

Low-pressure pneumoperitoneum could decrease postoperative alterations of hemodynamic variables and pulmonary function tests after laparoscopic cholecystectomy

Tarek Munier,^a MD; Mokhtar Abdelrahman Bahbah,^b MD

a) Department of Anaesthesia and I.C.U, Alazhar University, Cairo, Egypt.

b) Department of General surgery, Benha University, Benha, Egypt.

Abstract

Objectives: To evaluate the impact of pneumoperitoneum on pulmonary functions, hemodynamic variables and frequency and intensity of shoulder tip pain (STP) in patients undergoing laparoscopic cholecystectomy (LC).

Patients & methods: Fifty chronic calcular cholecystitis patients were allocated to high-pressure (HP) group (13-15 mmHg) and low-pressure (LP) group (9-11 mmHg). Mean arterial pressure (MAP), and heart rate (HR) measurements were obtained before (T1), after induction of anesthesia (T2), 5 min. before (T3), after insufflation (T4), 5 min. after tilting in reverse Trendelburg position (T5) and after exsufflation of CO₂ (T6). Duration of surgery, occurrence of intraoperative complications and conversion to laparotomy, time till first ambulation, first oral intake and length of postoperative (PO) hospital stay were recorded. Severity of PO STP was assessed using visual analogue scale at 3, 6, 12, 24, and 48 hours. Forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1) and FEV1/FVC ratio were estimated 24 hours prior to and after surgery.

Results: All patients passed smooth intraoperative course without complications or conversion to laparotomy. Mean operative data showed non-significant difference between both groups. At T4 and T5 HR and MAP measurements were significantly higher in HP group despite the significant difference compared to other measures in both groups. Twenty-three patients had STP with significantly higher frequency and intensity in HP group. Mean duration till request of analgesia was significantly longer in LP group. Pneumoperitoneum altered PO pulmonary function tests compared to preoperative values with significantly altered FEV1 evaluated as the percentage of change in HP group.

Conclusion: Pneumoperitoneum irrespective of the pressure used affects pulmonary function tests and induces hemodynamic changes with precipitation of STP; however LP allowed significant amelioration of these effects despite that it could not abolish it, so it allows getting the advantages of laparoscopic surgery with minimal hazards.

Key words: Pneumoperitoneum, low pressure, pulmonary function tests, shoulder tip pain.

Introduction:

Laparoscopic surgery has gained popularity in clinical practice; the fundamental differences between laparoscopic and open surgical approaches are the methods of access and exposure. Surgical access is generally obtained through an upper midline, right paramedian or Kocher's incision in open surgery and through four abdominal trocars in laparoscopic surgery. Surgical exposure of the operative field is

commonly performed using abdominal wall retractors in open surgery compared with carbon dioxide (CO₂) pneumoperitoneum in laparoscopic surgery.¹

The key element in laparoscopic surgery is creation of pneumoperitoneum and carbon dioxide is commonly used for insufflation. This pneumoperitoneum perils the normal cardiopulmonary system to a considerable extent. The physiologic effects of

pneumoperitoneum include systemic absorption of CO₂ and hemodynamic and physiologic alteration in a variety of organs due to the increased intra-abdominal pressure. CO₂ absorption across the peritoneal surface into systemic circulation can result in hypercarbia and eventual systemic acidosis. The increased intra-abdominal pressure during pneumoperitoneum has been shown to result in hemodynamic alteration and changes in femoral venous flow and renal, hepatic, and cardiorespiratory function.²⁻⁵

Minimized postoperative pain is one of the advantages of laparoscopic surgery; however, shoulder pain is considered one of distressing effects of pneumoperitoneum. Some authors maintain that it may be the result of diaphragmatic irritation of a chemical nature caused by the insufflated CO₂. Carbon dioxide may be transformed, by combining with fluid in the peritoneal cavity, to an irritative carbonic acid.⁶ However, Wallace et al.⁷ believed that shoulder pain after laparoscopy could be caused by overstretching of the diaphragmatic muscle fibers owing to the high rate of insufflations and so it would be the volume of the gas utilized for pneumoperitoneum that is causing diaphragmatic irritation.

Pneumoperitoneum increases pressure on the diaphragm, leading to its cephalic displacement and thereby decreasing venous return, which can be aggravated by the position of patient during surgery. Also, cephalic diaphragmatic displacement leads to alteration of pulmonary mechanics.⁸ Various therapeutic modalities were provided for minimization of the impact of pneumoperitoneum on general patients' condition and pneumoperitoneum-induced shoulder pain. Alijani et al.⁹ found that abdominal wall lift approach avoids fall in cardiac output associated with positive-pressure capnoperitoneum during laparoscopic surgery and is associated with a more rapid recovery of postoperative cognitive function compared with positive-pressure capnoperitoneum. However, abdominal wall lift increases the level of difficulty in the execution of the operation. Recent studies supported the need for pneumoperitoneum Azevedo et al.¹⁰ reported that the values of inter-peritoneal pressure and volume of insufflated gas at given time points during insufflation for creation of

the pneumoperitoneum, using the Veress needle, can be effective parameters to determine whether the needle is correctly positioned in the peritoneal cavity.

Thus, the current study aimed to evaluate the impact of steadily adjusted intra-peritoneal pressure on pulmonary functions, hemodynamic variables and frequency and intensity of shoulder tip pain in patients assigned for laparoscopic cholecystectomy.

Patients and methods:

The study comprised 50 chronic calculous cholecystitis patients of ASA grade I and II, assigned to undergo laparoscopic cholecystectomy at Algedaany group under Ibn Sina International Medical College throughout the period since May 2010 till and Jan 2012. Patients with cardiopulmonary diseases, renal or liver impairment or allergy to any of the used drugs were excluded from the study. Morbidly obese patients with body mass index (BMI) >35 kg/m² were not enrolled in the study. Patients who required emergency cholecystectomy or exploration of common bile duct were also excluded.

Patients were randomly, using sealed envelopes, allocated in two groups: high-pressure group (HP Group): consisted of 25 patients assigned to undergo LC under high intraperitoneal pressure ranging between 13-15 mmHg throughout the procedure and low-pressure group (LP Group): consisted of 25 patients assigned to undergo LC under low intraperitoneal pressure ranging between 9-11 mmHg.

All patients were premedicated with dormicum 3 mg, fentanyl 2 µg/kg IV given 5 minutes before induction of anesthesia. Before induction, patients were preoxygenated and base line mean arterial blood pressure (MAP), heart rate (HR), respiratory rate (RR) and peripheral arterial O₂ saturation (SaO₂) were recorded. Anaesthesia was induced with thiopentone 3-5 mg/kg and atracurium 0.5mg/kg. The trachea was intubated 3 min after administration of atracurium. Ventilation was controlled and minute ventilation was adjusted to maintain end tidal CO₂ at 35±5mmHg. Anaesthesia was maintained with 50/50 N₂O/O₂ supplemented with isoflurane 1.2%, and top up doses of neuromuscular

blocking agents were used as required. The patients received lactated Ringer's solution at a rate of 10 ml/kg/hr during anaesthesia and 2ml/kg/hr after anaesthesia until they tolerated oral fluids. At the end of surgery, atropine sulphate 0.02 mg/kg and neostigmine 0.04 mg/kg were administered I.V. for reversal of muscle relaxation and the trachea was extubated. Following extubation patients were maintained on supplemental O₂ until awake in the recovery room.

Laparoscopic cholecystectomy was performed according to the European "four-puncture" technique described by Dubois, et al.¹¹ The surgical technique involved intraperitoneal insufflation of CO₂ via Veress needle inserted into a small umbilical incision in the 15-20° Trendlenburg's position. An electronic variable-flow insufflator terminated when the intra-abdominal pressure reached 15mmHg. A cannula was inserted in place of the needle to provide and maintain intra-abdominal pressure of 13-15 mmHg in HP group, while in LP group, after a short duration of high pressure, low-pressure of 9-11 mmHg was maintained all the time of surgery. A video laparoscope was inserted through the cannula and the operative field was seen. The patient's position was changed to steep reverse Trendlenburg position (RTP), with a lateral tilt to facilitate retraction of the gall bladder fundus.

Intraoperative non-invasive monitoring included MAP, HR, RR and SaO₂. Measurements were obtained before induction of anaesthesia (T₁), after induction of anaesthesia (T₂), 5 min. before insufflation (T₃), 5 min. after insufflation (T₄), 5 min. after tilting in RTP (T₅), and after exsufflation of CO₂ (T₆). Duration of surgery and occurrence of bile spillage during operation, and the need to shift to open surgery were recorded.

The severity of postoperative shoulder-tip pain was assessed by means of a 100-point pain visual analogue scale (VAS) at 3, 6, 12, 24, and 48 hours after surgery with 0: no pain and 100: unbearable pain. Patients were asked to mark a point along the scale that represented their STP, at that time not to represent their generalized discomfort or wound pain. Duration till first request of postoperative rescue

analgesia was determined; postoperative rescue analgesia was provided in the form of intravenous lornoxicam 8 mg whenever patients request analgesia. Time till first ambulation, first oral intake and length of postoperative hospital stay were recorded.

Pulmonary function studies:

Pulmonary studies were performed with the patient in the sitting position, according to the guidelines of the American Thoracic Society.¹² Measurements were conducted the day before surgery and 24 hours after surgery. Estimated variables included forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV₁) and the FEV/FVC ratio were calculated.

Statistical analysis:

Results were expressed as mean±SD, range, numbers and percentages. Inter-group analysis was examined using Wilcoxon's Ranked test for related data (Z test). Statistical analysis was conducted using SPSS statistical program, (Version 10, 2002). P value <0.05 was considered statistically significant.

Results:

The study included 50 chronic cholecystitis patients; 11 males and 39 females with mean age of 37±8.8; range: 25-52 years and mean BMI of 32.1±2; range: 28.3-34.8 kg/m². There was non-significant (p>0.05) difference between both groups as regards enrollment data, **Table(1)**. All patients passed smooth intraoperative course without complications and no conversion to laparotomy.

Mean operative time was 44.9±5.6; range: 35-55 minutes, mean time till first ambulation was 2.3±1; range: 1-5 hours and mean time for first oral intake was 4.6±1.3; range: 2-7 hours with non-significant difference between both groups, but in favor of LP group. Mean postoperative hospital stay of HP group was 1.8±0.8 days and was significantly (Z=2.646, p=0.008) longer compared to hospital stay duration; 1.4±0.8 days in LP group. Moreover, the frequency of patients who required longer hospital stay was significantly (X²=6.112, p<0.05) higher in HP group compared to LP group, **Table(2)**.

Table (1): Patients enrollment data.

	HP group	LP group	Total
Age (years)	37.8±8.5 (26-51)	36.1±9.2 (25-53)	37±8.8 (25-53)
Sex; M:F	20:5	19:6	39:11
Weight (kg)	84.2±6.5 (75-92)	83.6±7.7 (72-93)	83.9±7 (72-93)
Height (cm)	161.6±3.8 (155-167)	161.8±4.2 (156-172)	161.7±3.9 (155-172)
BMI (kg/m ²)	32.2±2.1 (28.3-34.8)	31.9±1.9 (28.5-34.3)	32.1±2 (28.3-34.8)

Data are presented as mean±SD & ratio; ranges are in parenthesis.

Table (2): Operative and postoperative data.

	HP group	LP group	Total
Operative time (min)	44.2±5.7 (35-50)	45.6±5.6 (37-55)	44.9±5.6 (35-55)
Time till 1st ambulation (hr)	2.5 (1-5)	2±0.7 (1-3)	2.3±1 (1-5)
Time till 1st oral intake (hr)	4.8±1.4 (3-7)	4.4±1.2 (2-6)	4.6±1.3 (2-7)
Hospital stay (days)	1-day	11 (44%)	17 (68%)
	2-day	10 (40%)	5 (20%)
	3-day	3 (12%)	2 (8%)
	4-day	1 (4%)	1 (4%)
	Total	1.8±0.8	1.5±0.8

Data are presented as mean±SD & numbers; ranges & percentage are in parenthesis.

Both HR and MAP showed similar changes in both groups due to induction of anesthesia with non-significant ($p>0.05$) difference between both groups at T1-3, while at 5-minutes after CO₂ insufflation (T4) and 5-minutes after

RTP positioning (T5), both HR and MAP were significantly ($p<0.05$) higher in HP group compared to LP group despite the significant ($p<0.05$) difference compared to other measures in both groups, **Table(3)**, **Figure(1)**.

Table (3): Heart rate and MAP changes recorded throughout duration of surgery.

Time	HR (beats/min)		MAP (mmHg)	
	HP group	LP group	HP group	LP group
T1	78.9±5	78.7±4.7	91.3±4.5	90.6±5.3
T2	82.7±5.2	81±4.8	90.2±4.4	89.2±5.2
T3	80.3±5.1	80.6±4.8	88.3±4.3	86±5
T4	84.9±3.2	82.1±3.3*	97.4±5.7	92±5.4*
T5	87±3	83.7±2.9*	98.3±5.8	93.1±4.6*
T6	75.3±3.4	76.2±3.5	92.8±4.5	92±5.4

Data are presented as mean±SD.

*: significant versus HP group.

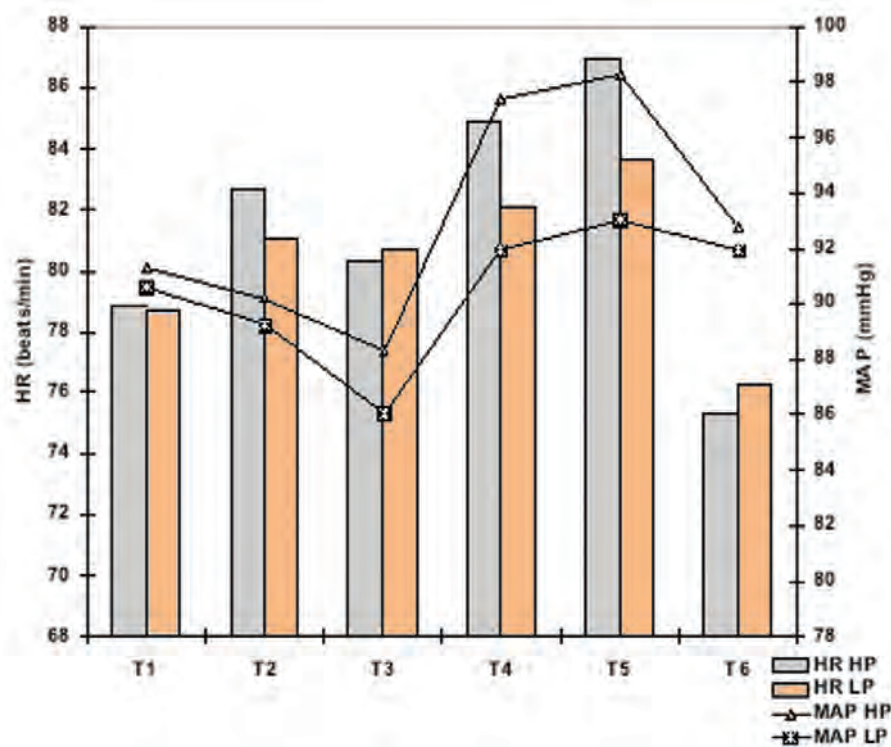


Figure (1): Mean HR and MAP changes throughout operative time.

Shoulder tip pain (STP) was reported in 23 patients (46%) in both groups; 14 in HP and 9 in LP group with significantly ($X^2=3.019$, $p<0.05$) higher frequency of STP in HP group compared to LP group. Seventeen patients had right STP, while 6 patients had fleeting pain between both shoulders with non-significant ($X^2=1.995$, $p>0.05$) difference between both groups. Two patients in HP group required rescue analgesia for 3 times, 7 patients; 5 in

HP and 2 in LP groups, requested it twice and 14 patients requested it once with significant ($X^2=5.217$, $p<0.05$) difference in favor of LP group. Mean total STP score at time of discharge was significantly higher ($Z=2.704$, $p=0.007$) in HP group compared to LP group. Moreover, among patients who had STP, the mean duration till request of analgesia was significantly ($Z=2.236$, $p=0.025$) longer in LP group compared to HP group.

Table (4): Postoperative STP data .

		HP group	LP group	Statistical analysis
Frequency of STP	Yes	14 (56%)	9 (36%)	$X^2=3.019$, $p<0.05$
	No	11 (44%)	16 (64%)	
Number of requested rescue analgesia	Once	7 (28%)	7 (28%)	$X^2=5.217$, $p<0.05$
	Twice	5 (20%)	2 (8%)	
	Thrice	2 (8%)	0	
Total STP score		26.4 ± 12.6	21.8 ± 10	$Z=2.704$, $p=0.007$
Duration till request of analgesia		3.9 ± 1.4	5 ± 1.5	$Z=2.236$, $p=0.025$

Data are presented as mean \pm SD & numbers; ranges & percentage.

Pneumoperitoneum, irrespective of pressure applied, altered pulmonary function tests estimated 24-hr after the end of surgery compared to its preoperative values. As regards the impact of pressure applied, HP significantly altered the forced expiratory volume in 1 sec

evaluated as the percentage of change of postoperative FEV1 in HP group compared to LP group, **Figure(2)** with non-significant changes of FVC inducing significant change of FEV1/FVC ratio at 24-hr after surgery and as percentage of change, **Table(3)**, **Figure(3)**.

Table (5): Postoperative pulmonary function tests compared to preoperative tests.

		HP group	LP group	Statistical analysis
FEV1	Preoperative	2.88±0.91	2.68±0.79	Z=0.806, p>0.05
	24-hr PO	1.97±0.45	2.35±0.69	Z=1.762, p>0.05
		t=7.418, p<0.001	t=5.249, p<0.001	
	% of change	(-45.5)±26.4	(-12)±10.4	Z=3.431, p=0.001
FVC	Preoperative	3.4±0.93	3.32±1.07	Z=0.206, p>0.05
	24-hr PO	3.13±0.82	3.11±0.93	Z=0.067, p>0.05
		t=10.035, p<0.001	t=5.691, p<0.001	
	% of change	(-8.4)±2.94	(-5.57)±4.87	Z=1.709, p>0.05
FEV1/FVC	Preoperative	0.85±0.13	0.83±0.16	Z=0.343, p>0.05
	24-hr PO	0.64±0.08	0.76±0.11	Z=3.673, p<0.001
		t=6.955, p<0.001	t=3.148, p=0.004	
	% of change	(-34)±23	(-6.7)±11.3	Z=3.404, p=0.001

Data are presented as mean±SD.

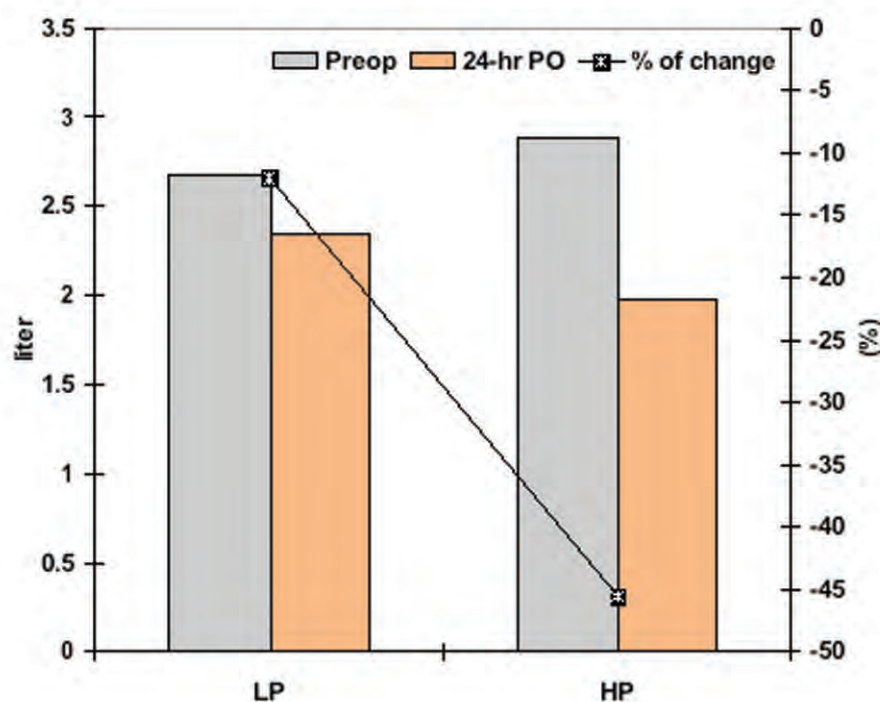


Figure (2):Mean preop and PO FEV1 with reference to percentage of change.

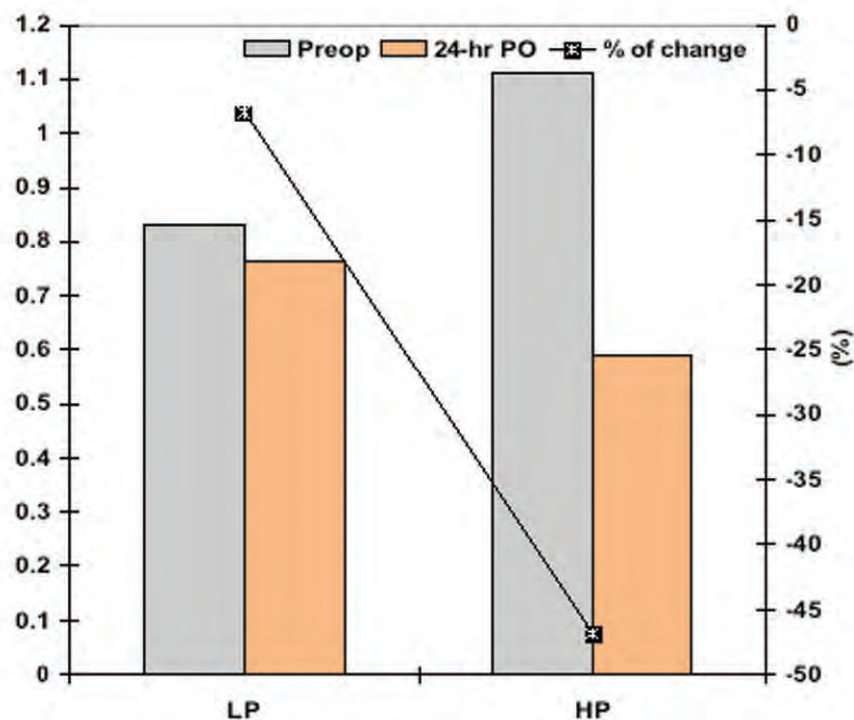


Figure (2): Mean preop and PO FEV1/FVC with reference to percentage of change.

Discussion:

Laparoscopic surgery nowadays is going to be the first choice in surgical management of various diseases and should be performed especially with well-trained laparoscopic surgeons. Laparoscopic surgery provides many advantages including short convalescence time and consequently hospital stay and sparing many side effects related to prolonged recumbency as development of phlebitis and chest infection and decreased the frequency of the possibility of nosocomial infections.¹³⁻¹⁶ However, no procedure was immune to complications or at least side effects; elevated intra-abdominal pressure hampers diaphragmatic movement with subsequent impairment of respiration and hemodynamic alterations and postoperative shoulder pain are the commonest side effects of laparoscopic surgery. Considering laparoscopic cholecystectomy as the standard procedure for evaluation of laparoscopic surgery especially for being the first procedure settled for laparoscopic approach, the current study tried to evaluate the impact of pneumoperitoneum insufflations pressure on hemodynamic variables, pulmonary function tests and shoulder pain.

At 5-minutes after CO₂ insufflations and at

5-minutes after RTP positioning, both HR and MAP were significantly higher in both groups compared to their previous measurements with significantly higher measures in HP group compared to LP group. Shoulder tip pain was reported in 46% of studied patients with significantly higher frequency and severity scores in HP group compared to LP, and among patients who had STP, the mean duration till request of analgesia was significantly longer in LP group compared to HP group. Thirdly, pneumoperitoneum, irrespective of pressure applied altered pulmonary function tests estimated 24-hr after end of surgery compared to its preoperative values and high pressure significantly altered the FEV1 evaluated as the percentage of change in HP group compared to LP group.

These findings indicated the impact of pneumoperitoneum on hemodynamic variables, initiation of STP and altering pulmonary function tests and such effect was pressure related as it is more pronounced by high pressure versus low pressure. These data go in hand with Joshipura et al.¹⁷ who found low pressure laparoscopic cholecystectomy significantly advantageous in terms of postoperative pain, use of analgesics, preservation of pulmonary function and hospital

stay. Sandhu et al.¹⁸ reported that low-pressure pneumoperitoneum tended to be better than standard-pressure pneumoperitoneum in terms of lower incidence of shoulder tip pain. Ekici et al.¹⁹ detected statistically significant increases of QT dispersion (QTd), and the corrected QT dispersion (QTcd), which are associated with an increased risk of arrhythmias and cardiac events during CO₂ insufflation in both high-pressure and low-pressure pneumoperitoneum with significantly higher changes in the high-pressure pneumoperitoneum group. Sandoval-Jimeez et al.²⁰ reported that low-pressure pneumoperitoneum significantly reduces abdominal and shoulder tip pain compared to standard pressure. Kandil & El-Hefnawy²¹ observed a significant difference in the prevalence of pain at different pressures and recommended the use of the lower pressure technique during LC.

In support of the advantages of low pressure pneumoperitoneum, Li et al.²² experimentally tried to determine the degree of impact of low and high pneumoperitoneum on liver and found CO₂ of 15 mmHg caused more substantial hepatic injury, such as increased levels of acidosis, mitochondrial damage, and apoptosis compared to pressure of 10 mmHg. Matsuzaki et al.²³ evaluated the impact of intraperitoneal pressure and duration of pneumoperitoneum on the peritoneal fibrinolytic system during laparoscopic surgery and found low intraperitoneal pressure and shorter duration of surgery appear to minimally impact the fibrinolytic system during a CO₂ pneumoperitoneum. Topal et al.²⁴ tried to determine the influence of the pneumoperitoneum at 10, 13, and 16 mmHg in laparoscopic cholecystectomy on thromboelastograph as an indication of platelet function and liability for operative site bleeding and found pneumoperitoneum at pressures of 10 and 13 mm Hg did not alter the thromboelastographic values which were significantly altered with pressure of 16 mmHg in comparison to other pressure values and recommended low intra-abdominal pressure for peritoneal insufflation for laparoscopic surgeries.

It could be concluded that pneumoperitoneum irrespective of pressure

used affects pulmonary function tests and induces hemodynamic changes with precipitation of shoulder tip pain. However, low pressure allowed significant amelioration of these effects compared to high pressure but could not abolish it. Low-pressure pneumoperitoneum is an appropriate modality to lessen pneumoperitoneum effects so as to get the advantages of laparoscopic surgery with minimal hazards and is advocated for being the standard and surgeons must try to acclimatize to work using low pressure pneumoperitoneum.

References:

- 1- Bosch F, Wehrman U, Saeger HD, Kirch W: Laparoscopic or open conventional cholecystectomy: Clinical and economic considerations. *Eur J Surg* 2002; 168: 270-277.
- 2- Sato K, Kawamura T, Wakusawa R: Hepatic blood flow and function in elderly patients undergoing laparoscopic cholecystectomy. *Anesth Analg* 2000; 90(5): 1198-1202.
- 3- Uemura N, Nomura M, Inoue S, Endo J, Kishi S, Saito K, Ito S, Nakaya Y: Changes in hemodynamics and autonomic nervous activity in patients undergoing laparoscopic cholecystectomy: Differences between the pneumoperitoneum and abdominal wall-lifting method. *Endoscopy* 2002; 34(8): 643-650.
- 4- Andersson L, Lindberg G, Bringman S, Ramel S, Anderberg B, Odeberg-Wernerman S: Pneumoperitoneum versus abdominal wall lift: Effects on central haemodynamics and intrathoracic pressure during laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2003; 47(7): 838-846.
- 5- Nguyen NT, Anderson JT, Budd M, Fleming NW, Ho HS, Jahr J, Stevens CM, Wolfe BM: Effects of pneumoperitoneum on intraoperative pulmonary mechanics and gas exchange during laparoscopic gastric bypass. *Surg Endosc* 2004; 18(1): 64-71.
- 6- Nyerges A: Pain mechanisms in laparoscopic surgery. *Semin Laparosc Surg* 1994; 1: 215-218.
- 7- Wallace DH, Serpell MG, Boxter JN, O'dwyer PJ: Randomized trial of different insufflations pressures for laparoscopic

- cholecystectomy. *Br J Surg* 1997; 84: 455-458.
- 8- Srivastava A, Niranjan A: Secrets of safe laparoscopic surgery: Anesthetic and surgical considerations. *J Minim Access Surg* 2010; 6(4): 91-94.
 - 9- Alijani A, Hanna GB, Cuschieri A: Abdominal wall lift versus positive-pressure capnoperitoneum for laparoscopic cholecystectomy: Randomized controlled trial. *Ann Surg* 2004; 239(3): 388-394.
 - 10-Azevedo JL, Azevedo OC, Sorbello AA, Becker OM, Hypolito O, Freire D, Miyahira S, Guedes A, Azevedo GC: Intraperitoneal pressure and volume of gas injected as effective parameters of the correct position of the Veress needle during creation of pneumoperitoneum. *J Laparoendosc Adv Surg Tech A* 2009; 19(6): 731-734.
 - 11-Dubois F, Icard P, Berthelot G, Levard H: Coelioscopic cholecystectomy preliminary report of 36 cases. *Ann Surg* 1995; 211: 60-62.
 - 12-American Thoracic Society: Standardization of spirometry: 1987 update. *Am Rev Resp Dis* 1987; 136: 1285-1298.
 - 13-Nguyen NT, Hinojosa MW, Fayad C, Varela E, Konyalian V, Stamos MJ, Wilson SE: Laparoscopic surgery is associated with a lower incidence of venous thromboembolism compared with open surgery. *Ann Surg* 2007; 246(6): 1021-1027.
 - 14-Iaria M, Capocasale E, Dalla Valle R, Mazzoni MP, Sianesi M: Laparoscopic versus open donor nephrectomy. An appraisal on surgical outcome and post-operative course. *Ann Ital Chir* 2009; 80(6): 449-451.
 - 15-Nguyen NT, Slone J, Reavis K: Comparison study of conventional gastric banding versus laparoendoscopic single site gastric banding. *Surg Obes Relat Dis* 2010; 6(5): 503-507.
 - 16-Pither S, Bayonne Manou LS, Mandji Lawson JM, Tchantchou TD, Tchoua R, Ponties JP: Surgical approaches to hysterectomy. *Sante* 2011; 21(2): 79-81.
 - 17-Joshipura VP, Haribhakti SP, Patel NR, Naik RP, Soni HN, Patel B, Bhavsar MS, Narwaria MB, Thakker R: A prospective randomized, controlled study comparing low pressure versus high pressure pneumoperitoneum during laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2009; 19(3): 234-240.
 - 18-Sandhu T, Yamada S, Ariyakachon V, Chakrabandhu T, Chongruksut W, Ko-iam W: Low-pressure pneumoperitoneum versus standard pneumoperitoneum in laparoscopic cholecystectomy, a prospective randomized clinical trial. *Surg Endosc* 2009; 23(5): 1044-1047.
 - 19-Ekici Y, Bozbas H, Karakayali F, Salman E, Moray G, Karakayali H, Haberal M: Effect of different intra-abdominal levels on QT dispersion in patients undergoing laparoscopic cholecystectomy. *Surg Endosc* 2009; 23(11): 2543-2549.
 - 20-Sandoval-Jimeez Ch, Medez-Sashida G, Cruz-Márquez-Rico L, Cárdenas-Victorica R, Guzmán-Esquivel H, Luna-Silva M, Dáaz-Valero R: Postoperative pain in patients undergoing elective laparoscopic cholecystectomy with low versus standard-pressure pneumoperitoneum. A randomized clinical trial. *Rev Gastroenterol Mex* 2009; 74(4): 314-320.
 - 21-Kandil TS, El Hefnawy E: Shoulder pain following laparoscopic cholecystectomy: Factors affecting the incidence and severity. *J Laparoendosc Adv Surg Tech A* 2010; 20(8): 677-682.
 - 22-Li J, Liu YH, Ye ZY, Liu HN, Ou S, Tian FZ: Two clinically relevant pressures of carbon dioxide cause hepatic injury in a rabbit model. *World J Gastroenterol* 2011; 17(31): 3652-3658.
 - 23-Matsuzaki S, Botchorishvili R, Jardon K, Maleysson E, Canis M, Mage G: Impact of intraperitoneal pressure and duration of surgery on levels of tissue plasminogen activator and plasminogen activator inhibitor-1 mRNA in peritoneal tissues during laparoscopic surgery. *Hum Reprod* 2011; 26(5): 1073-1081.
 - 24-Topal A, Celik JB, Tekin A, Yüceaktas A, Otelcioglu S: The effects of 3 different intra-abdominal pressures on the thromboelastographic profile during laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2011; 21(6): 434-438.