SCIENTIFIC ARTICLE

Stress response in open versus laparoscopic procedures: is laparoscopic surgery truly as beneficial to the patient as it promises to be?

S. Gambhir[1], M. Sukhadia[1], G. Bajpai[1], D. Sethi[1], A. Sethi[2]
[1]R.N.T. Medical College, Udaipur (Rajasthan), India.
[2]Ananta Institute of Medical Sciences, Kaliwas. Rajsamand (Rajasthan), India.

Keywords: Laparoscopic surgery, Open surgery, Stress response

Introduction

In a medical or biological context stress is a physical, mental, or emotional factor that causes bodily or mental tension. Stressors can be external (from the environment, psychological, or social situations) or internal (illness, or from a medical procedure). [1]

Surgical stress is the systemic response to surgical injury and is characterized by activation of the sympathetic nervous system, endocrine responses as well as immunological and haematological changes. The more the external stimuli i.e. incision size and tissue handling in this case, more is the stress response, which leads to delay in recovery of patient post operatively.

Laparoscopy, also called key-hole surgery or minimal access surgery, allows the surgeon to access the abdomen and pelvis without making a large incision in the skin. In conventional open surgical procedure because of larger incision and more handling of internal organs, the patient believed to have increased level of pain and longer recovery time, hence more stress.

Laparoscopic interventions have been increasingly used in surgical practice in recent years. The reported advantages of the laparoscopic approach in adults are: less wound infection, shortened postoperative recovery, less postoperative analgesic requirement and a faster return to normal activities.

In spite of the advancement in minimally invasive surgery, and it becoming standard of care for cholelithiasis and appendicitis, open (tension free mesh) repair for hernia continues to be the gold standard as the beneficial effects of laparoscopic repair must be achieved with better maintenance of cardiorespiratory, metabolic and endocrine homeostasis.

Majority of our patients belonged to tribal population (due to geographical location of Udaipur being in the tribal belt of Rajasthan, India) among whom the concept of laparoscopic surgery is still relatively new and it was difficult to get them to consent to laparoscopic surgery (esp. for hernia repair), as for them and their relatives, the open procedures have stood the test of time.

In an attempt to identify whether laparoscopic surgery is truly beneficial to the patients and thus in turn to understand the rationale behind the view of local population, in this case series of 50 patients we evaluated the difference between the stress response using 11 parameters in conventional open procedure versus laparoscopic surgery for cholelithiasis, appendicitis, hernia repair.

Materials and Methods

This is a prospective, observational and analytical case series study among 50 patients of cholelithiasis, appendicitis and inguinal hernia divided into 2 groups, Group-A (Open Procedures – 27 patients) and Group-B (Laparoscopic Procedures – 23 patients), to determine the less stressful procedure between open and laparoscopic surgery in patients of cholelithiasis, appendicitis and inguinal hernia, conducted in a tertiary care teaching institute at Department of General Surgery, Rabindra Nath Tagore Medical College and Maharana Bhupal Government Hospital, Udaipur. 313001. Rajasthan.

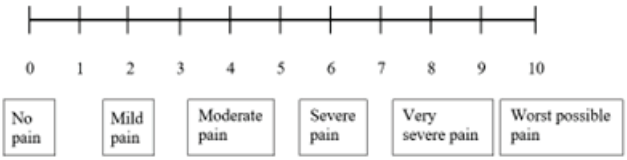
To measure the stress response between the two groups, following parameters were recorded at the time of admission, 6 hours and 24 hours after surgery and were analysed statistically for significant difference and correlation between the groups:

A) Physical parameters - pulse, blood pressure recorded as Mean Arterial Pressure, temperature and respiratory rate
B) Laboratory parameters via blood samples - serum cortisol, serum glucose, C-reactive Protein, interleukin-6,

Correspondence: A. Sethi
E-mail: dranjalisethi2011@gmail.com
https://orcid.org/0009-0009-5044-8253
Received: 18-08-2022 Accepted: 08-03-2023
DOI: http://doi.org/10.4038/sljs.v41i1.8989

prolactin and total leukocyte count.

C) Psychological Parameter recorded as **pain score** using **Visual Analogue Scale**. Patients were asked to score their pain on a scale of 0 to 10 with 0 being least or no pain while 10 being maximum/unbearable pain.



Statastical Analysis

The presentation of the Categorical variables was done in the form of number. On the other hand, the presentation of the continuous variables was done as mean ± SD and median values. The following statistical tests were applied for the results:

1. The comparison of the variables which were quantitative in nature were analyzed using Independent t test.
2. The comparison of the variables which were qualitative in nature were analyzed using Chi-Square test/Fisher's Exact test.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software ver. 21.0.

For statistical significance, p-value of less than 0.05 was considered as significant

Results

50 patients were studied in this case series to analyse the stress response between patients undergoing open procedures (Group A) and those undergoing laparoscopic procedures (Group B). The difference between the two groups in context of all the 11 stress parameters taken into account was statistically insignificant in the pre-operative period (p-value > 0.05).

There was no statistically significant difference between the 2 groups in terms of age (p-value=0.779) and sex (p-value=0.615)

The mean operating time in patients undergoing open procedure (55.2±22 minutes) was significantly lower (p-value=0.004) as compared to those undergoing laparoscopic procedures (76.8±28.8minutes) (Table 3).

Among the physical parameters(table 1)Mean ± SD of pulse rate (per minute) at 6 hours post-operative, 24 hours post-operative period in group A was 96.22 ± 7.65, 88 ± 6.2respectively which was significantly higher as compared to group B (82.96 ± 7.83(p-value<0.001), 82 ± 7.63 (p-value=0.003) respectively). It was also observed that 6 hours after surgery Mean Arterial Pressure (in mm Hg) of Group A patients fell while in Group B, the MAP had risen (however the difference was statistically not significant, p-value=0.254)

However at 24 hours after surgery, Mean Arterial Pressure of Group A patients had risen with Mean Arterial Pressure being significantly higher in Group A patients (p-value<0.001). Mean ± SD of the body temperature (ºF) at 6 hours post-operative and 24 hours post-operative period in group A and in group B were compared and no significant difference was found between them (p-value 0.566 and 0.702 respectively).Like the body temperature, the changes in respiratory rate (per minute) were not statistically significant in the post-operative period when compared in both the groups. (p-value 0.501 and 0.677 at 6 hours and 24 hours post-operatively).

When laboratory values (Table 2) were analysed, it was observed that Serum Glucose (mg/dl), C-Reactive protein (mg/l), Interleukin-6 (pg/ml) and Total Leukocyte Count (/mm3) were all significantly higher in Group A as compared to Group B at 6 hours and 24 hours post-operative periods. Though the mean Serum Cortisol (mcg/dl) level was higher in Group A patients throughout the observed post-operative period, the difference was significant only at 24 hours. On the other hand there was no significant difference between the two groups in terms of Prolactin (ng/ml) levels.

Psychological parameter recorded as pain score using Visual Analogue Scale was assessed in both the groups and there was no statistically significant difference in the early post-operative pain between the two groups. (p-value at 6 hours=0.264). However after 24 hours, pain was significantly lower in Group B patients; p-value at 24 hours=0.008) (Table 3).

The incidence of post-operative surgical site infection was significantly lower (p-value=0.024) in Group B patients (2 vs. 10 in Group A; Table 3). Concurring with the above findings of surgical site infection, Group B had significantly shorter post-operative hospital stay (3.48 ± 1.41days) vs. 4.48 ± 1.55 days in Group A (p-value=0.021; Table 3)

Table 4 shows the effect of general anaesthesia and spinal/regional anaesthesia on the variables of cortisol and glucose and shows no significant difference of the effect of anaesthesia on these two variables in the post-operative period. (p-value>0.05)

Table 1

Physical Parameters	Group A	Group B	p-value	Test Performed
Pulse per minute				
pre-operative	79.78 ± 8.62	78.96 ± 9.92	0.755	t test;0.313
6 hours post -operative	96.22 ± 7.65	82.96 ± 7.83	<.0001	t test;6.042
24 hours post -operative	88 ± 6.2	82 ± 7.63	0.003	t test;3.068
Blood Pressure as MAP in mm Hg				
pre-operative	96.2 ± 9.34	96.58 ± 9.96	0.889	t test;0.14
6 hours post-operative	94.42 ± 9.02	97.42 ± 9.35	0.254	t test;1.153
24 hours post -operative	106.07 ± 5.4	93.88 ± 5.79	<0.0001	t test;7.695
Temperature in °F				
pre-operative	98.44 ± 0.5	98.47 ± 0.41	0.851	t test;0.189
6 hours post -operative	98.72 ± 0.29	98.77 ± 0.22	0.566	t test;0.578
24 hours post -operative	98.4 ± 0.43	98.36 ± 0.27	0.702	t test;0.384
Respiratory Rate per minute				
pre-operative	17.48 ± 1.4	17.61 ± 1.12	0.727	t test;0.351
6 hours post -operative	19.26 ± 1.4	19 ± 1.28	0.501	t test;0.678
24 hours post -operative	17.3 ± 0.91	17.43 ± 1.41	0.677	t test;0.418

Table 2

Laboratory Parameters	Group A	Group B	p-value	Test Performed
Serum Cortisol (mcg/dl)				
pre-operative	10.24 ± 4.8	10.71 ± 3.13	0.69	t test;0.4
6 hours post-operative	22.77 ± 12.16	18.65 ± 13.74	0.266	t test;1.124
24 hours post -operative	22.35 ± 21.61	10.43 ± 6.41	0.01	t test;2.73
Serum Glucose (mg/dl)				
pre-operative	106.41 ± 21.8	103.83 ± 18.91	0.659	t test;0.443
6 hours post-operative	144.07 ± 37.98	125.3 ± 25.76	0.049	t test;2.008
24 hours post -operative	147.44 ± 28.22	127.48 ± 14.05	0.002	t test;3.235
C-Reactive protein (mg/l)				
pre-operative	25.08 ± 80.36	6.37 ± 7.04	0.239	t test;1.204
6 hours post-operative	19.17 ± 15.05	11.01 ± 11.38	0.038	t test;2.134
24 hours post -operative	80.38 ± 51.17	49.2 ± 43.65	0.026	t test;2.296
Interleukin -6 (pg/ml)				
pre-operative	14.48 ± 13.73	13.07 ± 9.48	0.68	t test;0.415
6 hours post-operative	92.89 ± 90.1	30.08 ± 16.22	0.001	t test;3.556
24 hours post -operative	57.07 ± 31.12	29.17 ± 26.61	0.001	t test;3.375
Prolactin (ng/ml)				
pre-operative	19.19 ± 10.52	30.03 ± 26.3	0.074	t test;1.855
6 hours post -operative	28.93 ± 19.2	25.5 ± 13.95	0.469	t test;0.73
24 hours post -operative	19.7 ± 11.64	25.35 ± 21.67	0.246	t test;1.172
Total Leukocyte Count (/mm ^{3})				
pre-operative	9922.96 ± 2146.18	9186.96 ± 2442.48	0.262	t test;1.134
6 hours post -operative	14009.63 ± 4285.35	11393.48 ± 2830.85	0.013	t test;2.58
24 hours post -operative	12200 ± 3809.92	9952.61 ± 2056.62	0.015	t test;2.530

Table 3

Parameters	Group A	Group B	p-value	Test Performed
Mean Duration of Surgery (in hours)	0.92 ± 0.37	1.28 ± 0.48	0.004	t test;2.997
Visual Analogue Score				
pre-operative	2.78± 2.94	2.96 ± 2.88	0.829	t test;0.216
6 hours post -operative	4.78± 1.67	4.22 ± 1.83	0.264	t test;1.13
24 hours post -operative	2.22± 1.31	1.35 ± 0.83	0.008	t test;2.759
Surgical Site Infection				
present	10 (37.04 %)	2 (8.70%)	0.024	Fisher Exact test
absent	17 (62.96 %)	21 (91.30 %)		
Post-operative hospital stay (in days)	4.48 ± 1.55	3.48 ± 1.41	0.021	t test;2. 374

Table 4

Parameters		Mean	Std. Deviation	t test	p-value
Serum Cortisol pre-operative	General Anaesthesia	11.00	2.47	0.288	0.775
	Spinal Anaesthesia	10.61	5.18		
Serum Glucose pre-operative	General Anaesthesia	100.82	12.96	1.036	0.307
	Spinal Anaesthesia	107.52	24.17		
Serum Cortisol 6 hours post-operative	General Anaesthesia	22.16	14.65	0.715	0.479
	Spinal Anaesthesia	19.00	13.18		
Serum Glucose 6 hours post -operative	General Anaesthesia	127.35	24.52	0.26	0.796
	Spinal Anaesthesia	125.00	30.78		
Serum Cortisol 24 hours post-operative	General Anaesthesia	13.43	8.11	1.325	0.193
	Spinal Anaesthesia	10.46	6.05		
Serum Glucose 24 hours post -operative	General Anaesthesia	132.82	22.82	0.311	0.758
	Spinal Anaesthesia	130.87	16.96		

Discussion

A surgery is said to be less stressful on the body if the changes produced in the sympathetic nervous system, endocrine responses as well as immunological and haematological systems are minimal. Thus an ideal surgery should also be easier to execute so as to cause less tissue damage and take less operating time, and hence in turn less stress to the patient's body. In that context, open tension free mesh repair proposed by Lichtenstein [2] continues to remain the gold standard till date for hernia repairs in spite of the advancement in minimally access surgery, which has become the standard of care for patients of cholelithiasis and appendicitis world over.

In our study, the mean operating time in patients undergoing laparoscopic surgery was significantly higher compared to those undergoing open repair similar to several other studies[3-11]. Contrary to our results, Eklund et al[12] refuted any claims regarding the difference in operating time between the 2 types of repair in cases of hernia, while another study[13] though acknowledging the fact of longer operating time during initial phase of surgical career concluded laparoscopic surgeries took lesser time in case of cholecystectomy. Similarly, certain studies found shorter operating times for laparoscopic appendicectomy even in the cases of complicated/perforated appendix. [14-16]

The analysis of physical parameters between the two groups showed no statistical difference in terms of body temperature and respiratory in the post-operative periods i.e. p-value>0.05 for both. A general trend though was observed in both the groups that the mean body temperature rose slightly within first 6 hours and then returned towards original pre-operative values at 24 hours after surgery.

Difference was noted between the pulse rates of the two groups, with that of Group A being significantly higher than that of Group B in both the post-operative time intervals (p-value <0.001 and 0.003 respectively). There was also difference in the blood pressures recorded as Mean Arterial Pressure (MAP) between the two groups. The MAP fell in Group A patients at 6 hours post-operative period but when compared to Group B - in whom the MAP had risen, this difference was not statistically significant. However at 24 hours after surgery, MAP of Group B patients returned towards pre-operative values, while that of Group A patients had risen with MAP being significantly higher in Group A patients (p-value <0.001). These changes can be probably explained by the effects of spinal anaesthesia in majority of the patients of Group A patients which is known to decrease the blood pressure[17] and produce continued analgesia in the early post-operative period.[18]

Laboratory parameters (Table 2) were significantly higher among the Group A patients with the exception of prolactin, which did not differ significantly between the two groups. The pain (Table 3) was significantly lower in group B patients 24 hours post-surgery. Conforming to our above findings, surgical site infections and post-operative hospital stay (Table 3) was significantly lesser in Group B patients as compared to those in Group A (p-values 0.024 and 0.021 respectively). Previous studies in this field which had observed one or more of the parameters analysed by us concurred with our findings. [7,9-10,13-14,19-26]

However, it is important to bring to notice that the patients of hernia did not comply with above trends of change in laboratory and psychological parameters and surgical site infections between the Group A and Group B patients and the difference between the two groups of inguinal hernia patients was not statistically significant in terms of above mentioned parameters. However, Group B patients of inguinal hernia had a significantly longer hospital as compared to their Group A counterparts (p-value=0.022), probably due to familiarity of the operating surgeons with the open repair, its complications and management. Very similar to the results obtained in our study, a prospective comparison of metabolic and inflammatory responses after laparoscopic and open inguinal hernia operations in 20 patients[27] showed that changes in the plasma levels of cortisol, growth hormone and prolactin - measured preoperatively and at fixed intervals up to 120 hours postoperatively - showed no statistically significant difference between the two groups. No significant changes in IL-6 levels were recorded in any group. Akhtar K et al. [27] however reported that changes in CRP levels were significantly higher (P< 0.006) in open hernia patients. Authors of previous studies have had varied results regarding the post-operative complications between the two groups, some suggesting laparoscopic group faring better[6,12] while others vice-versa[28]. Although some recent studies have shown that Laparoscopic hernioplasty (TAPP) is superior to Lichtenstein tension-free hernioplasty in terms of postoperative pain, hospital stay and return to daily activity[3] and may even be surgery of choice for unilateral inguinal hernia repair[3,29-31].

Since laparoscopic surgeries in our study had longer duration as compared to open surgeries, also to be taken into consideration while comparing the stress response between the two groups should be the effect of anaesthesia as general inhalation anaesthesia used in laparoscopic and open cholecystectomy patients produces a different stress response in body when compared to regional or local anaesthesia that is used during open hernia repair surgeries and appendectomy. Hence, a comparison of the effect of different types of anaesthesia (spinal/regional anaesthesia in open cases with

the exception of cholecystectomy and general anaesthesia in all laparoscopic surgeries) on the two groups was made using the two significantly affected variables of glucose and cortisol, excluding the patients of open cholecystectomy which was the only open surgery performed under general anaesthesia (Table 4). It was observed that these variables did not differ significantly in the post-operative phase at 6 hour and 24 hour intervals between those who underwent surgeries under regional anaesthesia compared to those who underwent surgeries under general anaesthesia.

Another consideration could be given to the fact that clean-contaminated cases are mixed with clean cases in both the groups. We would like to point out that number of clean contaminated cases were same between both the groups, thereby alleviating it as a confounding factor.

Follow up is needed post discharge to document the incidence of long term complications.

Conclusion

To conclude, laparoscopic surgery causes lesser stress compared to open surgery on the human body, and has the calibre to be the gold standard for cholelithiasis and appendicitis. However, further research is required to establish it as the standard of care for hernia repairs, where open hernia surgery based on the principles laid down by Lichtenstein continues to be the corner stone of hernia repair because of the following reasons:

1. Small sample size.
2. Longer duration of surgery in laparoscopic repair as learning curve for the same is longer.
3. Difference in anaesthesia between the two groups: region or local in open group while general anaesthesia in laparoscopic group.

Further detailed studies with greater sample size, taking into account the anaesthetic factors and long-term complications are required in future.

Even though the tribal population of Udaipur is embracing the newer advancements in the field of surgery as the standard of care for cholelithiasis and appendicitis, for the time being, open hernia repair continues to be a more popular option amongst the local population.

References

1.Desborough JP, The stress response to trauma and surgery, BJA: British Journal of Anaesthesia, Volume 85, Issue 1, 1 July 2000, Pages 109–117.

2.Lichtenstein IL, Shulman AG, Amid PK, Montllor MM. The tension-free hernioplasty. Am J Surg. 1989 Feb;157(2):188-93.doi: https://doi.org/ 10.1016/0002-9610(89)90526-6.

3.Akhtar MS, Mohammad Ali W, Ahmed Khan T, Raza MH, Ahmad M, Sajid M. Laparoscopic transabdominal preperitoneal versus open mesh lichtenstein repair of inguinal hernia: a comparative analysi. Int J Med Res Rev [Internet]. 2016Jul.31 [cited 2022Apr.12];4(7):1199-1206. Available from: https://ijmrr.medresearch.in/index.php/ijmrr/article/view/626

4.McCormack K, Scott NW, Go PM, Ross S, Grant AM; EU Hernia Trialists Collaboration. Laparoscopic techniques versus open techniques for inguinal hernia repair. Cochrane Database Syst Rev. 2003;(1):CD001785. doi: https://doi.org/10.1002/14651858.cd001785.

5.Schmedt CG, Sauerland S, Bittner R. Comparison of endoscopic procedures vs Lichtenstein and other open mesh techniques for inguinal hernia repair: a meta-analysis of randomized controlled trials. SurgEndosc. 2005 Feb;19(2):188-99. Epub 2004 Dec 2.doi: https://doi.org/10.1007/s00464-004-9126-0.

6.Dedemadi G, Sgourakis G, Karaliotas C, Christofides T, Kouraklis G, Karaliotas C. Comparison of laparoscopic and open tension-free repair of recurrent inguinal hernias: a prospective randomized study. SurgEndosc. 2006 Jul;20(7):1099-104. Epub 2006 Jun 8.doi: https://doi.org/10.1007/s00464-005-0621-8.

7.Guller U, Hervey S, Purves H, et al. Laparoscopic versus open appendectomy: outcomes comparison based on a large administrative database. Ann Surg. 2004;239(1):43-52. doi:10.1097/01.sla.0000103071.35986.c1

8.Chung RS, Rowland DY, Li P, Diaz J. A meta-analysis of randomized controlled trials of laparoscopic versus conventional appendectomy. Am J Surg. 1999;177(3):250-256. doi:10.1016/s0002-9610(99)00017-3

9.Garbutt JM, Soper NJ, Shannon WD, Botero A, Littenberg B. Meta-analysis of randomized controlled trials comparing laparoscopic and open appendectomy. SurgLaparoscEndosc. 1999;9(1):17-26.

10.Temple LK, Litwin DE, McLeod RS. A meta-analysis of laparoscopic versus open appendectomy in patients suspected of having acute appendicitis. Can J Surg. 1999;42(5):377-383.

11. Shukla, A., Seth, S., & Ranjan, A. (2017). A comparative study between laparoscopic and open cholecystectomy in cases of cholecystitis with cholelithiasis: one year experience in tertiary care center. International Surgery Journal, 4(3), 903-907. doi:http://dx.doi.org/10.18203/2349-2902.isj20170446

12.Eklund A, Rudberg C, Leijonmarck CE, Rasmussen I, Spangen L, Wickbom G, Wingren U, Montgomery A. Recurrent inguinal hernia: randomized multicenter trial comparing laparoscopic and Lichtenstein repair. SurgEndosc.

2007 Apr;21(4):634-40. Epub 2007 Feb 16.doi: https://doi.org/10.1007/s00464-006-9163-y.

13.Singh, P., Gupta, S., & Kumar, M. (2017). A comparative study of open cholecystectomy and laparoscopic cholecystectomy in patients with cholelithiasis. International Surgery Journal, 5(1), 253-256. doi:http://dx.doi.org/10.18203/2349-2902.isj20175905

14.Nazir A, Farooqi SA, Chaudhary NA, Bhatti HW, Waqar M, Sadiq A. Comparison of Open Appendectomy and Laparoscopic Appendectomy in Perforated Appendicitis. Cureus. 2019;11(7):e5105. Published 2019 Jul 9. doi:10.7759/cureus.5105

15.Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. Ann Surg. 2011;254(6):927-932. doi:10.1097/SLA.0b013e31822aa8ea

16.Yau KK, Siu WT, Tang CN, Yang GP, Li MK. Laparoscopic versus open appendectomy for complicated appendicitis. J Am Coll Surg. 2007;205(1):60-65. doi:10.1016/j.jamcollsurg.2007.03.017

17.Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. Anesthesiology. 1992 Jun;76(6):906-16. doi: 10.1097/00000542-199206000-00006. PMID: 1599111.

18.Naghibi K, Saryazdi H, Kashefi P, Rohani F. The comparison of spinal anesthesia with general anesthesia on the postoperative pain scores and analgesic requirements after elective lower abdominal surgery: A randomized, double-blinded study. J Res Med Sci. 2013 Jul;18(7):543-8. PMID: 24516483; PMCID: PMC3897018.

19. Makri GG, Karayiannakis AJ, Mantzioka A, Karousos D, Karatzas G. Systemic stress response after laparoscopic or open cholecystectomy: a randomized trial. br J Surg. 1997;84:467-71.

20.Haque Z, Rahman M, Siddique MA. Metabolic and stress responses of the body to trauma: produced by the laparoscopic and open cholecystectomy. Mymensingh Med J 2004;13:48-52.

21.FlorianG. General stress response to conventional and laparoscopic cholecystectomy. AnnalsofSurgery 1995;221:372.

22.Luo K, Li JS, Li LT, Wang KH, Shun JM. Operative stress response and energy metabolism after laparoscopic cholecystectomy compared to open surgery. World J Gastroenterol 2003; 9 (4): 847-850.

23.Sista F. A randomized prospective study of laparotomy vs laparoscopy in patients with acute cholecystitis complicated by peritonitis. World GastrointestSurg2013; 5 (4): 73-82.

24.Li P, Xu Q, Ji Z, Gao Y, Zhang X, Duan Y, Guo Z, Zheng B, Guo X, Wu X. Comparison of surgical stress between laparoscopic and open appendectomy in children. J Pediatr Surg.2005;40(8):1279-83.

25.Aktimur R, Gokakin AK, Deveci K, Atabey M, Topcu O. Oxidative stress markers in laparoscopic vs. open appendectomy for acute appendicitis: A double-blind randomized study. J Min Access Surg 2016;12:143-7

26.Bartın MK, Kemik O, Çaparlar MA, Bostancı MT, Öner MO. Evaluation of the open and laparoscopic appendectomy operations with respect to their effect on serum IL-6 levels. Ulus TravmaAcilCerrahiDerg 2016;22(5):466–470; doi: 10.5505/tjtes.2016.47650

27.Akhtar K, Kamalky-asl ID, Lamb WR, Laing I, Walton L, Pearson RC, et al. Metabolic and inflammatory responses after laparoscopic and open inguinal hernia repair. Ann R Coll Surg Engl. 1998;80 (2):125-30. PMID: 9623379; PMCID: PMC2503002.

28.Neumayer L, Giobbie-Hurder A, Jonasson O, Fitzgibbons R Jr, Dunlop D, Gibbs J, Reda D, Henderson W; Veterans Affairs Cooperative Studies Program 456 Investigators. Open mesh versus laparoscopic mesh repair of inguinal hernia. N Engl J Med. 2004 Apr 29;350(18):1819-27. Epub 2004 Apr 25.doi: https://doi.org/10.1056/nejmoa040093.

29.Tzovaras G, Symeonidis D, Koukoulis G, Baloyiannis I, Georgopoulou S, Pratsas C, Zacharoulis D. Long-term results after laparoscopic transabdominal preperitoneal (TAPP) inguinal hernia repair under spinal anesthesia. Hernia. 2012 Dec;16(6):641-5. doi: https://doi.org/10.1007/s10029-012-0934-1. Epub 2012 Jun 24.

30.Eklund AS, Montgomery AK, Rasmussen IC, Sandbue RP, Bergkvist LA, Rudberg CR. Low recurrence rate after laparoscopic (TEP) and open (Lichtenstein) inguinal hernia repair: a randomized, multicenter trial with 5-year follow-up. Ann Surg. 2009 Jan;249(1):33-8. doi: https://doi.org/10.1097/SLA.0b013e31819255d0.

31.Oguz H, Karagulle E, Turk E1, Moray G. Comparison of peritoneal closure techniques in laparoscopic transabdominal preperitoneal inguinal hernia repair: a prospective randomized study. Hernia. 2015 Dec;19(6):879-85. doi: https://doi.org/10.1007/s10029-015-1431-0. Epub 2015 Oct 20.