




# Cerebral oxygenation and its relation with blood gases and haemodynamic parameters in laparoscopic cholecystectomy with 5 cm H<sub>2</sub>O PEEP

5 cm H<sub>2</sub>O PEEP UYGULANAN LAPAROSKOPİK KOLESİSTEKTOMİLERDE SEREBRAL OKSİJENASYONUN KAN GAZLARI VE HEMODİNAMİ İLE İLİŞKİSİ

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## ABSTRACT

**Objective:** Pneumoperitoneum application during abdominal surgeries can have negative effects on haemodynamic and respiratory parameters. Cerebral oxygenation level is influenced by many factors; the partial arterial CO<sub>2</sub> pressure (PaCO<sub>2</sub>) level is the main determinant factor among them. We investigated the effects of CO<sub>2</sub> insufflation and the head-up position on haemodynamic parameters and cerebral oxygenation levels during laparoscopic cholecystectomy with the application of 5cm H<sub>2</sub>O positive end-expiratory pressure (PEEP).

**Materials and Methods:** Forty patients, between 18-65 of age, with an ASA physical status of I-II were included in the study. Following anaesthesia induction, 5 cm H<sub>2</sub>O PEEP was applied and CO<sub>2</sub> was insufflated into the abdominal space. Patients were operated in the 15° head-up position.

**Results:** Mean cardiac output was observed to be significantly higher after desufflation (5.80 ± 1.39) in comparison to the initial values prior to the pneumoperitoneum application (5.08 ± 0.95), (p < 0.05). There was no significant change in other haemodynamic parameters or cerebral oxygenation levels. PaCO<sub>2</sub> and end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) levels significantly increased during the pneumoperitoneum period (PaCO<sub>2</sub> = 33.37 ± 4.97, 36.77 ± 3.91, and 39.35 ± 3.51 mmHg, and EtCO<sub>2</sub> = 31.52 ± 2.80, 33.95 ± 3.38, and 35.72 ± 2.92 mm Hg; before, at 5 and 20 min after insufflation respectively; p < 0.05).

**Conclusion:** Application of 5 cm H<sub>2</sub>O PEEP does not improve the cerebral oxygenation but may contribute to preservation of baseline values with stable haemodynamic status after insufflation during laparoscopic cholecystectomy. Fluid administering strategy and use of opioids are important factors to achieve stable haemodynamic condition. In addition, mildly increased PaCO<sub>2</sub> levels may contribute to preserving cerebral oxygenation.

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**Keywords:** laparoscopic cholecystectomy, positive end expiratory pressure (PEEP), blood supply, near infrared spectroscopy (NIR Spectroscopy), blood gas analysis

### ÖZ

**Amaç:** Pnömooperitonyumun hemodinamik ve solunumsal parametreler üzerine olumsuz etkileri olabilmektedir. Serebral oksijenasyon, parsiyel arteriyel CO<sub>2</sub> basıncı (PaCO<sub>2</sub>) temel belirleyici olmakla birlikte birçok faktörden etkilenir. Bu çalışmada 5 cm H<sub>2</sub>O pozitif end ekspiratuar basınç (PEEP) uygulaması ile laparoskopik kolesistektomilerde CO<sub>2</sub> insüflasyonu ve baş yukarı pozisyonun hemodinamik parametreler ve serebral oksijenasyon üzerine etkilerini araştırdık.

**Gereç ve Yöntem:** Anestezi risk grubu ASA I - II olan, 18-65 yaş arası 40 hasta çalışmaya dâhil edildi. Anestezi indüksiyonunun ardından, 5 cm H<sub>2</sub>O PEEP uygulandı ve abdomen CO<sub>2</sub> ile insüfle edildi. Hastalar 15° baş pozisyonunda opere edildi.

**Bulgular:** Pnömooperitonyum periyodu ile karşılaştırılınca, desüflasyon sonrası dönemde kardiyak debinin (CO) arttığı gözlemlendi (sırasıyla 5,08 ± 0,95 ve 5,80 ± 1,39; p <0,05). Diğer hemodinamik parametrelerde veya serebral oksijenasyon seviyelerinde değişiklik yoktu. Pnömooperiton periyodunda PaCO<sub>2</sub> ve end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) seviyelerinde yükselme saptandı (PaCO<sub>2</sub> = 33,37 ± 4,97, 36,77 ± 3,91 ve 39,35 ± 3,51 mm Hg ve EtCO<sub>2</sub> = 31,52 ± 2,80, 33,95 ± 3,38 ve 35,72 ± 2,92 mm-Hg; insüflasyon öncesi, insüflasyondan 5 ve 20 dakika sonra, p <0,05).

**Sonuç:** Laparoskopik kolesistektomi sırasında 5 cm H<sub>2</sub>O PEEP uygulamasının serebral oksijenasyonu arttırmadığı, fakat insüflasyon sonrası bazal değerlerin korunmasına katkıda bulunabileceği kanısına varıldı. Sıvı uygulama stratejisi ve opioid kullanımı, stabil hemodinamik durumun sağlanmasında önemlidir. Buna ek olarak PaCO<sub>2</sub> düzeyinde ılımlı yükselme serebral oksijenasyonun korunmasına katkıda bulunabilir.

**Anahtar Sözcükler:** laparoskopik kolesistektomi, pozitif basınçlı solunum, kan sağlama, yakın kızıl-ötesi spektroskopisi, kan gazı analizi

Recently, laparoscopic abdominal surgeries are preferred instead of open surgeries because they have the advantages of small incision and early recovery. During laparoscopic cholecystectomy, carbon dioxide (CO<sub>2</sub>) gas is insufflated into the abdominal space to create a pneumoperitoneum and the patient is placed in the head-up position. However, pneumoperitoneum application and patient position can result in haemodynamic and respiratory changes.. Inflation of the abdomen with CO<sub>2</sub> increases intraabdominal pressure, thus leads to increment in systemic vascular resistance (SVR), mean arterial pressure (MAP) and causes decrement in cardiac output (CO) (1-3). In addition, application of the head-up position and positive end-expiratory pressure (PEEP) leads to reduced cardiac filling and CO (4-7).

Cerebral oxygen saturation reflects the balance between cerebral oxygen supply and demand. It depends

on the arterial oxygenation levels, cerebral blood flow (CBF), haemoglobin (Hb) content, and cerebral metabolic rate (8). Partial arterial CO<sub>2</sub> pressure (PaCO<sub>2</sub>) is the most important determinant factor of the CBF when MAP is between 70 and 150 mmHg values (9). Peritoneal insufflation can affect CBF and arterial oxygenation, which may result in alteration in oxygen delivery, especially in critically ill patients. Trendelenburg and head-up positions can both lead to decreased cerebral oxygenation during pneumoperitoneum application in laparoscopic abdominal procedures (7, 10, 11).

Previous studies demonstrated that application of PEEP could preserve arterial and cerebral oxygenation during pneumoperitoneum (5, 12). However, some studies have suggested that cerebral oxygenation does not change during the application of PEEP both in the Trendelenburg and in head-up positions (4, 5). Additionally, some studies

have shown that PEEP can also affect the haemodynamic parameters (13).

In this study, we aimed to investigate the effect of abdominal insufflation and the head-up position on the haemodynamic parameters and cerebral oxygenation levels during laparoscopic cholecystectomy with the application of 5 cm H<sub>2</sub>O PEEP. It was stated that high PEEP values have negative haemodynamic effect even if cerebral oxygenation is maintained (4, 5). Therefore, we used 5 cm H<sub>2</sub>O, as a low PEEP level that we think would not affect hemodynamic parameters.

## MATERIALS AND METHODS

### Study design and measurements

This study was performed with the approval of the Ethics Committee (23.07.2020; 2014/162) of our institution. The patients who underwent laparoscopic cholecystectomy at our University Research and Training Hospital were enrolled to the study. 18–65 years old, forty patients with an ASA physical status of I–II were included after obtaining written informed consent. Patients with pulmonary, cardiovascular, renal, or cerebrovascular diseases or those that were pregnant were excluded.

Electrocardiography, pulse oximetry, and noninvasive blood pressure measurement devices were applied to all patients before the induction of anaesthesia. Propofol (2 mg/kg), atracurium (0.5 mg/kg), and fentanyl (2 µg/kg) were administered to the patients for induction of anaesthesia. After intubation, a 6–8 mL/kg tidal volume, 12/min respiratory rate, and 5 cm H<sub>2</sub>O PEEP were applied to all patients. Tidal volume and respiration rate were set to maintain a stable minute ventilation rate with a P<sub>insp</sub> value of 30 cmH<sub>2</sub>O or above after insufflation. Anaesthesia was maintained with 50/50% fresh O<sub>2</sub>/N<sub>2</sub>O and 3–6% desflurane. After intubation, a 20 G cannula was inserted in the radial artery to enable measurement of haemodynamic parameters (FloTrac/VigileoTM; Edwards Lifesciences, Irvine, USA) and sample collection for arterial gas analyses (ABL 800 flex; Radiometer Medical ApS, Copenhagen, Denmark). Tissue oximetry system based on Near Infrared Spectroscopy (NIR Spectroscopy) was used for monitoring cerebral oxygenation. Both cerebral oximeter sensors (Foresight®; Casmed Medical, CT, USA) were placed on the

forehead. Administration of fentanyl (1 µg/kg) was repeated when an increase of 30% or more was observed in heart rate (HR) or systolic blood pressure.

Intraabdominal pressure was set at 12 mmHg in the supine position during the pneumoperitoneum period, and the patients underwent surgery in the 15° head-up position. HR, MAP, SVR, CO, end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>), and regional oxygen saturation (rSO<sub>2</sub>) measurements were recorded before (T<sub>0</sub>), 5 min after insufflation (T<sub>1</sub>), 20 min after insufflation (T<sub>2</sub>), and 5 min after desufflation (T<sub>3</sub>). The results were presented as mean ± standard deviation (mean ± SD).

### Statistical analysis

The Shapiro–Wilk test was used to determine the normality of data distribution, and the measurements were found to have normal distribution. Data were analysed using repeated analysis of variation (ANOVA) measurements with the Bonferroni correction. We calculated differences between measurements to investigate correlations between parameters. Pearson's test was used to determine correlations. A p value of <0.05 was considered statistically significant. The MedCalc® v.10.3 program was used for the statistical analysis.

## RESULTS

Demographical and certain surgical data were presented in Table 1. Mean duration of pneumoperitoneum and surgery were 64.52 ± 11.23 and 96.20 ± 14.42 min, respectively.

**Table 1.** Demographic and clinical characteristics of the patients were summarized

Age (years)	46.97 ± 11.82
Sex (M/F)	19/21
Mean duration of surgery (min)	96.20 ± 14.42
Mean duration of pneumoperitoneum (min)	64.52 ± 11.23
Mean volume of fluid infused (mL)	1010.00 ± 254.24
Mean dose of fentanyl (µg)	145.00 ± 35.44
Mean measured blood loss (mL)	160 ± 41.13

Haemodynamic parameters, arterial blood gas analyses results, and cerebral oxygenation levels during the operation were presented in Table 2. There were no statistically significant differences in haemodynamic parameter, PaO<sub>2</sub>, and rSO<sub>2</sub> levels before, during, and after the operation. However, CO levels were significantly higher before the pneumoperitoneum period as compared to the after desufflation period. Mean PaCO<sub>2</sub> and EtCO<sub>2</sub> values were significantly higher during the operation (PaCO<sub>2</sub> = 33.37 ± 4.97, 36.77 ± 3.91, and 39.350 ± 3.51 mmHg, and EtCO<sub>2</sub> = 31.52 ± 2.80, 33.95 ± 3.38, and 35.72 ± 2.92

mmHg, at T<sub>0</sub>, T<sub>1</sub>, and T<sub>2</sub> respectively; p < 0.05), but there were no significant differences after desufflation. Mean Hb values were significantly lower after desufflation in comparison with the values before and during insufflation (Table 2). Cerebral desaturation was not observed in any of the study group patients.

We found significant correlations between the changes in the following parameters: L/R rSO<sub>2</sub> and PaCO<sub>2</sub>; L/R rSO<sub>2</sub> and CO; L/R rSO<sub>2</sub> and MAP (p < 0.05; Figure 1, 2, 3).

Table 2. Mean haemodynamic parameters, cerebral oxygenation values, and blood gas sample measurements of the patients.

	T <sub>0</sub> (before PP)	T <sub>1</sub> (5 min after PP)	T <sub>2</sub> (20 min after PP)	T <sub>3</sub> (5 min after desufflation)
HR (min <sup>-1</sup> )	71.15 ± 12.66	75.62 ± 10.22	75.05 ± 9.52	75.77 ± 11.55
MAP (mmHg)	85.25 ± 16.81	94.12 ± 19.43	89.62 ± 13.73	88.32 ± 14.40
CO (L/min)	5.08 ± 0.95*	5.36 ± 1.03	5.48 ± 1.13	5.80 ± 1.39 <sup>γ</sup>
SVR (dyn·s·cm <sup>-5</sup> )	1261.30 ± 357.23	1422.70 ± 494.55	1314.20 ± 436.66	1247.00 ± 430.20
rSO <sub>2</sub> (L/R) (%)	72.02 ± 4.65 72.20 ± 4.64	72.22 ± 5.69 73.90 ± 6.78	72.12 ± 5.22 73.25 ± 5.08	72.70 ± 4.76 73.90 ± 4.45
EtCO <sub>2</sub> (mmHg)	31.52 ± 2.80 <sup>*αβ</sup>	33.95 ± 3.38 <sup>*βγ</sup>	35.72 ± 2.92 <sup>αγ</sup>	35.57 ± 3.13 <sup>αγ</sup>
PaCO <sub>2</sub> (mmHg)	33.37 ± 4.97 <sup>αβ*</sup>	36.77 ± 3.91 <sup>*βγ</sup>	39.350 ± 3.51 <sup>αγ</sup>	40.25 ± 3.77 <sup>αγ</sup>
PaO <sub>2</sub> (mmHg)	178.37 ± 52.55	179.95 ± 51.39	172.22 ± 50.98	184.37 ± 55.23
Hb (mg/dL)	11.53 ± 0.95*	11.49 ± 0.96*	11.44 ± 0.87*	11.15 ± 0.94 <sup>αβγ</sup>

PP: induction of pneumoperitoneum, HR: Heart Rate, MAP: Mean Arterial Pressure, CO: Cardiac Output, SVR: Systemic Vascular Resistance, rSO<sub>2</sub>: regional oxygen saturation, EtCO<sub>2</sub>: end-tidal CO<sub>2</sub>, PaCO<sub>2</sub>: Partial arterial CO<sub>2</sub> pressure, PaO<sub>2</sub>: Partial arterial O<sub>2</sub> pressure, Hb: hemoglobin

\*: p < 0.05, statistically significant difference compared with measurement after desufflation

<sup>α</sup>: p < 0.05, statistically significant difference compared with measurement 5 min after insufflation

<sup>β</sup>: p < 0.05, statistically significant difference compared with measurement 20 min after insufflation

<sup>γ</sup>: p < 0.05, statistically significant difference compared with measurement before pneumoperitoneum

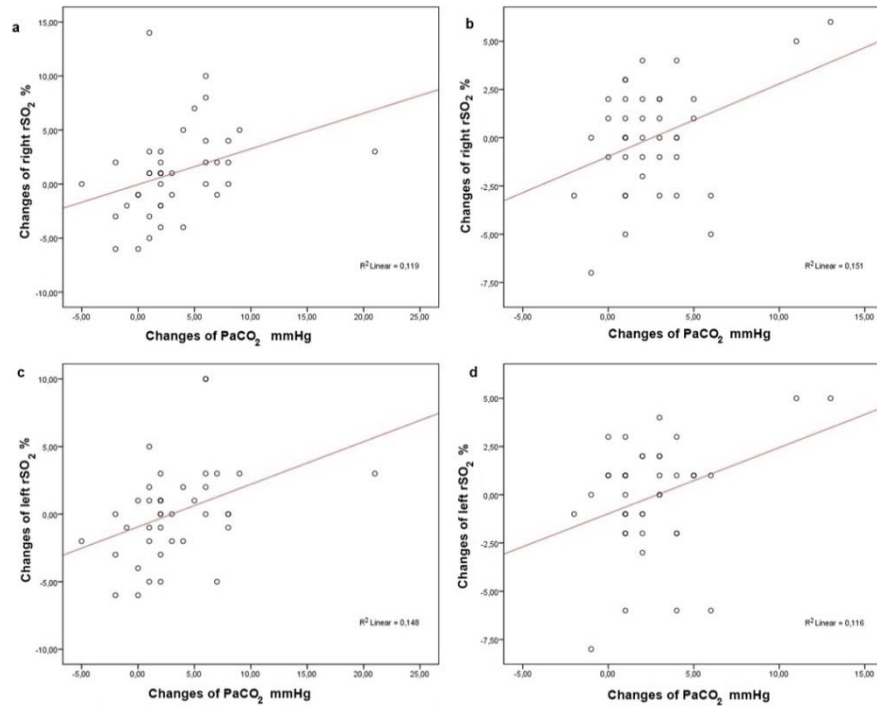


Figure 1: Correlation between the changes in PaCO<sub>2</sub> level and right/left cerebral oxygen saturation.

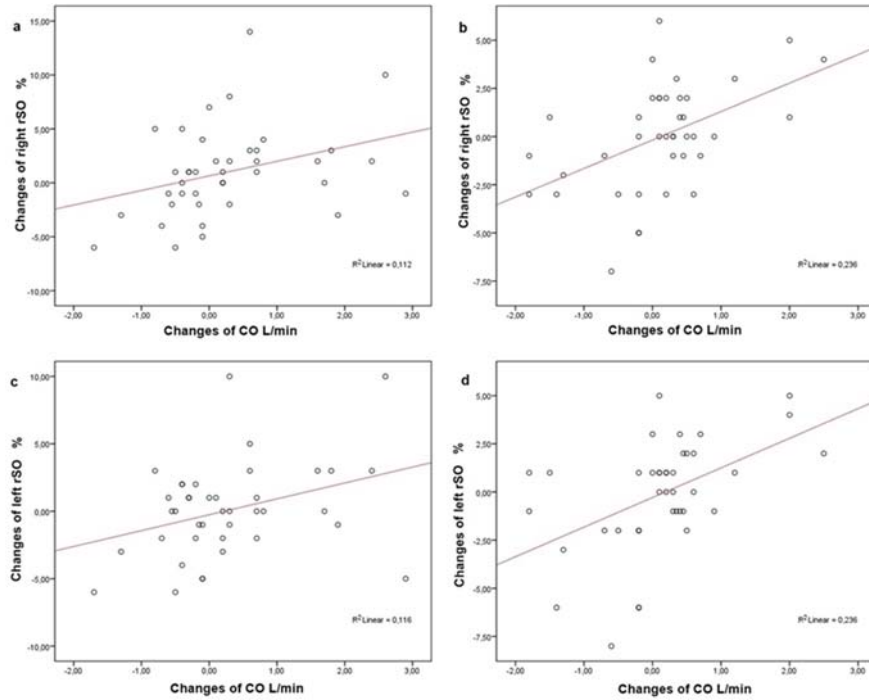
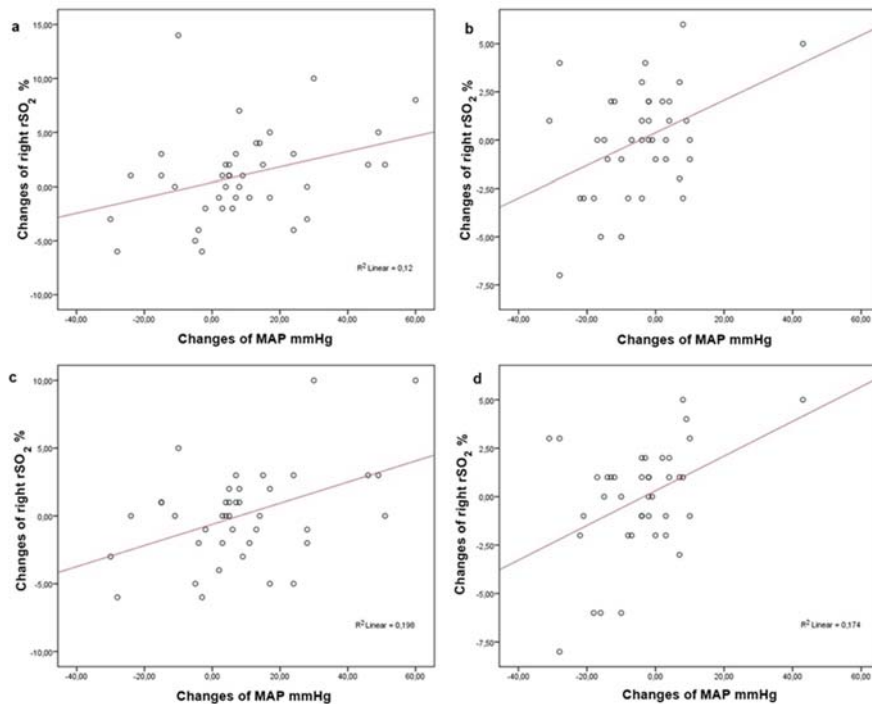


Figure 2: Correlation between the changes in cardiac output (CO) and right/left cerebral oxygen saturation.



**Figure 3:** Correlation between the changes in MAP level and right/left cerebral oxygen saturation.

## DISCUSSION

This study demonstrated that the head-up position, and 5 cm H<sub>2</sub>O PEEP employment did not significantly change the cerebral oxygenation levels and haemodynamic parameters for patients who underwent laparoscopic cholecystectomy under the application of pneumoperitoneum. However, PaCO<sub>2</sub> and EtCO<sub>2</sub> levels significantly increased during the pneumoperitoneum period. It can be suggested that the increased PaCO<sub>2</sub> levels might have had beneficial effects on the cerebral oxygenation levels (14). It should be noted that intravascular fluid and fentanyl were also administered to aid in the maintenance of the appropriate haemodynamic conditions and optimal oxygenation levels during the surgery, in our study.

It is well known that the application of pneumoperitoneum has unfavorable effects on the haemodynamic parameters (15). HR, SVR, central venous pressure (CVP), MAP increase, and CO values may change during pneumoperitoneum employment. Decreased

cardiac index and CO levels have been observed with pneumoperitoneum application. On the other hand; fluid replacement prior to the onset of the pneumoperitoneum application has been demonstrated to, increase the CO levels (16). We found no significant differences in HR, SVR, and MAP before, during, and 5 minutes after the end of the pneumoperitoneum period. However, CO values did not change significantly during the pneumoperitoneum period but increased after 5 minutes of desufflation as compared with the initial levels ( $p < 0.01$ ). Our fluid administration strategy might have provided the preservation of the CO during insufflation and the increase after desufflation. Watanebe et al. showed that HR and MAP did not change with the remifentanyl infusion during laparoscopic cholecystectomy (15). We think that, PEEP application in addition to the opioid and fluid administration strategy prevented the increment in MAP values and provided haemodynamic stability in our study. The decreased Hb concentration after desufflation was probably related to the fluid administration in our study, because there was negligible blood loss during the surgery.

Insufflation of CO<sub>2</sub> into the abdominal space may result in reduction of cerebral oxygenation by influencing both the levels of PaO<sub>2</sub> and CBF. Moreover, the sitting position contributes to the decreased cerebral oxygenation (10). Previous research showed that CBF and oxygenation decrease after insufflation in the head-up position, and another study showed that cerebral oxygenation decreases time dependently after the onset of pneumoperitoneum during laparoscopic cholecystectomy in the head-up position (2, 17). Although these reduced rSO<sub>2</sub> values were not below critical levels, they may be crucial in critical patients.

The mechanism of cerebral oxygenation during laparoscopic surgery is complicated and remains unclear, because there are many determinant factors playing a role during surgery, such as cerebral metabolic rate, CBF, Hb content, and arterial blood oxygenation. CBF remains stable in the presence of physiologic MAP values, but may change according to PaCO<sub>2</sub> levels in particular (9, 18), and several studies have demonstrated that changes in the PaCO<sub>2</sub> levels lead to the changed rSO<sub>2</sub> levels (19, 20). The PaO<sub>2</sub> level also affects the rSO<sub>2</sub> values, it has been shown that adjustment of FiO<sub>2</sub> from 0.3 to 1.0 and to increase of the EtCO<sub>2</sub> levels from 30 to 45 mmHg resulted in 5% and 9% increment in rSO<sub>2</sub> values, respectively (21). In this study, we found that rSO<sub>2</sub> levels significantly correlated with the PaCO<sub>2</sub> levels during the pneumoperitoneum period (but not after desufflation), but were not correlated with the PaO<sub>2</sub> levels. In addition, we did not find significant decrement in either the rSO<sub>2</sub> or PaO<sub>2</sub> levels. According to our study results we can judge that; Although the PaCO<sub>2</sub> level is the main determinant factor of cerebral oxygenation, other parameters such as PaO<sub>2</sub> or Hb concentration also play an important role in physiological clinical settings. However, the effects of these factors on cerebral oxygenation are less pronounced when compared to the PaCO<sub>2</sub> levels. In concordance with our findings, previous investigators also revealed that increased CO<sub>2</sub> levels have a preserving effect on cerebral oxygenation through increased CBF during laparoscopy (17).

Another factor that might have provided to preserve the rSO<sub>2</sub> levels in this study might be the increased MAP levels after insufflation. Correlations have been found

between rSO<sub>2</sub>, MAP, and CO in certain studies (22-24) We also found correlations between differences in the rSO<sub>2</sub>, MAP, and CO measurements during insufflation.

Application of PEEP increases PaO<sub>2</sub> levels but requires individual adjustment for each patient in the clinical settings. Futier et al. showed that increased cerebral oxygenation cannot be achieved by PEEP application alone, and additional recruitment manoeuvres are necessary (25). In addition, another study reported that the application of 10 cm H<sub>2</sub>O PEEP does not improve cerebral oxygenation after abdominal insufflation (5). High PEEP levels can have negative effects on cerebral oxygenation due to decreased CBF (26). A study investigating the effect of PEEP on cerebral oxygenation showed that rSO<sub>2</sub> levels did not change after the application of 10 cmH<sub>2</sub>O PEEP but haemodynamic parameters were affected adversely (4). Contrary to these results, another study which conducted on laparoscopic cholecystectomy has suggested that 10 peeps increase oxygenation compared to 5 peeps but do not cause any hemodynamic disturbance (27). PEEP levels that result in an increase of driving pressure were also related with more postoperative pulmonary complications (28). Although ideal peep was reported to be 7 cm H<sub>2</sub>O in patients in the trendelenburg position, another study that measures the driving pressure found an ideal PEEP value of 8 cmH<sub>2</sub>O in laparoscopic cholecystectomy operations in the reverse-trendelenburg position (29, 30). We used a low PEEP level to avoid negative cardiovascular effects and found no change in cerebral oxygenation or haemodynamic parameters. Moreover, we did not need to open closed alveoli with recruitment manoeuvres owing to use 5 cmH<sub>2</sub>O at the start of the operation. This implementation did not increase but might have maintained the cerebral oxygenation levels. This aspect may be important in critically ill patients.

This study had certain limitations. First, ventilator parameters were closely monitored and readjusted when necessary according to peak airway pressure. However, to maintain the integrity of the study, these values were not recorded. Second, BIS monitoring to enable adjustment of the depth of anaesthesia was not carried out. Third, CVP values were not monitored. We considered central venous

catheterisation as an invasive monitoring method for these operations.

Increased intraabdominal pressure may cause a decrease in cerebral oxygenation. However, no any significant effect was observed during abdominal insufflation on hemodynamics and cerebral oxygenation values with 5 cm H<sub>2</sub>O PEEP level. Application of 5 cm H<sub>2</sub>O PEEP does not improve the cerebral oxygenation but could contribute to preservation of preceding values with stable haemodynamic status after insufflation during laparoscopic cholecystectomy. The PaCO<sub>2</sub> level is the most important determinant factor of cerebral oxygenation. Mild increment in CO<sub>2</sub> levels may aid in preserving cerebral oxygenation.

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