

Assessment of systemic inflammatory response after total extraperitoneal repair and Lichtenstein repair for inguinal hernia

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Abstract

Purpose The aim of the study was assessment of the systemic inflammatory response (SIR) intensity by measuring the blood serum levels of high sensitivity C—reactive protein (hsCRP), Interleukin-6 (IL-6) and Total Leukocyte Counts of patients. The estimations were done before and after the patient underwent either open Lichtenstein or endoscopic TEP inguinal hernia repair. This is a prospective observational type of study.

Methods Sixty patients with a diagnosis of unilateral uncomplicated inguinal hernia were included in the study. Patients were divided into two groups. In the first group, endoscopic total extraperitoneal repair (TEP) was done, while the other group underwent Lichtenstein repair. The patient selection was random. Serum markers for SIR were measured prior to and 24 h post-surgery.

Results Total extraperitoneal repair (TEP) and open Lichtenstein inguinal hernia repair both cause a significant Systemic Inflammatory Response in the body. The rise in serum markers for SIR post-surgery was statistically significant in both the groups. The rise in serum hsCRP and IL-6 concentrations was observed to be equivocal among the two groups. Statistically significant difference was

observed in serum TLC rise: Lichtenstein repair group having a higher value.

Conclusion Both, open and endoscopic surgical techniques incite a systemic inflammatory response in the body. However, it cannot be conclusively stated that TEP is associated with lesser SIR compared to the Lichtenstein repair on the basis of this study.

Keywords Inguinal hernia · Systemic inflammatory response · Endoscopy · CRP · Interleukin-6

Introduction

Inguinal hernia is one of the commonest surgical diseases with which a patient presents to a surgeon. The probability of having an inguinal hernia is 27% for males and 3% for the females [1]. The treatment of inguinal hernia has undergone significant development resulting in better and effective outcomes and smooth post-operative recovery for the patients [2].

The three milestones in the evolution of hernia repair surgery are:

1. Tissue repair by Eduardo Bassini in the year 1884.
2. Onlay tension-free mesh repair by Irving Lichtenstein in the year 1984.
3. Laparoscopic hernia repair by Ger, Schultz, Corbitt, etc. 1990 [3].

The Lichtenstein inguinal hernioplasty was one of the first procedures to use a prosthetic mesh. Consequently, the repair was tension free, which resulted in the success of the technique. The Lichtenstein's method of hernia repair has been associated with lower percentage of post-operative complications and low recurrence rates. It is probably the

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most widely practised technique today. The technique involves the placement of a polypropylene mesh tailored to fit along the inguinal canal floor and form a new and tighter deep ring. This new internal ring is more medial in position as compared to the previous anatomical internal ring [4].

In TEP, the peritoneum is not breached and thereby eliminating the risks of small bowel injury or obstruction. An incision is made infraumbilically, and the anterior rectus sheath on the ipsilateral side is incised. The rectus muscle is retracted laterally, and the preperitoneal space is bluntly dissected. A port is placed in this space for a balloon, which is insufflated to make room for dissection. Two additional ports are placed between this port and pubic symphysis. Peritoneum is dissected downwards and vas and testicular artery are visualized. A prosthetic mesh is then placed into the preperitoneal space [5].

Surgical procedures cause trauma to the patient's body and, as a result, inflammatory responses are induced. A higher degree of intra-operative injury is likely to induce greater inflammatory response and subsequently more complications post-operatively thereby prolonging recovery time [6].

Although a lot of research has taken place in the attempt to declare a possible winner amongst the open and endoscopic hernia repair procedures, the debate still continues. In this study, we will measure the change in the serum inflammatory markers post-surgery and compare one group with the other. A measurement of the inflammatory markers (TLC, hsCRP and IL-6 concentrations) in the pre- and post-operative period in patients undergoing Total Extra peritoneal inguinal hernia repair and Lichtenstein inguinal hernia repair can be used to estimate the magnitude of the inflammatory response. The results will enable us to reach a conclusion.

Materials and methods

The study was conducted in the Department of Surgery, Lady Hardinge Medical College and associated Smt. Sucheta Kriplani Hospital, New Delhi from November 2012 to March 2014. Sixty (60) patients with diagnosis of unilateral uncomplicated inguinal hernia were included in the study. These were divided randomly, using a randomly generated sequence from the website www.randomizer.org [7], into two groups each of thirty (30) patients: one undergoing endoscopic TEP repair and the other open Lichtenstein repair. All, except one patient, were men aged between 18 and 76 years.

All patients undergoing elective endoscopic TEP and open Lichtenstein inguinal hernia repair with the diagnosis of unilateral uncomplicated primary inguinal hernia were

included in the study. Informed consent was obtained from all individual participants included in the study.

Patients with any systemic infection or any foci of infection, who developed perioperative complications, who were immunocompromised or had bilateral inguinal herniae, were excluded from the study.

All the patients operated on in the TEP group had been given general anaesthesia and were operated on by the same surgeon. The procedure duration did not exceed 120 min. All the patients operated on in the Lichtenstein group had been given spinal anaesthesia and were operated on by the same surgeon. The procedure duration did not exceed 80 min. Polypropylene (PROLENE®) mesh for Lichtenstein procedure and Polypropylene (PROLENE SOFT®) mesh for endoscopic TEP repair of size 3" × 6" inches were used (Type 1: Macroporous [8]).

In the perioperative period, prophylactic antibiotic therapy (Inj. Amoxicillin + Clavulanic acid 1.2 g i.v.) was administered and continued till next 24 h post-operatively. The patients in both groups received analgesics (Inj. Diclofenac Sodium 75 mg i.m. 12 hourly for 48 h) as a standard during the post-operative period.

Patients for inguinal hernia surgery eligible to the study groups were admitted 2 days before the procedure. All selected patients granted their informed consent to the procedure. Venous blood sampling was done twice, 24 h before and 24 h after the surgery, to determine the serum concentrations of IL-6, hsCRP levels and TLC counts.

High sensitivity CRP (hsCRP) estimation is based on the principle of a solid-phase enzyme-linked immunosorbent assay. Plasma IL-6 was determined by the quantitative immune-enzymatic test. TLC counts were determined with the aid of autoanalyser (SYSMEX KX-21).

The data were collected and analysed using SPSS version 20 software. Since the data obtained were non-parametric, variables were compared using the Mann–Whitney and Wilcoxon Signed Ranks Tests.

Table 1 Age distribution

Age groups (years)	Number (total = 60)	Percentage
<20	5	8.3
21–30	18	30.0
31–40	14	23.3
41–50	9	15.0
51–60	6	10.0
>60	8	13.3

Results

Table 1 shows the age distribution of participants in the study. The majority of the patients belonged to the 21–30 years age group (30%). Out of the 60 patients in the study, only one was female and underwent endoscopic TEP inguinal hernia repair. All patients who underwent Lichtenstein repair were males.

The patients undergoing the surgery were classified using the EHS classification system [9] for inguinal hernia. Table 2 shows the distribution among each group.

The serum TLC, hsCRP and IL-6 levels in patients of endoscopic TEP and open Lichtenstein repair are shown in Table 3. Statistically significant rise (P value <0.05) in the serum TLC, hsCRP and IL-6 values was seen in the post-operative period in both the groups.

Since the mean values of the variables, i.e. serum TLC, hsCRP and IL-6 in the two groups, during the pre-operative and post-operative periods are comparable; the magnitude of change can be compared statistically. As the data are non-parametric, Mann–Whitney test (U) and Wilcoxon Signed Rank test (W) are used. The Mann–Whitney test compares statistically the change in the values of the three variables amongst the two groups. A lower value of U suggests the possibility of the null hypothesis being false, i.e. there is a significant statistical difference. This is further supported by the P value. Significant difference was observed in the magnitude of rise in TLC values post-operatively, higher values being seen in the group that underwent Lichtenstein repair. Table 4 shows the comparison of the magnitude of difference in the two groups.

Table 2 EHS classification of patients included in the study

	P			
	0	1	2	3
TEP				
<i>L</i>	–	10	10	2
<i>M</i>	–	2	4	2
<i>F</i>	–	–	–	–
Lichtenstein				
<i>L</i>	–	9	11	3
<i>M</i>	–	1	3	3
<i>F</i>	–	–	–	–

P primary hernia, L lateral/indirect hernia, M medial/direct hernia, F femoral hernia, 0 no hernia detectable, 1 <1.5 cms (one finger), 2 <3 cms (two fingers), 3 >3 cms (more than two fingers)

Note: patients with recurrent (R) hernia were not included

Table 3 Serum levels of inflammatory markers in the study group

Type of surgery		TLC values in study groups		hsCRP values in study groups		IL-6 values in study groups	
		Before surgery (/ml)	After surgery (/ml)	Before surgery (mg/L)	After surgery (mg/L)	Before surgery (pg/mL)	After surgery (pg/mL)
TEP	Mean $\pm$ SD	6853.33 $\pm$ 1444.0	8480 $\pm$ 1797.39	2.17 $\pm$ 2.34	21.3 $\pm$ 6.7	7.0 $\pm$ 9.9	64.2 $\pm$ 27.3
Lichtenstein	Mean $\pm$ SD	6586.67 $\pm$ 1859.5	9093.33 $\pm$ 2499.6	2.45 $\pm$ 2.1	24.4 $\pm$ 7.3	8.8 $\pm$ 7.2	64.4 $\pm$ 22.7

* Significant value <0.05 (Using Wilcoxon Signed Rank Test)

Table 4 Comparison of the magnitude of difference in the two groups

	Difference in TLC	Difference in hsCRP	Difference in IL-6
Mann–Whitney <i>U</i>	267.5	350.5	448.5
Wilcoxon <i>W</i>	732.5	815.5	913.5
<i>Z</i> score	−2.7	−1.471	−0.022
<i>P</i> value	0.007*	0.141	0.982

* Significant value <0.05 (using Wilcoxon Signed Rank Test)

Discussion

Inguinal hernia repair has undergone considerable changes in the surgical techniques and as technology advances, further progress is expected. The recent advancement is the endoscopic repair of the inguinal hernia. However, contrary to some other procedures, such as cholecystectomy, where laparoscopic technique has replaced the open technique and is said to be the gold standard, such a phenomenon has not been witnessed yet in inguinal hernia repair. Thus, the debate continues: which procedure is the best for the patient, open or laparoscopic? Since, multiple surgical techniques are available in both the groups; numerous studies have taken place comparing one to the other.

Damage or injury to the body tissues is an event which initiates the inflammatory response within the body. The presence of the primary defence elements in the blood circulation is the reason behind the prompt and instant development of inflammation at the injured site. The inflammatory response prevents the spread of damaging agents to neighbouring tissues, disposes off dead cells and pathogens and enables the initiation of the repair process. The five classic signs of inflammation are redness, heat, swelling, pain and impairment of function. The inflammatory process begins with the release of a group of inflammatory chemicals in the extracellular fluid. Injured tissue cells, phagocytes, lymphocytes, mast cells and blood proteins are all capable of releasing inflammatory mediators, the most significant of which are histamine, kinins, prostaglandins, complement, and lymphokines. These chemicals make the local capillaries more permeable. These chemicals result in localized oedema or swelling which presses upon adjacent nerve endings causing pain. Pain is also caused by the release of bacterial toxins, the absence of nutrition to the cells in the area, and due to the action of released prostaglandins and kinins [10].

Cytokines consist of low-molecular weight proteins which include the interleukins and interferons. They are synthesized from activated leucocytes, fibroblasts and endothelial cells. This step is an initial response to tissue injury and has a significant role in mediation of immunity and inflammation [11]. The cytokines play a pivotal role in the inflammatory response to surgery and trauma. Their

local effects comprise of mediating the inflammatory response to tissue injury. Cytokines also initiate some of the systemic changes which occur. Post-surgery, the key cytokines that are released include Interleukin-1 (IL-1), Tumour Necrosis Factor- α (TNF- α), and Interleukin-6 (IL-6). The first step is the release of IL-1 and TNF- α from activated macrophages and monocytes of the injured tissues. This stimulates the synthesis and secretion of further more cytokines, out of which IL-6 is the predominant one responsible for inducing systemic changes. These changes are known as the acute phase response [12]. Within half to 1 h after the start of surgery, IL-6 concentration rises. Cytokine production and serum level are directly proportional to the degree of tissue trauma sustained. Hence, cytokine synthesis is the lowest with procedures that are less invasive and less traumatic, such as laparoscopic surgery. IL-6 stimulates the production of ‘acute phase proteins’ in the liver [12]. These include CRP, fibrinogen, α 2-macroglobulin and other anti-proteinases. Laparoscopic surgery causes a lesser tissue injury when compared to open procedures and, therefore, the magnitude of rise in concentrations of biochemical markers of inflammation is not as high [13].

Ever since the use of mesh in the surgical repair of groin hernia, numerous research studies have taken place investigating its role and the effects it has on the final outcome. In today’s era, meshes have been recommended as the general standard for hernia repair [14]. The first question which needed to be answered was obviously, which mesh was ideal for groin hernia repair? Klinge et al. thoroughly discussed the various ‘Textile implants’ or the so-called ‘meshes’ in their work, appropriately titled, “The Ideal Mesh?” Due to the extensive variety of surgical procedures which utilize meshes, the quest for one ideal mesh for all defects and purposes is almost impossible to achieve. However, the authors did suggest certain guidelines to aid the surgeon in the selection of the suitable mesh for a particular procedure [15]. The type of filament, tensile strength and porosity of the mesh are considered to be of utmost importance. These properties contribute to the weight of the mesh and its actual biocompatibility. The other properties of mesh include elasticity, constitution and shrinkage. The mesh has evolved significantly ever since its advent, some 30 years ago, to become a more

biocompatible product today. Over this period, it became evident that the tensile strength that a mesh must possess to withstand the maximum abdominal pressure was actually only one-tenth that of most meshes in use. This discovery gave way to the development of light weight meshes. Light weight meshes are supposed to be better than the conventional heavy weight meshes due to increased flexibility, large pore size, reduced risk of infection and shrinkage and better comfort. Composite meshes and bioprosthesis are the recent materials which find little use in routine groin hernia repair, but are of immense potential elsewhere. Most common complications of mesh use are local infection, dense adhesions, pain, seroma formation, mesh degradation and recurrence [16]. Even though research has given, and will continue to do so in the future, the surgeon a vast variety and the latest of 'textile implants' to choose from for a particular hernioplasty; the surgical skill remains indispensable. The method in which the mesh is placed has a significant role in preventing future complications [17].

Researchers have compared the inflammatory response incited by various procedures in the past. The procedures include Shouldice herniorrhaphy, Bassini's herniorrhaphy and Lichtenstein's hernioplasty. One such study is "The Comparison of Inflammatory Responses and Clinical Results After Groin Hernia Repair Using Polypropylene or Polyester Meshes". The authors divided the patients into two groups, one who underwent Shouldice herniorrhaphy and the other Lichtenstein hernioplasty (using polypropylene/polyester mesh). Serum levels of IL-6 and CRP were measured pre- and post-operatively. Post-operative pain and time to return to normal activities were observed. The results showed that the serum IL-6 levels returned to the baseline levels in both the groups after 48 h; however, the serum CRP levels remained significantly elevated in the Lichtenstein group even after 48 h, while they returned to pre-operative levels in the herniorrhaphy group. Clinical evaluation found that the Lichtenstein repair group had earlier recovery and lesser post-operative pain. The study concluded that there was no significant difference in the inflammatory response incited by each of the two procedures [18].

In contrast to the aforementioned study results, a group of researchers led by Di Vita proposed that Lichtenstein hernioplasty causes a greater inflammatory response as compared to the Bassini's herniorrhaphy in their report titled "Tension-free hernia repair is associated with an increase in inflammatory response markers against the mesh". The investigators obtained venous blood samples prior to surgery and multiple samples post-operatively at fixed time intervals. Patients who underwent Lichtenstein repair had higher elevated levels of serum fibrinogen, CRP, alpha 1—antitrypsin and IL-6 as compared to those who underwent Bassini's herniorrhaphy. Consequently, patients

who had undergone mesh hernioplasty had lesser pain and earlier recovery as compared to those who underwent herniorrhaphy. The higher inflammatory response is possibly attributed to the presence of polypropylene mesh [19]. The study shows that the group of patients undergoing Lichtenstein repair recovered earlier and complained of less post-operative pain, although there is evidence of a higher inflammatory response in the group.

Bender and colleagues, in their prospective randomized trial, compared the systemic inflammatory response after Kugel repair and laparoscopic groin hernia repair (TEP). With a sample size of forty patients, equally distributed amongst the two groups, the investigators compared the operation duration, hospital stay, pain severity, systemic inflammatory and hormone response, time to return to normal activities and cost between the two procedures. The results of the study suggested that the two procedures did not differ much in terms of operation duration, length of hospital stay, pain and time to return to normal activities. The rise in serum Cortisol, hsCRP and IL-6 concentrations after Kugel repair did not seem to differ significantly as those observed in the TEP repair group. However, the cost of the procedure per patient was substantially lower in the Kugel group. Hence, the authors concluded that Kugel repair offers all the advantages of the laparoscopic repair (TEP) in addition of being less costly [20].

In a study titled "Assessment of inflammatory response intensity in early post-operative period in patients after hernioplasty operated on with classic Stoppa method and videoscopic TEP method", the researchers measured serum TLC, CRP and IL-6 in the post-operative period. The inflammatory response estimated with CRP, IL-6 concentration in blood serum was considerably higher in patients who underwent Stoppa method. There was a significant increase in serum CRP and IL-6 in the post-operative period in the Stoppa method compared to the TEP method. A significant difference was not observed in increase of white blood cells' concentration in both the groups. The hospitalization time was considerably shorter in patients operated on with endoscopic method. Patients who underwent Stoppa procedure experienced stronger pain in the post-operative period. Wound healing occurred with a stronger inflammatory reaction when compared to the TEP procedure [2]. In contrast, the present study shows a significant rise in serum TLC in the open method compared to the endoscopic method. There was no significant difference in the serum CRP and IL-6 rise between the open and endoscopic groups [2]. In the above-mentioned study by Libiszewski M et al., the plane of dissection was same in both the endoscopic TEP and classic Stoppa techniques. In the present study, the planes of dissection are different in the Lichtenstein and endoscopic TEP techniques.

Schwab R et al. published a study to determine whether laparoscopic repair techniques are also preferable to conventional procedures. Biochemical monitoring of cytokine activity (CRP, prostaglandin F1 α , neopterin, interleukin-6) was done prospectively in 101 patients [TEP $n = 32$, Shouldice $n = 69$,] before and until 3 days after surgery. The inflammatory response immediately post-endoscopic hernia surgery was significantly higher, as suggested by elevated levels of prostaglandin F1 α and IL-6, in comparison to the Shouldice repair. This study concluded that the Shouldice procedure appears to cause a lower inflammatory response when compared with the endoscopic TEP technique [21].

Advantages of endoscopic surgery include early return to routine activities and a lesser persisting pain and numbness [22]. In his research article, Fegade concluded that a considerably lower inflammatory response was present in the patients who underwent endoscopic repair, which accounted for the reduced post-operative pain and reduction in hospital stay [3].

There are conflicting reports in the literature regarding as to which surgery incites a lesser inflammatory response, as is evident from the above discussion. In a randomized control study comparing the operating time, pain scores, time to return to work, complications and cosmesis between open Lichtenstein repair and endoscopic TEP, Lal et al. concluded that patients undergoing TEP recover earlier. Furthermore, TEP causes significantly lesser pain in the post-operative period, is associated with early return to work, and has a better cosmetic outcome although the mean operating time was significantly more [23]. However, laparoscopic hernia repair costs more, has a steep learning curve and has an increased risk of injuries [24]. Moreover, conditions such as strangulated hernia, sliding hernia and irreducible hernia are not amenable to laparoscopic repair. Elderly patients and those having co morbid conditions are also not suitable candidates to undergo laparoscopic repair. Also, the surgery cannot be done as a 'day care' procedure [25]. Recurrence of hernia after surgery is perhaps the most important parameter deciding the success or failure of the procedure. Recurrence of hernia depends on the type of hernia repair, the presence or absence of any co morbidities and duration of time from the original repair [26]. The available literature suggests no significant difference in recurrence between open and laparoscopic methods of hernia repair [27–29]. A group of researchers led by Koning GG, after evaluating 13 trials with a high risk of bias, conclude in their systematic review with meta-analyses and trial sequential analyses of randomized clinical trials that there is no evidence of a difference between TEP and Lichtenstein in terms of chronic pain, recurrences and severe adverse events [30].

The type of analgesic technique used determines the degree to which the responses are altered. Blockade of stress responses is seen to be highest in neural blockade with local anaesthetics. There is some evidence to suggest

that analgesia given using neural blockade enhances the recovery. The type of the surgical technique has a significant role in the process of recovery; laparoscopic procedures are followed with a speedy recovery and early discharge. The response to the surgery, however, is also governed by the behavioural and subjective changes. The use of minimally invasive surgical techniques will lessen the effects of tissue damage [12]. In experienced hands, hernia repair done endoscopically is safe, is associated with less post-operative morbidity and advantageous over the open procedure. Laparoscopic approach has been recommended for bilateral and recurrent inguinal hernias [4].

This study confirms the increase in inflammatory markers post surgery, in both the groups. There is also a statistically significant difference in one of the variables (serum TLC), between the two groups. However, based on these results, it cannot be conclusively stated that the inflammatory response is more in open Lichtenstein mesh hernioplasty when compared to endoscopic TEP repair. Keeping in mind this discussion, we come to the conclusion that the available literature does not clearly indicate which procedure of the two is superior. Hence, the surgeon's preference shall continue to determine the procedure chosen in the near future [26].

This study does not conclusively demonstrate that inflammatory response is lower in endoscopic TEP compared to the open repair. One of the reasons for this can be that the area of dissection is more in endoscopic TEP than in open Lichtenstein repair; however, this is only a hypothesis. An important point to note here is that endoscopic surgery is done under general anaesthesia whereas the Lichtenstein procedure is done under regional anaesthesia. The advantages of endoscopic hernia repair are probably because of a smaller skin incision and not just because of the relatively decreased rise in the inflammatory markers when compared to the open repair group. This aspect requires further research, which would investigate the role of the extent of dissection, size of skin incision, post-operative pain scoring and further follow-up with serum inflammatory markers in a larger sample size.

Conclusion

Endoscopic TEP and open Lichtenstein inguinal hernia repair both cause a rise in the inflammatory markers in the body. A pre-operative and post-operative measurement of the values of serum TLC, hsCRP and IL-6 has helped us to confirm the rise in the post-operative period in both the groups. This rise was statistically significant in both the groups (P value = 0.001). When the rise in inflammatory markers of one group was compared with the other, a significant difference was observed in serum TLC only (P value = 0.007), higher value being observed in

Lichtenstein repair group. The difference in hsCRP between Lichtenstein and endoscopic TEP repair group was not statistically significant (P value = 0.141). The rise in IL-6 was equivocal (P value = 0.982). Based on our results, it cannot be stated conclusively that endoscopic TEP is associated with lesser inflammatory response compared to open hernia repair.

A more extensive study, with assessment of response in multiple variables, may be recommended. The study may include parameters like post-operative pain score, extent of dissection intra-operatively, size of the skin incision, hospital stay and duration of absence from work to further compare the open and laparoscopic hernia repair procedures.

Compliance with ethical standards

Declaration The authors declare that the study experiments comply with the current laws in India.

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Conflict of interest MV, DP, SS, NT, GS, MA, and AK have declared no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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