

## ORIGINAL RESEARCH

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# Effect of alveolar recruitment maneuver on ischemia-modified albumin and oxidative stress in laparoscopic cholecystectomy

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### Abstract

The effect of intraoperative recruitment maneuver on ischemia-modified albumin (IMA) and oxidative stress in performed laparoscopic cholecystectomy with intra-abdominal 12 mmHg pressure was investigated. Fifty patients undergoing laparoscopic cholecystectomy were included in the study by separating the two groups. Basal ventilator settings in both groups were set as tidal volume: 6-8 ml / kg, respiratory rate: 12 breaths / min, I: E = 1: 2, flow: 4 l / min. In group R, after intubation, 5 cm H<sub>2</sub>O PEEP was adjusted in addition to basal ventilator settings. Five minutes after CO<sub>2</sub> insufflation and exsufflation, PEEP was step by step raised to 10-15-20 cm H<sub>2</sub>O, and patients were ventilated for 10 breaths. Venous blood samples were taken from the patients for three times in perioperative periods to measure IMA and oxidative stress. There was no difference between the groups in terms of demographic data, surgery and insufflation times. Significant differences in IMA, TOS, TAS and OSI levels within the group were observed but no difference was between groups. The recruitment maneuver that we used in laparoscopic cholecystectomies was found to have no effect reducing tissue ischemia and oxidative stress response in the intraoperative period.

**Keywords:** Cholecystectomy, laparoscopic, ischemia-reperfusion injury, ischemia-modified albumin, oxidative stress, positive-pressure respiration

### Introduction

In laparoscopic cholecystectomy operations, the pneumoperitoneum is achieved by applying intraperitoneal carbon dioxide (CO<sub>2</sub>) via insufflation. Increased intraperitoneal pressure due to pneumoperitoneum leads to pathophysiological changes in pulmonary and hemodynamic functions [1]. These changes cause ischemia in the splanchnic area and also cause reperfusion injury after deflation. The deterioration of gas exchange between the tissues and increasing CO<sub>2</sub> absorption due to increased intra-abdominal pressure cause hypercarbia and acidosis [2,3]. The resulting ischemia, hypercarbia and acidosis cause changes in serum oxidative stress markers [4].

In the study, the effect of intraoperative recruitment maneuver application on ischemia modified albumin, total oxidant status,

and complete antioxidant status is evaluated in laparoscopic cholecystectomies performed with an intra-abdominal pressure of 12 mmHg.

### Material and Methods

This study was performed with the permission of the Necmettin Erbakan University Meram Faculty of Medicine Ethics Committee (protocol no. 2014/47). ASA I-II 50 patients aged between 18 and 60 years who will be applied laparoscopic cholecystectomy with written and oral consent are enrolled in the study. Chronic hypertension, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease, ischemic heart disease, decompensated heart failure, burger disease, chronic renal failure, chronic liver disease, neoplastic disease, hyperlipidemia, hypertriglyceridemia, statin use, hypoalbuminemia, smoking history and those who are allergic to the drugs used are removed from the study.

After taking the patients on the operation table, the vascular access

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was established using 20G intravenous cannula, and the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), peripheral oxygen saturation (SpO<sub>2</sub>) were monetarized (Datex-Ohmeda Cardiacap/5®).

Anesthesia induction is applied with intravenous lidocaine, 2 mg/kg propofol and 0.6 mg/kg rocuronium in both groups after preoxygenation. After the tracheal intubation, the basal ventilation parameters of patients were set as tidal volume of 6-8ml/kg, respiration rate of 12 min<sup>-1</sup>, I:E=1:2, and flow rate of 4 l/min. Then, the patients were connected to anesthesia device (Datex-Ohmeda). Anesthesia was maintained using 0.05-0.2mcg/kg/min remifentanyl, 50% O<sub>2</sub>+air, and 1-2% sevoflurane. The muscle relaxant effect was antagonized with 0.04 mg/kg neostigmine and 0.02 mg/kg atropine at the end of the surgical procedure. The patients, who would be undergone laparoscopic cholecystectomy under 12 cmH<sub>2</sub>O intra-abdominal pressure, were divided into control group (Group K) and study group (Group R) by using closed envelopes containing numbers. While the patients in the Group K undergo anesthetic follow-up with baseline ventilator settings, the patients in the Group R were applied alveolar recruitment maneuver in addition to basal ventilator settings. In addition to the basal ventilator settings, PEEP was set to 5 cmH<sub>2</sub>O after the intubation for the patients in Group R, and the PEEP value was gradually increased to 10-15-20 cmH<sub>2</sub>O twice after 5 minutes from insufflation and exsufflation. In each of PEEP increase, the plateau and peak pressure limits were set below 30-50 cmH<sub>2</sub>O limits, and the recruitment maneuver was performed by implementing 10 times ventilation to the patient. Intraoperative follow-up of all patients was performed with end-tidal carbon dioxide (ETCO<sub>2</sub>) values of 35-45 mmHg and SpO<sub>2</sub>: 95-100%. Values of HR, SBP, DBP, MBP, SpO<sub>2</sub>, and ETCO<sub>2</sub> were recorded before induction and every 5 minutes after induction. When the mean blood pressure is reduced by 25% compared to the basal value, 0.5 mg ephedrine was given; 100 mg of nitroglycerin was given in case of an increase. When the heart rate decreased below 50 beat/min, 0.02 mg/kg atropine was pushed intravenously. 5ml venous blood samples were taken from the patients into the biochemistry gel tube for ischemia-modified albumin (IMA), total antioxidant status (TAS), and total oxidant status (TOS) analyses at preoperative (T0), 20 minutes after insufflation (T1), and postoperative 6th hour (T2). The venous blood sample was allowed to clot for 30 minutes at room temperature and then centrifuged at 3000 G for 20 minutes and the serums were separated. Separated samples were stored at -80 C until the working day. Samples are centrifuged again before

working after dissolution at working day.

IMA level measurement was measured with Human Ischemia Modified Albumin (IMA) ELISA kit (Shanghai Sunred Biological Technology Co., Ltd, Shanghai, China). The results were expressed in U/ml.

TOS and TAS levels were measures using Total Oxidant Status (TOS) and Total Antioxidant Status (TAS) commercial kits (Rel Assay Diagnostics, Megatip Sanayi Ticaret Ltd. Şti., Gaziantep, Turkey) and Prestige 24i clinic chemical auto-analyzer (Tokyo Boeki Ltd., No.13.8 2-Chome Hachobori Chuo-ku, Tokyo, JAPAN). The results were expressed in Trox equivalent millimole per liter for TAS (mmol Trolox equiv/L), and H<sub>2</sub>O<sub>2</sub> equivalent micromolar per liter for TOS (µmol H<sub>2</sub>O<sub>2</sub> equiv/L).

The TOS values were proportioned to TAS values as percentage, and the oxidative stress index (OSI) that is accepted as the indicator of oxidative stress was calculated. (*While calculating the oxidative stress, TAS concentrations were converted to µmolTroloxEquiv./L and OSI = (TOS = µmol/H<sub>2</sub>O<sub>2</sub> Equiv/L) / (TAS = mmolTroloxEquiv./L x 1000) x 100 formula was used in calculation.*)

Demographic data, duration of operation and duration of insufflation were compared between groups using Student's t-test and Chi-square test. ANOVA was used for repeated measurements and Bonferroni correction paired t-test was used as the second test of this test in-group comparisons. The difference between the groups was made by covariance analysis (ANCOVA).

## Results

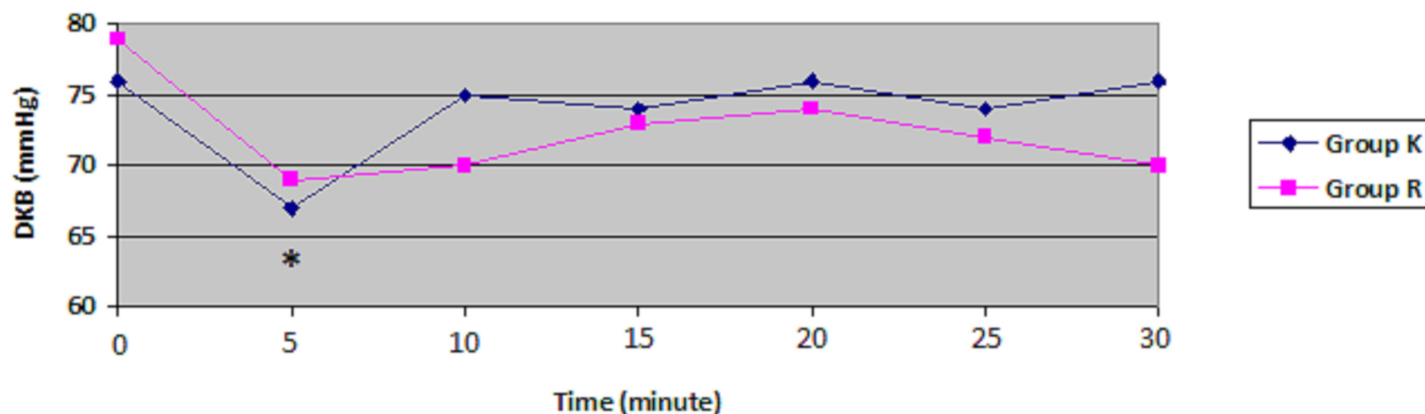
There were no differences between the groups in terms of demographical data, and surgery and insufflation durations (Table 1). The systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate and peripheral oxygen saturation values were not statistically significant difference between the groups. But there were statistically significant differences in intragroup comparison in terms of diastolic blood pressure (p=0.022) (Figure 1) and mean blood pressure (p=0.027) at 5th minute (Figure 2).

There was statistically significant difference in intragroup comparison of ischemia-modified albumin (p<0.001), total oxidant status (p<0.001), total antioxidant status (p<0.001) and oxidative stress index (p<0.001). But there was no difference between the groups (Table 2) (Figure 3).

**Table 1.** Demographic data of patients

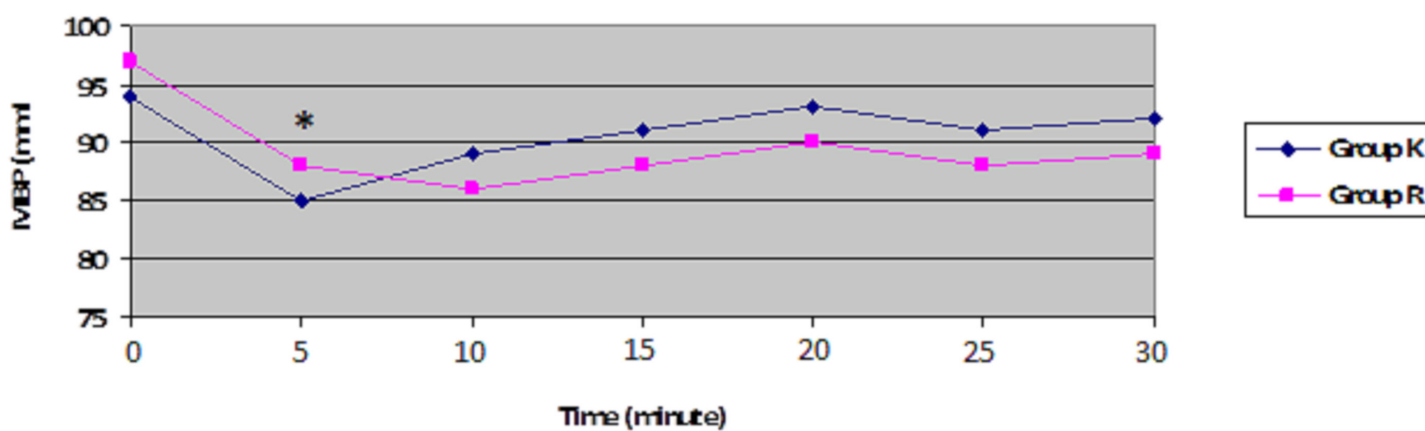
|                         | Group K<br>(n=25) | Group R<br>(n=25) | p      |
|-------------------------|-------------------|-------------------|--------|
| Age (years)             | 40.96±13.145      | 35.04±10.338      | 0.083* |
| Sex (Male/Female)       | 5/20              | 6/19              | 0.733‡ |
| Weight (kg)             | 72.36±14.728      | 73.28±13.085      | 0.816* |
| Height (cm)             | 165.68±6.388      | 164.44±8.559      | 0.564* |
| Operation time (min)    | 49.24±17.826      | 47.56±12.162      | 0.699* |
| Insufflation time (min) | 35.76±15.262      | 32.76±12.056      | 0.444* |

\* Student's t tests, ‡ Pearson chi-square test



**Figure 1.** Diastolic Blood Pressure

\* Bonferroni paired t test ( $p=0,022$ )



**Figure 2.** Mean Blood Pressure

\* Bonferroni paired t test ( $p=0,022$ )

**Table 2.** IMA, TAS, TOS and OSI

|     |                | T0          | T1          | T2           | P      |
|-----|----------------|-------------|-------------|--------------|--------|
| IMA | Group K (n=25) | 32.49±13.68 | 62.24±32.57 | 136.55±98.15 | 0.001* |
|     | Group R (n=25) | 32.58±12.34 | 91.85±42.63 | 163.04±80.62 | 0.252‡ |
| TAS | Group K (n=25) | 1.07±0.29   | 1.32±0.19   | 1.44±0.21    | 0.001* |
|     | Group R (n=25) | 1.15±0.28   | 1.31±0.18   | 1.45±0.17    | 0.173‡ |
| TOS | Group K (n=25) | 4.17±1.55   | 6.58±2.38   | 18.46±10.47  | 0.001* |
|     | Group R (n=25) | 4.65±2.34   | 7.71±4.28   | 14.56±8.54   | 0.403‡ |
| OSI | Group K (n=25) | 0.40±0.14   | 0.49±0.16   | 1.18±0.18    | 0.001* |
|     |                | 0.52±0.40   | 0.57±0.39   | 0.93±0.07    | 0.203‡ |

IMA: ischemia-modified albumin (U/ml)  
 TAS: Total antioxidant status (mmol Trolox equiv/L)  
 TOS: Total oxidant status (μmol H<sub>2</sub>O<sub>2</sub> equiv/L)  
 OSI: Oxidative stress index

T0: Preoperative  
 T1: 20 minutes after insufflation  
 T2: 6th hour postoperative

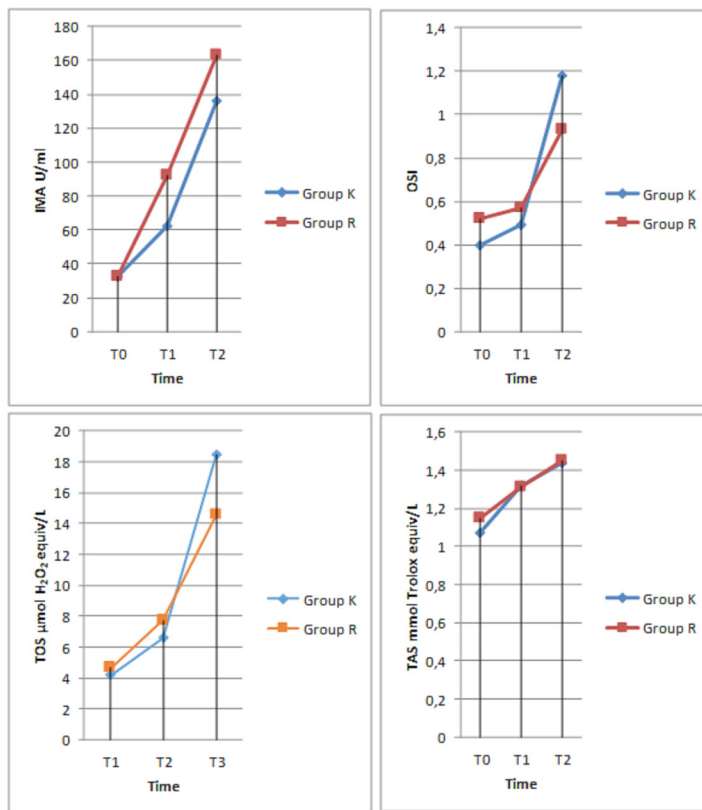


Figure 3. IMA, TAS, TOS and OSI

## Discussion

The increased intra-abdominal pressure in laparoscopy abdominal surgeries leads to changes in the circulation and respiratory system. Complications related to these changes are trying to be reduced by keeping the CO<sub>2</sub> insufflation pressure as low as possible, appropriate anesthesia management, application of ventilation strategies, proper position, cardiac monitoring and close observation [5-7]. For this purpose, the efficacy of alveolar recruitment maneuver which has been investigated in many studies applied to reduce the adverse effects of laparoscopic surgery on the respiratory system has been shown to increase partial arterial oxygen pressure and pulmonary compliance [8-12].

Ischemia-modified albumin is used in early diagnosis of ischemic heart diseases as well as it is seen to be used in the diagnosis of other diseases with ischemia to [13-15]. It has been shown that increased intra-abdominal pressure in laparoscopic cholecystectomy leads to decreased tissue perfusion in the abdominal organs and ischemia [16-18]. Koksall et al.; have been shown that the increase in intra-abdominal pressure due to pneumoperitoneum during the laparoscopic cholecystectomy has an increasing effect on IMA and the increase can be used to determine the changes in the blood flow of splanchnic area and intra-abdominal organs [14]. In our study, the difference in intra-group comparison of IMA values at preoperative (T0), 20 minutes after insufflation (T1), and postoperative 6th hour (T2) are significant ( $p < 0.0001$ ) and this results supports that the increased intra-abdominal pressure changes the blood flow of the abdominal organs [14]. However, although there was no difference between the groups in terms of IMA ( $p = 0.252$ ), the increase the IMA value is higher in the Group R than Group K, indicates that the applied recruitment maneuver

may contribute to the tissue ischemia.

At the end of laparoscopic cholecystectomy surgeries, the perfusion of tissues increases and, together with the perfusion, the oxidative reactions, in which the free radicals arise in tissues, occur. Together with the cellular damages, the free radicals cause tissue damages [4,19]. The oxidative stress increases occurring due to ischemia in laparoscopic cholecystectomies were shown using different methods [20-23]. In our study, the measurement methods based on total antioxidant status (TAS) and total oxidant status (TOS), which are easier and more affordable than separately measuring the oxidants and antioxidants, was employed [24,25].

The increase in oxidative stress on the pulmonary system by the increase in intra-abdominal pressure has been demonstrated by measuring oxidant and antioxidants in bronchoalveolar lavage fluid [26,27]. In open abdominal surgeries, in which the standard ventilation is implemented, the displacement of the diaphragm due to general anesthesia and use of muscle relaxant, cause atelectasis. It was shown that the cytokines increased due to atelectasis in the taken bronchoalveolar lavage fluid sample [28,29]. In studies comparing the recruitment maneuver and standard ventilation in open abdominal surgeries found that respiratory complications such as pleural effusion and atelectasis were less and FEV and FVC capacity were higher in the recruitment maneuver group patient [29]. In our study, the statistically significant difference ( $p < 0.001$ ) found in the intragroup comparison of TOS, TAS, and OSI values measured at preoperative (T0), 20 minutes after insufflation (T1), and postoperative 6th hour (T2) indicated that increased intra-abdominal pressure increases the oxidative and antioxidative response [20-23,26]. But, despite that there was no difference between the groups, the rise in TOS in the sixth hour postoperatively was lower in the Group R compared to the Group K, suggests that the recruitment maneuver that was applied reduced the oxidative response.

Even though there are studies reporting that vasopressor usage decreases in surgical operations, in which the alveolar recruitment maneuver is implemented, no significant hemodynamic effect originating from maneuver was observed [8,12,29]. In our study, no significant hemodynamic change was observed in any of two groups but both groups' post-induction diastolic blood pressure and mean blood pressure values that were lower than the initial values suggest that it is related with the cardiac depressant effect of the anesthetic agent used in induction.

## Conclusion

In conclusion, the recruitment maneuver that we use in laparoscopic cholecystectomies was found to have no effect reducing tissue ischemia and oxidative stress response in intraoperative period. But they might contribute to reducing the ischemia reperfusion damage in postoperative period. In order to demonstrate this effect, more comprehensive studies are needed.

## Competing interests

The authors declare that they have no competing interest

## Financial Disclosure

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## Ethical approval

Ethics committee approval was received from konya necmettin erbakan university meram faculty of medicine.

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