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ANALYSIS OF PHYSIOLOGICAL RESPONSE TO A SURGICAL TRAUMA WITH LAPAROSCOPIC AND OPEN CHOLECYSTECTOMY (a prospective randomized study)

SUMMARY

By monitoring the post laparoscopic cholecystectomy (LC) & open cholecystectomy (OC) cortisolemia we have objectified neuroendocrine reaction to a surgical trauma and confirmed the LC is a weaker stimulus for cortisol secretion. Recorded higher and prolonged post OC cortisolemia is consonant with the intensity of the surgical trauma. Our study suggests that the laparoscopic approach in the perioperative period results in the diminished neurodocrine response to the surgical trauma. As for the indicators of the muscular-tissue destruction, we have shown that the LC represents the smaller surgical trauma, i.e. during OC, lesions of tissues rich with CK, AST, ALT enzymes (skeleton muscules, liver) are more pronounced. The results of both gas analysis of capillary blood and spirometry suggest the following advantages of the LC: 1–less decline of pCO_2 postoperative values 2–better O_2 saturation, 3–improved postoperative spirometry, meaning less and shorter disturbance of pulmonary function. The laparoscopic surgery, however, involving CO_2–pneumoperitoneum, can lead to undesired hemodynamic effects and significant complications. With more abdominal surgeries performed by laparoscopic technique, it became clear that surgeons must be more informed and aware of disadvantages, taking corresponding measures to prevent possible Co_2–pneumoperitoneum related complications.

Key words: **laparoscopic cholecystectomy, neuroendocrine reaction, physiological response**

INTRODUCTION

Medicine is a science which has constantly been changing and its history represents an everlasting struggle against disease, pain and suffering. In that, however, surgeons have been using instruments and methods leaving wounds and pain after them. What is evident is a strange symbiosis of opposites, so although a patient sees salvation from his disease, he, at the same time, fears the surgeon and his knife. That is why medicine is in a continuous and persistent search for treatment methods which are minimally invasive to a patient's body. Thus, at the end of the 20th century, the development of medical technology led to revolutionary changes in surgery by the introduction of laparoscopic surgical technique.

The laparascopic approach to digestive diseases has a short history. It owes its origin and development to gynecology and urology. At the beginning of the 1950s, laparoscopy was a purely explorative technique, and as the time went by, it developed into an operative method. The first laparoscopic operation was appendectomy carried out by a gynecologist Kurt Semm in 1983. At that time no one was visited with the idea to perform cholecyste-

ctomy in a laparoscopic manner because it had been carried out as an open cholecystectomy (OC) successfully for over one hundred years, and it had almost reached the level of perfection. The first OC was performed by Carl Langenbuch in 1882, and then he set an important principle: the gallbladder should be removed not because it contains calculi but because it forms them. The first successful laparoscopic cholecystectomy (LC) was performed by a French surgeon, Phillipe Mouret, in Lion, in 1987. That operation entered the history of surgery together with a laparoscope as a new surgery symbol, which, for the patient, represents the victory over surgical wound and pain.

The increasing application of a 'laparoscopic approach in the surgical treatment of cholelithiasis is the result of numerous advantages of this technique over the OC, the most significant being: the reduced surgical morbidity in the immediate postoperative stage, less postoperative pain, minimal postoperative immobility of the patient, shorter hospitalization time, avoided cosmetic defects by eliminated of laparotomy, less frequent postoperative ileus and less incidence of abdominal adhesions and smaller metabolic response to stress; it is also more economical because of both shorter hospitalization of the patient and his faster return to work (1–7).

On the basis of many experimental and clinical researches, the LC has been evaluated from various aspects. In our opinion the presented facts obviously necessitate a global evaluation of the LC vs OC, with the emphasis on the analysis of physiological responses to various levels of surgical trauma and influences of laparoscopic surgery (LC) on chemodynamic parameters.

AIMS

The evaluation of laparoscopic cholecystectomy (LC) in relation to open cholecystectomy (OC) in the surgical treatment of symptomatic cholelithiasis. We based our research on the analysis of physiological response of the body to the LC and OC as different forms of a surgical trauma, as well as on the global analysis of specific intra–and postoperative parameters. In order to reach our aim objectively, we made a comparative, quantitative and qualitative analysis of the following parameters:

1. Quantitative analysis of the postoperative values of cortisol, as the parameter of neuroendocrine response to the postoperative stress (the results compared after the LC and OC);

2. Quantitative analysis of postoperative values of creatine-kinase (CK, transaminase (AST, ALT), Na and K, as the indicators of muscular-tissue destruction and the metabolic response to the surgical trauma (the comparison of results after the LC and OC);

3. Analysis of chemodynamic response as well as the potentially beneficial influences of the LC to the postoperative cardiopulmonary function, in contrast to the harmful intrasurgical influences of the CO_2 – pneumoperitoneums, based on pre- and postoperative value comparisons of gas analyses of capillary blood and spirometry.

MATERIAL AND METHODS

Our prospective randomized study comprised 100 patients with symptomatic cholelithiasis. Using the random choice method, two groups of 50 patiens were formed. One group was treated by the laparoscopic surgery, and the other by the conventional - open method. In relation to the pre- intra- and postoperative status, a comparable homogenization of samples was made, pursuant to the previously determined protocol.

On the surgery day, at 6 PM, a vein blood sample was taken from all patients to determine cortisol, creatine-kinase *(CK),* transaminase *(AST, ALT)*, Na, K. These values were compared with the tested and the control group in order to evaluate the neuroendocrine and metabolic response to the operative stress, as well as to test the parameters of muscular-tissue destruction. The cortisol level was also monitored with both groups of patients on the first postoperative day, at 10 AM (circadian rhythm of the cortisol was respected, being higher in the later half of the sleep, between 3 and 9 o'clock). DELFIA system - flouroimmunoassay was used for the determination of cortisol.

On the surgery day, at about 6 PM, all patients underwent gas analyses of capillary blood from mechanically hypermicized lobus of auricle. The values of pH, pCO_2, pO_2, O_2 saturation and HCO_3 were monitored and compared both between the groups and with the preoperative values, in order to evaluate the influence of the LC and OC on the postoperative cardiopulmonary function.

Spirometry was carried out with both groups on the first and the fifth postoperative days. The following parameters were monitored and mutually compared: vital capacity (VC), forced vital capacity (FVC), forced expiry volume in the first second (FEV-1), Tiffeneau's index (100 FEV-1/FVC) and the forced expiratory flow between 25–75% FVC (FEF_{25-75}). The VC and FVC are the tests to determine possible restrictive obstacles to ventilation; FEV-1 and Tiffeneau's index determine the obstructive changes in the larger bronchial tubes, and the FEF_{25-75} is a test to determine obstructive obstacles in the smaller bronchial tubes. On the basis of these parameters, the potential beneficial influences of the LC to the pulmonary function were evaluated, against the harmful influences of CO_2 – pneumoperitoneums during this surgery.

RESULTS

Neuroendocrine response to a surgical trauma

Cortisol postoperative values in serum:
I –On the surgery day;
II –The 1st postoperative day.

In an attempted objectification of neuroendocrine response to a surgical trauma by monitoring cortisol level in serum, we found increased values with both groups, though with the OC group they were statistically not only substantially higher ($p<0.01$) but also longer lasting which manifested in its more sluggish decrease on the 1st postoperative day (figures 1–5).

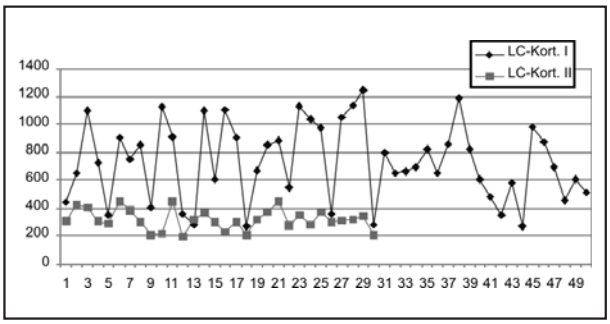

Figure 1. Post LC cortisolemia

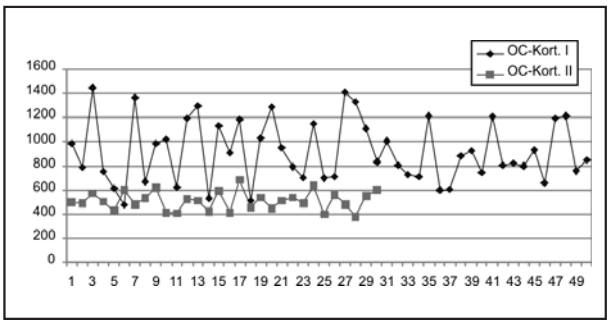

Figure 2. Post OC cortisolemia

Comparision post LC & OC cortisolemia:

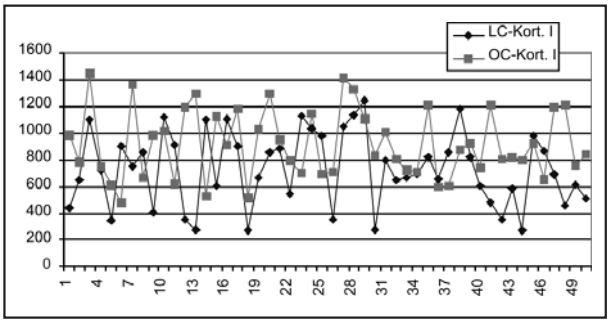

Figure 3. Comparision post LC & OC cortisolemia on the surgery day

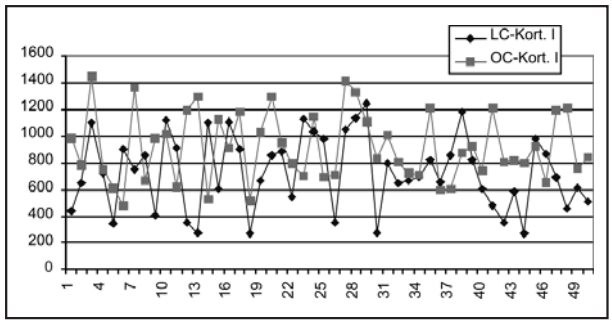

Figure 4. Comparision post LC & OC cortisolemia the 1st postoperative day

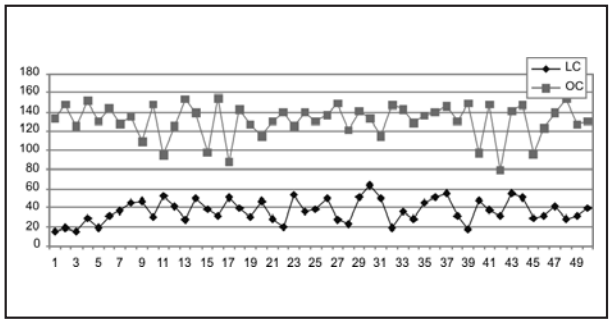

Figure 5. CK postoperative values in serum on the surgery day

The indicators of the muscular-tissue destruction and metabolic rasponse to trauma

The CK value (table 1), showing a level of the muscle destruction in relation to the applied procedure, has not exceeded the average with the LC group of patients, while with the OC ones it was on the upper limit of the normal values, and such an increase is statistically highly significant compared to the LC ($p<0.01$).

The postoperative AST values in serum were statistically substantially higher with the OC group of patients (figure 6).

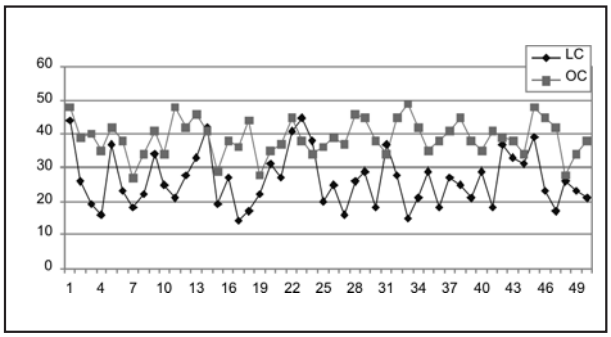

Figure 6. AST psotoperative values in serum on the surgery

The ALT postoperative values are somewhat higher with the OC group than with the LC one (though statistically substantial) (figure 7).

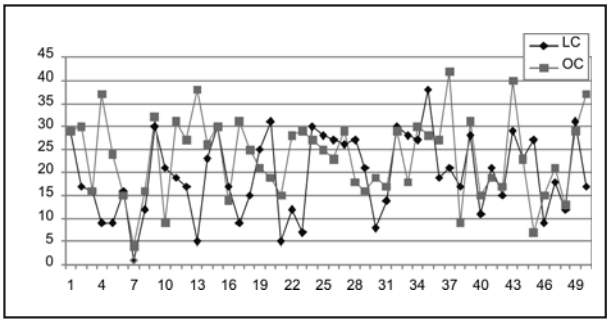

Figure 7. ALT postoperative values in serum on the surgery day

The K^+ in serum value with both groups were within the average, although the K^+ concentration is lower with the OC group, having the high statistical significance ($p< 0.01$) (figure 8).

The postoperative serum Na^+ values with both groups were within standard values; there was no substantial statistical difference between the OC and LC groups ($p > 0.01$) (figure 9).

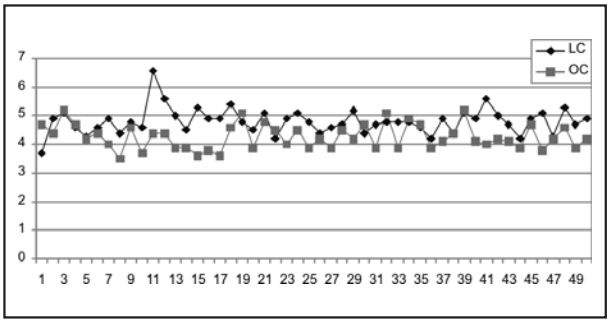

Figure 8. K^+ postoperative values in serum serum on the surgery day

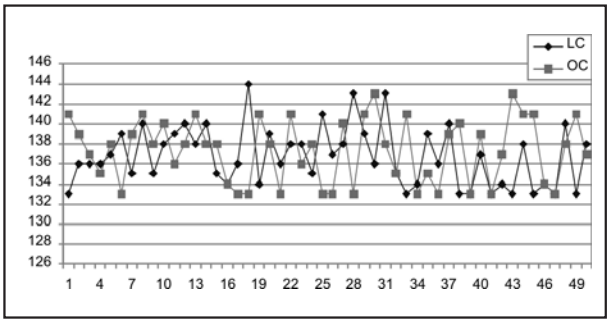

Figure 9. Na^+ postoperative values in serum serum on the surgery day

Gas analyses of capillary blood

(1) – preoperative
(2) – postoperative

In this study there is no statistically significant difference of pre- and postoperative pH values in both the OC and LC groups ($p>0.01$). All pH results were within the normal state (figure 10).

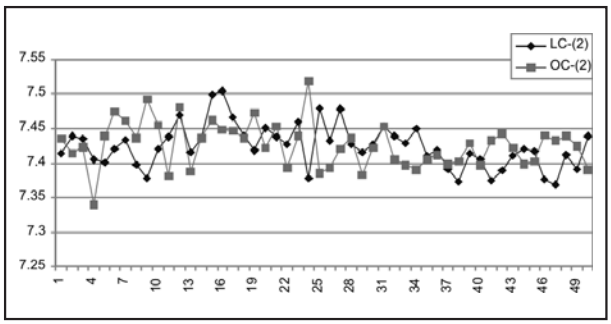

Figure 10. Comparison postoperative pH

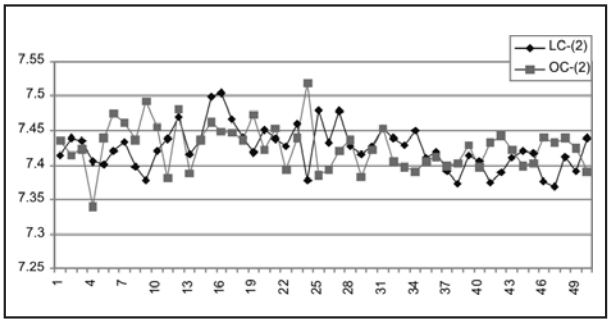

Figure 11. Comparison postoperative pCO_2

With both patient groups, decreased pCO_2 (figure 12) and HCO_3 (figure 13) postoperative values were evident (with the high statistical significance, $p<0.01$), but within the limits of reference values. A smaller drop of $pC0_2$ postoperative values was noted with the LC group, having high statistical significance ($p<0.01$) (table 2)

With both patient groups there was a postoperative decresase of pCO_2 and O_2 - SAT values having high statistical significance ($p<0.01$); a slight O_2 -drop was found with the LC group with high statistical significance ($p<0.01$).

Table 1. As an indicator of a muscular-tissular destruction, enzyme postoperative values were analyzed with both groups of patients

	LC vs	OC
1	CK not above normal values	CK at the upper limit and statistically highly significant ($p<0.01$)
2		AST in serum statistically essentially higher ($p<0.01$) due to a considerable difference of catalytic concentration in tissue and blood serum
3		Postoperative ALT slightly higher, but still statistically significant

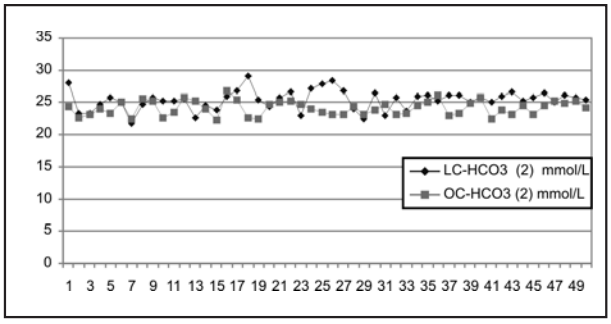

Figure 12. Comparison postoperative HCO_3

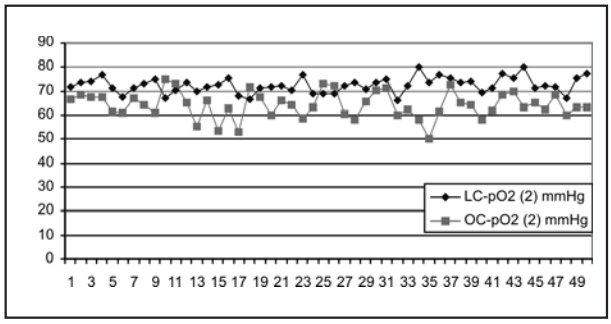

Figure 13. Comparison postoperative pO_2

Table 2. Comparasion gas analyses of capillary blood

	LC vs OC	
pH	All results within limits. No statistically significant difference (p>0.01)	
pCO_2, HCO_3 & alkaline difference	Smaller drop of pCO_2 (p<0,01) attributed to CO_2 - pneumoperitoneum	Larger drop of pCO_2 explained as an offset pCO_2 decrease caused by primary HCO_3 decline
	With all patients - alkaline excess (+BE) : low metabolic acidity	
		Lower postoperative HCO_3 and pCO_2 - more prominent temporary slight metabolic acidosis

Spirometry

(1)- the preoperative values

(2)- the 1 st postoperative day

(3)- the 5 th postoperative day

The spirometry value analysis in this controlled study displayed a postoparative reduction of the following parameters with both the LC and OC groups of patients: (1) vital capacity – VC (figure 14), (2) forced vital capacity – FVC (figure 15), (3) forced expiry volumen in the 1st second - FEV – 1 (figure 16), (4) Tiffeneau index - 100 FEV – 1/FVC (figure 17), (5) forced expiratory flow between 25 – 75% FVC – FEV_{25-75} (figure 18). The preoperative values of these parameters are comparable, i.e. there is no statistically significant difference in values between the OC and LC groups (table 3).

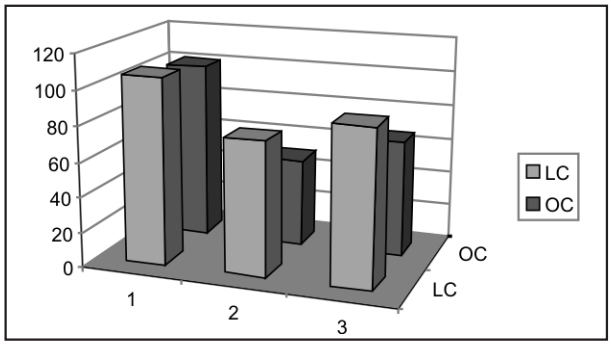

Figure 14. Postoperative reduction in VC

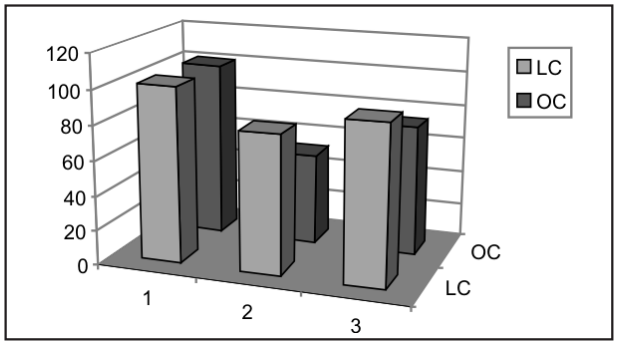

Figure 15. Postoperative reduction FEV-1

DISCUSSION

Numerous advantages of the LC have extensively been presented to professional circles and confirmed by many papers (2,3,5,8–17), evidently including those of Minimally Invasive Surgery like,

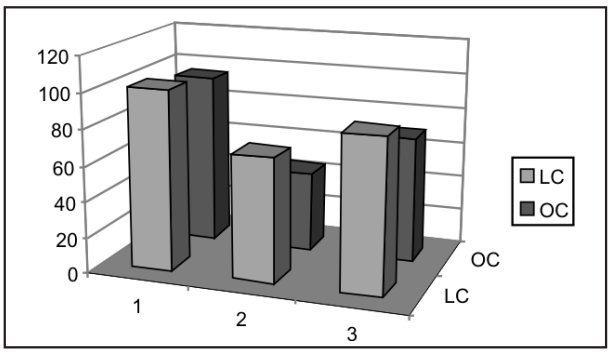

Figure 16. Postoperative reduction in FVC

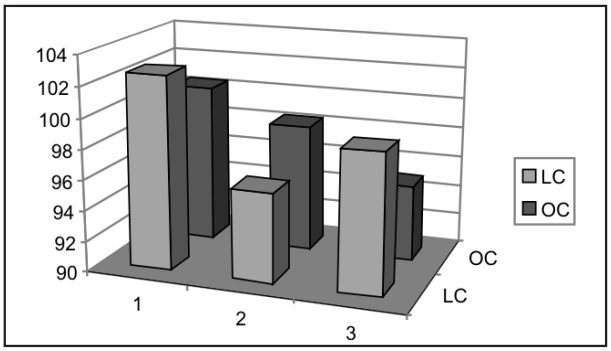

Figure 17. Postoperative reduction in Tiff. index

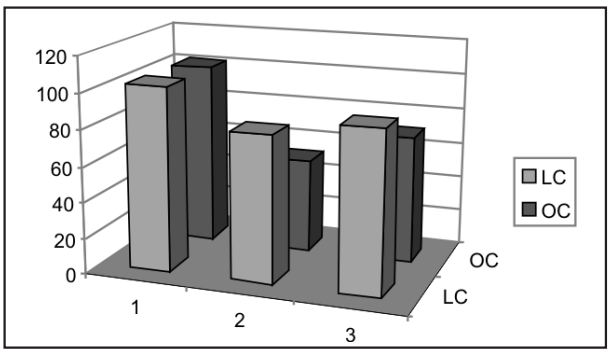

Figure 18. Postoperative reduction in FEF 25/75

above all, less surgical morbidity during an immediate postoperative stage, alleviated pain, sooner mobilization, shorter hospitalization, early regained work ability, smaller neuroendocrine-, metabolic- and tissue reaction to a surgical trauma, manifestly smaller postoperative cicatrix, higher thriftiness. An examination of a neurohumoral response to a surgical trauma discovers many papers in the literature dealing with: (1) Hormonal Medium (CRH, ACTH, Corticosteroids, Prolactin, AVP, Glucagon, T3, T4, Insulin); (2) Cytokines (IL-1, IL-6, THF); (3) Other Mediators (Eicosanoides, Mediators of Endotheloid Cells, Intracellular Mediators, Kallikrein, Kinin, Histamine, Interferon), as well as (4) Acute Phase Hepatic Proteins (CRP, Ceruloplasmin, Fibrinogen, Haptoglobin, Alpha-1 Antitrypsin, Alpha-2 Macroglobulin, Albumins). Analyses of metabolic responses to a surgical trauma are mainly focused to determine how the surgical trauma influences glucose metabolism, carbohydrate, protein and fat metabolism as well as a hydroelectrolytic balance. In recent years, however, a surgical trauma immunological reactions are being examined more often. Examinations of both animals and humans have proved premilinarily and complementarily that an immune function was less disturbed after a laparoscopic surgical intervention then after an open one (5,17).

We believe that our domestic professional world needed a general evaluation of the LC vs. OC, emphasising an anlysis of physiological responses to various levels of tissue damages, trying so to objectify parameters of the surgical trauma. Thus, in that context our prospective study of 100 consecutive patients (splitted in two of 50 ones) was designed as shown in the Methods. After having analysed the examination results, the following facts should be pointed out:

Table 3. The spirometry value analysis

LC	vs	OC
On the 1st postoperative day, reduction in VC, FVC, FEV–1 and FEF_{25-75} less by 20–30%		
(1) Smaller reduction of VC & FVC ($p<0.01$)-less ventilation restrictive obstructions.	/	
(2) FEV 1 & FEF_{25-75} also less reduced - less pronounced ventilation obstructions in both larger and smaller respiratory channels	/	
(3) Tiffeneau's Index; below 7% with LC & OC and reduction difference not statistically significant ($p>0.01$) – exceptionally low rate of ventilation obstructions in the larger respiratory channels.		
Substantial improvement of postoperative spirometry values & pulmonary function more rapidly restored to its basic value		On the 1st and 5th postoperative day, higher reduction of spirometry values

➢ In an attempt to objectify the neuro-endocrine reaction to a surgical trauma, the postoperative cortisol level in serum was monitored showing in both groups-the LC and the OC – an increase of values, statistically substantially higher and prolonged as such with the OC group, dropping slowly on the 1st postoperative day. As a consequence, that higher cortisol level, with the OC patients reflected more pronouncedly on: cells of liver, skeleton musculature, adipose tissue, glucose metabolism and immune system control (lymphocite blastogenesis suppression). Since the pain medication approach with both groups was the same (a postoperative applied analgesia was similar), the smaller response with the LC group couldn't be atributed to the used analgetics.

➢ As an indicator of a muscular-tissue destruction with both the LC and the OC, the postoperative values of sarcoplasmic reticulum muscle cells enzyme were analysed: CK, AST, ALT.

(1) The CK value, showing a level of the muscle destruction in relation to the applied procedure, has not exceeded the average with the LC group of patients, while with the OC ones it was on the upper limit of the normal values, and such an increase is statistically highly significant compared to the LC ($p<0.01$). It is clear that higher values in the OC group are the result of more extensive muscular tissue destruction caused by laparotomy.

(2) The postoperative AST values in serum were statistically substantially higher with the OC group of patients. This happens due to high difference of catalitic concentration in tissue and blood serum. Duirng the OC, lesions of AST rich tissues (skeleton muscles, liver) are bigger, so it goes into circulation and reflects on increased AST activity in serum.

(3) The ALT postoperative values are somewhat higher with the OC group than with the LC (though statistically substantial), the reason being in its relatively small content in other tissues and organs, except for the liver rich in AST.

➢ As the parameters of the metabolic response to trauma, the postoperative values of K^+ and Na^+ in serum were measured; they are less specific for the surgical trauma, but sufficient enough in correlation with other results. The K^+ in serum value with both groups were within the average, although the K^+ concentration is lower with the OC group, having the high statistical significance ($p< 0.01$) – These lower K^+ values with the OC group of patients (where the trauma level is higher), are explained by an increased renotubular excretion, due to secondary hyperaldosteronism and stressed cortisolemia which draft K^+, water and nitrogen from cells to extracellular liquid. Since changes in K^+ levels could be caused by quite a number of factors, those results must be taken with some precaution. The postoperative serum Na^+ values with both groups were within standard values; there was no statistical substantial difference between the OC and LC groups ($p > 0.01$). The reason is probably the fact that the organism has a rather developed sodium-static mechanism being "vigilant in guarding Na" from bigger losses, as well as IV compensation of liquids and electrolites (0.9% NaCl sol.) during surgery and perioperative period (2,5,16,18,19).

➢ In order to evaluate potential beneficial effects of LC to the postoperative cardiopulmonary function against detrimental intrasurgical influences of CO_2- pneumoperitoneum, values of capillary blood gas analysis and spirometry were monitored (table 2).

Gas analysis values

♦ pH of the blood

The most important effect of a disturbed H+ ion concentration balance is its influence on enzyme activity of an organism. The enzyme systems have an optimal pH at which the reaction rate is maximal.

♦ pCO_2, HCO_3, alkaline difference

Higher pCO_2 values with the LC can be partially atributed to the CO_2 –pneumoperitoneum, i.e. a possibility of CO_2 systematic absorbtion from the abdomen; the absorbed CO_2 can cause substantial chemodynamic changes, being in the most cases avoided by changed ventilation regime of patients (higher insufflation pressure and/or hyperventilation). The pCO_2 value drop was more pronounced with the OC group of patients; it could be understood as a compensational decrease of pCO_2 caused by $HC0_3$ primary drop. With all patients, an excess of base (+BE) was found: buffer bases are less engaged by organic acids, so there is base surplus –low metabolic acidity. With regard that HCO_3 and pCO_2 postoperative values are lower with the OC group, (the group with a bigger surgical trauma), than with the LC one, it is supposed that with the OC a temporary low metabolic acidosis is more pronounced.

♦ pCO_2 , O_2 - SAT

It could be concluded that with the LC group oxygen saturation was better (higher pCO_2 and O_2 - SAT values), which is the result, amongst others, of a smaller pulmonary function disturbance during laparoscopic surgery; that is in correlation with results of the LC large series confirming pulmonic complications of less than 0.5% with the LC vs. 2% of the OC. With the OC group, showing lower O_2 values, more pulmonic complications are likely to be expected in terms of hypoxia and atelectasis. We believe laparotomy is one of the reasons for more pulmonic complications with the OC group, i.e. spared respiration muscle system due to more intensive pain caused by laparotomy.

Spirometry values

On the 1st postoperative day, reductions of VC, FVC, FEV-1 and FEV_{25-75} were by 20–30% less after the LC than OC. That smaller VC and FVC reductions on the 1st postoperative day with the LC group was statistically highly significant ($p< 0.01$), leading to a conclusion that the restrictive obstructions of ventialtion are less after the LC than after the OC. FEV -1 and FEV_{25-75} on the 1st operative day were also less reduced with the LC than the OC group, so it could be concluded that the ventilation obstructive disturbances in both larger and smaller respiratory ways are less pronounced with the group treated with the laparoscopic technique (LC). The postoperative reduced Tiffeneau - index with the OC and LC is below 7%, and the reduction difference is not statistically significant ($p > 0.01$), confiming thus that the ventilation obstructive disturbances in the larger respiratory ways are exceptionally of low grade.

Reductions of postoperative spirometry values on the 1st and the 5th days were higher with the OC group, meaning that patients undergoing LC show substantially improved postoperative spirometry values and, with the most of them, the pulmonary function was reinstated to the basic value more efficently, comparing with the OC treated patients (such results are in correlation with data from the literature).

It is known that after abdominal surgical interventions and general anesthesia, the pulmonary function is significantly disturbed. The general anesthesia typically leads to a temporary disturbance of gas exchange due to reduced lungs volumen and changes in breathing mechanism. An influence of the upper abdominal open cholecystectomy (OC) on the pulmonary function, compared with the laparoscopic one (LC), is longer and more pronounced. These changes of the pulmonary function become clinically significant when they are adjuncted to pathological states like atelektasis, hypoxemia and pneumonia. It is probable that thanks to the minimal muscular system destruction with the LC of the abdominal wall which is a component of a ventilation pump the pulmonary function disturbance is reduced. A smaller postoperative pain with the LC is also significant in reduction of pulmonary disfunction; the pain resulting from a deep inspiring influences a whole line of occurences and because of changed thorax movement, the pulmonary disfunction is increased (20–24).

CONCLUSION

- By monitoring the post LC & OC cortisolemia we have objectified neuroendocrine reaction to a surgical trauma and confirmed the LC as a weaker stimulus for cortisol secretion. Recorded higher and prolonged the post OC cortisolemia is consonant with the surgical trauma intensity. Our study suggests that the laparoscopic approach in the perioperative period results in the diminished neuroendocrine response to the surgical trauma.

– Taking in consideration nonspecific parameters of the metabolic response to the surgical stress and indicators of the muscular – tissue destruction, we have shown that, for a patient, laparoscopic cholecystectomy represents the smaller surgical trauma than the open cholecystectomy.

– The results of both gas analysis of the capillary blood and spirometry, as well as monitoring of the postoperative pain indicate the following advantage of the LC: 1–less decline of pCO_2 postoperative values 2–better 02 saturation, 3–improved the postoperative spirometry, 4–reduced the analogous accompanying pain meaning a smaller and shorter impairment of the pulmonary function with the LC thanks to the minimal muscular destruction of the abdominal wall and the smaller postoperative pain. The laparoscopic surgery, however, involing CO_2-–pneumoperitoneum, might lead to undesired hemodynamic effects and significant complications. With more abdominal surgeries performed by the laparoscopic technique, it became clear that surgeons must be better informed and aware of unwanted effects i.e. take corresponding measures to prevent possible CO_2– pneumoperitoneum related complications.

On the basis of the above conclusions, it could be stated that the laparoscopic cholecystectomy is really "a patient's friend" increasingly substituting conventional surgeries as a "golden standard" in the treatment of symptomatic cholelithiasis although it requires certain technical preconditions.

Entering the era of a modern endoscopic surgery and adopted laparoscopic technique in the cure of cholelithiasis, it is possible to perform cholecystectomy with the minimal trauma respecting so the principle set by Langenbush and searched by alternative methods.

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ANALIZA FIZIOLOŠKOG ODGOVORA NA HIRURŠKU TRAUMU KOD LAPAROSKOPSKE I OTVORENE HOLECISTEKTOMIJE (prospektivna, randomizovana studija)

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SAŽETAK

Prateći nivo kortizolemije nakon LC i OC objektivizirali smo neuroendokrini odgovor na operativnu traumu i potvrdili da je LC slabiji stimulus za lučenje kortizola. Zabeleženi veći i dugotrajniji porast kortizolemije nakon OC je u skladu sa intenzitetom operativne traume. Ovom studijom sugerišemo da laparoskopski pristup u perioperativnom periodu rezultira u smawenom neuroendokrinom odgovoru na hirušku traumu. Uzimajući u obzir indikatore mišićno-tkivne destrukcije, pokazali smo da LC predstavlja manju operativnu truamu, odn. prilikom OC dolazi do većih lezija tkiva bogatih enzimima CK, AST, ALT (skeletni mišići, jetra).

Razmatranjem vrednosti gasnih analiza kapilarne krvi i spirometrije, dolazimo do zaključka da LC rezultira: 1-manjim padom postoperativnih vrednosti pCO_2, 2-boljim zasićenjem kiseonikom, 3-poboljšanjima u postoperativnoj spirometriji. Ovo govori da je kod LC došlo do manjeg i kratkotrajnijeg poremećaja pulmonalne funkcije. Međutim, laparoskopska hirurgija koja uključuje CO_2-pneumoperitoneum, može da dovede do neželjenih hemodinamskih efekata i značajnih komplikacija, što se više abdominalnih operacija izvodi laparoskopski, to više postaje imperativ da hirurzi postanu informisaniji o neželjenim efektima i da preduzmu odgovarajuće mere kako bi sprečili potencijalne komplikacije koje su vezane za CO_2-pneumoperitoneum.

Ključne reči: **laparoskopska holecistektomija, neruoendokrini i metabolički odgovor, indikatori mišićno-tkivne destrukcije.**