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Randomised Controlled Trial

# Laparoscopic surgery: A randomised controlled trial comparing intraoperative hemodynamic parameters and arterial-blood gas changes at two different pneumoperitoneal pressure values

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ABSTRACT

*Background:* The benefits of laparoscopic surgery are well known. However, clinic and metabolic consequences of pneumoperitoneum, achieved by insufflation of gas carbon dioxide, are still debated. Cardiovascular system suffering due to the compression of intra-abdominal venous structures can cause life-threatening complications. Increased partial pressure of carbon dioxide induces metabolic acidosis with further vascular suffering. Pneumoperitoneum reduces the pulmonary exchange volumes and bring renal suffering.
*Methods:* The aim of this study is to evaluate the alterations in hemodynamic and hemogasanalysis parameters during the laparoscopic surgery at different pressure settings of pneumoperitoneum in order to assess the best pressure value.
We evaluated and compared intraoperative hemodynamic and hemogasanalytic alterations in two groups of patients respectively subdue to laparoscopic cholecystectomy at a pneumoperitoneum pressure of 12 mmHg (group A) and at a pressure of 8 mmHg (group B).
*Results:* In both groups, after the induction of anesthesia we observed a flexion in the heart rate, with no significant difference between the two groups. During the intervention, group A showed a significantly higher respiratory rate than the group B. The average blood pressure decreased mostly in group B. The oxygen saturation increased at the end of the procedure in group A, more than in the group B. The pH value was higher in group B. The hydrogen carbonate ion settled at lower levels in group A.
*Conclusion:* Although significant differences between the two groups were appreciated on several parameters, they were never of such magnitude to prefer the induction of pneumoperitoneum at 8 mmHg.

## 1. Introduction

The benefits of laparoscopic surgery have been extensively reported in the Literature. However, laparoscopic surgery presents some aspects whose interpretation is still under study. One of the main steps consists in the realization of pneumoperitoneum through the insufflation of gas, in almost all cases carbon dioxide. The consequences of gas injection into the peritoneum are widely discussed in the Literature. Some Authors reported the onset of cardiovascular system suffering due to the compression of intra-abdominal venous structures [1,2]. In particular, deep vein thrombosis and pulmonary embolism after more complex laparoscopic surgical procedures showed an incidence of up to 23%, and can represent a lethal complication, especially if surgery is performed for oncological indications [3,4]. Increased partial pressure of carbon dioxide in the blood is a predisposing factor for metabolic acidosis and therefore promotes further vascular suffering. Pneumoperitoneum also reduces the pulmonary exchange volumes and induces renal suffering, the latter due to a decreased contractile cardiac activity and to the compression of the vascular structures. Moreover, the pressure on the peritoneal serosa induced by pneumoperitoneum could be the cause of

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inflammatory alterations, which could explain the surprisingly high serum values of acute phase proteins observed after major laparoscopic surgery [4].

The aim of this study is to search for possible differences in hemodynamic and hemogasanalysis parameters during the execution of laparoscopic surgery at different pressure settings of pneumoperitoneum and the possible advantages obtainable from applying a specific pressure value.

This case report has been reported in line with the SCARE Criteria [5].

## 2. Materials and methods

The aim of the study was to evaluate the benefits of performing the pneumoperitoneum at a lower pressure and at the standard pressure. We evaluated intraoperative hemodynamic and hemogasanalytic alterations in two groups of randomized patients respectively operated at a pneumoperitoneum pressure of 12 mmHg (group A) and at a pressure of 8 mmHg (group B) to highlight any significant alterations. The patients were chosen by the method of block randomization, which is a method designed to randomize subjects into small balanced groups having always equal sample sizes. The blocks' size was of four patients each with an amount of six blocks overall. The drawing of the block was performed on the day of surgery of the first patient of the block itself.

The clinical sample used in the study is composed by patients aged between 15 and 85 years affected by cholelithiasis and treated with laparoscopic cholecystectomy at the Surgical Clinic of the Policlinic University Hospital in Catania in the period between July 2019 and February 2020.

The Ethical Committee of the Policlinico University Hospital in Catania, Italy, approved the study. Written informed consent was obtained from the patients.

The exclusion criteria were: immunodeficiency disorders, chronic use of corticosteroids, non-compensated diabetes mellitus, major morbidity with a life expectancy of less than 30 days, significant anemia (hemoglobin <7 gr/Dl or hematocrit <21%), coagulopathies, ascites, chronic pain treatment, severe comorbidities (atrial fibrillation, pulmonary hypertension, etc.) and any severe comorbidities.

20 patients, 9 men and 11 women, were enrolled.

Group A included 10 patients, 5 men and 5 women, with an average age of 47.9 years. Group B included 10 patients, 4 men and 6 women, with an average age of 50.7 years.

The parameters evaluated were: heart rate (HR), average blood pressure (BP), respiratory frequency (RF), oxygen saturation (SaO2), hemogasanalysis (PaO2, PaCO2, pH and HCO3-).

The measurements were made at four stages: before the induction of anesthesia, after the anesthesia induction but before incision, 30 min after the pneumoperitoneum induction, 5 min after the pneumoperitoneum releasing.

The hemodynamic parameters (HR, RF, BP, SaO2) were extrapolated from the multiparameter monitor for each evaluation. The hemogasanalytic values (PaO2, PaCO2, pH and HCO3) were evaluated by the radial arterial sampling. The average and standard deviation were calculated for the quantitative data normally distributed. For the comparison of the quantitative data, the t-student test was used. A value of $p \leq 0,05$ was considered statistically significant.

The study has been registered in the Research Registry with the number NCT05367557 at the link https://clinicaltrials.gov/show/NCT05367557.

The work is compliant with the CONSORT criteria.

## 3. Results

The two groups were homogeneous for demographic parameters.

Regarding the heart rate, in both groups we observed an initial stability in the values of beats per minute from the first evaluation until the induction of anesthesia. Subsequently, a flexion of beats per minute was observed (Fig. 1). The average trend did not deviate significantly comparing the two groups ($p > 0.05$).

The respiratory rate had a wider oscillation. In the pre-anesthesia evaluation, the group B showed a significantly higher respiratory rate than the group A ($p < 0.05$). During the intervention, there was an increase in respiratory rate in both groups 30 min after the induction of anesthesia. In the last observation, in group A, a further increase in respiratory rate compared to the group B was recorded; on the contrary, in group B it slightly decreased (Fig. 2).

The average blood pressure decreased discontinuously during the intervention in both groups (Fig. 3). In the pre-anesthesia evaluation, the group B had a lower mean blood pressure than the group An until the post-anesthesia evaluation, and slightly increased for the group A. At the end of the operation, we saw a further decrease in the mean blood pressure, which was significantly higher in the group B ($p < 0.05$).

The trend of oxygen saturation from the first to the second stage, increased in both groups, higher in patients of group A. Subsequently, there was a progressive flexion at 30 min from the anesthesia induction and at 5 min after the release of pneumoperitoneum (Fig. 4). Although the major reduction occurred in group B, the difference of the average blood pressure between the two groups of patients was slight, especially 30 min after the induction of anesthesia, and was not statistically significant ($p > 0.05$).

The partial blood pressure of oxygen substantially increased from the first to the second stage. Subsequently, PaO2 decreased 30 min after the induction of the anesthesia, and in the final stage, at the pneumoperitoneum release (Fig. 5). The flexion was significantly greater in group A than in group B ($p < 0.05$).

The partial pressure of carbon dioxide in the arterial blood decreased from the first to the second stage in both groups, settling at lower values in group A. However, during the intervention, PaCO2 increased at 30 min after the induction of anesthesia in group A, and exceeded the average value of PaCO2 of the group B, which instead underwent only a slight increase. At the pneumoperitoneum release, there was a slight decrease of PaCO2 in both groups, which was lower in the group B (Fig. 6).

The pH value decreased in both groups, from the pre-anesthesia stage to the anesthesia induction stage, remaining at slightly lower values in group B. From the 30-min stage until the release of pneumoperitoneum, we saw a reversal of the values in the two groups. In group B, the pH tended to slightly re-establish on higher values, while in group A the pH further decreased and remained within the normal range (Fig. 7).

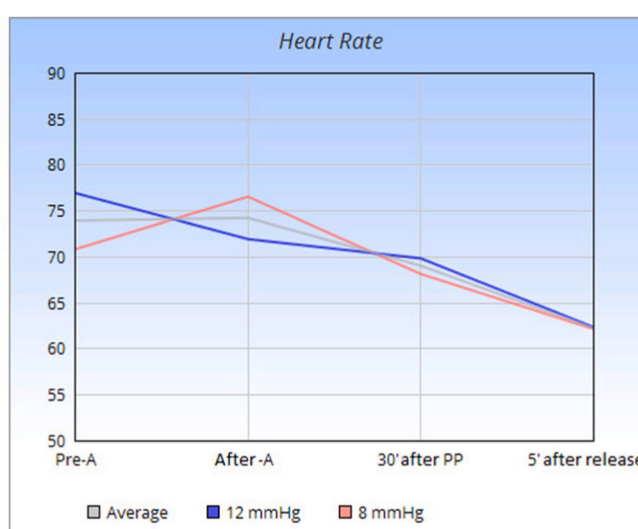


**Fig. 1.** Heart rate.

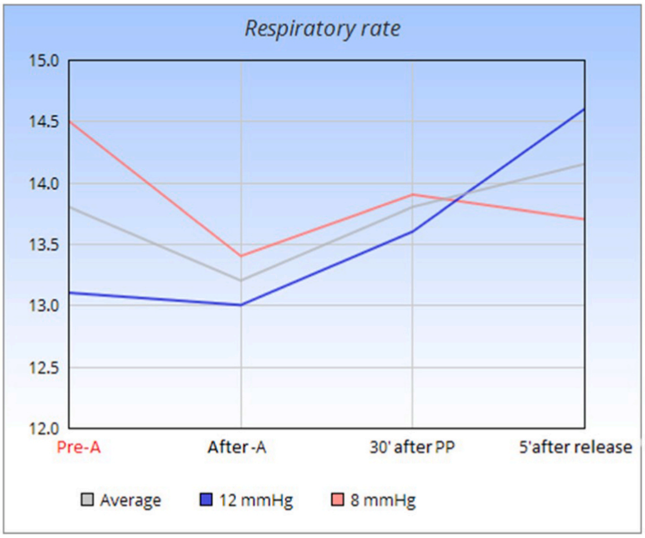


**Fig. 2.** Respiratory rate.

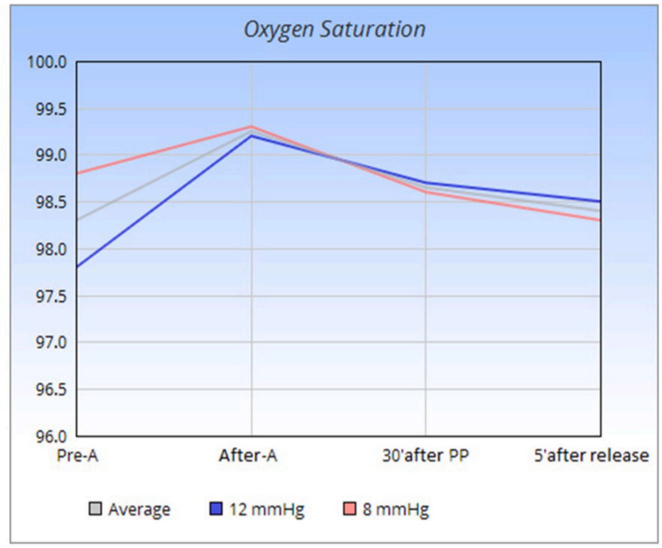


**Fig. 4.** Oxygen saturation rate.

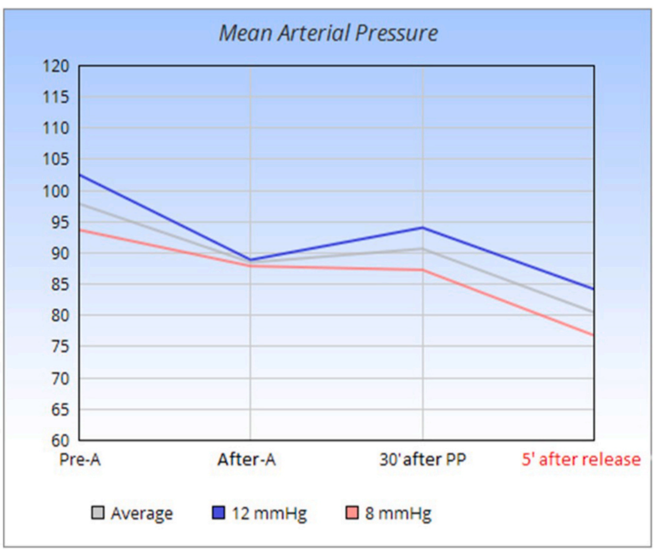


**Fig. 3.** Mean arterial pressure.

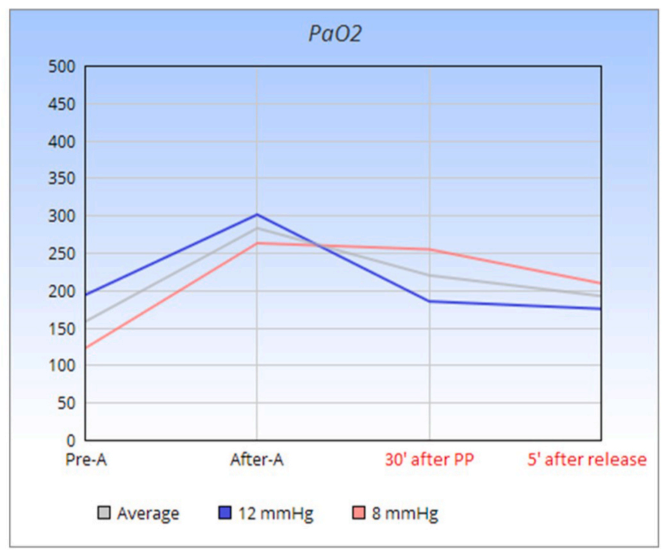


**Fig. 5.** PaO2 rate.

The hydrogen carbonate ion (HCO3-) underwent a non-linear trend. It initially decreased between the first and the second stage, settling at slightly lower levels in group A. Subsequently, in group B, it maintained a stable value up to 30 min from the beginning of the intervention and then slightly flexed at the end of the intervention. In group A, its value rised up to exceed the value of the group B at the observation made 30 min after the pneumoperitoneum induction, and then it decreased at the end of the intervention or at the observation made 5 min after the pneumoperitoneum release with the same trend of the other group (Fig. 8).

## 4. Discussion

During laparoscopic surgery, pneumoperitoneuom and anti-Trendelemburg position are performed to create the intra-abdominal surgical field.

The hemodynamic changes recorded during the laparoscopic technique have a multifactorial origin subsequent to pneumoperitoneum, including the compression on the abdominal aorta, the action of humoral factors including catecholamines, prostaglandins and renin, and the increase in the peripheral vascular resistance.

Increased intra-abdominal pressure is known to have an effect on hemodynamics. These effects include a reduction in cardiac output, changes in the blood circulation of the abdominal organs such as kidney, liver and bowel, an increased risk of deep vein thrombosis and of pulmonary thromboembolism, respiratory effects and even arrhythmias.

The increased return, the increased peripheral vascular resistance, the anti-Trendelemburg position and the increased intra-thoracic pressures can explain the pathophysiology of cardiac output reduction during pneumoperitoneum.

Many Authors have described the hemodynamic variations during laparoscopy.

Joris et al. highlighted a 50% reduction in cardiac index and a substantial increase in systemic and pulmonary peripheral vascular resistance by using a catheter in the pulmonary artery in a group of healthy patients subdue to laparoscopic cholecystectomy [1].

Similarly, in a study conducted by McLaughling et al., there was a statistically significant increase in mean blood pressure, systolic blood pressure, diastolic blood pressure an central venous pressure during laparoscopic cholecystectomy, which reduced the cardiac performance

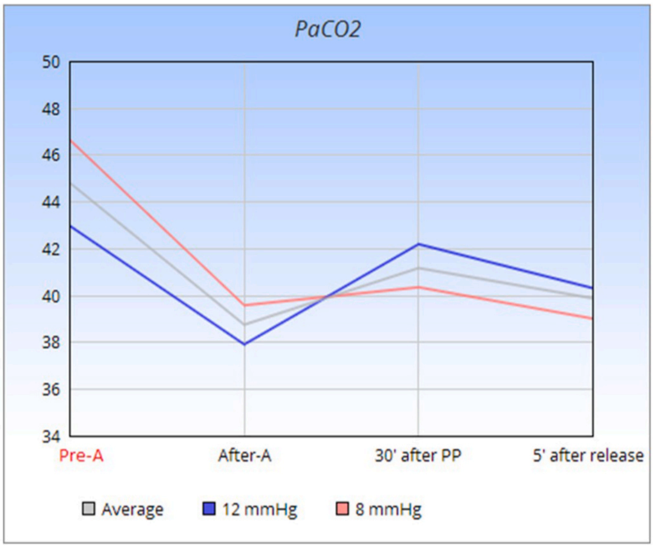


**Fig. 6.** PaCO2 rate.

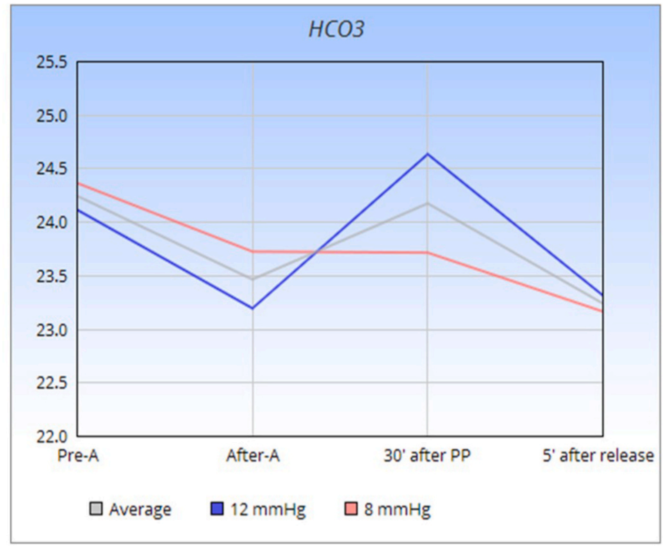


**Fig. 8.** HCO3$^-$ rate.

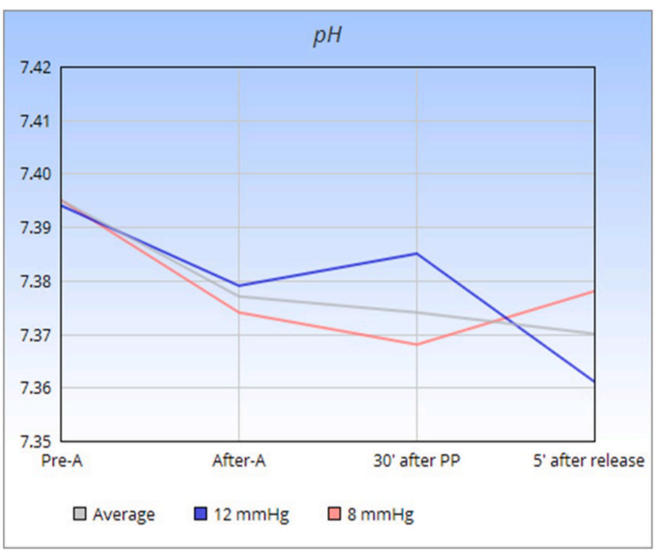


**Fig. 7.** pH Rate.

[2].

Cunningham et al. observed through the *trans*-esophageal echocardiography an important maintenance of the left ventricular output either during CO2 insufflarion or during patient's position changes, but also observed a reduction in the ventricular compliance concurrently with an increased systemic blood pressure during laparoscopic cholecystectomy [6].

A study by Safran et al. reported a significant reduction in cardiac output and an increase in the peripheral vascular resistance in a group of women at high cardiovascular risk, treated laparoscopically for gynecological pathologies [7].

Additionally, the reverse-Tremdelemburg position usually causes a decrease in the cardiac output and blood pressure, and accentuates the hemodynamic changes induced by pneumoperitoneum. The greater the inclination, the greater the fall in cardiac output.

A study by Hainsworth et al. reported that when the angle of inclination reached 30°. The mean blood pressure increased in both Trendelemburg and reverse-Trendelemburg positions [8].

Since the pneumoperitoneum increases the blood retention in the lower limbs, any additional factors involved in circulatory abnormalities should be avoided. Increased intrathoracic pressure, changes in venous return and cardiac function can cause an increase in pulmonary blood pressure. These changes are more evident at the reverse-Trendelembug position than at the Trendelemburg position [9].

The increase in peripheral vascular resistance is strongly linked to the increase of the abdominal pressure. Furthermore, CO2 has also a direct hemodynamic effect on the depression of the cardiac contractility and the dilation of peripheral arterioles.

Intra-abdominal organs are particularly sensitive to these hemodynamic variations. The reduction in blood flow at the mesenteric and renal level would be proportionally greater than the measured cardiac output drop. In a study by Chiu et al., the renal function parameters such as diuresis, renal plasma flow and glomerular filtration rate reached less than 50% of baseline during laparoscopic cholecystectomy and it was significantly lower than those recorded during open cholecystectomy. In addition, diuresis increased significantly after the end of the pneumoperitoneum [9,10].

These hemodynamic changes during pneumoperitoneum highlights the problem of tolerance to these changes by cardiac sick patients.

All surgical procedures are burdened by a non-negligible incidence of thromboembolic complications. Deep vein thrombosis represents one of the most serious complications in patients undergoing abdominal surgery. The most recent cases showed that in the absence of prophylaxis, the frequency of deep vein thrombosis was considerable. A study by Mastrojeni et al. stated that there are no substantial differences in the incidence rate of thromboembolic events between laparoscopic and open sugery, since both the techniques have conditions predisposing for thrombosis: the longer the duration of the laparoscopic surgery, and the longer post-operative bedding in patients subdue to open surgery [3]. In our study, the possible negative effects of the pneumoperitoneum seems to be compensated by the lower thrombogenic activation of the coagulation system during laparoscopy.

Furthermore, the insufflation of CO2 in the abdomen hinders the movement of the diaphragm, causing a decrease in the volume exhaled per minute, with increasing in the CO2 load to be eliminated. Putensen et al. reported a reduction in residual functional capacity with a tendency to atelectasis and an increased alteration in the ventilation/perfusion ratio [11]. Laparoscopic surgery, therefore, is not recommended in sujects with absolute respiratory insufficiency such as decompensated emphysema, because it will complicate an already evident insufficiency, and a careful monitoring of PaCO2 is essential.

Arrhythmias during laparoscopy can have several causes. Increased vagal tone may result from a sudden stretching of the peritoneum and may cause bradycardia, cardiac arrhythmias and asystole. Cardiac irregularities usually occur at an early stage of insufflation, when hemodynamic and pathophysiological changes are more intense. For this reason, arrhythmias can be a wake-up call to intolerance to hemodynamic disorders, especially in patients with known or latent heart disease.

Hemogasanalytic alterations depend on changes in respiratory dynamics and on CO2 absorption by the peritoneum. The increase in intra-abdominal pressure causes a cranial displacement of the diaphragm with compression of the lungs caudal lobes. This phenomenon causes the closure of the small airways and the atelectasis of these lobes, leading to a decrease in pulmonary compliance.

Several studies have shown a 30–50% decrease in the respiratory system compliance in healthy patients during the laparoscopic surgical treatment [12,13]. Nevertheless, in the study of Tan et al., no significant changes in physiological dead space and shunt occurred in patients without cardiovascular dysfunction, at an intra-abdominal pressure of 14 mmHg and the Trendelemburg or Anti-Trendelemburg position [14].

The pneumoperitoneum achieved through CO2 insufflation causes the partial pressure of arterial carbon dioxide to increase. PaCO2 increased progressively up to the plateau at 15–30 min after the onset of the pneumoperitpneum, and this has been seen during gynaecological laparoscopies in Trendelemburg in the study of Mullet et al. [15], and during laparoscopic cholecystectomies in the study of Nyarwaya et al. [16].

During pneumoperitoneum with CO2, the increase in PaCO2 can be multifactorial: direct absorption of CO2 through the peritoneum, impairment of perfusion and pulmonary ventilation by mechanical factors such as abdominal distension, anti-trendelemburg position and ventilation depression caused by anesthetics. The increase in PaCO2 when CO2 is used to induce pneumoperitoneum, is mainly due to gas absorption, rather than being caused by the mechanical repercussions on ventilation given by the increase in intra-abdominal pressure, as stated in the studies by Bongard et al. [17] and Rademaker et al. [18].

Our study evaluated the development of hemodynamic parameters, such as heart rate, respiratory rate, mean blood pressure and oxygen saturation, and of hemogasanalytic parameters, such as PaO2, PaCO2, pH and HCO3-, in two groups of patients subdue to laparoscopic cholecystectomy at pneumoperitoneum pressure respectively of 8 mmHg and 12 mmHg. The insufflation of CO2 in the abdominal cavity caused a reduction in the cardiac output and in the average blood pressure values, changes in hemodinamics and a decrease in the volume exhaled per minute. The increased alteration of the ventilation/perfusion ratio induced hypercapnia and a reduction in pH during pneumoperitoneum, up to respiratory acidosis in extreme cases.

Based on our results, the responses of hemodynamic parameters confirmed the data from the Literature, such as decreased heart rate, respiratory rate and mean blood pressure as well as a slight decrease in oxygen saturation. The flexion of hemodynamic parameters was greater, albeit slightly, in patients treated with 8 mmHg induced pneumoperitoneum.

The data obtained from our study also showed that the hemogasanalytic parameters have followed a trend in agreement with those present in the Literature. The values of PaO2 were higher than normal values, but this increase was attributable to the preventive intubation during surgery and the concomitant administration of O2. However, this increase occurred in both groups. The other hemogasanalytic parameters, as PaCO2, pH and HCO3, also had a trend in direction of acidosis but never reaching serious pictures. In both groups there was a progressive lowering of pH, more pronounced in the 12 mmHg treated group, of PaCO2, more pronounced in the 8 mmHg treated group, and of HCO3 ion, more pronounced in the 8 mmHg treated group.

In conclusion, our study has shown that, although significant differences between the two groups were appreciated on several parameters studied, the variations found were never of such magnitude to prefer the induction of pneumoperitoneum at 8 mmHg which would lead to a lower pH reduction than the group treated at 12 mmHg.

For this reason, being the hemodynamic and hemogasanalytic trends quite similar in the two groups of patients, the surgical technique performed with a pneumoperitoneum pressure of 12 mmHg would be preferable, due to the more facility of maneuvers execution and to the minor complications associated.

The limitation of this study is related to the small size samples, due to the very selective inclusion and exclusion criteria.

## Ethical approval

The study has been approved by the Ethical Committee of the Policlinico University Hospital in Catania, Italy.

## Sources of funding

There are no sources of funding.

## Author contribution

All the Authors contributed to conceptualization, data curation, investigation, methodology and writing. Rosolia Guglielmo and Vecchio Rosario, in addition, supervised and reviewed the manuscript.

## Registration of research studies

1. Name of the registry: ClinicalTrials.gov.
2. Unique Identifying number or registration ID: NCT05367557.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/show/NCT05367557.

## Guarantor

Prof. Rosario Vecchio is the Guarantor of the study.

## Consent

Written informed consent was obtained from the patients for publication of this study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Provenance and peer-review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

None.

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