

## Original Research Article

# Incidence and predictors of intraoperative hypertension during laparoscopic cholecystectomy for acute cholecystitis: retrospective cohort study

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## ABSTRACT

**Background:** The authors noticed during their practice that most of patients scheduled for laparoscopic cholecystectomy (LC) owing to acute cholecystitis are associated with increased intraoperative blood pressure especially during manipulation on the gallbladder which may increase the risk of bleeding. A retrospective analysis was carried out to estimate the risk and the potential risk factors of intraoperative hypertension.

**Methods:** A retrospective analysis of the data of patients who underwent LC for acute cholecystitis in our university hospitals from June 2022 to December 2023. The patients' documents and records were revised with exclusion of patients with incomplete data. The data of age, gender, ASA class, BMI, co-morbidities, preoperative CRP, preoperative TLC, preoperative temperature, and preoperative bilirubin were collected and reported. The data of duration of surgery, time for devascularization of the gallbladder, and the changes in the blood pressure were also recorded.

**Results:** Seventy-three patients underwent LC for acute cholecystitis during the study period, 44 (60.27%) of them developed intraoperative hypertension with statistically significant difference between the patients who did not develop intraoperative hypertension in BMI ( $p=0.0003$ ), preoperative CRP ( $p=0.008$ ), preoperative TLC ( $p=0.001$ ), duration of surgery ( $p=0.034$ ), and time to devascularization of the gallbladder ( $p=0.027$ ). The regression analysis revealed an increased risk of intraoperative hypertension with decreased age ( $p=0.0191$ ), increased BMI ( $p=0.034$ ), and increased preoperative TLC ( $p=0.038$ ).

**Conclusions:** The risk of intraoperative hypertension during LC for acute cholecystitis increased with decreased age, increased BMI, and increased preoperative TLC.

**Keywords:** Age, BMI, Cholecystectomy, CRP, Hypertension

## INTRODUCTION

Acute cholecystitis is a common and severe critical illness that is defined as acute inflammation in the gallbladder with or without gallstones. It is commonly caused by cystic duct obstruction.<sup>1</sup> It is typically presented by acute pain in the right upper quadrant, fever, and eating problems. It can be suspected by presence of

right upper quadrant tenderness and the diagnosis is confirmed by ultrasonography or CT scan.<sup>2</sup> It may be hemorrhagic, gangrenous, emphysematous, or ruptured gall bladder.<sup>3</sup>

Early LC in acute cholecystitis in the first 3 days is preferred over the late intervention as it improves the patient outcome, decreases the postoperative

complications, and shortens the hospital stay. Moreover, early intervention improves the mortality rate in patients over 65 years.<sup>1</sup>

The prognosis of acute cholecystitis is relatively good, especially in adequate early management. However, it may be complicated with secondary bacterial infection. Septicemia is a common complication of acute cholecystitis especially in elderly and immunocompromised patients. Sepsis may result from cholecystitis itself, from cholangitis, or from peritonitis in ruptured and gangrenous gallbladders.<sup>3,4</sup> The risk of morbidity and mortality increases with increasing certain variables as age more than 65, male gender, leukocytosis, neutrophilia, and elevated liver enzymes.<sup>5</sup>

Patients with septic or potentially septic conditions are at high risk of developing severe hypotension requiring vasopressor support after induction of anesthesia due to severe vasodilation resulting from release of inflammatory mediators.<sup>6</sup> The risk of hypotension increases with increased age, gangrenous or perforated gallbladder, and presence of preoperative uncontrolled morbidities as diabetes mellitus.<sup>7</sup> In addition, hemoperitoneum can aggravate or induce hypotension from decrease the venous return.<sup>8</sup>

On the other hand, the authors noticed in their center that most patients undergoing LC for acute cholecystitis are associated with significant increase in the blood pressure during manipulation on the inflamed gallbladder even if they were not known hypertensive patients. So, this retrospective analysis of the previously managed cases in the last period was carried out to estimate the incidence of intraoperative hypertension and the potential risk factors.

## METHODS

This retrospective cohort study was carried to evaluate the incidence of increase in mean arterial pressure and manipulation on acute inflamed gallbladder during LC in adult patients diagnosed with acute cholecystitis and undergone LC under general anesthesia in Tanta university hospitals from June 2022 to December 2023. The study is approved by institutional ethical committee.

The documents of patients presented with acute cholecystitis from June 2022 to December 2023 were reviewed by two physicians who were blinded to the patients. Discordant results were reviewed until reaching decision. Then, the medical records of the patients were reviewed by trained physician chart reviewers.

The patient's data was collected and reviewed. It included the age, gender, the presence of co-morbidities, preoperative body temperature, and preoperative blood pressure. Moreover, the laboratory investigations of the patients were reviewed to find the preoperative total leucocytic count and the preoperative CRP. Furthermore,

the operative data was reviewed to find out the operative time, time from induction of anesthesia to vascular control of cystic artery, the blood pressure before devascularization, and the blood pressure after devascularization. Patients with absent or incomplete documentation were rolled out from the analysis.

Acute cholecystitis was diagnosed by moderate to severe abdominal pain starting in the right upper quadrant of the abdomen and the diagnosis was confirmed by ultrasonography. CT abdomen with intravenous contrast was requested only in the suspicion of complications or unclassified diagnosis. Preoperative laboratory investigations included complete blood picture, liver function tests, renal function tests, and coagulation studies. Cardiological consultation was requested only in cardiac patients, patients older than 65 years, or patients with limited functional capacity.

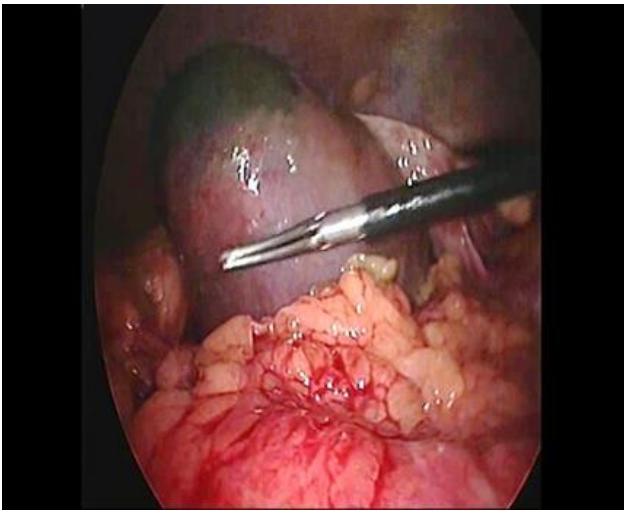
## Anesthesia technique

After adequate preoperative assessment and obtaining informed written consent, the patient is admitted to the operating room with connection to a monitor device consisting of 5-leads ECG, pulse oximeter, and non-invasive blood pressure. Moreover, intravenous access is established with starting preload in the form of lactated ringer solution. Anesthesia is induced by fentanyl 1 ug/kg, propofol (1-2 mg/kg), and atracurium (0.5 mg/kg) with endotracheal intubation by suitable sized tube with connection of the patient to mechanical ventilator whose parameters is adjusted to maintain end-tidal CO<sub>2</sub> 32- 36 mmHg. The anesthesia was maintained by sevoflurane 1 MAC in a mixture of oxygen and air 1:1. The patient is connected to Bispectral index monitor (BIS) to assess the depth of anesthesia with its readings maintained 40-60. The sevoflurane is switched off at the end of the surgery with reversal of muscle relaxation by neostigmine plus atropine with fully awake extubation. The patient is discharged from the recovery room when Aldrete's score reaches 10 or more.

Intraoperative hypotension (defined as mean arterial pressure less than 65 mm Hg) is managed by incremental doses of ephedrine 6 mg and by intravenous fluid administration until reaching mean arterial pressure above 65 mmHg. Intraoperative bradycardia (defined as decrease in the heart rate below 50 beats/min) is managed by atropine 0.3 mg intravenous and revision of the intra-abdominal pressure. Hypertension (increase in the mean arterial pressure by more than 30% of preop value) is managed by increase concentration of sevoflurane, incremental doses of fentanyl 0.5 ug/kg intravenous, and ensure reading of BIS 40-60. Re-assessment of blood pressure is done after that, persistent hypertension is managed by lidocaine 1.5 mg/kg slow intravenously/metoprolol 1-5 mg intravenous infusion over 20 minutes. Intraop tachycardia is managed by an additional dose of fentanyl 0.5 ug/kg intravenous bolus and ensuring the depth of anesthesia.

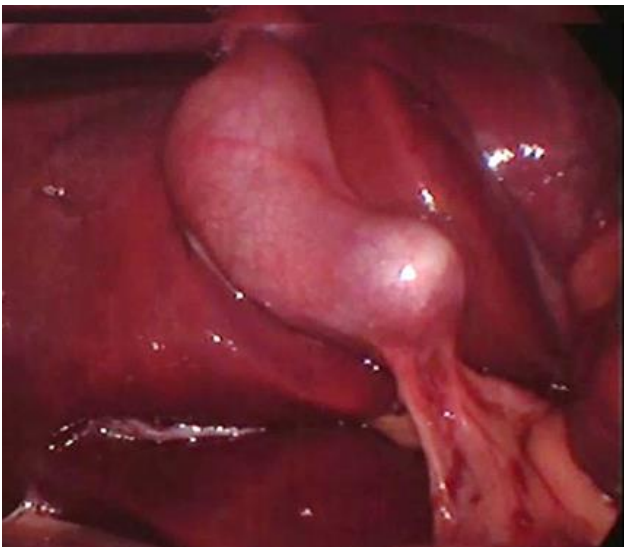
### Technique of LC

All patients were put in supine position and after sterilization of the abdomen, initial access was gained by direct safety trocar placement without prior pneumoperitoneum then carbon dioxide insufflation with pressure of 12-14 mmHg. Table tilted in a reverse Trendelenburg position and rotated to patient's left side, then remaining trocars were then introduced under vision. Any adhesions between gall bladder and duodenum, colon or omentum were taken down using Maryland's dissector with less cautery, (Figure 1). When gallbladder was tense, decompression was done before attempting to the grasp it.



**Figure 1: Taking down adhesions in gangrenous acute cholecystitis.**

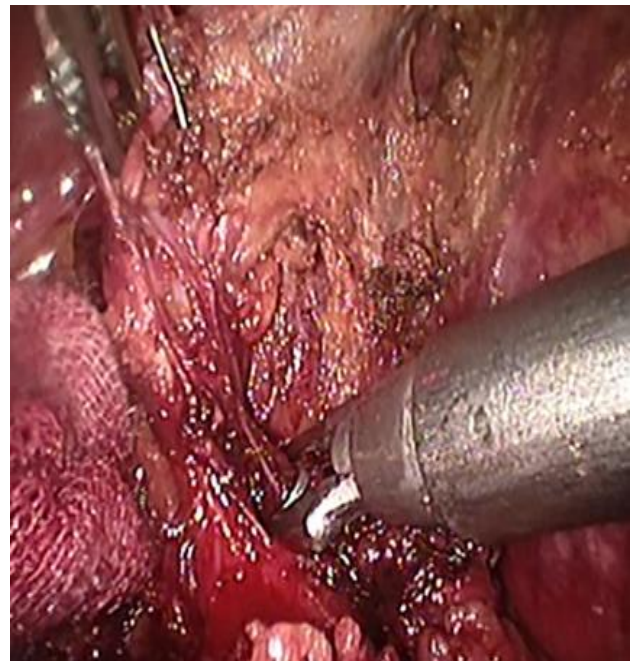
Two graspers to fundus and Hartmann's pouch used as traction and counter traction for proper dissection. If a stone was impacted in Hartmann's pouch, (Figure 2), it was dislodged into the body of the gallbladder.



**Figure 2: Impacted stone in Hartmann's pouch.**

We used the suction irrigation cannula with direct blunt dissection with pressured saline irrigation for clearance the field and usually with a repetitive inserted gauze for the blunt dissection to expose the cholecystohepatic triangle.

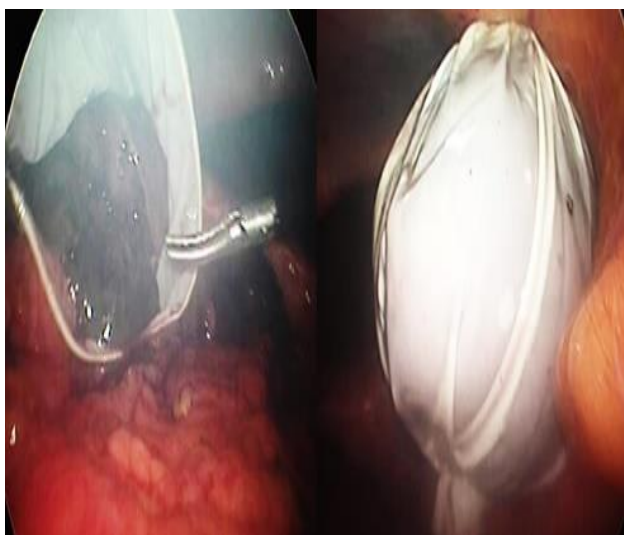
The dissection was continued close to the wall of the gallbladder with careful attention to hemostasis. Clearance of the surrounding tissues, such as the fat and fibrous tissue with the oedema present with the acute inflammation leaving the cystic duct and artery ready for clipping, after achieving critical view of safety, the cystic artery was clipped, (Figure 3), followed by duct control. The period taken for vascular control recorded with the blood pressure measurements on monitor was also recorded.



**Figure 3: Applying clip to cystic artery, with seen gauze assisted for dissection and hemostasis.**

The continuous irrigation and suction were very helpful for clearance the camera vision and eyes of operator for proper control. In some cases, with dilated or inflamed cystic duct we used a surgical polyglactin 910 (Vicryl<sup>®</sup>) 2/0 ligature instead for clips. The remainder of the operation consists of dissection of the gallbladder from its bed as we used a hook cautery "hot" or the blunt stone forceps "cold" without cautery, as forceps used by pushing the gallbladder away from liver as the edema of the tissues caused by acute inflammation facilitate way of dissection with traction and counter traction until complete separation from liver bed obtained.

This was always followed by irrigation of saline and suction with clearance of operative field after extraction of gall bladder inside glove irrigated by the saline used as specimen bag from the epigastric port, (Figure 4), with or without insertion of a drain in Morrison s pouch.



**Figure 4: Glove irrigated by saline used as a specimen (gall bladder) bag.**

### Statistics

The recorded data were analyzed statistically using the SPSS software program (SPSS Inc., Chicago, IL, USA). Parametric data were expressed as mean and standard deviation after being analyzed with unpaired t test, while categorical data were expressed as numbers and percentages after an analysis with a chi-square test. The regression analysis was carried out by ANOVA. The statistical significance was considered when the p value < 0.05.

### RESULTS

Ninety-four patients were found to undergo LC for acute cholecystitis in Tanta University Hospitals in the period from June 2022 to December 2023, 21 of them had incomplete data, so, they were excluded from analysis and the other 73 patients had their data available. 44 patients were found to develop intraoperative hypertension during manipulation on the gallbladder (group A), while the other 29 patients did not develop intraoperative hypertension (group B), so the incidence of intraoperative hypertension was 60.27%.

Comparison between the group of patients who developed intraoperative hypertension (group A) and the group of patients who did not develop it (group B) revealed statistically insignificant difference between the two groups as regards age, gender, ASA class, and the comorbidities of diabetes mellitus, hypertension, and cardiac disorders (p=0.271, 0.851, 0.764, 0.839, 0.980, and 0.956 respectively). On the other hand, the body mass index was significantly higher in group A than group B (p=0.0003) (Table 1).

According to clinical and laboratory data preoperatively, we found the level of C-reactive protein (CRP) was

significantly higher in group A ( $125.05 \pm 64.08$  mg/dl) than group B ( $86.28 \pm 50.29$  mg/dl) (p=0.008). Also, the total leucocytic count was higher in group A ( $17.32 \pm 2.48 \times 10^3/\text{mm}^3$ ) than group B ( $15.21 \pm 2.77 \times 10^3/\text{mm}^3$ ) (p=0.001). However, there was statistically insignificant difference between the two groups in the preoperative total bilirubin level and the preoperative temperature level (p=0.624 and 0.169 respectively) (Table 2).

The duration of surgery was significantly prolonged in group A to  $72.84 \pm 36.72$  min than in group B  $56.55 \pm 24.65$  min (p=0.034). In addition, time from start of surgery to devascularization of gallbladder (controlling cystic artery) was significantly higher (p=0.027) in group A  $37.22 \pm 20.97$  min than group B  $27.07 \pm 15.03$  min (Table 3).

The changes in the mean arterial pressure were statistically insignificant between the two groups regarding the preoperative assessment and assessment after de-vascularization of gallbladder (p=0.147 and 0.076 respectively), however, there was statistically significant increase in the MAP during pre-devascularization in group A in comparison two group B (p<0.0001). Moreover, there was statistically significant increase in MAP during pre-devascularization period in comparison to preoperative values in group A (p 0.0001) with insignificant difference between preoperative values and values after devascularization (p=0.09). Furthermore, there was statistically significant decrease in MAP at pre-devascularization period in comparison to preoperative values in group B (p<0.0001) with insignificant difference between preoperative values and values after devascularization (p=0.189) (Table 4).

The regression analysis of the data revealed that the risk if intraoperative hypertension significantly increased with decreased age (coefficient; -0.013, odds ratio; 0.976, and p=0.0191), significantly increased with increased BMI (coefficient; 0.013, odds ratio; 1.120, and p=0.034), and significantly increased with increased preoperative total leucocytic count (coefficient; 0.051, odds ratio; 1.353, and p=0.038). On the other hand, there was a statistically insignificant inverse relationship between intraoperative hypertension and duration of surgery (coefficient; -.0007, odds ratio; 1.018, and p=0.771) and number of diabetic patients (coefficient; -0.0336, Odds ratio; 1.243, and p=0.757).

Furthermore, there was statistically insignificant direct relationship between intraoperative hypertension and male gender (coefficient; 0.0039, odds ratio; 1.228, and p=0.969), the number of hypertensive patients (coefficient; 0.062, odds ratio; 2.228, and p=0.682), the number of cardiac patients (coefficient; 0.264, odds ratio; 1.368, and p=0.145), the preoperative CRP (coefficient; 0.0012, Odds ratio; 1.011, and p=0.203), and the time to devascularization of gallbladder (coefficient; 0.0045, odds ratio=1.033, and p=0.300) (Table 5).

**Table 1: Basic demographic data of the studied patients.**

Variables	Group A, (n=44) (%)	Group, B (n=29) (%)	P value
<b>Age (in years)</b>	45.27±10.04	48.24±12.79	0.271
<b>Gender</b>	Male	19 (43.18)	0.851
	Female	25 (56.82)	
<b>BMI (kg/m<sup>2</sup>)</b>	37.43±9.67	29.93± 5.46	0.0003*
<b>ASA class</b>	ASA I	3 (6.82)	0.764
	ASA II	20 (45.45)	
	ASA III	21 (47.73)	
<b>Co-morbidity</b>	DM	19 (43.18)	0.839
	Hypertension	9 (20.46)	0.980
	Cardiac	6 (13.64)	0.956

Data were presented as mean ± SD or number and percent. \*Denotes significant changes. Group A, patients who developed intraoperative hypertension, group B, patients who did not developed intraoperative hypertension. BMI, Body mass index. ASA=American society of anesthesiologist physical status.

**Table 2: Preoperative CRP, total leucocytic count, total bilirubin, and body temperature in the studied patients.**

Variables	Group A, (n=44)	Group B, (n=29)	P value
<b>CRP (mg/dl)</b>	125.05±64.08	86.28±50.29	0.008*
<b>TLC (10<sup>3</sup>/mm<sup>3</sup>)</b>	17.32±2.48	15.21±2.77	0.001*
<b>Total bilirubin (mg/dl)</b>	2.58±1.11	2.70±1.00	0.624
<b>Body temperature (°C)</b>	38.27±0.39	38.12±0.49	0.169

Data were presented as mean ± SD. \*Denotes significant changes. Group A, patients who developed intraoperative hypertension, group B, patients who did not developed intraoperative hypertension. CRP=C-reactive protein, TLC=total leucocytic count.

**Table 3: Duration of surgery and time to devascularization of gallbladder.**

Variables (min)	Group A, (n=44)	Group B, (n=29)	P value
<b>Duration of surgery</b>	72.84±36.72	56.55±24.65	0.034*
<b>Time to devascularization of gallbladder</b>	37.22±20.97	27.07±15.03	0.027*

Data were presented as mean ± SD. \*Denotes significant changes. Group A, patients who developed intraoperative hypertension, group B, patients who did not developed intraoperative hypertension.

**Table 4: Changes in the mean arterial pressure (MAP) in the studied patients.**

Variables	Group A, (n=44)	Group B, (n=29)	P value
<b>Preoperative MAP (mmHg)</b>	95.25±9.90	98.65±9.42	0.147
<b>Pre-devascularization MAP (mmHg)</b>	130.98±13.10 <sup>#</sup>	86.00±7.39 <sup>#</sup>	<0.0001*
<b>Post-devascularization MAP (mmHg)</b>	92.16±6.43	95.48±8.75	0.076

Data were presented as mean ± SD. \*Denotes significant changes between two groups, # denotes significant change as compared to baseline values. Group A-patients who developed intraop hypertension, group B-patients who did not developed intraop hypertension.

**Table 5: Regression analysis of the risk factors in the studied patients.**

Variables	Coefficients	Odds ratio	Standard error	T stat	P value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
<b>Intercept</b>	-0.366	1.061	0.4069	-0.899	0.372	-1.179	0.446	-1.179	0.447
<b>Age (in years)</b>	-0.013	0.976	0.0056	-2.405	0.019*	-0.024	-0.002	-0.024	-0.002
<b>Gender</b>	0.004	1.228	0.1041	0.038	0.969	-0.204	0.212	-0.204	0.212
<b>DM</b>	-0.034	1.243	0.108	-0.310	0.757	-0.250	0.182	-0.250	0.231
<b>HTN</b>	0.062	2.228	0.1520	0.410	0.682	-0.241	0.366	-0.241	0.366
<b>Cardiac</b>	0.264	1.368	0.1793	1.476	0.145	-0.093	0.623	-0.093	0.623
<b>BMI</b>	0.013	1.120	0.0062	2.161	0.034*	0.001	0.026	0.001	0.026
<b>TLC</b>	0.051	1.353	0.0240	2.122	0.038*	0.003	0.099	0.003	0.099
<b>CRP</b>	0.001	1.011	0.0009	1.285	0.203	-0.001	0.003	-0.001	0.003
<b>Time of surgery</b>	-0.0007	1.018	0.0026	-0.291	0.771	-0.006	0.005	-0.006	0.005
<b>Time to revascularize</b>	0.005	1.033	0.0043	1.044	0.300	-0.004	0.013	-0.004	0.013

\*Denotes significant changes

## **DISCUSSION**

LC has become the standard approach for gallbladder removal, offering advantages such as reduced postoperative pain and shorter hospital stays. However, intraoperative hypertension during LC can pose challenges and may have implications for patient safety. While the exact causes of intraoperative hypertension can vary, factors such as pneumoperitoneum, patient positioning, and surgical manipulation can contribute to hemodynamic changes. Several previous studies have touched on this issue, our research aims to provide a comprehensive analysis of the factors contributing to intraoperative hypertension and its implications.

This retrospective study demonstrated that patients with acute cholecystitis undergoing LC are at high risk of developing intraoperative hypertension during manipulation on gallbladder and before devascularization of it as 44 out of 73 patients developed intraoperative hypertension (60.27%). Similarly, Desborough et al reported that the manipulation of tissues during surgery can trigger the sympathetic nervous system, leading to an increase in catecholamine release. Catecholamines, such as adrenaline and noradrenaline, can raise heart rate and systemic vascular resistance, impacting blood pressure.<sup>9</sup> Moreover, Bisgaard et al suggested in his study that surgical manipulation and tissue injury can induce a pain response, contributing to increased sympathetic activity. Pain-induced stress responses may lead to higher levels of circulating catecholamines, affecting blood pressure.<sup>10</sup>

Nguyen et al hypothesized that one of the primary factors affecting blood pressure during LC is the creation of pneumoperitoneum, which involves insufflating the abdominal cavity with carbon dioxide gas. Increased intra-abdominal pressure can lead to elevated systemic vascular resistance and elevated blood pressure.<sup>11</sup>

Both Al Knawy et al and Gan et al supported in their analysis that the positioning of the patient during laparoscopic surgery can affect venous return and cardiac output, potentially impacting blood pressure. The Trendelenburg position may contribute to increased venous return and elevated blood pressure.<sup>12,13</sup>

In the current study, the risk of intraoperative hypertension increased with increased body mass index, the relationship between increased body mass index (BMI) and intraoperative hypertension is a complex interplay involving multiple physiological factors. Several studies have explored this association, shedding light on the mechanisms by which elevated BMI may contribute to changes in intraoperative blood pressure. Grassi et al attributed the intraoperative hypertension with elevated BMI to the association with increased sympathetic nervous system activity, leading to heightened baseline levels of circulating catecholamines. This heightened sympathetic tone may predispose individuals with higher BMI to an exaggerated response

to surgical stress.<sup>14</sup> On the other hand, Muniyappa et al reported that obesity is linked to insulin resistance and endothelial dysfunction which may impair vascular function and contribute to an imbalance in vasodilatory and vasoconstrictor factors, potentially impacting blood pressure regulation.<sup>15</sup> Furthermore, Cascorbi et al stated that the distribution and metabolism of anesthetic agents and vasoactive drugs may be altered in individuals with increased adiposity, confirming on the importance of understanding the pharmacokinetic implications of obesity and titrating anesthetic and antihypertensive medications effectively during surgery.<sup>16</sup>

Increased preoperative CRP and TLC were among the risk factors in our study, there isn't an extensive body of literature specifically examining the relationship between increased preoperative CRP levels, TLC, and intraoperative hypertension in LC, but we can discuss the potential mechanisms and implications based on broader knowledge of inflammation, CRP, and perioperative cardiovascular changes. The existing knowledge suggests potential links between inflammation, endothelial dysfunction, and perioperative stress responses. Understanding these relationships is essential for optimizing patient care and tailoring perioperative management strategies for individuals with elevated CRP and TLC levels.<sup>9,17,18</sup>

Additionally, prolonged surgery and time to gallbladder devascularization in our patients increased the risk for intraoperative elevated blood pressure. It is reasonable to consider that prolonged surgical manipulation, exposure to pneumoperitoneum, and patient-specific factors (e.g. compromised cardiovascular system) could contribute to cardiovascular changes during LC.<sup>9,11,19</sup> Surgeons and anesthesiologists should be attentive to these factors and work together to manage perioperative conditions to minimize the risk of intraoperative hypertension.

Management of intraoperative hypertension in our case series was by increase sevoflurane concentration, and intravenous fentanyl increments, and for persistent hypertension, lidocaine or metoprolol intravenous infusion was used. Paul et al. suggested the use of magnesium. Sulfate attenuates the elevation of MAP and heart rate during pneumoperitoneum and thereby provides perioperative hemodynamic stability during laparoscopic surgery.<sup>20</sup>

This study is limited by being retrospective study and by limitation in the available data to be analyzed as risk factors. Moreover, the missed data of many patients limited the studied sample size. Furthermore, the lack of assessment of risk of bleeding added to the study limitations.

## **CONCLUSION**

It can be concluded that patients with acute cholecystitis undergoing LC are at high risk to develop intraoperative

hypertension (60.27%) and the risk is increased with decreased age, increased body mass index, and increased preoperative TLC. Moreover, the risk of intraoperative hypertension may be increased with male gender, increased preoperative CRP, and prolongation of time of surgery.

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