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The effect of type of anesthesia (general versus spinal) on postoperative levels of brain natriuretic peptide in parturient women with cardiovascular diseases undergoing cesarean section and related cardiac impacts

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ABSTRACT

Background: Dealing with parturient women with cardiac disease is still a challenge for anesthesiologists due to the presence of physiologic burden of pregnancy in addition to the already existing compromised cardiovascular system. A variety of cardiac indices have been utilized to forecast the risk of perioperative cardiac complications, yet limitations in their predictive value exist. Perioperative brain natriuretic peptide (BNP) level is used as a prognosticator of cardiac complications following surgery in cardiac and non-cardiac individuals.

Aim of study: To compare the effect of general and spinal anesthesia during cesarean section in parturient with cardiac disease on BNP levels and on predicting adverse cardiac events.

Methods: Thirty cardiac parturient with cesarean section were assigned randomly into two groups of equal size. Group A: participants received general anesthesia (GA); Group B: participants received spinal anesthesia. Preoperative and 2 and 24 h postoperative BNP levels were measured. Intraoperative and 24 h postoperative cardiac complications were observed.

Results: Preoperative and 2 and 24 h postoperative BNP mean levels were similar in the two groups. In each group, the 2 and 24 h postoperative rise in BNP mean levels was insignificant compared to the preoperative mean levels of BNP. Incidence of complications was comparable in both groups, but it was associated with the already high preoperative levels of BNP.

Conclusions: The study concludes that safely conducted certain type of anesthesia has no effect on the perioperative BNP levels nor incidence of complications which is associated with the already high preoperative BNP levels.

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1. Introduction

Managing parturient with heart diseases is considered a challenge in anesthetic practice. In addition to the already existing cardiovascular compromise related to both the primary disease and pregnancy, the surgical stress response to surgical manipulation and perioperative pain of cesarean section (CS) is another risk factor [1]. Mastering the suitable analgesic and anesthetic approach to keep the most possible stability of cardiovascular system (CVS) and hemodynamics during CS requires a comprehensive understanding of pregnancy physiological changes and the effect of different anesthetic drugs and technique as well [2].

Prediction of CVS risk factors is very important to avoid perioperative complications. Various investigations and cardiac indices have been used for predicting cardiac risks. Eagle's risk index, Goldman multifactorial risk index and Detsky's cardiac index are well-known cardiac indices that are simple to use [3–6]; however, they are inconvenient and of limited predictive value [4].

An indicator for diagnosis and forecasting the prognosis of many cardiac conditions is the brain natriuretic peptide (BNP), which is a cardiac hormone produced in ventricular myocytes in response to ventricular dysfunction [7]. Research has revealed that in general population, increased levels of BNP in serum can predict first cardiovascular event and death [7,8]. Moreover, measurement of BNP levels prior to major surgeries can serve as an effective indicator for postoperative cardiac complications [9,10]. Few studies [11–13] have evaluated the predictive value of BNP in pregnant women with cardiovascular diseases (CVD) during antenatal and postnatal period; however, this is the first study to compare the effect of the type of anesthesia on BNP levels to predict complications during CS in such population.

The aim of this study is to compare the impact of two different types of anesthesia (general and spinal) in CS in parturient with cardiac disease on perioperative levels of BNP and its correlation with predicting the adverse cardiac events.

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2. Methods

This study received approval from Kasr AlAiny Hospital's ethics committee and the Faculty of Medicine, Cairo University (N-2-2018), with clinical trial registration at ClinicalTrials.gov (ID: NCT03460184). This prospective randomized trial was carried out at Kasr AlAiny Hospital from March 2018 till June 2018 on 30 parturient patients with different CVD coming for elective CS. Patients included were within the age range of 20–50 and presented with mild to moderate valvular heart lesions, cardiomyopathic lesions with ejection fraction (EF) more than 40%, hypertension, ischemic heart disease and non-fatal arrhythmias, e.g., controlled atrial fibrillation (AF).

Patients excluded from the study were those presented with cardiomyopathy with EF less than 40%, valvular lesions of tight stenosis or severe regurgitation, pregnancy-induced hypertension and fatal arrhythmia, e.g., ventricular tachycardia and renal insufficiency with creatinine level more than 1.2 mg/dl (leads to false increase in BNP). Dropouts were patients with surgery-related complications, which are operation longer than 120 min, patient needed intravascular fluids resuscitation with more than 3 l and intra-operative blood loss more than 1 l.

Patients' assessment was done through detailed history taking, comprehensive physical examination and routine preoperative labs. Preoperative electrocardiograph (ECG) and echocardiography was done. An 18-gauge peripheral cannula was inserted in a suitable peripheral vein. Preoperative BNP level was measured through patient's blood sample. Prophylactic antibiotic was given 30 min prior to skin incision, with appropriate selection in cases at risk of rheumatic heart disease. Intravenous (iv) metoclopramide 20 mg and ranitidine 50 mg were administrated.

Patient monitoring with ECG, non-invasive blood pressure and pulse oximeter was conducted, and the baseline values of heart rate (HR), mean arterial blood pressure (MABP) and arterial oxygen saturation (SaO_2) were listed.

Random allocation of patients in two equal groups was done through computer-generated random tables, and senior anesthesia staff kept the random numbers in closed opaque envelopes (Figure 1).

Group A (*n* = 15): patients had CS under general anesthesia

General anesthesia (GA) and rapid sequence induction and intubation were done using iv propofol 2 mg/kg and succinylcholine 1.5 mg/kg. GA was maintained by 100% oxygen and isoflurane 0.8%, keeping MABP within 20% of the baseline reading. Neuromuscular block was maintained by atracurium infusion with a rate of 0.5 mg/kg/h, administrated in a separate line, and iv fentanyl 1 µg/kg was given after fetus delivery. Neuromuscular blockade reversal was done at the end of the surgery according to train of four using 0.01 mg/kg atropine and 0.07 mg/kg neostigmine. Endotracheal extubation was done after adequate anesthesia reversal.

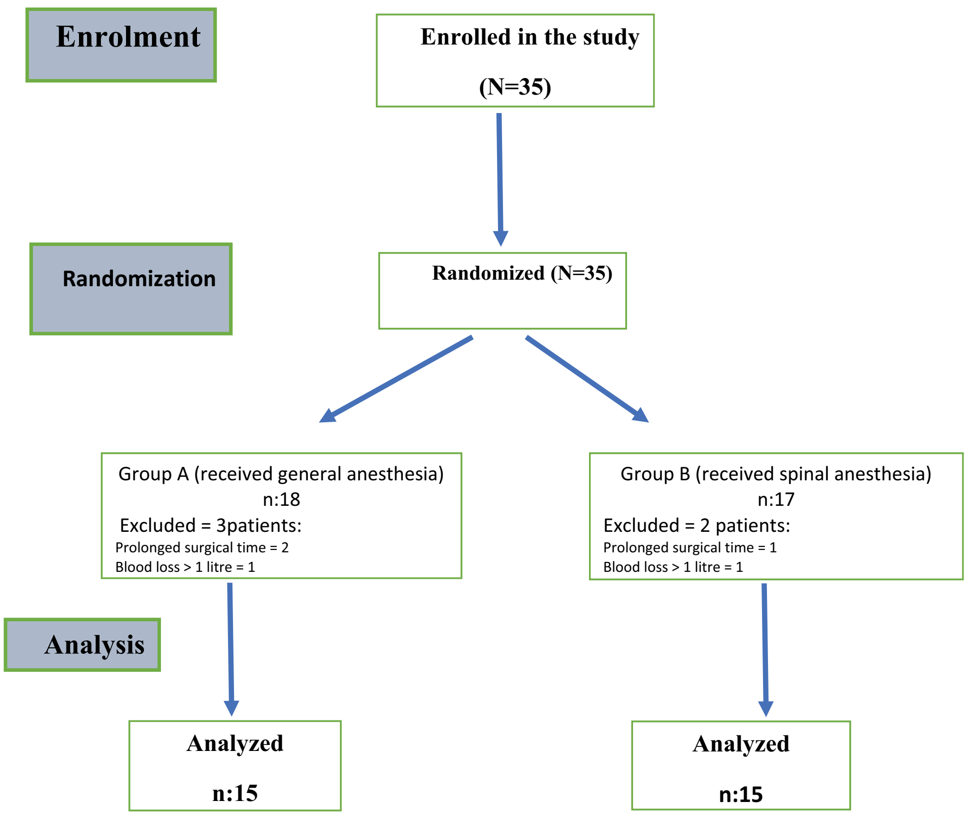


Figure 1. Consort flow chart.

Group B (*n* = 15): patients had CS under spinal anesthesia

Having the patient in a sitting position, the back was properly sterilized. After local skin infiltration with 2–3 ml lidocaine, spinal anesthesia (SA) was done at interspace L3–4 or L4–5, using either midline or paramedian approach. A 22-gauge Quincke needle was inserted with lateral bevel direction and a mixture of 2.5 ml hyperbaric bupivacaine 0.5% and 25 µg fentanyl (0.5 ml) was injected into the subarachnoid space. In the supine position, a wedge under the right loin of the patient was put for left uterine displacement. Sensory block was confirmed by losing pinprick sensation (sensory level was at T4–T5 in all participants).

Intraoperatively, patients in both groups received 2 ml/kg/h Ringer lactate infusion till the end of surgery and iv infusion of 20 IU oxytocin after fetus delivery. Monitoring of HR, MABP and SaO_2 was recorded at 5 and 15 min after completion of anesthesia induction, then every 15 min till the end of surgery. In case of hypotension (20% decrease from MABP baseline), iv increments of 3 mg ephedrine was given.

All patients were monitored closely for any signs of cardiac adverse effects, such as arrhythmias, frequent atrial extrasystoles, supraventricular tachycardia, rapid AF, non-fatal MI and sudden cardiac death until the end of surgery.

Postoperatively, patients in both groups had a continuous monitoring for HR, MABP and SaO_2 in postoperative care unit and then in the ward hourly till the completion of 24 h.

Postoperative pain was managed by 1 g acetaminophen every 8 h if mild and additional iv 30 mg ketorolac if needed, maximum of 120 mg with 6-h interval.

Postoperative PNB levels measurement, ECG and echocardiography were done at 2 and 24 h postoperatively. All patients were monitored closely for any signs of cardiac adverse effects, such as arrhythmias, frequent atrial extrasystoles, supraventricular tachycardia, rapid AF, non-fatal MI and sudden cardiac death until discharged.

Primary outcome was detecting postoperative PNB levels changes in relation to the type of anesthesia.

Secondary outcomes were intraoperative and postoperative hemodynamics and detecting the efficiency of the absolute values of BNP (≥100 pg/ml) in predicting perioperative cardiac complications.

3. Statistical analysis

3.1. Sample size

Based on a pilot study, sample size was calculated according to the insignificant difference in the mean value of difference in BNP between GA group (1.17 ± 2.89) and SA group (1.54 ± 3.24) in two-tailed unpaired t-test, with α = 0.05, power of 80% and an effect size of 0.94. So, a sample size of 15 patients/group would be required and increased to 17 women to allow for a 15% dropout rate (G-Power 301; www.psycho.uni-duesseldorf.de).

4. Method of analysis

Depending on the context, the obtained data are displayed as mean ± standard deviation (SD) or number and percentage. The chi-square test, the Student's t-test and the analysis of variance were the three methods used to compare the data. Data analysis was done using both Microsoft Office 2013 and SPSS (20, 2012). Statistical significance was presumed when the *p* value was ≤0.05.

5. Results

Thirty-five participants were included in this study, and five patients were excluded due to prolonged surgery duration of more than 120 min (three patients) and more than 1 l intraoperative blood loss (two patients) (Figure 1).

Both groups were comparable to one another in terms of patients' characteristics, such as age, the existing cardiac diseases and duration of surgery (Table 1).

Intraoperative and postoperative HR (Figures 2 and 4 respectively) and MABP (Figures 3 and 5 respectively) in the two studied groups were comparable.

Preoperative baseline and 2 and 24 h postoperative mean BNP levels were comparable in the two groups (Table 2).

In each group, the 2 and 24 h postoperative rise in BNP mean levels was insignificant compared to the preoperative mean levels of BNP (Table 2).

Incidences of intraoperative cardiac complications were comparable in both groups (Table 3).

Incidence of cardiac complications was not associated with the rise in postoperative levels of BNP and type of anesthesia; however, it was associated with the already high preoperative levels of BNP (Table 3).

6. Discussion

Understanding the physiological burden that occurs during pregnancy on CVS has been the major focus in the recent anesthetic practice, especially in parturient with already compromised CVS. Physiological cardiovascular changes in pregnancy include volume overload as there is almost 50% increase in maternal blood volume and increased left ventricular wall thickness and end-diastolic dimensions. Different studies are being conducted for better management in such patients (dealing with surgical stress response, hemodynamic instability and postoperative pain, all

Table 1. Patients characteristics.

	Group A ($n = 15$)	Group B ($n = 15$)	P value
Age (years), mean ± SD	30.13 ± 6.05	31 ± 5.23	0.694
Number of patients with history of			
o RHD	8	11	
o RHD and AF	3	2	0.4
o IHD	2	0	
o IHD and HTN	2	2	
Echocardiography valvular findings			
o Moderate MS	2	3	
o Mild MS	5	4	
o Mild MR	3	2	
o Mild TR	2	1	
o Mild AS	0	2	
o Mild AR	1	2	
Surgery duration (min), mean ± SD	51.92 (±3.81)	53.82 (±3.89)	0.065

P value ≤ 0.05 considered significant. RHD: rheumatic heart disease; AF: atrial fibrillation; IHD: ischemic heart disease; HTN; hypertension; MS: mitral stenosis; MR: mitral regurgitation; TR: tricuspid regurgitation; AS: aortic stenosis; AR: aortic regurgitation.

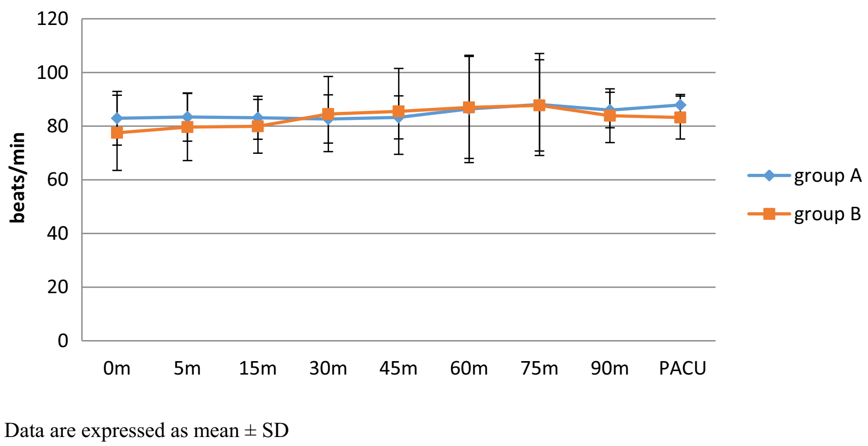


Figure 2. Intraoperative HR (beats/minute) between the two studied groups. Data are expressed as mean ± SD.

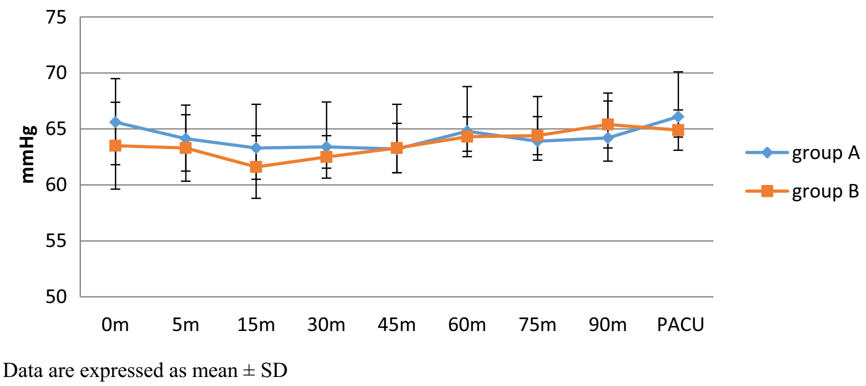
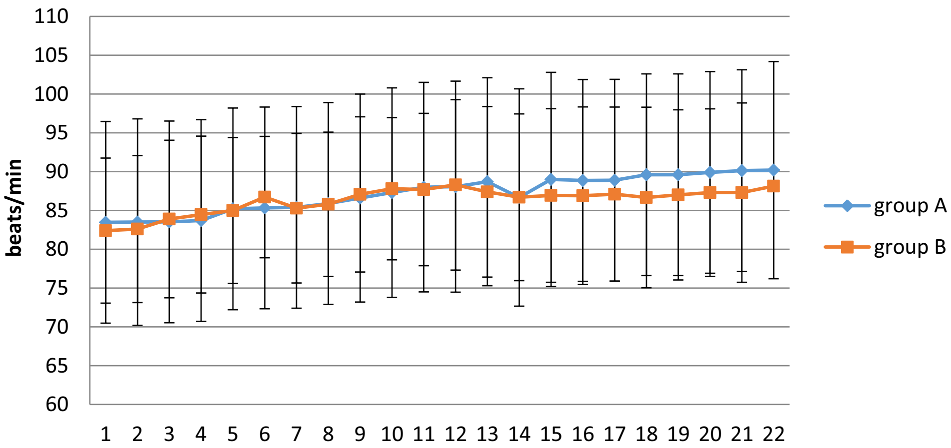


Figure 3. Intraoperative MABP (mm hg) between the two studied groups. Data are expressed as mean ± SD.

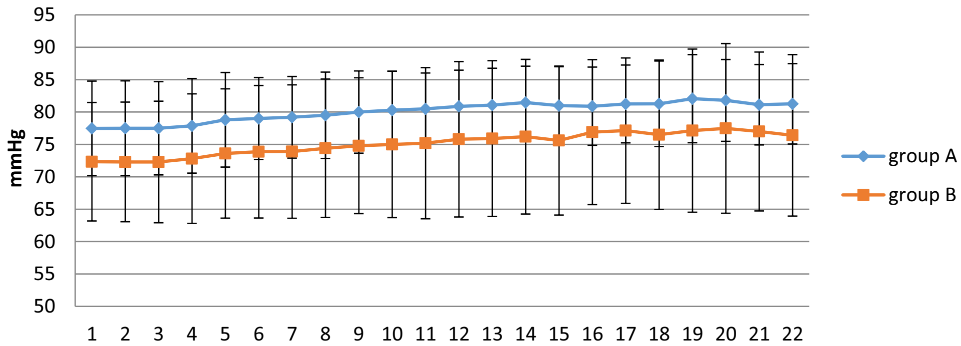
negatively affect the CVS), and prediction of the cardiac risk factors in cardiac parturient is among the most essential procedures involved in managing any of them [1,2].

It is well recognized nowadays that BNP levels are used to predict adverse cardiac consequences like AF, heart failure and coronary heart disease. Both N-terminal-pro-BNP and BNP have been used as helpful prognostic tests in predicting cardiac complications in ICU [14,15] and after vascular [16,17], cardiac [18,19] and noncardiac surgeries (NCS) [20,21–23]. These previous studies have demonstrated a clear link between high BNP levels preoperatively and the possibility of postoperative cardiac adverse effects such as acute pulmonary edema, arrhythmias, non-fatal myocardial infarction and cardiac death [20,16–19,21–23]. In addition, it is described as Class I indication to measure BNP level preoperatively in noncardiac operations for patients vulnerable to postoperative cardiac complications, as guided by the Canadian Cardiovascular Society for Perioperative Care [24].



Dataare expressed as mean ± SD

Figure 4. Postoperative HR (beats/minute) between the two studied groups. Data are expressed as mean ± SD.



Dataare expressed as mean ± SD

Figure 5. Postoperative MABP (mm hg) between the two studied groups. Data are expressed as mean ± SD.

Table 2. Mean values of BNP.

	Total no. of patients ($n = 30$)	Group A ($n = 15$)	Group B ($n = 15$)	*P* value
Preoperative Mean (±SD) pg/ml	88.4 (±33.5)	85 ± 28.48	90.8 (±38.48)	0.482
2 h postoperative Mean (±SD) pg/ml	99.6 (±35.59)	98.15 (±33.98)	101.13 (±38.3)	0.823
	P value compared to preoperative level	0.708	0.55	
24 h postoperative Mean (±SD) pg/ml	102.67 (±40.54)	101.67 (±36.1)	103.67 (±45.84)	0.896
	P value compared to preoperative level	0.17	0.31	

Data are presented as mean and standard deviation. *P* value ≤ 0.05 is considered significant.

Table 3. Number of patients who had intraoperative and postoperative complications with and without high preoperative BNP levels.

	With normal preoperative BNP			With high preoperative BNP (≥100 pg/ml)		
Complications vs preoperative BNP level	Group A $N = 11$	Group B $N = 10$	Total $N = 21$	Group A $N = 4$	Group B $N = 5$	Total $N = 9$
Intraoperative complications	1 (9%)	1 (10%)	2 (9.5%)	2 (50%)	3 (60%)	5 (55%)
Postoperative complications	0	0	0	4	3	7 (77%)

Data are presented as number and percentage.

Although the use of BNP to predict perioperative cardiac complications is widely accepted, there is no agreement on a definite cutoff of the BNP serum levels at which perioperative cardiac complications are most suspected. However, a BNP level of 100 pg/ml is agreed as a threshold for heart failure diagnosis, however; complications can occur at BNP levels less than this threshold [8,25].

Normal BNP levels in healthy women during pregnancy have not been precisely confirmed yet. In relation to pregnancy, Hameed et al. [26] found that there are twofold increase in BNP levels in healthy pregnant women [19 (10–143) pg/ml] than that in nonpregnant women [10 (10–37) pg/ml] ($p = 0.003$). In healthy pregnant women, Kimura et al. [11] found an increase in BNP levels within 4 days after delivery (23.5 pg/ml, IQR: 14.0–38.2 pg/ml) in relation to those measured during 28–30 weeks' gestation (13.2 pg/ml, IQR: 8.5–20.8 pg/ml) and lasts for 6 weeks postpartum. This increase was associated with echocardiographic findings of gestational cardiac chamber enlargement and the postpartum fall in hemoglobin. All the increases in levels noticed in the previous studies have not reached the level of heart failure prediction.

In our study, we hypothesized that preoperative and postoperative levels of BNP may be helpful in predicting adverse cardiac event related to different anesthetic techniques that may have an impact on cardiac parturient undergoing CS. However, what we actually found is that both GA and SA have similar postoperative impacts on BNP levels after CS in parturient with CVD. BNP levels measured preoperatively and 2 and 24 h after induction of anesthesia were comparable on both groups. Incidences of intraoperative and postoperative cardiac complications were comparable in both general and spinal groups. Patients in both groups demonstrated comparable statistically insignificant degrees of increase in postoperative BNP and comparable incidence of complications. However, patients in both groups with elevated preoperative levels of BNP demonstrated significantly higher incidence of complications, either intraoperative or postoperative, than those with normal preoperative levels of BNP. These findings suggest that in this type of population, parturient with mild to moderate heart disease, when the anesthetic technique is conducted safely and properly with stable hemodynamics, it would have a minimal effect on postoperative cardiac complications regardless of the type of anesthesia used.

In the current study, the fact that all participants had an EF more than 40% may have contributed to the lower BNP level than that measured in some previous trials such as that observed in the study by Leibowitz et al. [27] who included 44 patients having NCS presenting with more severe cardiac affection than our included patients, such as history of congestive heart failure, severe aortic stenosis or EF less than 40%. Thirty-four percent of patients had postoperative cardiac complications, with a mean BNP level in patients with and without events being 1366 ± 1420 pg/ml and 167 ± 194 pg/ml, respectively ($p < 0.001$). However Dos Santo et al. [12] had similar observations as ours. They compared the PNB levels in normal parturients ($n = 43$) and in parturients with congenital heart diseases ($n = 30$) at different stages of pregnancy, and they found comparable levels of BNP in parturient with and without congenital heart disease with no BNP measurement being more than 40.0 pg/ml in the third trimester of both groups. They explained the relatively lower (than other studies and comperable BNP levels between the two groups in thier study by thier relatively small sample size and the well compensated cardiac status of most of thier included participants, as similar as our participants.

Mirkheshti et al. [28] allocated 120 noncardiac patients undergoing lower limbs orthopedic surgeries into three groups; 40 patients had GA and postoperative epidural analgesia, 40 patients had GA and postoperative iv patient-controlled analgesia (PCA) and 40 patients had SA and postoperative PCA. However, in disagreement with our results, their findings suggested that SA and PCA have the most protective cardiac effects with the least increase in postoperative pro-BNP levels (51.5 ± 8.5 ng/L), where GA with epidural analgesia and GA with PCA had BNP levels of 63.8 ± 10.1 ng/L and 83.2 ± 12.3 ng/L, respectively, $P = 0.01$. However, the different type of the included noncardiac population could explain the difference in results.

On 60 patients with coronary artery disease undergoing lower limb surgery and allocated into three equal groups ($n = 20$), Atalay et al. [10] studied the effect of GA and then postoperative iv PCA, lumbar epidural anesthesia and analgesia and combined GA with thoracic epidural anesthesia and analgesia on the BNP release during surgery in such population. They found that the combined GA with thoracic epidural anesthesia and analgesia group had the lowest postoperative level of BNP (69.0 ± 6.9 pg/ml), then the lumbar epidural anesthesia group (110.6 ± 12.2 pg/ml) and then the GA with iv PCA group which had the highest BNP release (162.4 ± 29.4 pg/ml), $P < 0.05$. They explained that the combined use of local anesthetics with opioid in the two epidural groups had an effect in decreasing BNP synthesis.

7. Study limitations and recommendations

- A relatively small sample size is one of the limitations, so future study with larger number of participants is recommended.
- Only individuals with more or less maintained cardiac functions were included in this study, so we recommend including patients with more severe systolic and diastolic dysfunction in further studies.
- Further, the correlation between BNP and other cardiac indices like cardiac troponin is needed to be studied in these types of patients in future studies.

8. Conclusion

We conclude that when conducted safely, type of anesthesia in CS in cardiac parturient has no effect on perioperative BNP levels nor on intraoperative and postoperative cardiac complications, and the absolute value of preoperative BNP levels, either normal or high, is the most important factor.

Authors' contributions

Heba Omer and Michael Wahib contributed to the conception and design of the study, analysis of the data and writing the manuscript.

Sahar Marzouk, Ahmed Abdalla, Ashraf Mohamed Abdelreheem and Mohamed Hussein Helmy collected the data and wrote the manuscript.

Sahar Marzouk, Ahmed Abdalla, Ashraf Mohamed Abdelreheem, Mohamed Hussein Helmy, Heba Omar and Michael Wahib revised the manuscript and contributed to the approval of final manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethical approval and consent to participant

- Ethical approval was obtained from Cairo University hospitals research committee (N-2-2018). Approval date: 17-2-2018.
- Study was conducted at Kasr Al Ainy Hospital.
- Written informed consents were obtained from participants before inclusion.

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