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Original article

Implications of Anesthetic Techniques on Cardiocirculatory Stability in Laparoscopic Cholecystectomy

Biljana Stošić[1,2], Marija Stošić[2], Jelena Živadinović[2], Ines Veselinović[2]

[1]*University of Niš, Faculty of Medicine, Niš, Serbia*
[2]*University Clinical Center Niš, Clinic of Anesthesiology and Intensive Care, Niš, Serbia*

SUMMARY

Background and Aim: The aim of the present study was to compare the effect of volatile induction and maintenance of anesthesia (VIMA) and target controlled infusion (TCI) on cardiovascular stability in New York Heart Association (NYHA) grade II patients who underwent laparoscopic cholecystectomy.
Patients and methods: In the present study, 90 patients were randomized into two groups depending on whether they received VIMA or TCI. Heart rate, systolic, diastolic and mean arterial pressure were monitored continuously and recorded in five time intervals.
Results: Statistical analysis showed that VIMA with sevoflurane provides better cardiocirculatory stability (less than 10% deviation from basal values for each measured parameter) than TCI group (p < 0.01).
Conclusion: Volatile induction and maintenance of anesthesia with sevoflurane provides better hemodynamic stability for NYHA II patients with concomitant cardiovascular diseases compared to TCI.

Keywords: **anesthesia, cholecystectomy, laparoscopic, cardiovascular diseases**

Corresponding author:
Biljana Stošić
e-mail: b.stosic@yahoo.com

INTRODUCTION

Laparoscopic cholecystectomy (LC) is the most common technique for surgical treatment of uncomplicated chronic choledocholithiasis. Considering the results, LC compares equally to the best achievements in classic cholecystectomy worldwide (1). It is a minimal invasive video endoscopic type of surgery with many advantages, both for patients and hospitals: less tissue trauma, lower intensity of pain, shorter hospitalization time, lower treatment costs, and shorter time to full recovery (2).

Nevertheless, there are some issues considering specific pathophysiological changes that occur during LC. Specific patient positioning (anti-Trendelenburg and left decubitus), greater intra-abdominal pressure, and iatrogenic pneumoperitoneum caused by carbon dioxide insufflations, all of which can have a negative impact on cardiovascular system and cause hemodynamic instability. It is clear that certain methods of laparoscopic technique can worsen an already existing ischemic heart disease, heart insufficiency, or heart valve disease in New York Heart Association (NYHA) II classified patients. Therefore, it is of great significance to determine which type of anesthesia is the best for providing favorable conditions for hemodynamic stability. According to the literature, different authors have not yet reached an agreement about this problem (2 – 4).

The aim of the present study was to compare the effect of volatile induction and maintenance of anesthesia (VIMA) and target controlled infusion (TCI) on cardiovascular stability in NYHA II patients who underwent laparoscopic cholecystectomy.

PATIENTS AND METHODS

In our prospective, comparative study, the patients were divided into two groups depending on whether they received VIMA or TCI. Ninety patients were assigned to groups randomly (45 in each group), right after they were called to the operating theater for surgery. All of them had been assigned for laparoscopic surgical treatment of chronic cholelithiasis. The study took place at the Department of Anesthesiology and Intensive Care and the Department of Hepatobiliary Surgery at the University Clinical Center Niš.

The inclusion criteria were: a diagnosis of chronic cholelithiasis, a set indication for laparoscopic surgical treatment, and NYHA II classification of a patient based on previous patient examination. The exclusion criteria were: hypersensitivity to opioids and general anesthetics used in this study, a history of drug or/and alcohol abuse, pregnancy, and morbid obesity.

All the patients were given a premedication 30 minutes before the surgery: 0.1 mg/kg BW midazolam and 0.5 mg atropine i.m.

In the first group of patients we used VIMA technique with sevoflurane and remifentanil for analgesia. A single-breath vital capacity technique with fresh gas flow at 8 l/min and 8 vol% of sevoflurane was used for the induction of anesthesia. After preoxygenation, each patient was told to inhale as deeply as possible and then to exhale to the residual volume. Their anesthesia circuit was primed with 8% sevoflurane and 50% nitrous oxide in oxygen at a fresh gas flow of 8 l/min ($FiO_2 = 0.5$). At end-expiration, the mask connected to the primed circuit was placed firmly over the patient's face. Patients were encouraged to perform a vital capacity breath as long as they could. If they exhaled again before losing consciousness, patients were encouraged to take additional deep breaths until they were asleep. The loss of consciousness occurred approximately in 1 minute. For the maintenance of anesthesia, the inspiratory concentration of sevoflurane was reduced to 1.5 – 2.5 vol% with End Tidal (ET) concentration being approximately 1.7%. During maintenance, the fresh gas flow was reduced to 1 l/min (low-flow anesthesia). For analgesia we used TCI of remifentanil (Minto model), 7 ng/ml during the induction and 5 ng/ml during the maintenance of anesthesia. Twenty minutes before emergence from anesthesia, patients received 30 mg of ketorolac. Ten minutes before emergence, TCI of remifentanil was stopped.

In the other group of patients, we used TCI of propofol, together with TCI remifentanil to achieve analgesia. For TCI of propofol, we used Shnider's effect mode, 4 μg/ml during induction, 3 μg/ml during maintenance, down to 0.5 μg/ml during emergence from anesthesia. TCI of remifentanil was used by the same protocol as in VIMA group of patients.

In both groups we used the same non-depolarizing neuromuscular blocking agent, rocuronium bromide, at 0.6 mg/kg BW intubation dose, and 0.15 mg/kg BW maintenance dose. The residual neuromuscular block at the end of surgery was antagonized with 0.035 mg/kg neostigmine and 0.015 mg/kg atropine.

In both groups we used bispectral index (BIS) monitoring system to ensure the equal depth of anesthesia. For this purpose we used BIS™ Complete 2-Channel Monitor (Medtronic).

The Dräger Fabius® (Drägerwerk AG&Co) anesthetic machine was used for mechanical ventilation in all patients. To measure inspiratory and ET concentrations of sevoflurane, O_2 and N_2O we used Dräger Vamos plus® analyzer (Drägerwerk AG&Co). TCI was performed by using Perfusor® Space BBraun (B. Braun Medical Inc.) devices.

Hemodynamic parameters (heart rate, systolic, diastolic and mean arterial pressure) were monitored continuously with Datex-Engstrom AS/3 monitor and recorded in six time intervals. We calculated the percentage deviation from the starting values for every patient, and registered the frequency of variations greater than 20% from the baseline values. We graded the cardiovascular stability as follows: grade I – 0-10% variations from the starting values; grade II – 11-20%; grade III – 21-30%; grade IV – more than 30% variations.

Heart rate, systolic, diastolic and mean arterial pressure were recorded in six time intervals: t_0 – before the induction of anesthesia, t_1 – after the induction of anesthesia and before the skin incision; t_2 – after the skin incision; t_3 – 5 minutes after creating a pneumoperitoneum; t_4 –30 minutes after creating the pneumoperitoneum; t_5 – 5 minutes after release of pneumoperitoneum.

For every hemodynamic parameter, mean arithmetic value and standard deviation were calculated. Statistical analysis was done by SPSS for Windows (version 7.2) and the tests used were: Friedman's χ^2 test and Student's t-test. Additionally, a time-series analysis was conducted in order to determine any trends in the changes of the value of parameters. In order to determine which model is the most appropriate for the given data sets, the following procedures and principles were used: measurement of the magnitude of the residuals through squared differences paired with the principle of parsimony. As a result, the first-order autoregressive model was used on the collected data sets. Due to the nature of the data collected, it was hypothesized that the values will indeed auto-correlate. The significance level was at $\alpha = .05$.

RESULTS

Demographic characteristics of patients and joined cardiovascular diseases are presented in Table 1.

The difference in cardiovascular stability grades between the groups was statistically highly significant at all recorded time intervals. All the patients at VIMA group presented grade I deviations of the measured cardiovascular indices. In TCI group, a different number of patients (even more than 30%) belonged to grade II. One patient in TCI group had a grade III cardiovascular instability recorded at t5 interval.

The heart rate was monitored continuously and recorded at six time intervals (t_0 – t_5). In each group separately, the difference between heart rates at all time intervals was statistically tested using the Friedman's χ^2 test. This test shows that in both groups there was a high statistically significant difference between the heart rate values (VIMA: χ^2 F = 33.7, p < 0.01; TCI: χ^2F = 37.7, p < 0.01). The greatest

Table 1. *Demographic characteristics of patients and joined cardiovascular diseases*

Patient's characteristics	VIMA (n = 45)	TCI (n = 45)
Average age (age span)	61.4 (41 – 73)	61.2 (42 – 71)
Sex		
male (n)	19	20
female (n)	26	25
Cardiovascular comorbidities (n)		
Ischemic heart disease	17	21
Arterial hypertension	28	29
Heart valve disease	7	7

VIMA-Volatile Induction and Maintenance Anaesthesia; TCI- Target Controlled Infusion

Table 2. *Patient distribution by cardiovascular instability grades considering heart rate*

Time interval and grade of cardiovascular instability	VIMA (n)	TCI (n)	VIMA:TCI *p*
t_1			
I grade	45	36	< 0.01
II grade	0	9	
III grade	0	0	
t_2			
I grade	45	30	< 0.01
II grade	0	15	
III grade	0	0	
t_3			
I grade	45	29	< 0.01
II grade	0	16	
III grade	0	0	
t_4			
I grade	45	34	< 0.01
II grade	0	11	
III grade	0	0	
t_5			
I grade	45	35	< 0.01
II grade	0	9	
III grade	0	1	

VIMA-Volatile Induction and Maintenance Anaesthesia; TCI- Target Controlled Infusion

change in heart rate values happened between t_0 and t_1 interval when the heart rate increased, and between t_4 and t_5 interval when it decreased.

Table 2 shows patient distribution by cardiovascular instability grades considering heart rate in both groups at all time intervals.

Systolic, diastolic and mean arterial pressure were monitored continuously and recorded at six time intervals ($t_0 – t_5$). Separately in each group, the difference between systolic blood pressure at all time intervals was statistically tested using the Friedman's χ^2 test. This test shows that in both groups there was a high statistically significant difference between the values of systolic blood pressure (VIMA: $\chi^2 F = 66.8$, $p < 0.01$; TCI: $\chi^2 F = 83.5$, $p < 0.01$). This difference is a result of a systolic blood pressure reduction at t_0-t_1 and t_4-t_5 time intervals. Time series analysis provided the information that the t-statistic for the first-order autoregressive model using the .05 level of significance was statistically significant ($t = 54$, $df = 5$, $p < 0.05$).

Also, in each group separately, the difference between diastolic blood pressure at all time intervals was statistically tested using the Friedman's χ^2 test. This test shows that in both groups there is a high statistically significant difference between the values of diastolic blood pressure (VIMA: χ^2 F = 41.0, $p < 0.01$; TCI: χ^2 F = 49.5, $p < 0.01$). This difference is a result of the diastolic blood pressure reduction at t_0-t_1 and t_4-t_5 time intervals. This result was further confirmed with the results of the time series analysis as the t-statistic for the first-order autoregressive model using the .05 level of significance was statistically significant ($t = 38$, $df = 5$, $p < 0.05$).

The same type of statistical testing was done for mean arterial pressure in both groups separately. The results show that in both groups there was a high statistically significant difference between the values of mean arterial pressure (VIMA: χ^2 F = 46.7, $p < 0.01$; TCI: χ^2 F = 52.5, $p < 0.01$). This difference is a result of the reduced mean arterial pressure at t_0 - t_1 and t_4 - t_5 time intervals. Again, further confirmation was ob-

Table 3. *Patient distribution by cardiovascular instability grades considering systolic, diastolic and mean arterial pressure*

Time interval and grade of cardiovascular instability	Systolic pressure		p	Diastolic pressure		p	Mean arterial pressure		p
	VIMA	TCI		VIMA	TCI		VIMA	TCI	
	(n)			(n)			(n)		
t_1									
I grade	45	30	< 0,01	45	21	< 0,01	45	30	< 0,01
II grade	0	14		0	23		0	11	
III grade	0	1		0	1		0	4	
t_2									
I grade	45	45		45	30	<0,01	45	39	< 0,05
II grade	0	0		0	15		0	6	
III grade	0	0		0	0		0	0	
t_3									
I grade	45	43		45	35	< 0,01	45	40	< 0,05
II grade	0	2		0	10		0	5	
III grade	0	0		0	0		0	0	
t_4									
I grade	45	41		45	34	< 0,01	45	40	< 0,05
II grade	0	4		0	11		0	5	
III grade	0	0		0	0		0	0	
t_5									
I grade	45	33	< 0,01	45	25	< 0,01	45	36	< 0,01
II grade	0	12		0	20		0	8	
III grade	0	0		0	0		0	1	

VIMA-Volatile Induction and Maintenance Anaesthesia; TCI- Target Controlled Infusion

tained from the time series analysis and the information that the t-statistic for the first-order autoregressive model using the .05 level of significance was statistically significant ($t = 38$, $df = 5$, $p < 0.05$).

Patient distribution by cardiovascular instability grades considering systolic, diastolic and mean arterial pressure in both groups at all time intervals is presented in Table 3.

The difference in cardiovascular instability grades considering systolic blood pressure between the groups was statistically highly significant at t_1 and t_5 time intervals. All the patients from the VIMA group had grade I of cardiovascular stability. In TCI group, a different number of patients (even more than 30%) belonged to grade II at t_1 and t_5 intervals. One patient in TCI group had grade III cardiovascular instability recorded at t_1 interval. In the rest time intervals, the difference was not statistically significant.

The difference in cardiovascular instability grades considering diastolic blood pressure between the groups was statistically highly significant at all recorded time intervals. All the patients from the VIMA group had grade I of cardiovascular stability. In TCI group, different number of patients (25 - 50%) belonged to grade II. One patient in TCI group had grade III cardiovascular instability recorded at t_1 interval.

Also, the difference in cardiovascular instability grades considering mean arterial pressure between the groups was statistically significant at all recorded time intervals. The statistical significance was high at t_1 and t_5 intervals. All the patients from the VIMA group had grade I of cardiovascular stability. In TCI group, different number of patients (25 - 30%) belonged to grade II. Five patients in TCI group had grade III cardiovascular instability (four of them at t_1 and one at t_5 interval).

DISCUSSION

Laparoscopic surgery is a widely used technique in most hospitals. It is usually more convenient for patients, in some studies proven to be safer in elderly patients (5, 6), but on the other hand it requires specific anesthesia management.

Specific positioning of a patient and iatrogenic pneumoperitoneum compromise cardiovascular and respiratory function, possibly causing many complications during anesthesia (3). The age limit for patients undergoing laparoscopic surgeries continues to rise adding to operative risk and complications in anesthesia management, since elderly people often have accompanying cardiovascular or respiratory diseases, such as arterial hypertension, ischemic heart disease, myocardiopathy, chronic obstructive pulmonary disease, and emphysema. The rising number of NYHA II patients undergoing laparoscopic surgeries has opened a whole new chapter of problems in anesthesia management of the patients with reduced functional capacities and reduced ability to compensate changes in their cardiovascular and respiratory systems that occur during laparoscopic procedures.

The creation of moderately elevated intraabdominal pressure (IAP) in healthy and/or young individuals has minimal effects on stroke volume and cardiac output. Putting patients in anti – Trendelenburg position leads to a significant reduction of these parameters. IAP greater than 10 mmHg has a potentially negative influence on the cardiovascular system. The reduction in preload and increase in afterload, as a result of increased IAP, have negative effects on patients with impaired heart function, anemia or hypovolemic status. A decrease in cardiac output, and increases in arterial pressure, systemic and pulmonary vascular resistance are often seen in these patients. A recent study showed that there is a decrease in hepatic and renal blood flow caused by positive pressure pneumoperitoneum in LC (7).

The patients with congestive heart failure are more likely to develop cardiovascular complications than those with ischemic heart disease during LC. Despite surgical stress, there is a significant reduction of cardiac output in these patients compared to preoperative values, but the increases in blood pressure and heart rate, which are potentially harmful in ischemic heart disease patients, are not as significant. Is laparoscopy more dangerous than laparotomy for these patients? This problem has not been extensively addressed yet and deserves a careful and serious approach. It is of great importance for these patients to weight postoperative benefits against intraoperative risks. Because of significant intraoperative risk, NYHA II classification of a patient was an absolute contraindication for laparascopic surgery twenty years ago, but later on it became a relative contraindication. The number of NYHA II patients undergoing LC continues to rise, but the agreement on which anesthesia technique provides the best conditions and hemodynamic stability has not been reached so far (1 – 4).

According to our results, the TCI anesthesia technique in NYHA II patients did not provide a satisfactory degree of hemodynamic stability. Considering its characteristics, the VIMA technique should theoretically provide the greatest degree of hemodynamic stability to NYHA II patients. The time intervals for recording vital signs were chosen based on the main pathophysiological changes that affect cardiovascular system's stability. At t_0, we registered the initial values of hemodynamic parameters and by comparing them to values in other time intervals we were able to determine a grade of hemodynamic instability. At t_1, we could observe potential negative effects of administered anesthetics and intubation on cardiovascular stability. At t_2, the skin incision was the first surgical stimulant that could affect hemodynamic stability. At t_3, the first negative impact of increased IAP was already evident. The hemodynamic deviations were usually present early during carbon dioxide insufflation since the greatest pathophisiologycal changes were happening at that time. At t_4, we measured hemodynamic parameters after prolonged increase of IAP, while t_5 time interval was important to observe whether CO_2 draining contributes to acute hypotension, bradycardia and hypoxemia.

Considering heart rate values in our study, we concluded that in both groups of patients the changes of these parameters were statistically highly significant. However, in VIMA group all the patients had grade I deviations, which means their heart rate did not change by more than 10% compared to the initial values. In TCI group, the patients belonged to grade II and grade III of hemodynamic instability.

VIMA, compared to TCI, provided better cardiovascular stability during the time intervals when there is a maximum negative impact of increased IAP and patient positioning.

Considering the differences in diastolic blood pressure values, there was a high statistically significant difference in t_1 and t_5 between the groups. The patients in VIMA group were hemodynamically stable during the whole intraoperative period, while in TCI group the cardiovascular instability of grade II and III was present at all time intervals. It favors the fact that anesthetics (sevoflurane) used in VIMA group had minimal negative cardiovascular effects compared to the intravenous agent (propofol) used in TCI group.

Comparing the mean arterial pressure values between the groups, the difference was statistically highly significant at all time intervals except at t_4 (the difference was not statistically significant).

Our study showed that all the patients in VIMA group had grade I of hemodynamic instability, which means that their cardiovascular parameters did not show more than 10% deviation compared to the initial values at all time intervals. The cardiovascular stability achieved by this anesthesia technique was satisfactory, as opposed to the TCI technique, that showed deviation in cardiovascular parameters greater than 10%, and under which the patients presented statistically significant instability at most time intervals.

In both groups we used TCI of remifentanil to achieve analgesia. Remifentanil effect site concentrations of 5 ng/ml for tracheal intubation and 2 ng/ml for skin incision are required to blunt sympathetic response when combined with TCI of propofol (8, 9). Watanabe et al. showed that high dose of remifentanil suppresses stress response from pneumoperitoneum during laparascopic colectomy (10). This blocking of sympathetic response by remifentanil combined with TCI of propofol, supports the results of greater hemodynamic instability in our TCI group. Propofol and remifentanil are commonly administered together in clinical anesthesia. Remifentanil reduces cardiac index, and in addition to that it increases the plasma concentration of propofol (11), which may contribute to a greater hemodynamic changes. One study shows that sedation with propofol for upper endoscopy procedure has a significant effect on cardiovascular stability in patients up to 70 years old. Low preoperative blood pressure (< = 125 mm Hg) was more often associated with hypotension (12).

Since hypotension, as a mark of cardiovascular instability, can adversely affect anesthesia maintenance, patients response to vasopressor medications is of great clinical importance. Even though the interaction of anesthetics and vasopressor drugs are not fully understood and researched, it is reported that using ephedrine is more effective in reversing propofol-related hypotension than that of a volatile agent like sevoflurane (13). In our study, we treated severe hypotension with boluses of phenylephrine equally in both groups, and did not notice any difference in effectiveness in one or another.

In their study, Atallah and Othman concluded that total intravenous anesthesia is a better technique than inhalation anesthesia for laparoscopic procedures (14). This fact does not support our results that show greater cardiovascular stability during VIMA technique.

Some studies show that there is no significant difference in cardiovascular stability between different anesthesia techniques (regardless whether propofol or inhalation agents are used) (15, 16).

Stosic et al. concluded in their study that VIMA technique with sevoflurane for LC provides faster and more qualitative recovery of patients (4). Some authors observed different anesthetic characteristics between propofol-remifentanil and sevoflurane-sufentanyl groups in laparascopic cholecystectomy, and concluded that both techniques had advantages and disadvantages and none of the techniques was superior. Considering the hemodinamics in this study, the observation was that a need for anthypertensive drug was greater in sevoflurane group (17). The reason for this may be in depressive effect of remifentanil-propofol combination on hemodinamics.

Other authors have come to similar results as those of the present study. In their studies, inhalation agents provided a better cardiovascular stability, compared to intravenous anesthesia with propofol (18 – 20).

In this study, we did not take into consideration the age of patients when assigning to groups, they were chosen and assigned randomly. We had all different age categories in both VIMA and TCI groups. Also, the surgical teams were different in different cases, so we tried to minimize the effect of this factor by choosing the measurement points at certain times that could not be affected by surgical skills.

CONCLUSION

Volatile induction and maintenance of anaesthesia with sevoflurane provides better hemodynamic stability than TCI for NYHA II patients with concomitant cardiovascular diseases who undergo LC.

Conflict of interest

None.

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Uticaj tehnika anestezije na kardiovaskularnu stabilnost pacijenata podvrgnutih laparoskopskoj holecistektomiji

Biljana Stošić[1,2], Marija Stošić[2], Jelena Živadinović[2], Ines Veselinović[2]

[1]*Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija*
[2]*Univerzitetski klinički centar Niš, Klinika za anesteziju i intenzivnu terapiju, Niš, Srbija*

SAŽETAK

Uvod i cilj. Cilj ove studije bio je da se uporedi efekat volatilnog uvoda i održavanja anestezije (VIMA) i ciljano kontrolisane infuzije intravenskim anestetkom (TCI) na kardiovaskularnu stabilnost kod pacijenata stepena II klasifikacije Njujorškog udruženja za srce (NIHA), koji su bili podvrgnuti laparoskopskoj holecistektomiji.
Pacijenti i metode. U ovoj studiji, 90 pacijenata je nasumično podeljeno u dve grupe u zavisnosti od toga da li su primali VIMA ili TCI. Broj otkucaja srca, sistolni, dijastolni i srednji arterijski pritisak, praćeni su kontinuirano i beleženi u pet vremenskih intervala.
Rezultati. Statistička analiza je pokazala da VIMA sa sevofluranom obezbeđuje bolju kardiocirkulatornu stabilnost (manje od 10% odstupanja od bazalnih vrednosti za svaki mereni parametar) od TCI grupe ($p < 0,01$).
Zaključak. Inhalaciona indukcija i održavanje anestezije sevofluranom obezbeđuje bolju hemodinamsku stabilnost za pacijente NIHA II klasifikacije sa pratećim kardiovaskularnim oboljenjima u poređenju sa TCI.

Ključne reči: **anestezija, holecistektomija, laparoskopija, kardiovaskularne bolesti**