may indicate discrete inhibition of oxidative metabolism. Consistent with this view, lower OER in group D indicates that oxygen delivery was reduced to a lesser extent than oxygen uptake. Such an effect has not been reported previously in cardiac-surgical patients. The slightly higher lactate level after ICU admission in group D points to decreased oxygen metabolism, rather than decreased energy demand, as the cause of decreased oxygen consumption. An increase of brain and blood lactate levels has recently been demonstrated in mice under isoflurane anaesthesia [21]. It is difficult to interpret the meaning of this information in the context of patients' clinical conditions. Reduced oxidative metabolism may limit energy supply, which would represent a potentially deleterious effect. However, it can also induce conditioning, protect from oxidative damage and improve oxygen balance in patients anaesthetised with desflurane for off-pump coronary surgery. Further studies are required to investigate details of desflurane influence on oxygen metabolism, but it is possible that decreased oxygen metabolism could be closely related to mechanisms of anaesthetic conditioning.

This study was very pragmatic. It was not designed to prove desflurane's conditioning effect on the myocardium, something that has been demonstrated previously by many authors. The potential value of our study was that it demonstrated the influence of desflurane anaesthesia on haemodynamic parameters and oxygen balance in the setting of everyday clinical practice, including factors that can limit myocardial anaesthetic protection.

LIMITATIONS OF THE STUDY

There are several limitations of this study, including the potential bias of a single centre study. The choice of the anaesthetic, for obvious reasons, was not blinded to the

attending anaesthesiologist who was also responsible for haemodynamic measurements. The study was underpowered for the assessment of the difference in troponin I concentration and in cardiac output between the groups. With respect to these parameters, this study should be regarded as a pilot study. As the reduction of VO_2 by desflurane was an unexpected finding, the study was not adequately conducted to provide deeper insight into oxygen metabolism. This could be assessed in detail by microdialysis or transmyocardial lactate concentration gradient.

CONCLUSION

We conclude that in our group of off-pump coronary surgery patients, desflurane compared to propofol presented no reduction of myocardial injury markers and no clinically meaningful improvement of haemodynamic parameters, besides slightly faster recovery of LVSWI. Nor was any significant effect on long term survival and MACCE reported.

FINANCIAL DISCLOSURE

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