Drugs For Attenuation of Hemodynamic Responses In Patients Undergoing Elective Off-Pump Coronary Artery Bypass Graft: A Randomized Clinical Trial

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Abstract

Objective: We aimed to compare the effectiveness of esmolol (ESM) vs. dexmedetomidine (DEX) in the treatment of increased hemodynamic response during coronary artery bypass. Methods: Following the approval of the Local Committee Research and Ethics Health Research, a controlled randomized clinical trial, in patients undergoing elective coronary revascularization during off-pump coronary artery bypass surgery, was performed under standardized general anesthesia. Patients randomly received infusions of ESM 0,5 mg /kg or DEX 0,5 ?cg/kg/hr. Hemodynamic variables of study: heart rate and MAP were analyzed at different times: t1) baseline, t2) sternotomy, t3) time of coronary anastomosis and t4) sternal closure. Results: In group DEX, a statistic significance was found in the heart rate sternotomy (t2) p=0,004 and heart rate (t3= time of coronary anastomosis) p=0,026 and MAP during (t3) p=0,002. Conclusions: Although ESM and DEX attenuate hemodynamic response during coronary artery bypass, in the DEX group, hemodynamic stabilization was observed in heart rate and MAP during coronary artery bypass.

Original Research

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ABSTRACT

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Results : In group DEX, a statistic significance was found in the heart rate sternotomy (t2) p=0,004 and heart rate (t3= time of coronary anastomosis) p=0,026 and MAP during (t3) p=0,002.

Conclusions: Although ESM and DEX attenuate hemodynamic response during coronary artery bypass, in the DEX group, hemodynamic stabilization was observed in heart rate and MAP during coronary artery bypass.

Keywords : "Esmolol" [MeSH], "dexmedetomidine" [MeSH], "cardiac surgery" [MeSH], "median sternotomy" [MeSH] "Off-Pump Coronary Artery Bypass" [MeSH].

INTRODUCTION

Off-pump coronary artery bypass surgery (off-pump CABG) has become a common surgical procedure. An important goal in the perioperative management of patients undergoing off-pump CABG, is to maintain cardiac function, organ perfusion and oxygen delivery. Recent and innovative approaches in cardiac surgery have led to complement the conventional objectives of anesthesia such as: hemodynamic stability, coronary perfusion parameters, and adequate anesthetic depth. New objectives are added after cardiac surgery, such as: rapid recovery of brain activity, spontaneous respirations and a minimal load on the intensive care unit (ICU). The benefits of early extubation include improved cardiac function and patient comfort, reduction in respiratory complications, as well as an ease in management.

Dexmedetomidine

Dexmedetomidine (DEX) has been shown to decrease anesthetic induction doses and decreased use of intraoperative opioid and halogenated requirements for the maintenance of anesthesia. DEX decreases the preoperative concentrations of catecholamines and promotes perioperative hemodynamic stability (**1**).

Dexmedetomidine (DEX) is an alpha (2A)-adrenergic receptor with a selectivity ratio between α2: α1 receptors of 1600: 1, which is eight times more selective for the alpha (2A)-adrenergic receptor in comparison to clonidine. Dexmedetomidine is a relatively new drug approved by the end of 1999 by the Food and Drug Administration (FDA) for human use due to its sedative, analgesic and anxiolytic action, its reduction in delirium and agitation, its perioperative sympatholysis, cardiovascular stabilizing effects, and preservation of respiratory function (**4**).

Metabolism. DEX is extensively metabolized by the liver and excreted in urine. More than 90% is bound to proteins.

Pharmacokinetics . The elimination half-life (t1 / 2β) of DEX is 2 - 3 h. The context-sensitive half-life is approximately 4 min - 8 min. which allows the suspension of DEX infusion minutes before the end of the surgery.

Central Nervous System . Activation of the α2 receptor of the CNS (central nervous system) produces sedation, analgesia, and anxiolysis. Sedation is mediated by the activation of the alpha (2A)-adrenergic receptor in the locus coeruleus. Analgesic effects are mediated mainly at spinal cord level. It is known that DEX lowers the minimum alveolar concentration (CAM) of inhalation anesthetics and at higher concentrations it may affect memory and recollection.

Respiratory effects . While DEX reduces minute ventilation (VE), it maintains a ventilatory response to increased CO2 levels. DEX appears to decrease the tidal volume (VC) without affecting the respiratory rate (FR). The combination of DEX along with an opioid, improves analgesia but does not seem to enhance respiratory depression.

Cardiovascular system. Through its sympathetic effects of central action and included in cardiovascular effects, there are frequent decreases in heart rate, BP, systemic vascular resistance (SVR) and cardiac output (CO). This is believed to be the result of agonist effects on the peripheral alpha (2A)-adrenergic receptor. A bolus injection of DEX causes a biphasic response, with an initial increase in BP and a decrease in heart rate (**5**)(**6**).

In cardiac surgery, DEX is a clinical alternative amidst numerous pharmacological alternatives because it does not cause depression of the respiratory centers, and furthermore reduces the use of opioids up to 66% in the postoperative period.

Esmolol

Another group of drugs that are used in off-pump CABG, belongs to β-adrenergic antagonists (β blockers) among them, Esmolol (ESM), by reducing the extent of myocardial injury during ischemia and coronary reperfusion. It is believed that the negative inotropic and chronotropic effects of these drugs concomitantly reduce myocardial oxygen consumption (MVO2) and decrease sympathetic tone, thereby exerting a beneficial effect on the ischemic myocardium. However, most β blockers are known for prolonged negative inotropic properties, which limits their use during cardiac surgery (**2**)(**3**).

Esmolol (ESM) belongs to the B blocker drug group (ultra-short-acting β1 selective-adrenergic blocker). It presents a rapid action onset of 1-2 minutes in which it is quickly metabolized by red blood cell esterase; its elimination half-life (T $\frac{1}{2}$) is 9 -10 min. The rapid onset of action of this agent and its short duration of effect is an advantage in the perioperative period. The drug can be administered either as a bolus injection or as a continuous intravenous infusion. It is commonly administered in doses of 0,5mg/Kg and its effect stops within 10-20 minutes of discontinuing the infusion (**7**).

In clinical studies (following hemodynamic resuscitation) ESM administration has shown a reductive effect of myocardial damage in the context of acute ischemia. A hemodynamic benefit has also been accepted by decreasing contractility, economizing cardiac work and decreasing cardiac energetic costs with a consequent reduction in oxygen consumption (MVO_2) (**8**).At the cellular level, these drugs reduce mitochondrial respiration and phosphorylase activity, thus buffering the production of free radicals. Because hemodynamic changes are common in laryngoscopy, lidocaine is often administered intravenously 90 seconds before intubation in order to suppress laryngeal reflexes, and ESM may be used to reduce heart rate and blood pressure in response to post-laryngoscopy. ESM is an excellent option for attenuation of cardiovascular responses to airway instrumentation (**9**).

Surgical exposure and Hemodynamics

Hemodynamic monitoring is critical in patient care during cardiac surgery. The participation of the anesthesiologist is indispensable in patient care during this procedure. The ever-increasing advances in surgical techniques and the multidisciplinary teams' experience have extended the use of off-pump CABG, to include patients with an increasing prevalence of comorbidities.

Off-pump CABG, presents a unique set of technical challenges for the anesthesiologist and surgeon; perhaps the most critical being to monitor and maintain stable hemodynamics and rhythm in an environment during surgical manipulations that occur in a "beating heart".

In order to attain an adequate heart for exposure of the coronary arteries, a tissue stabilizing device (Octopus Medtronic) and a cardiac positioner (Medtronic Starfish) are placed, their function being, to lift the heart and expose the posterior vessels (Figure 1), this facilitates the making of anastomosis. The order of distal versus proximal anastomosis can often vary or be changed to adjust to various coronary anatomies and tolerances to grafting (**10**).

Appropriate preparation, guided therapy, and technical maneuvers can lessen such adverse hemodynamic changes. The total exposure of the heart for multiple coronary revascularizations (2-3 vessels), including the circumflex artery (AC) and posterior descending artery (ADP), is only possible with the use of stabilization devices that restrict the regional wall's movement, either via suction or mechanical compression. These manipulations in a "beating heart" depress cardiac contractility and cause some hemodynamic impact (**11**).

In this clinical environment, CO monitoring becomes a useful tool for optimal anesthetic care. Fluid therapy remains a challenge in critical patient settings. Fluid overload will cause organic edema, consequently increasing mortality, while an inadequate circulation volume will result in coronary perfusion pressure and insufficient and inadequate oxygen supply.

Therefore, fluid status control (volume) is essential in critically ill patients. During the past decades, there have been significant developments in hemodynamic monitoring techniques, such as *FloTrac / Vigileo* ? and PiCCO system (*Pulse-Induced Contour Cardiac Output*), which incorporates a transpulmonary thermodilution technique (TPTD) (**12**)(**13**).

The objective of this essay is to compare the administration of ESM and DEX infusion, in the hemodynamic response of patients undergoing off-pump CABG.

METHODS

Our protocol was approved by the local Research and Ethics Committee on Health Research No. 3502 of the General Hospital "Gaudencio Gonzalez Garza" of the La Raza, National Medical Center (IMSS), registered in BioMed Central *ISRCTN 17397629* , and the study was conducted in accordance with the principles laid out in the Declaration of Helsinki, 2000. Written informed consent was obtained from the patients. This clinical trial was conducted following the guidelines of the CONSORT Statement (**14**).

Study design

We conducted a prospective, randomized and controlled clinical trial in 20 adult patients of the Cardiothoracic surgery service.

Study Participants

Inclusion criteria: Patients with stable coronary artery disease undergoing elective off-pump CABG. In physical state ASA II and III, according to risk classification by the American Society of Anesthesiology (**15**). Patients older than 18 years of age, with renal function were included: creatinine <1,4 mg / dL and left ventricular ejection fraction (LVEF) [?] 40%, Cardiac Index [?]2.5 L, evaluated by echocardiogram.

Exclusion criteria: Patients with hepatic or renal impairment, patients with hemodynamic instability (cardiogenic shock), patients requiring coronary revascularization with extracorporeal circulation and candidates for cardiac reoperation.

Interventions

A controlled clinical study in patients undergoing elective off-pump CABG, under standardized general anesthesia. Randomly received infusions of Esmolol 0.5 mg /kg/1 min (Group E, n=10) or Dexmedetomidine 0.5 mcg/kg/hr. (Group DEX, n=10). Through administration with*Fresenius-Kabi(r)* volumetric infusers. The monitored parameters were: invasive blood pressure, oxygen saturation, electrocardiogram, bispectral index for the depth of anesthesia, and central venous catheter. The hemodynamic data outcome variables of this study are heart rate and invasive blood pressure which were analyzed at different times:

t1) baseline,

t2) sternotomy,

t3) time of coronary anastomosis,

t4) sternal closure,

We have compared the analysis of the hemodynamic profile, narcotics and muscle relaxant rate; arterial blood gas and hemogram parameters were recorded during surgery. All patients underwent balanced general anesthesia with desflurane and invasive monitoring for the measurement of hemodynamic parameters. At the end of the surgical procedure, the patients were transferred to the Intensive Care Unit (ICU).

Outcomes

Patients underwent standardized balanced general anesthesia and invasive monitoring, to obtain the hemodynamic variables measured through a central venous catheter which was recorded by the *FloTrac / Vigileo System* (*Monitor Edwards Life sciences*) in real-time. The gasometric parameters utilize an arterial line to measure lactate, serum electrolytes, and mean arterial pressure (MAP). Fentanyl consumption was noted in both groups. Hemodynamic constants, such as heart rate (bpm), respiratory rate (FR), temperature (degC), blood pressure (BP), mean arterial pressure (MAP), peripheral oxygen saturation (SPO_2%), Cardiac output (CO), venous oxygen saturation (SVO2%), systemic vascular resistance (SVR) and central venous pressure (CVP) were obtained on a *Datex-Ohmeda monitor* .

Primary outcome measure

The primary measure was: heart rate and invasive blood pressure (MAP) which were analyzed at different times:

t1) baseline,

t2) sternotomy,

t3) time of coronary anastomosis,

t4) sternal closure,

Standard monitoring was performed according to the official Mexican Standard NOM-006-SSA3-2011 for the practice of anesthesiology.

Secondary outcome measures

1. A Swan Ganz catheter was placed for the assessment and monitoring of arterial pulmonary pressure. This catheter was placed in all 20 cardiac surgery patients undergoing off-pump CABG.

2. Low systemic vascular resistance during cardiac surgery was assessed using a pulmonary artery catheter, and *Vigileo* monitor for data outcome variables.

3. Difference in perioperative arterial blood pressure measured by Arterial blood pressure was assessed using an arterial radial catheter after ICU admission.

4. Mixed venous oxygen saturation (SVO_2) will be assessed by analysis of blood gases by *Vigileo* monitor.

5. A multidisciplinary team monitored throughout the entire process, the variables of hemodynamics and laboratory results related to cardiogenic shock, post operatory bleeding or other complications by using *Vigileo Monitor Edwards Lifescience* s, in cardiac surgery patients undergoing off-pump CABG, monitoring the cardiac output of surgical patients who required continuous invasive monitoring during ICU stay. Start in induction of anesthesia, sternotomy, grafting of coronary descending, post-revascularization after ICU.

e. Implementation

During the intra-operative period once the sternotomy was performed, the administration of the drugs was divided in two groups, E group and DEX group which aim to maintain heart rate at 50-60 (bpm). Coronary arteriotomy is performed, in the area previously chosen and assessed by the Cardiothoracic surgeon, a clip of coronary artery retraction is placed and the anastomosis was made.

Methods of hemodynamic monitoring. During the perioperative period all patients were monitored with *FloTrac/Vigileo?* a widely used method that uses CVP and vascular tone to calculate stroke volume and CO; we compared heart rate and MAP in both groups (ESM and DEX) at the following times:

- t1 = baseline,
- t2 = time of sternotomy,
- t3 = time of coronary anastomosis,
- t4 = time of sternal closure,

The graft was obtained from the internal mammary artery. The mediastinum and pleural cavities were drained intraoperatively, and the sternum closed. Both ESM and DEX infusions were suspended, once the placement of the sternal closure was completed, each patient was then transferred to the ICU.

Randomization

Randomization was carried out through a random number generator, by means of repetitions divided into two treatments, using *R-2.15.1 Statistics* . Treatment assignments were performed at random according to a blocked randomization by the researchers allowed to use the program with a username and password, Group Esmolol (ESM) 0,5mg / kg, Group Dexmedetomidine (DEX) group 0,5-0,8µcg / kg / h.

Statistical Analysis

The data of the demographic variables were tabulated in the spreadsheet of the Microsoft Excel 2010 program. The data is expressed as the mean ± standard deviation. The independent *t*- test was used to compare the study groups. The paired *t*- test was used to compare the variables before and after the intervention. A *P* value of less than *0,05* was considered statistically significant. The package IBM SPSS Statistics 20 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

In this clinical trial, 143 adult patients were randomly assigned to undergo off-pump CABG surgery. The flow of the patients throughout the trial is shown in Figure 2 and their baseline characteristics are summarized in Table 1 .

The diagnosis of ischemic heart disease was the cause of hospitalization of our population, mainly alongside relaxation and hypokinesia disorders in ten patients (50%), contractility and wall akinesia in three patients (15%) and akinesia in five patients (25%).

On average, 2,25 anastomosis per patient were performed. The internal mammary artery was routinely used for the anterior descending artery (LAD). 45 anastomoses were performed on the 20 patients included in the study.

A comparison of narcotic consumption and comparisons between gasometric and electrolytic parameters in both groups are mentioned in *Tables 2 - 3.*

We obtained the records of hemodynamic variables at the following times during transoperative in both groups: t1 = baseline; t2 = sternotomy, t3 = time of coronary anastomosis, t4 = sternal closure. We analyzed the results at different times, regarding the heart rate, we obtained during the sternal closure (t4) p = 0,004 and during the coronary anastomosis (t3), with a value of p = 0,002, in the DEX group. (*Tables 3)*

Regarding the difference in the MAP in both groups, we observed hemodynamic stability in the DEX group mainly during the performance of anastomosis; during sternotomy and the placement of sternal closure, no differences were observed.

DISCUSSION

In our study, we found that DEX infusion has a predictable cardiovascular effect, which was observed during the impregnation of the infusion, a 20% drop in blood pressure is reported in the literature and a 10-20% drop in heart rate over baseline parameters is also expected. We also observed a reduction in narcotic consumption by the DEX group.

The results obtained with the use of DEX, hemodynamic stability during coronary anastomosis was beneficial, and also facilitated the technique on a beating heart in patients undergoing off-pump CABG (**3**)(**16**).

The hemodynamic data was collected at four different times: baseline, at the time of sternotomy, coronary anastomosis, and placement of the sternal closure. These off-pump CABG surgical times were chosen because they are reasonably considered the most significant painful stimuli during sternotomy and the placement of sternal closure at the time of coronary grafting (**17**)(**18**)(**25**).

Tachycardia is poorly tolerated in patients with heart failure, as this may predispose the patient to cardiac arrhythmias during the transoperative period. Consequently, atrial fibrillation and subsequent myocardial ischemia may occur, thus leading to fatal complications in some cases (**19**)(**26**).

The use of DEX, due to its pharmacological property, can be used to prevent tachycardia and attenuate the hemodynamic response during cardiac surgery.

Studies suggest that the perioperative use of DEX may result in a decreased risk of adverse cardiac events, including myocardial ischemia. Stimulation of α-adrenergic receptors can modulate coronary blood flow during myocardial ischemia, by preventing the redistribution of blood flow, which leads to improvement of coronary perfusion. (**27-28**)

This specific effect, along with hemodynamic stability and**reduced** surgical stimulus-response, make DEX an ideal adjuvant anesthetic, particularly in patients undergoing coronary bypass grafting.

Hemodynamic monitoring should be applied within the context of therapeutic interventions, which have proven effective in the reversal of the disease process (**20**)(**21**).

The risk of adverse events in off-pump CABG, increases in patients with specific comorbidities, such as recent myocardial infarction, left ventricular ejection fraction (LVEF <40%), a history of lung disease or renal dysfunction. The impact of comorbidities on postoperative morbidity and the outcome have also been studied in cardiac surgery where the use of hemodynamic therapy in the perioperative period has been associated with a decrease in the incidence of overall complications or length of postoperative stay in cardiac surgery. Several interventions in the ICU after cardiac surgery have been investigated, but the results have yet to significantly change clinical practice (**22**).

Currently, these critically ill patients are hemodynamically optimized with "early goal-directed therapy" (EDGT), which in high-risk surgery has been associated with a reduction in postoperative morbidity and mortality along with a decrease in cardiac complications, particularly in the case of arrhythmias (**12**)(**29**).

Clinical studies that have been performed individually for cardiac surgery, with a hemodynamic approach aimed at the goal of therapy during the perioperative period, the hemodynamic objectives have been to maintain: MAP 60–100 (mmHg); heart rate [?]90 (bpm); Hb [?]8 (g/dl); SVO_2 [?]60(%), CVP 6-8 (mmHg), Stroke Volume Variation (SVV) 10 (%); stroke volume index (SVI) 30–65 ml; SVRI 1500–2500 (dyne x sec x cm^{-5} x m^{-2}); Oxygen delivery (DO_2) 450–600 (ml/ min/ m^2); Hct [?]30(%); pH 7.35–7.45; PO_2 100mm Hg; PCO_2 35–45 mm Hg; SpO_2 [?]95%, Lactate [?]2 (mmol/l) after 8 h from the postoperative period (**23**)(**24**).

Limitations

The present study has some limitations. This is because we only studied the perioperative time up until surgery and during the patients' stay in the ICU.

We did not need to use the transesophageal echo Doppler echocardiography (TEDE), nevertheless the echocardiography continues to be limited by the need of full-volume data sets to capture the entire region of interest, which may not be possible in patients with irregular rhythms.

By analyzing the data with *FloTrac/Vigileo?* the additional information related to cardiac function and peripheral oxygen supply can be obtained during cardiac surgery.

CONCLUSIONS

The hemodynamic profile during off-pump CABG, can be optimized by continuous infusion of DEX during the time of coronary anastomosis, due to the properties of this adjuvant in anesthesia.

Off-Pump CABG, surgery has contributed to enhancing surgical techniques, anesthesia, and pharmacological management, as well as hemodynamic monitoring, during the transoperative period and in the ICU. Knowledge of this new information that describes the behavior of hemodynamic variables under this specific instability is essential.

Hemodynamic monitoring is the cornerstone for adequate resuscitation, improving results in the patient undergoing off-pump CABG. Knowing the timing of cardiac manipulation can be useful to predict trends in hemodynamic variables and thus direct pharmacological interventions to best manage patients undergoing off-pump CABG.

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Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the institutional ethics committee/review board of the Hospital General Medical Center "La Raza" (No. 3502), which waived the requirement for informed consent owing to the study design.

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TABLE 1

UNIDADES Y PARAMETROS REFERENCIA

Demographic data of the study's population

	Group E (n=10)	Group DEX (n=10)
Age (years)	63±7	64±9
Sex (M/F)	7/3	8/2
BMI	28,99±2.24	28,2±2,5
Comorbidity	**Comorbidity**	**Comorbidity**
Myocardial infarction	3	2
Type 2 Diabetes Mellitus (T2DM)	3	3
Hypertension	10	10
Smoker	3	7
Dyslipidemia	8	7
Ejection fraction (%)	43(43-65)	55(45-75)
Physical status ASA	**Physical status ASA**	**Physical status ASA**
ASA II	5	3
ASA III	5	7
Surgical time (min)	185±4	208 ±27

ASA= American Society of Anesthesiologist

Table 2

Gasometric parameters during the perioperatory of patients subjected to coronary revascularization

	Group E (n=10)	Group DEX (n=10)	*P value*
Glucose (mg/dL)	118 (±13)	139 (±70)	0,369
Lactate (mmol/L)	1,27 (±0,105)	1,16 (±0,275)	0,254
BD	5,89 (±1,31)	5,65 (±2,22)	0,772
Arterial blood partial PCO_2 pressure (mmHg)	36 (±0,823)	35 (±1,83)	0,175
Arterial blood partial PO_2 pressure (mmHg)	240 (±67)	253 (±68)	0,675
Na^+ (mmol/L)	143 (±1.05)	143 (±1,56)	0,259
K^+ (mmol/L)	3,67 (±0,24)	3,43 (±0,33)	0,167
Ca^{++} (mmol/L)	1,03 (±0,7602)	1,08 (±0,62)	0,134
Hto (%)	34,4 (±1,17)	33,4 (±3)	0,343
Hb (g/dL)	11,4 (±0,11)	11,31 (±0,50)	0,594
pH	7,27 (±0,135)	7,30 (±0,427)	0,052

BD- Base deficit, Ca-Calcium, Hto - Hematocrit, Hb-hemoglobin, PO2- oxygen arterial pressure, PCO2-Carbon dioxide arterial pressure.

Table 3

Hemodynamic profile during the perioperatory

Variables	Group ESM (n=10)	Group DEX (n=10)	P value
Sevoflurane %	1,50 (±0,94)	1,56 (±0,171)	0,345
Muscle relaxant (Vecuronium) µcg/Kg/hr	128 (±8,23)	129 (±16,39)	0,825
BIS	41 (±3,23)	39 (±3,09)	0,175
Narcotic (Fentanyl) µcg/Kg/h	11,4 (±1,71)	8,6 (±0,96)	0,012
Heart rate $_{t1}$ (lpm)	65 (±4)	59 (±5)	0,060
Hear rate $_{t2}$ (lpm)	62 (±10)	56 (±4)	0,026
Heart rate $_{t3}$ (lpm)	62 (±5)	58 (±4)	0,004
Heart rate $_{t4}$ (lpm)	60 (±12)	58 (±4)	0,662
MAP $_{t1}$ (mmHg)	66 (±14)	70 (±5)	0,537
MAP $_{t2}$ (mmHg)	77 (±7)	73 (±5)	0,522
MAP $_{t3}$ (mmHg)	78 (±4)	72 (±4)	0,002
MAP $_{t4}$ (mmHg)	72 (±9)	68 (±9)	0,471
CVP (cmH_2O)	13,9 (±2,80)	14,9 (±2,02)	0,373
MPAPm (mmHg)	11,1 (±1,37)	10,9 (±1,19)	0,732
VOS_2 (%)	80 (±2,66)	78 (±5,35)	0,309
CO (L x min)	4,9 (±1,036)	4,6 (±1,012)	0,442
Temp °C	32,2 (±0,46)	32,5 (±0,57)	0,266

BSI- Bispectral Index, MAP-Mean arterial pressure, t1= baseline, t2= time sternotomy, t3=time of coronary anastomosis, t4= time sternal closure placement. CVP-Central venous pressure, MPAP - Mean pulmonary arterial pressure, VOS2% -Percentage of venous oxygen saturation, CO-Cardiac output, Temp-Temperature.

Values are expressed as mean standard deviation (SD).

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