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Responsiveness to Infusion Load under Regional Anesthesia after Off-Pump Coronary Artery Bypass Graft Surgery

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Summary

Objective. To evaluate the effect of erector spinae plane block (ESPB) and epidural anesthesia on responsiveness to infusion load after coronary bypass surgery on a beating heart.

Materials and methods. A prospective randomized single-center study included 45 patients who were grouped into 3 equal arms based on anesthesia techniques: general anesthesia in combination with ESPB (GA+ESPB), general anesthesia and epidural anesthesia (GA+EA) and general anesthesia without regional techniques (GA). Patient's response to volume loading was assessed using dynamic and orthostatic tests after transfer from the operating room and at the end of the first postoperative day. Passive leg raise (PLR) and standard bolus injection tests were done at the first stage; changes in hemodynamic parameters during verticalization were additionally evaluated at the second stage. Patients with >10% cardiac index (CI) increase after PLR test and >15% increase after bolus injection test were categorized as responders.

Results. The concordance of obtained results in PLR and bolus injection tests for the GA+ESPB, GA+ EA and GA groups at the first stage was 0.53 (95% CI 0.12–0.94), 0.68 (95% CI 0.30–1.00) and 0.61 (CI 0.24–0.99), at the second stage — 0.70 (0.32–1.00), 0.84 (95% CI 0.55–1.00) and 0.82 (95% CI 0.47–1.00), respectively. There were no differences in distribution of responders between the groups. CI dynamics did not differ between the groups during verticalization, and there were no associations of CI changes during verticalization with the preceding PLR test results. The dynamics of troponin T and NT-proBNP did not differ between the groups.

Conclusion. Methods of regional anesthesia (SPB or EA) do not significantly affect the responsiveness to infusion therapy in the postoperative period after coronary bypass surgery on a beating heart.

Keywords: regional anesthesia; epidural anesthesia; coronary bypass surgery; responsiveness to infusion therapy; orthostatic reactions

Conflict of interest. The authors declare no conflict of interest.

Introduction

Assessment of fluid responsiveness has long been a cornerstone of critical care medicine, as fluid therapy is a key method to optimize hemodynamics and perfusion and should be administered when indicated with appropriate assessment of efficacy [1]. Traditionally, dynamic tests have been used to evaluate the effects of fluid therapy. One of these is the standard bolus challenge (infusion of 7 mL/kg) [2, 3], which is irreversible and increases the risk of hyperhydration and tissue edema [4]. A viable alternative to this test is the passive leg raising (PLR) test, which has a hemodynamic effect equivalent to an infusion of 300–500 mL of crystalloid solution. In addition to reversibility, the PLR test has high sensitivity and specificity, providing a good predictive value for fluid therapy responsiveness [5]. Other dynamic tests, including mini-bolus challenge, end-expiratory occlusion test, and assessment of plethysmogram variability, are not sufficiently accurate, especially during spontaneous breathing [6].

In addition to dynamic tests, static and dynamic preload parameters can be used to assess the effects of fluid therapy. Unlike dynamic parameters, including stroke volume variation, pulse pressure, and plethysmogram, static parameters have not been shown to be reliable for assessing volume status, but central venous pressure (CVP) remains a valuable measure of right ventricular filling [7]. Meanwhile, right ventricular failure is a limiting factor affecting the accuracy of dynamic methods to assess responsiveness to fluid loading and should be considered when performing such methods [8].

The rate of adaptation of the cardiovascular system to changes in body position is mainly determined by the autonomic nervous system. Thus, if the chronotropic or vasomotor response to baroreceptor activation is disturbed, the change in body position will result in orthostatic responses [9]. However, no single method has been proposed to diagnose orthostatic hypotension. For its indirect assessment, a head-up tilt table test or an active standing approach have been proposed [10]. The hemodynamic effects of upright positioning are equivalent to a 500–1000 mL decrease in preload due to blood pooling in the lower extremities,

splanchnic and pulmonary circulation [11]. In cardiac surgery, the use of regional anesthetic techniques, which can affect several hemodynamic parameters, increases the incidence of orthostatic reactions by up to 33% [12]. However, the effect of regional anesthesia techniques, including erector spinae plane block (ESPB), on fluid responsiveness after cardiac surgery remains controversial [13].

The aim of the study was to evaluate the effect of erector spinae plane block (ESPB) and epidural anesthesia on fluid responsiveness after off-pump coronary artery bypass grafting (CABG).

Materials and methods

The study was approved by the local ethics committee of the Northern State Medical University of the Ministry of Health of the Russian Federation (Arkhangelsk) (protocol 03/04-20 of April 29, 2020).

A single-center, prospective, randomized, controlled pilot study of patients undergoing elective off-pump CABG under sevoflurane anesthesia was conducted at the E. Volosevich First Regional City Clinical Hospital (Arkhangelsk). The study was not blinded. Patients were randomized 1:1:1 using the envelope method into the following groups: 1) combination of general anesthesia (GA) with sevoflurane and erector spinae plane block (ESPB) at the Th5 level using 20 mL of 0.5% ropivacaine intraoperatively followed by prolonged infusion of 0.2% ropivacaine after CABG (GA + ESPB group), 2) combination of sevoflurane general anesthesia with epidural anesthesia (EA) with 10–14 mL of 0.75% ropivacaine at the Th2-4 level followed by prolonged infusion of 0.2% ropivacaine (GA+EA group), 3) sevoflurane general anesthesia without regional anesthesia (GA group).

Inclusion criteria were signed voluntary informed consent to participate in the study, age greater than 18 years and not greater than 70 years, elective stand-alone off-pump CABG, ejection fraction greater than 40%, and sustained sinus rhythm.

Exclusion criteria were refusal to participate in the study, refusal of regional anesthesia (EA or ESPB), myocardial infarction within the previous 30 days, severe chronic obstructive pulmonary disease (GOLD stage II and greater, need for continuous therapy with inhaled steroids), chronic kidney disease stage IV and V, poor control of diabetes mellitus (glycated hemoglobin more than 8%), obesity with body mass index more than 40 kg/m². Intraoperative conversion to cardiopulmonary bypass or inadequate regional anesthesia were considered criteria for post-randomization exclusion from the study.

On admission to the operating room, patients in the GA+ESPB group underwent peripheral vein (Vasofix Braunule, BBraun, Germany) and radial artery (Arteriofix, BBraun, Germany) catheterization. In the supine position under ultrasound guidance (Philips CX-50, USA), catheterization of the neurofascial space of the erector spinae muscle at the level of the transverse process of Th5 (Perifix, BBraun, Germany) was performed bilaterally and the catheter was guided cranially at a distance of 4–5 cm from the tip of the needle. A 20 mL bolus of 0.5% ropivacaine was injected through the catheter on each side. After induction of anesthesia (propofol 1–2 mg/kg, fentanyl 2–3 μg/kg, pipecuronium bromide 0.08 μg/kg), tracheal intubation and lung ventilation (Datex Ohmeda Aespire View, GE Carestation 650, GE Healthcare technologies, USA) were performed with a tidal volume of 6 mL/kg and parameters necessary to maintain saturation greater than 96% and normocapnia. Under anesthesia, patients underwent right internal jugular vein catheterization (Intradyn F8, BBraun, Germany) followed by pulmonary artery catheterization (Corodyn TDF7, BBraun, Germany). Anesthesia was maintained with sevoflurane at MAC 0.7–1.5. In the postoperative period, analgesia was provided by continuous infusion of 0.2% ropivacaine at a rate of 5–12 mL/hour until the patient was transferred from the ICU.

In the GA+EA group, epidural catheterization (Perifix, BBraun, Germany) was performed before induction of anesthesia through a midline approach at the level of Th2–Th3 or Th3–Th4. Anesthesia was maintained during the intraoperative period with sevoflurane 0.7–1.5 MAC. The analgesic component of anesthesia included intermittent injection of 10–14 ml of 0.75% ropivacaine. Postoperative analgesia was provided by continuous infusion of ropivacaine 0.2% at a rate of 3–6 mL/h and fentanyl 4–10 μg/h.

In the GA group, induction of anesthesia and tracheal intubation were performed according to the same procedure. Anesthesia was maintained intraoperatively with sevoflurane 0.7–1.5 MAC, analgesia was achieved by fentanyl administration at 2–3 μg/kg/hour.

The intraoperative infusion consisted of 1000 ml of balanced solutions in all patients. The first-line drug for control of perioperative hypotension was norepinephrine 0.2–0.3 μg/kg/min. In case of insufficient hemodynamic effect (mean arterial pressure (MAP) less than 65 mm Hg), dobutamine 5–7 μg/kg/min or change of surgical approach, in particular conversion to cardiopulmonary bypass, were considered. Patients remained in the ICU for the first two days of the postoperative period. Fluid therapy was adjusted by the attending physicians according to the patient's condition.

Forty-eight patients who underwent elective off-pump CABG between May 2020 and February 2023 were included in the study (Fig. 1). After excluding one patient from each group, 45 patients (37 men and 8 women) were included in the analysis.

Mean arterial pressure (MAP), heart rate (HR), CVP, mean pulmonary artery pressure (PAP), pul-

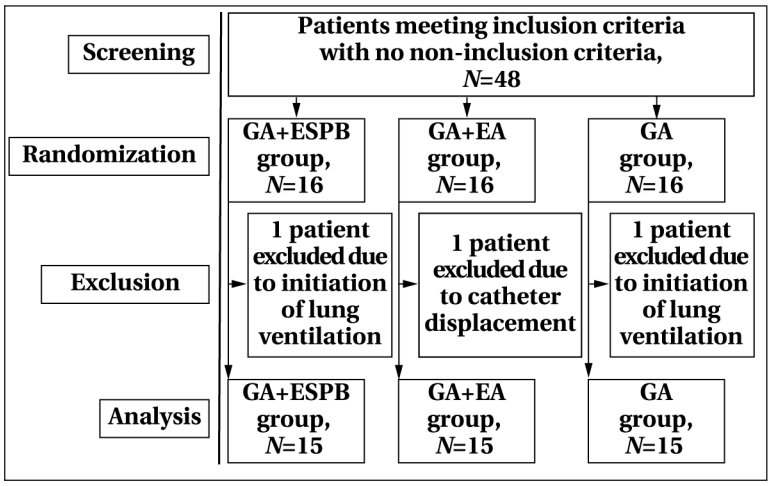

Fig. 1. Flowchart of the trial.
Note. GA — general anesthesia; EA — epidural anesthesia; ESPB — erector spinae plane block.

monary artery wedge pressure (PAWP), cardiac index (CI), stroke volume index (SVI), systemic vascular resistance index (SVRI), pulmonary vascular resistance (PVR) (Nihon Kohden monitors, Japan) were measured immediately after the patient was transferred from the operating room to the ICU and on the next postoperative day when the patient was transferred to the cardiac surgery unit. In both stages of the study, arterial and venous blood gas parameters, as well as changes in troponin T and NT-proBNP on day 1 of the postoperative period were determined compared to preoperative values.

After transport to the ICU with continued propofol sedation at a dose of 1–2 mg/kg/hour to achieve synchronization with the ventilator at the RASS sedation level of 2–3 points, all patients were tested for fluid responsiveness. First, the PLR test was performed, followed 10 minutes later by the standard bolus challenge (500 mL of balanced crystalloid solution over 5 min). At the end of the first postoperative day, before the patient was transferred out of the ICU, these tests were repeated, followed by an assessment of the hemodynamic effects during upright positioning of the patient, for which CI, HR, and SVI were measured in the sitting position on the bed and then in the standing position. Thermodilution measurements were performed after a 5 min period of position stabilization with continuous assessment of subjective comfort and monitoring of vital signs (Fig. 2).

Patients were considered to respond to fluid loading if the CI increased by more than 10% from baseline in the PLR test and by more than 15% in the bolus test (BT).

Statistical analysis was performed using SPSS v 21.0 (SPSS Inc, USA) and Python 3.11.0 with packages Numpy 1.24.1, Pandas 1.5.2, Matplotlib 3.6.2. Data distribution was assessed using the Shapiro-Wilk criterion. For normal distributions, analysis of variance was used for between-group comparisons, and the Kruskal–Wallis test was used for non-normal distributions. Within-group changes were assessed using the Wilcoxon test with Bonferroni correction for multiple comparisons. The relationship between categorical variables was assessed using Pearson's χ^2 test. The kappa-Cohen coefficient was used to determine the consistency between dynamic tests. Two-sided significance level criteria were used. Data were presented as mean (standard deviation) *[M (SD)]* for normal distribution or as median (interquartile range) *[Me (IQR)]* for non-normal distribution. Categorical variables were presented as frequencies. Differences were considered significant at $P<0.05$.

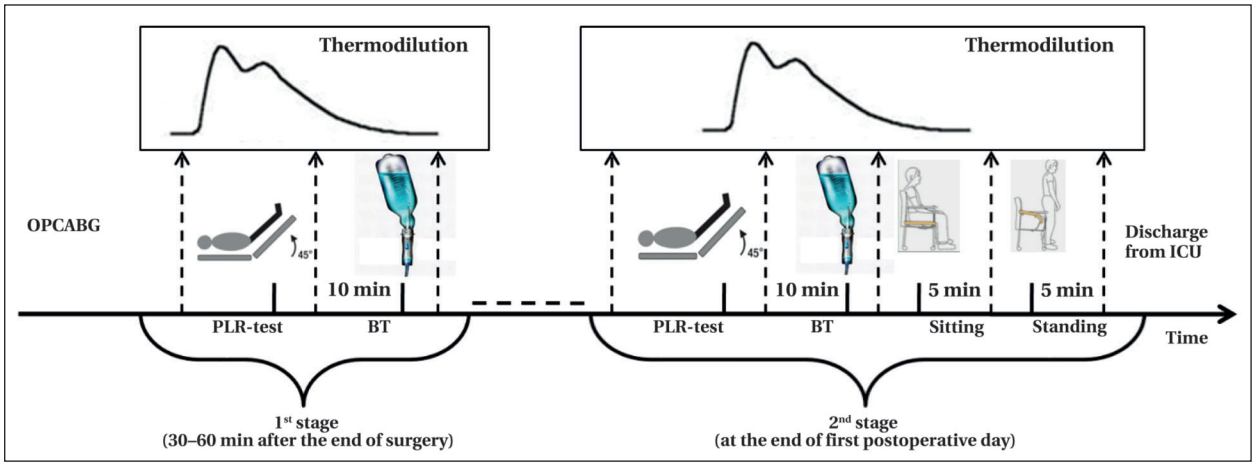

Fig. 2. Sequence of thermodilution test for fluid responsiveness assessment and during upright positioning.
Note. OPCABG — off-pump coronary artery bypass grafting; PLR — passive leg rising; BT — bolus test.

Table 1. Perioperative characteristics of patients.

Parameter	Values in groups			*P*
	GA+ESPB	GA+EA	GA	
Preoperative				
Age, years	60.1 (4.8)	60.7 (8.0)	62.7 (7.3)	0.53
Percentage of men, %	73	80	93	0.35
Body mass index, kg/m²	26.2 (2.8)	28.2 (4.3)	27.1 (3.0)	0.41
Euroscore II, %	1.07 (0.73)	0.85 (0.43)	1.34 (0.77)	0.06
CHF, NYHA class	2.0 (0.2)	2.0 (0.3)	2.0 (0.1)	0.47
Intraoperative				
Duration of surgery, min	174.3 (18.2)	178.3 (31.8)	179.8 (28.8)	0.85
Intraoperative fluid balance, mL	612.0 (206.0)	641.3 (262.1)	648.0 (159.9)	0.89
Postoperative				
Fluid balance during day 1, mL	336.0 (615.6)	599.3 (570.9)	630.7 (382.5)	0.26
Fluid infusion during day 1 of postoperative period, mL	1700 (25)	1700 (200)	1700 (500)	0.72
NT-proBNP, ng/mL	398.9 (275.4)	642.0 (1183.0)	725.4 (1121.8)	0.65
Troponin T, pg/mL	179.6 (161.0)	199.2 (109.6)	243.5 (250.3)	0.62

Table 2. Cardiac index changes during tests of fluid responsiveness and orthostatic tests.

Period	Parameter	Values in groups			*P*
		GA+ESPB	GA+EA	GA	
Admission to ICU	CI_{rest}	2.40 (0.54)	2.22 (0.67)	2.16 (0.58)	0.521
	CI_{PLR}	2.53 (0.58)	2.44 (0.70)	2.44 (0.66)	0.914
	*P-value**	0.048	0.012	0.001	
	CI_{BT}	2.82 (0.70)	2.59 (0.83)	2.35 (0.47)	0.203
	*P-value**	0.005	0.011	0.055	
End of Day 1	CI_{rest}	2.47 (0.34)	2.78 (0.65)	2.58 (0.44)	0.243
	CI_{PLR}	2.61 (0.47)	2.94 (0.71)	2.83 (0.59)	0.291
	*P-value**	0.169	0.026	0.026	
	CI_{BT}	2.73 (0.45)	2.97 (0.62)	2.64 (0.41)	0.193
	*P-value**	0.007	0.064	0.277	
	$CI_{sitting}$	2.75 (0.50)	3.20 (0.83)	2.83 (0.53)	0.152
	*P-value**	0.029	0.172	0.035	
	$CI_{standing}$	2.24 (0.41)	2.59 (0.61)	2.62 (0.65)	0.151
	*P-value**	0.173	0.391	0.934	

Note. CI — cardiac index; PLR — passive leg raising; BT — bolus test. * — when compared to the resting value.

Results and Discussion

The mean age of the patients was 61.2 (6.7) years, the body mass index was (27.3 (0.4) kg/m²), the class of chronic heart failure was 2.0 (0.4), and the preoperative risk according to the Euroscore II scale was 1.1 (0.6) %. All parameters did not differ between the two groups. The average revascularization index was 2.4. Intraoperative fluid administration was prearranged, and no differences in fluid volume and balance were found in the postoperative period (Table 1).

On admission to the ICU, fluid responsiveness tests showed a significant increase in CI: after the PLR test, CI increased in the GA+EA and GA groups, after the bolus infusion — in the GA+ESPB and GA+EA groups (Table 2). At the end of day 1, CI was significantly increased only during the bolus test in the GA+ESPB group due to the increase in SVI (*P*=0.004) (Fig. 3). This can be explained both by the variable severity of the hemodynamic effects of the different regional anesthesia techniques and by differences in the hemodynamic effects of the methods used to assess fluid responsiveness.

When analyzing the parameters that determine CI, the GA+ESPB group showed an increase in HR during upright positioning (*P*=0.001) (Fig. 3). This may indicate the consistency of the baroreceptor reflex in ESPB [21]. Godfrey et al. also found a greater significance of HR increase compared to stroke volume during the PLR test [6].

When analyzing fluid responsiveness, there was no significant difference between groups in either the PLR test or the bolus test. Thus, the PLR test immediately after surgery showed that 7 (47%), 10 (67%), and 9 (60%) patients in the GA+ESPB, GA+EA, and GA groups, respectively, were responders (*P*=0.53), while the bolus test showed 4 (27%), 7 (47%), and 7 (47%) responders (*P*=0.43). The lack of between-group differences in response to fluid therapy confirms previous findings [14]. In addition, no significant differences in mean PAP, PAWP, SVRI and PSR were observed between groups.

The agreement between PLR and bolus test in the GA+ESPB, GA+EA and GA groups was 0.53 (95% CI 0.12–0.94), 0.68 (95% CI 0.30–1.00) and 0.61 (CI 0.24–0.99), respectively. The same fluid responsiveness on both tests was found in 9–11 patients from each group, representing 80% of the total cohort. This suggests the limited consistency of PLR and bolus tests immediately after CABG and

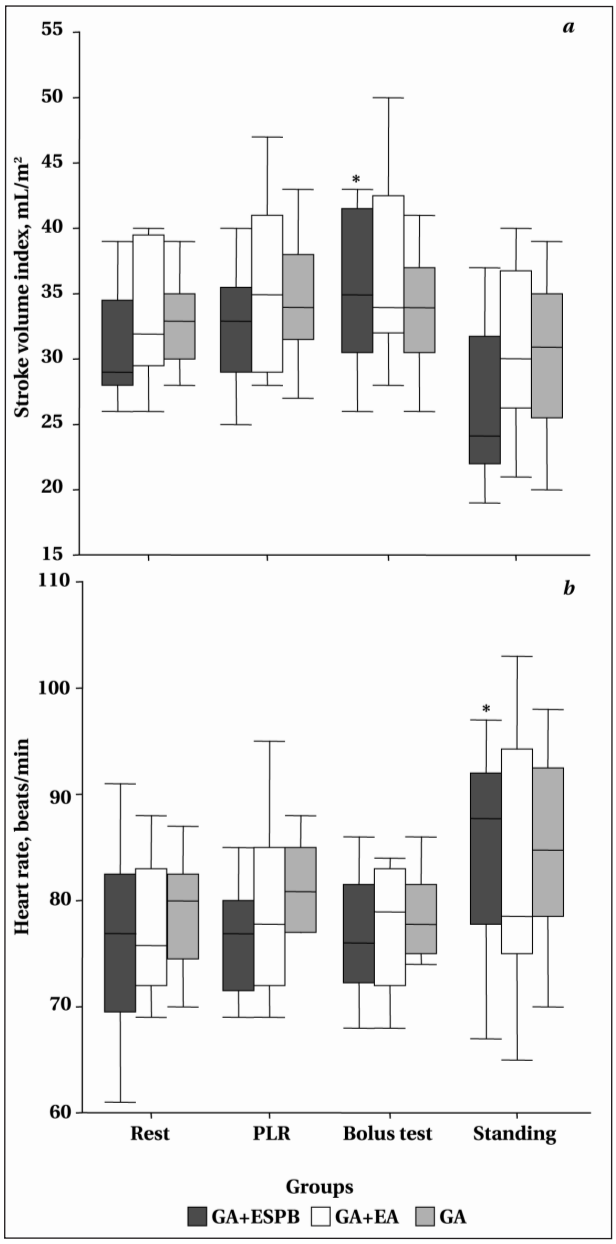

Fig. 3. Heart rate and stroke volume index at the end of first postoperative day.
Note. * — $P<0.05$ compared to the resting value within the group.

the need for cautious interpretation of their results at this stage. Based on different methods of CI assessment, several investigators have shown a moderate correlation between changes in CI during PLR and bolus testing [15]. In our study, the consistency of the tests increased at the end of the first postoperative day and was 0.70 (0.32–1.00), 0.84 (95% CI 0.55–1.00), and 0.82 (95% CI 0.47–1.00) in the GA+ESPB, GA+EA, and GA groups, respectively. The number of fluid responders in the groups was 6 (40%), 4 (27%), and 5 (33%) for the passive leg raise test (P=0.74) and 4 (27%), 3 (20%), and 4 (27%) for the bolus test (P=0.89). The same fluid responsiveness on both tests was found in 14 patients in the GA+ESPB group, 14 patients in the GA+EA group, and 14 patients in the GA group, representing 95% of patients in the total cohort.

The decrease in the number of responders on the first day after CABG may be a natural consequence of the positive postoperative balance. Thus, when analyzing within-group changes, the number of responders in the bolus test during the first postoperative day decreased from 18 to 3 with no between-group differences. On the other hand, 8 patients (18%) of the 27 non-responders immediately after surgery became responders to fluid therapy by the end of the first postoperative day despite a positive postoperative balance. This is probably due to the effect of myocardial revascularization and optimization of left ventricular inotropic and lusitropic function, transition to spontaneous breathing and improvement of right ventricular dysfunction [16], and tissue perfusion with fluid therapy [17]. However, the hemodynamic effects of fluid therapy administered to all patients in the postoperative period are often transient [18]. For example, even in responders, CI begins to decrease 60 minutes after bolus infusion [19], with complete loss of the volume effect of crystalloid solution in 120 min [20]. Meanwhile, the hemodynamic effects of fluid therapy can be prolonged when vasopressor support which reduces venous capacitance is used [21].

Although stable parameters, particularly CVP, have not been shown to be a reliable measure of preload [3], changes in CVP may reflect the severity of right ventricular dysfunction [7]. For example, Vlahakes et al. demonstrated that after pericardial closure and change in preload during cardiac surgery, the increase in left and right ventricular pressures no longer showed a linear relationship, reducing the potential for optimizing right ventricular preload to increase left ventricular performance [22]. While the changes in the passive leg-raise test were consistent in all groups, the subsequent bolus challenge resulted in an increase in CVP only in the EA and ESPB groups (Fig. 4). Several authors have suggested a decrease in right ventricular systolic function with the use of regional anesthetic techniques, particularly EA [23], but these results are controversial [24]. For example, Cooke et al. found that the maximal hemodynamic effect of fluid was in those patients who did not have an increase in CVP with increasing MAP and CI after bolus infusion [25]. However, the PLR test, which increases CVP, may have potential limitations. In addition, non-responders to dynamic testing may include patients with a decrease in cardiac output of more than 15% in response to bolus infusion [25], which is particularly undesirable in cardiac surgery.

The lack of between-group differences in CI values at the end of the first postoperative day during upright positioning of patients suggests a minor contribution of the studied regional anesthetic

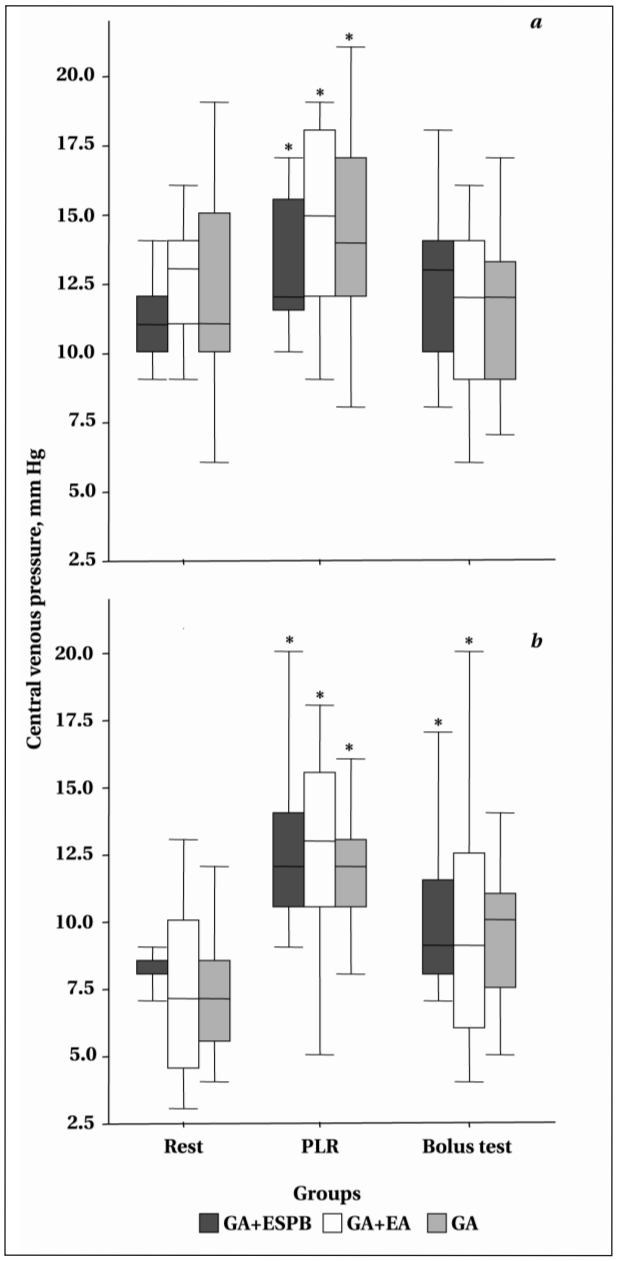

Fig. 4. Central venous pressure at the ICU admission (*a*) and at the end of first postoperative day (*b*).
Note. * — $P<0.05$ compared to the resting value within the group.

techniques at the thoracic level, in particular EA and ESPB, to the severity of autonomic nervous dysfunction [26]. Discomfort during upright positioning occurred in 15 patients, again without differences between groups, with two patients (one each from the GA and GA+ESPB groups) refusing the orthostatic test due to low tolerance. Although the effect of upright positioning is equivalent to a loss of 500–1000 mL of volume [24], we did not observe significant changes in CI and SVI, except for an increase in HR in the sitting (P=0.004) and standing (P=0.001) positions, which highlights the complexity of the adaptation mechanisms to changes in circulating blood volume, that are difficult to predict.

Limitations of the assessment of CI changes in PLR and upright positioning tests include the fact that the bolus test, which has an irreversible and independent effect on volume status, was performed between these two tests, and the combined hemodynamic effect of all three tests is poorly predictable.

No between-group differences were found when evaluating changes in blood gases and troponin T; troponin rise was 14.6 (10.3), 14.3 (11.5), and 11.2 (12.1) fold in the GA+EA, GA, and GA+ESPB groups, respectively (P=0.92). NT-proBNP levels at the end of the first postoperative days exceeded preoperative levels by 4.3 (3.6), 2.9 (2.3) and 2.9 (1.8) times, respectively (P=0.27), while postoperative fluid balance parameters did not differ between groups. Thus, the use of epidural anesthesia and ESPB does not cause excessive myocardial damage, and neurohumoral markers of systolic or diastolic dysfunction showed concordant changes attributed to perioperative surgical stress.

Another limitation of the study is its pilot nature without pre-specified statistical power. Further studies with a larger number of patients are warranted.

Conclusion

The use of EA and ESPB during off-pump CABG results in an increase in CVP when the bolus test is performed at the end of the first postoperative day. There were no differences in the severity of orthostatic response between groups. During upright positioning with ESPB, heart rate increased, whereas no changes in cardiac output and stroke volume were observed.

Thus, the use of regional anesthesia techniques does not significantly affect the responsiveness to fluid therapy after coronary artery bypass grafting and does not exacerbate perioperative myocardial injury or dysfunction. In the postoperative period after coronary artery bypass grafting, there is moderate concordance between the PLR test and the bolus challenge test, with a subsequent increase in concordance by the end of the first postoperative day, suggesting that responsiveness to fluid therapy on ICU admission could be assessed using the bolus test alone.

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