Cardiovascular effects of different peep levels in a clinical setting of increased abdominal pressure

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ABSTRACT

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The interaction between increased Intra Abdominal Pressure (IAP) and Intrathoracic Pressure under different Positive End Expiratory Pressure (PEEP) levels is intriguing, since these two conditions coexist frequently in several clinical settings. The aim of our study was to investigate the interaction between different PEEP levels and increased IAP during laparoscopic cholecystectomy. In fifty two patients, who underwent scheduled laparoscopic cholecystectomy, cardiovascular parameters were determined by an Oesophageal Doppler Monitor device during two different time periods, before and after pneumoperitoneum, and under five conditions: (i) PEEP 0 cmH₂O. (ii) PEEP 5cm H₂O (iii)

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⁵Anesthesiology Department, Interbalkan Medical Center (Private Hospital) Thessaloniki, Greece. PEEP 10cm H₂O (iv) PEEP 15cm H₂O and (v) in the absence of PEEP or ventilation. Cardiac output and stroke volume showed a statistically significant decrease compared to the baseline value after the application of different PEEP levels, when there was no pneumoperitoneum (p<0.05). However, both parameters increased, when PEEP and pneumoperitoneum were applied together (p<0.001). Corrected flow time, peak flow velocity in the descending thoracic aorta and

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mean acceleration showed similar alterations but not at all PEEP levels. Finally, αt the no PEEP or ventilation phase, the negative effects of increased IAP on the cardiocirculatory function were predominant. According to these results, application of PEEP seems to counterbalance the negative hemodynamic effects of increased IAP. Moreover, it could also be concluded that 'ideal' PEEP level might be the one that borders the IAP level, since the best cardiac output and stroke volume values were reported at that point.

INTRODUCTION

Application of Intermittent positive pressure ventilation (IPPV) induces cyclic changes in left and right ventricle loading. Transpulmonary pressure increase during inspiration induces a decrease in the preload and an increase in the afterload of the right ventricle (RV).¹ This combination results in a reduction of RV stroke volume (SV) and cardiac output (CO).²⁻⁶ Notably, CO decrease is directly associated with airway pressure elevation and the resultant proportional intrathoracic pressure (ITP) increase.^{7,8}

General anesthesia and mechanical ventilation (MV) can evoke intraoperative hypoxemia, even in patients with healthy lungs. The main causative pathophysiological mechanisms are airway collapse and subsequent occurrence of atelectasis. Moreover, cyclic closing and opening of the alveoli and small bronchi during MV is strongly associated with ventilator induced lung injury.⁹⁻¹³

Application of positive end expiratory pressure (PEEP) is generally recommended as a routine anesthesia practice, in order to prevent atelectasis and hypoxemia. Furthermore, PEEP has been widely applied both intraoperatively and in the Intensive Care Unit (ICU) setting in several cases, such as in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), in obese patients, during one lung ventilation in thoracic surgery and after cardiac surgery.¹⁴⁻¹⁸

Despite the undoubted^a beneficial effects of PEEP on respiratory mechanics, its impact on cardiac function is complex and often unpredictable. According to the results of several studies, application of PEEP is associated with a negative influence on CO.¹⁹⁻²³ The PEEP-induced increase in ITP leads to a restriction of venous return to the right ventricle, resulting in a fall in CO.⁷ In fact, this fall in CO is completely attributed to the decrease of left ventricle SV and the alteration of its determinants; heart rate is generally not affected by PEEP.^{24,25}

As far as the left heart is concerned, PEEP induces a decrease in left atrium preload and in left ventricle afterload. Furthermore, in some studies it is implied that PEEP leads to the release of humoral agents, which decrease cardiac contractility, alter coronary blood flow and induce myocardial ischemia.^{26,27} Patients with increased intra-abdominal

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pressure (IAP) are part of the routine anesthesia practice, as the number of laparoscopic procedures performed has increased significantly over the past few years. In laparoscopic surgery, increased IAP is a result of carbon dioxide (CO₂) insufflation into the peritoneal cavity. Moreover, increased IAP is seen in many other clinical conditions, such as in patients with intraabdominal pathology (trauma etc). Increased IAP is associated with respiratory, cardiovascular and central nervous system sequelae.²⁸⁻³¹

As far as the respiratory system is concerned, increased IAP causes cephalic transposition of the diaphragm resulting in a decrease in functional residual capacity (FRC) and in respiratory system compliance, along with airway pressure elevation. This decrease in respiratory system compliance is attributed more to the reduction in chest wall compliance (which in physiological terms consists not only of the bony thorax but also of the diaphragm and the abdominal wall) and less to that of the lung compliance.³¹⁻³⁵

Haemodynamic effects of increased IAP are reflected in decreased CO, which is primarily caused by a reduction of venus return and secondarily by systemic vascular resistance elevation.³⁶⁻³⁷ However, in many studies it has been implied that venous return is not decreased until IAP reaches a value of 15mmHg. In fact, lower levels of IAP may even be accompanied by an increase in preload.^{38,39} Moreover, other factors such as the type of insuf-

flated gas, the amount of absorbed CO₂ (in case of ©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ΕταιρείαΑναισθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος

capnoperitoneum), patient positioning, intravascular volume status etc, may have an impact on overall haemodynamic effects.^{40,41}

Importantly, the thoracic cage with the lungs, and the abdominal cavity comprise a closed system with the diaphragm as the connecting interface. Hence, the inevitable interaction between the pressure changes in the two parts of the system, may be the cause of unexpected cardiovascular effects.^{25,27,42-44.}

Coexistence of increased IAP and PEEP is frequently encountered in many clinical conditions and is challenging, since their interaction and their combined hemodynamic effects remain unclear. The results of many studies in the literature are controversial. In some, the combination of PEEP and increased IAP seems to be detrimental for the cardiovascular system, whereas in others PEEP is considered beneficial due to its positive influence on respiratory mechanics without any negative hemodynamic effects.^{45,46}

The aim of our study was to investigate the hemodynamic effects of different PEEP levels in a setting of increased IAP, namely in patients undergoing laparoscopic cholecystectomy.

MATERIAL AND METHODS

Fifty two patients scheduled for laparoscopic cholecystectomy were included in this study. All of the patients agreed to the study protocol by signing a written Informed Consent Form, which was approved by the Ethics Committee of our hospital. The exclusion criteria were oesophageal obstruction and recent upper gastrointestinal surgery or bleeding.

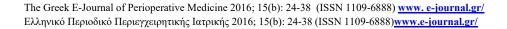
Before anesthesia induction, all patients received an initial Ringer's Lactate bolus adapted to their body weigh,t in order to remedy the deficit due to preoperative fasting (approximately 1000ml), which was followed by an infusion of 2ml/kg/hr of crystal-loids. After preoxygenation, anesthesia was induced similarly in all patients, via propofol 1.5-2mg/kg, fentanyl 4-6µg/kg and cis-atracurium 0.15mg/kg and maintained with sevoflurane and fentanyl.

After anesthesia induction and onset of MV, an arterial line and a Folley catheter were placed on each patient. Moreover, an Oesophageal Doppler Monitor device (ODM II) (G 974, Abbott Laboratories) was placed into the esophagus to determine the CO. ODM was advanced to a position of 30 to 35cm from the incisors in order to obtain the best waveform display on the monitor screen. The rest of the monitoring included ECG, invasive and noninvasive blood pressure measurement, capnography, BIS and respiratory parameters.

All the parameters of the study were recorded during two different time periods, before and after pneumoperitoneum establishment (periods A and B respectively) and under five conditions: (i) PEEP $0 \text{cmH}_2\text{O}$, (ii) PEEP 5cm $H_2\text{O}$, (iii) PEEP 10cm $H_2\text{O}$ (iv) PEEP 15cm $H_2\text{O}$ and (v) in the absence of both PEEP and ventilation (protocol phases). Before each measurement, a 5min interval was allowed for the patient to stabilize and acclimate to ©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ErcupeíaAvaioθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος

the new condition. In the absence of PEEP and ventilation phase, oxygen was insufflated to the patient using a catheter inserted through the endotracheal tube and positioned just above the carina, in order to avoid hypoxaemia. Recorded parameters included stroke volume (SV), cardiac output (CO), heart rate (HR), corrected flow time (FTc), peak flow velocity in the descending thoracic aorta (PV) and mean acceleration (MA) (Figures 1,2). For the statistical analysis the General Linear Model for repeated measures (ANOVA) was employed. Mean \pm standard deviations are presented in the pertinent Tables. Statistical significance was set at p<0,05. PASW 18.0 (SPSS Inc., Chicago, IL) was used for data analysis.One-Sample Kolmogorov Smirnov test was applied at the beginning and for each individual parameter in order to find out whether data follow a normal distribution. In case were normally distributed, Mauchly's data Sphericity was used to validate the correction method of the grades of freedom, which in all cases was the conservative Greenhouse-Geisser. The effects of pneumoperitoneum alone, of PEEP alone and of their combination on each parameter were examined. If the main effect of each separate factor was not significant, any parameter differences along the different study phases were ignored. If the main effect of each factor separately was significant, differences of the parameter along the different study phases were analyzed.

Figure 1. Period A: ODM Waveforms



(traces)

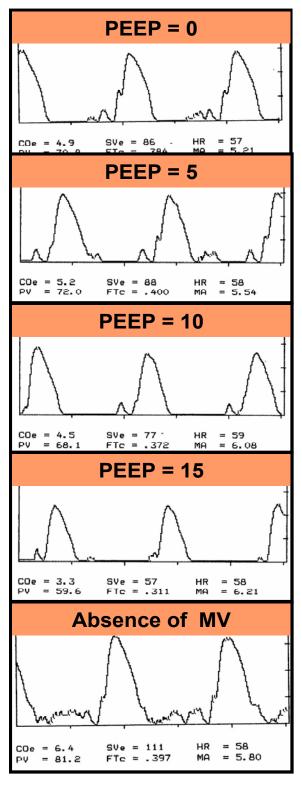
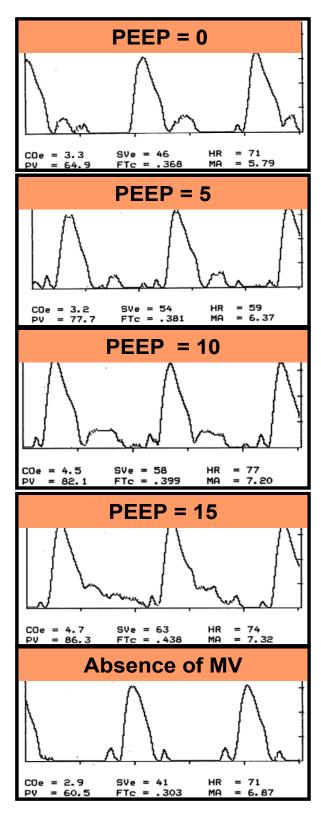


Figure 2. Period B: ODM Waveforms

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Results

Fifty two patients were enrolled in this study. Demographic data of the patients and their ASA-PS classification are presented in Table 1.

Table 1. Demographic data and ASA-PSclassification

PARAMETERS	N	52		
	AGE (Years)	49,5±14,4		
	BODY WEIGHT (kg)	77,8±18,4		
	HEIGHT (cm)	166±25,6		
	BMI	27,29±3,9		
	ASA-PS	I-III		

Values are mean \pm SD

CO, SV, HR, FTc, MA, and PV alterations during A and B periods under the five protocol conditions are presented in Tables 2 and 3 respectively.

During time period A, CO and SV showed a statistically significant decrease, compared to the baseline value at 10 and 15cm H_2O PEEP and a significant increase in the absence of MV. On the contrary, during time period B, CO and SV showed a statistically significant increase at all PEEP levels, with the highest CO value present at

©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ΕταιρείαΑναισθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος 10cmH₂O PEEP and a significant decrease in the absence of MV.

Table 2. CO, SV and HR alterations during thetwo study periods under five protocol conditions

	CO		SV		HR		
	PERIOD		PERIOD		PERIOD		
	А	В	A	В	А	В	
PEEP:0cmH ₂ O	4,7	4,2	72,1	65,2	66,4	65,1	
	±1,7	±1,5	±23,4	±18,2	±9,4	±18,2	
PEEP:5cmH ₂ O	4,6	4,6	70,2	69,2	66,2	69,2	
	±1,6	±1,4*	±23,7	±18,5*	±9	±18,5	
PEEP:10cmH ₂ O	4,1	4,9	64,3	72,3	64,7	72,3	
	±1,6*	±1,5*	±22,4*	±18,5*	±9,1**	±18,5	
PEEP:15cmH ₂ O	3,6 ±1,7*	4,7 ±1,5*	57,7 ±22,7*	73,5 ±19,9*	$64,7 \\ \pm 8,8^{**}$	73,5 ±19,9**	
ABSENCE	5,1	3,5	79,7	52,6	$\begin{array}{c} 66 \\ \pm 8,8 \end{array}$	52,6	
OF MV	±1,9*	±1,2*	±25,8*	±17,3*		±17,3	

MV: Mechanical Ventilation, *p<0,001: Compared with baseline value, **p<0,05: Compared with baseline value. **Table 3.** PV, FTc and MA alterations during the

two stuc	ly perioc	ls unde	er five	protocol	conditions

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	PV PERIOD		FTc PERIOD		МА	
					PERIOD	
	А	В	A	В	A	В
PEEP:0cmH ₂ O	68,9 ±20,4	65,4 ±19	0,38 ±9,4	$0,40 \\ \pm 0,05$	6,3 ±1,7	6,4 ±1,7
PEEP:5cmH ₂ O	69,86 ±21,4	66,7 ±21,5	0,39±9	0,41 ±0,06	6,41 ±1,7	6,71 ±1,6
PEEP:10cmH ₂ O	$68,6 \pm 20,9$	69,4 ±20,7*	0,36 ±9,1*	0,42 ±0,06**	6,36 ±1,6	6,74 ±1,8
PEEP:15cmH ₂ O	65,2 ±21,8*	68,5 ±21,1*	0,34 ±8,8*	0,42 ±0,07	6,13 ±1,6**	6,80 ±1,7**
ABSENCE OF MV	71,3 ±20,8**	59,5 ±19,8*	$0,40 \\ \pm 8,8^{**}$	0,38 ±0,6*	6,5 ±1,7**	6,2 3±1,7

MV: Mechanical Ventilation, *p<0,001: Compared with baseline value, **p<0,05: Compared with baseline value. The comparison of the two time periods revealed a statistically significant difference at all protocol phases, except at the baseline level and at 5cmH₂O PEEP (Table 2, Figures 3,4).

Figure 3. Stroke volume alterations during the study period

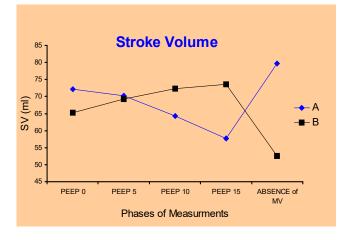
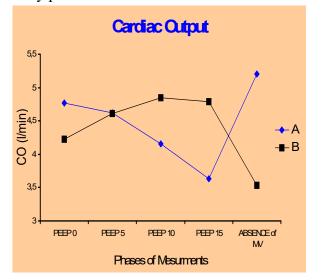


Figure 4. Cardiac output alterations during the study period



As far as HR is concerned, there was no statistically significant difference between the two study periods at any protocol phase. HR showed a statistically significant decrease at 10 and 15cmH₂O PEEP during period A, whereas it showed a statistically significant increase at 15cmH₂O PEEP during period B (Table 2).

©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ΕταιρείαΑναισθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος FTc, which is considered as an in indicator of cardiac preload,⁴⁷ showed a statistically significant decrease compared to the baseline value at 10 and 15cm H₂O PEEP and a significant increase in the absence of MV during period A. During time period B, FTc showed a borderline statistically significant increase only at 10cmH₂O PEEP and a statistically significant decrease in the absence of MV. The comparison of the two time periods revealed a statistically significant difference at all protocol phases (Table 3).

PV, which is an indicator of the left ventricular contractility,⁴⁷ showed a statistically significant decrease at 15cm H2O PEEP and a significant increase in the absence of MV, compared with the baseline value, during study period .. During time period B, PV showed a statistically significant increase at 10 and 15 cmH₂O and a statistically significant decrease in the absence of MV. The comparison of the two time periods revealed a statistically significant difference only in the absence of MV (Table 3).

Finally, MA, which is a parameter mainly influenced by cardiac contractility and secondarily by after- and preload, showed a statistically significant decrease at 15cmH₂O PEEP and an increase in the absence of MV during period A and an increase at 15cmH₂O PEEP during period B. The comparison between the two periods A and B revealed a statistically significant difference only at 15cmH₂O PEEP level (Table 3).

DISCUSSION

The negative impact of IPPV and PEEP on the cardiovascular system is well known and established in the literature.^{5,25,43,44}

As far as the respiratory system is concerned, beneficial effects of PEEP application in the enhancement or preservation of oxygenation, the increase in FRCand the restoration of the ventilation perfusion disturbances are clear and beyond any doubt.^{12,13,15}

However, the haemodynamic effects of high PEEP levels have been proven to be hazardous.^{7,19-21} This can be explained by PEEP induced preload decrease, afterload increase and alterations in the cardiac contractility.

Moreover, IAP elevation with or without MV has also negative effects on cardiovascular system.³⁶⁻⁴⁰ The magnitude of these effects is related to parameters such as the applied PEEP level, VT, IAP values and intravascular volume status. Hypovolemic patients are more susceptible to the adverse effects of increased ITP and IAP.

Since simultaneous presence of MV, PEEP and increased IAP is quite often in routine clinical practice both in the operating theatre and in the ICU, the interaction between IAP and ITP under different PEEP levels is of great importance.

It seems only rational to assume that if increased IAP, MV and PEEP are simultaneously present, they will have cumulative cardiovascular effects.

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However, the results of previous studies in the literature about the combined hemodynamic effects of these two conditions remain controversial.^{14,16,46} Kraut et al studied the haemodynamic influence of the application of 10cm H₂O PEEP in nine patients, who underwent laparoscopic cholecystectomy under 15mmHg IAP in anti-Trendeleburg position.⁴⁵ They demonstrated preload and SV reduction in the presence of both PEEP and increased IAP, whereas the cardiovascular effects of increased IAP alone without any PEEP were well tolerated. They concluded that it would be advisable to avoid the combination of these two parameters in the daily routine clinical practice. Whenever this cannot be avoided, it is mandatory to monitor cardiac function and preload closely.

On the other hand, the results of a similar, more recent study by Meininger et al are different.⁴⁸ They studied the respiratory and haemodynamic effects of the application of 5cm H₂O PEEP in twenty patients who underwent laparoscopic prostatectomy. The combination of PEEP and pneumoperitoneum resulted in better arterial oxygen partial pressure without any negative haemo-dynamic effects. The authors of this study concluded that the application of low PEEP level and pneumoperitoneum can be useful, especially during laparoscopic procedures of long duration.

In our clinical trial, we evaluated the effect of different PEEP levels in a high intra – abdominal pressure setting during laparoscopic cholecystectomy. ODM was selected as capable of calculating real time SV and CO by measuring blood flow velocity in the descending aorta beat-by-beat.^{47,48} Besides SV and CO, other parameters such as PV, MA and FTc, which are correlated to ventricle contractility and preload, can be measured by this technique. ODM is a non invasive and more reliable method compared to the Swan-Ganz catheter thermodilution technique.⁵⁰⁻⁵²

In our study, we confirmed the negative influence of the incremental application of PEEP on CO and SV. Nevertheless, this influence was statistically significant only when PEEP exceeded 10cm H_2O . Moreover, in the absence of both PEEP and MV, a great CO and SV increase was recorded. These results are consistent with previous studies in the literature.

After CO₂ was insufflated and an intraperitoneal pressure of 12mmHg was obtained, CO and SV increased with the application of all three PEEP levels. Nevertheless, the most excessive increase in CO and SV was recorded with the application of PEEP of 10cm H2O and 15cmH2O, respectively, namely at the time when PEEP tends to counterbalance/equalize IAP. On the contrary, in the absence of both PEEP and MV, and while increased IAP was obtained, CO and SV showed a tremendous decline.

According to these results, PEEP application seems to counterbalance the negative haemodynamic effects of increased IAP. This can be derived from the statistical significant CO and SV increase compared to the basal measurement after ©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ΕταιρείαΑναισθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος the application of different levels of PEEP. Moreover, this correlation between PEEP and increased IAP may be more obvious by the detrimental CO and SV decline during time period B (pneumoperitoneum) and at the moment when both PEEP and MV are absent.

In addition to the above, we analyzed alterations of FTc as an index of cardiac preload.^{47,49,53} During period A, FTc showed a statistically significant decrease at 10 and 15cm H₂O PEEP and a significant increase in the absence of MV compared to its baseline value, which are well reported effects of PEEP in previous studies. However, during pneumoperitoneum, FTc showed a gradual increase at all PEEP levels (statistically significant at 10cmH₂O) and a statistically significant decrease in the absence of MV. This observation is very important since it implies that, during increased IAP, cardiac preload could be enhanced by PEEP application.

According to these results, we could also conclude that 'ideal' PEEP level may be the one that borders on the IAP level, since at that point we have reported the best CO and SV value.

Finally, MV alterations are also of importance, since they mainly represent changes in contractility. ^{47,49,53} In our study, MV showed a decline at high PEEP levels during period A, whereas it increased essentially at all PEEP levels. This suggests that the combination of PEEP with increased IAP may be helpful for the cardiac contractile function. A possible limitation of our study might be the use of ODM for CO measurements. ODM uses a normogram to estimate CO, which is based on flow measurements in the descending aorta and it seems that there is a good correlation between standard invasive methods such as thermodilution and ODM measurements.⁵²⁻⁵⁴ However, the fact that ODM calculates CO based on the assumption that 30% of the total blood flow goes to the upper body could cause errors in CO calculations in some situations with blood flow redistribution (such as aorta cross-clamping). Nevertheless, this was not the case in our clinical setting. Moreover, it is beyond any doubt that ODM provides a good guide of hemodynamic changes and clinicians should focus on trends rather than absolute values. Our results have clinical implications, since increased IAP is a very common clinical condition not only in severely ill patients but also in patients undergoing any surgical laparoscopic procedure. In addition, MV with PEEP application is a standard ventilation strategy in general anesthesia. Indeed, PEEP application is often not just desirable but mandatory, because of ventilation/perfusion disturbances, especially in severely ill patients with intra-abdominal pathology of different causes. Therefore, specifically under these circumstances, the possible beneficial effect of PEEP not only on respiratory mechanics but also on the cardiovascular system seems very promising.

However, in situations when PEEP and increased IAP are applied at the same time, it is strongly ©2016 Society of Anesthesiology and Intensive Medicine of Northern Greece ©2016 ΕταιρείαΑναισθησιολογίαςκαιΕντατικήςΙατρικήςΒορείουΕλλάδος recommended to closely monitor the heart function and to optimize preload, since both ITP and increased IAP have a negative effect on venous return.

Despite the positive results of this study and the possible favorable correlation of PEEP and increased IAP in relation to the cardiovascular system, more research and clinical studies are necessary to confirm this observation and to determine the 'ideal' PEEP level.

In conclusion, PEEP application at levels between $5 \text{cm H}_2\text{O}$ to $15 \text{cm H}_2\text{O}$ during MV of patients undergoing laparoscopic cholecystectomy seems to protect the cardiovascular system from the negative hemodynamic effects of the increased intraabdominal pressure induced by pneumoperitoneum.

CONCLUSION

In order to optimally apply NIV in everyday clinical practice, there is a necessary learning curve. It is very important to be able to identify those patients most likely to benefit from NIV as opposed to those that will likely not and recognize signs of early NIV failure in order to escalate respiratory support. There are still major questions for which we lack high quality data, such as optimal patient selection, duration of NIV, patient-ventilator interface and ventilator parameters.

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Author Disclosures:

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