

Systemic immune response after open tension-free inguinal hernia repair under different anesthetic alternatives: a prospective comparative study

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SUMMARY: Systemic immune response after open tension-free inguinal hernia repair under different anesthetic alternatives: a prospective comparative study.

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Purpose. The purpose of the present study was a comparison of the systemic inflammatory response intensity through the estimation of C-reactive protein and albumin levels before and after open tension free inguinal hernia repair performed under different anesthetic alternatives.

Patients and methods. Totally, 125 inguinal hernia patients scheduled for unilateral primary open tension free inguinal repair un-

der local (50 patients), spinal (50 patients) and general anesthesia (25 patients) have been included in this prospective study.

Results. The group of local anesthesia was associated with the higher postoperative serum levels of albumin compared to the group of general anesthesia (P 0.013). Local anesthesia was also associated with higher postoperative serum albumin levels compared to regional anesthesia but however the difference was not statistically significant (P 0.282). The group of local anesthesia was also associated with the lower postoperative levels of CRP compared to the regional (P 0.0094) and general anesthesia (P 0.0009) groups.

Conclusion. Local anesthesia proved superior to regional or general anesthesia for open tension free inguinal hernia repair in the given patient sample from the standpoint of the inflammatory and acute phase response.

KEY WORDS: Systemic immune response - Open inguinal hernia repair - Tension free - Local anesthesia.

Introduction

Surgery initiates a systemic inflammatory response that is, generally, proportional to the magnitude of the surgical trauma (1). Minimally invasive surgical procedures are considered of being less traumatic than conventional techniques (2). Laparoscopic colorectal cancer resections and laparoscopic cholecystectomy have been evaluated with respect to the immunologic impact on human organism and their advantages over the conventional open procedures have been well-documented (3). Using the same methodological principles, studies also evaluated the role of the laparoscopic repairs in inguinal

hernia with not however respective homogeneity in the reported results (4-6). Despite however, the relatively recent introduction of these innovative approaches, open tension-free inguinal hernia repair with mesh placement is still considered a valid procedure with certain well-established advantages (7).

Regarding the methods of anesthesia, local anesthesia under a strictly determined application protocol represents an efficient method of anesthesia for open tension-free inguinal hernia repair (7). Only young, extremely anxious or obese patients might not be ideal candidates for the proposed technique (7). However, the adaptation of these guidelines in daily clinical practice appears problematic. Still, in many especially northern European countries, general anesthesia remains the mostly utilized anesthetic method for surgical procedures such as open inguinal hernia repair (8).

Within this framework of notable diversity, a

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study that would compare in terms of systemic immune response open tension free inguinal hernia repair performed under different anesthetic options appeared especially attractive. Aiming to throw some additional light in this highly debated area i.e. the optimal method of anesthesia for open inguinal hernia repair, we conducted this prospective study taking into account only parameters of the immunological impact of each procedure on human organism. Therefore, the purpose of the present study was a comparison of the inflammatory response intensity through the estimation of C- reactive protein (CRP) and albumin levels before and after open tension free inguinal hernia repair performed under different anesthetic alternatives.

Patients and methods

Internal board approval and ethics committee permission was obtained prior to the initiation of this prospective study. Since October 2007, 125 inguinal hernia patients scheduled for unilateral open primary surgical repair have been included in the study. Patients with scrotal, recurrent, bilateral, strangulated and incarcerated hernias or patients who were on immunosuppressive medication, up to six months prior to the operation, were excluded from the study. In addition, we excluded patients where the intra-operative findings dictated the use of a drain or those where a relatively long incision - > 8 cm in length - was undertaken due to difficulties in achieving adequate exposure.

In our daily clinical practice, at the Department of Surgery, University Hospital of Larissa, open tension free inguinal hernia repair is performed under three different types of anesthesia: local, regional or general. In any case, the decision about the anesthetic technique was left at the patient's discretion after a detailed informative discussion with the surgeon.

Anesthetic techniques

All patients received a standard sedation protocol with 50 mg pethidine I.M. and premedication with 0.1mg atropine I.V. prior to the operation. Local

anesthesia was performed with the infiltration of 40ml of lidocaine 1% at the site of incision (subcutaneous fat and intradermic level) and then at deeper layers as well as underneath the external oblique aponeurosis, inside the inguinal canal. Regarding spinal anesthesia, with the patient in the right lateral decubitus position, a 25-gauge pencil-point spinal needle was introduced into the subarachnoid space at the L2-L3 intervertebral space, under aseptic conditions. After free flow of cerebrospinal fluid was obtained, 3 mL of hyperbaric bupivacaine .5%, .25 mg of morphine, and 20 µg of fentanyl were injected intrathecally. Finally, standard general anesthesia with endotracheal intubation was the last anesthetic option. Patients were monitored continuously during the operation by both clinical observation and intensive hemodynamic monitoring.

Surgical technique

After a 7 to 8 cm skin incision, the external oblique aponeurosis was incised. With careful manoeuvres we aimed at identifying and preserving the ilio-inguinal and ilio-hypogastric nerves. The spermatic cord was carefully dissected free from the hernia sac, which was always reduced. The inguinal ligament was dissected towards the pubis up to the anterior superior iliac spine. A wide dissection of the conjoined tendon and the rectus muscle aponeurosis was performed up to the pubic tubercle in order to create the space required to spread out the mesh. Direct or indirect inguinal hernias were treated with the same principles. An absorbable plug (Gore BIO A hernia plug®) was placed in the internal ring of the inguinal canal preperitoneally and fixed with one or two absorbable sutures. This manoeuvre was common in all open repairs irrespective of the hernia type i.e. direct or indirect. Then, an expanded Polytetrafluoroethylene (e-PTFE) non-absorbable patch (GORE-TEX® Soft Tissue Patch) was placed into the inguinal canal, and it was secured in place with non-absorbable sutures. Finally, the external oblique aponeurosis was closed and refashioned, superficially to the spermatic cord, by continuous non-absorbable suture.

Antibiotic prophylaxis was not routinely used

and only patients who required a Foley catheter placement received a single dose of a second generation cephalosporin. Low molecular weight heparin subcutaneously and proton pump inhibitors intravenously were routinely administered. A standard postoperative analgesic protocol was followed in all cases with oral administration of Paracetamol 500mg every 6 hours and 40mg Parecoxib sodium twice a day iv. On-demand analgesics were administered in cases where the standard protocol did not achieve adequate pain control. All operations were performed according to the same predetermined principles from the study design by four specialized surgeons with years of experience in open hernia repair.

According to the available anaesthetic alternatives patients were assigned into one of the following categories: open repair under local anesthesia, open repair under spinal anesthesia, open repair under general anesthesia. The systemic inflammatory response was quantified for comparison purposes by the anticipated reduction in serum albumin levels and the rise of serum CRP levels following the procedure. So, blood samples were obtained from each patient pre- and 24 hours postoperatively in order to determine the aforementioned parameters in patient's serum. We aimed to a minimum of fifty (50) patients per group for preliminary analysis.

The statistical analysis was made using the SPSS® software (Statistical Package for Social Sciences) version 15. Unpaired t tests were used to compare the mean values \pm standard deviation. A result is consid-

ered statistically significant when the P value is under 0.05.

Results

Totally, 125 patients were included in the final analysis. Fifty (n.50) patients were submitted to open repair under local anesthesia, fifty (n.50) patients to open repair under spinal anesthesia and finally twenty-five (n.25) patients were submitted to open repair under general anesthesia. Regarding the parameters that reflect the systemic inflammatory response in the three groups according to study design, the mean values \pm standard deviation of albumin (gr/dl) and CRP (mg/l) either pre- or 24 hours postoperatively are shown at Tables 1 and 2 respectively. The statistical analysis revealed a statistical significant variation between the pre- and the postoperative levels of each parameter i.e. albumin and CRP in all three patient groups (P 0.0001).

As the preoperative serum levels of either albumin or CRP were equivalent and within normal range in all three groups, a comparison of the groups regarding the postoperative levels of albumin and CRP seemed appropriate. The comparison of the postoperative serum levels of albumin and CRP in the three groups of the study is shown at Table 3. Regarding serum albumin levels, open inguinal hernia repair performed under local anesthesia was associated with the higher recorded mean postoperative serum levels of albumin compared to the open repair

TABLE 1 - PRE- AND POSTOPERATIVE SERUM ALBUMIN (GR/DL) LEVELS (MEAN \pm STANDARD DEVIATION) IN EACH GROUP OF THE STUDY AND THE COMPARISON (P VALUE) BETWEEN THE PRE- AND THE POSTOPERATIVE LEVELS IN EACH GROUP.

	Pre - op Albumin	Post - op Albumin	P value
Open local	3,89 \pm 0,37	3,47 \pm 0,38	0.0001
Open regional	3,83 \pm 0,36	3,39 \pm 0,36	0.0001
Open general	3,85 \pm 0,33	3,23 \pm 0,4	0.0001

TABLE 2 - PRE- AND POSTOPERATIVE SERUM CRP (MG/L) LEVELS (MEAN ± STANDARD DEVIATION) IN EACH GROUP OF THE STUDY AND THE COMPARISON (P VALUE) BETWEEN THE PRE- AND THE POSTOPERATIVE LEVELS IN EACH GROUP.

	Pre - op CRP	Post - op CRP	P value
Open local	2,6 ± 1,6	9,9 ± 5,3	0.0001
Open regional	2,4 ± 2,1	13,4 ± 7,7	0.0001
Open general	2,4 ± 2,8	15,4 ± 8,4	0.0001

TABLE 3 - COMPARISON OF THE THREE GROUPS OF THE STUDY (P VALUE) REGARDING THE POSTOPERATIVE SERUM ALBUMIN LEVELS (SUPERIOR TABLE HALF) AND SERUM CRP LEVELS (INFERIOR TABLE HALF).

CRP \ Albumin	Open local	Open regional	Open general
Open local		0.282	0.013
Open regional	0.0094		0.084
Open general	0.0009	0.307	

under general anesthesia (P 0.013). Open repair under local anesthesia was also associated with higher serum albumin levels compared to the open repair under regional anesthesia but however the difference was not statistically significant (P 0.282).

Regarding CRP levels, the group of open hernia repair performed under local anesthesia was associated with the lower postoperative levels of CRP compared to the open repair under regional (P 0.0094) and general anesthesia (P 0.0009). Conversely, open

inguinal hernia repair performed under typical general anesthesia with endotracheal intubation provoked the greater systemic inflammatory response compared to the other patient groups.

Discussion

Acute-phase proteins are a class of proteins whose plasma concentrations increase - positive acute

phase proteins - or decrease - negative acute phase proteins - in response to tissue injury and subsequent inflammation as a part of a systemic organic reaction called the acute phase response (9). In response to tissue trauma, inflammatory cells aggregate locally and secrete a number of cell-signaling protein molecules, the cytokines, into the bloodstream (10). Interleukins IL-1, IL-6 and IL-8, and tumor necrosis factor - α (TNF- α) are the most potent that stimulate the liver to produce a large number of acute phase reactants such as CRP, ferritin and ceruloplasmin - positive response (11). Simultaneously, the liver production of other proteins such as albumin, transferrin and antithrombin is decreased - negative response (12). Therefore, the measurements of the serum levels of these acute phase proteins are especially useful markers of systemic inflammation (1).

However, besides trauma or infection, several different forms of stimuli such as stress or neoplasia can also activate the acute phase response (1). Aiming to reestablish homeostasis after a stressful event and promote the healing process after tissue injury, the response serves as a core of the innate immune system (1). The quantification of this response in terms of individual acute phase protein measurements can provide a relatively accurate assessment of the impact on the organism caused by the triggering event (1). By definition, anesthesia and surgery significantly disturb the internal environment of the human organism promoting the activation of the acute phase response.

Inguinal hernia repair is a surgical field of constant debate. The optimal technique for the repair has not been solidly established yet. Laparoscopic techniques, either the totally extraperitoneal (TEP) or the trans-abdominal preperitoneal (TAPP) approach, have been added to the existing open tension free repairs rendering the searching process for the optimal technique extremely problematic. Long term comparison parameters such as the incidence of recurrences and of chronic pain as well as the short term complications such as the incidence of hematoma formation and/or infection have been utilized in order to compare the existing modalities and consequently highlight the best available technique.

However, as studies comparing the open and the laparoscopic approach report generally similar and comparable results, a consensus has not been practically reached (7). Virtually, either the open tension free inguinal hernia repair or the laparoscopic approach are evenly indicated for the repair of primary unilateral uncomplicated inguinal hernias (7).

In order to provide a more objective assessment in the field of surgical hernia repair studies have also used the methodology of acute phase response quantification for the comparison between the available surgical alternatives. However, many of these studies were mainly aligned in the direction of comparing the newly introduced laparoscopic variant in inguinal hernia repair surgery with the conventional open approaches such as the Shouldice, the Stoppa or the Lichtenstein technique, yielding relatively expected results in favor of the former (4, 6, 13, 14). As open tension free repair with mesh placement remains the mainstream in inguinal hernia repair in many specialized centers worldwide, a study that would evaluate, from the physiologic viewpoint, the optimal method of anesthesia for this surgical approach could add precious data to the existing knowledge. The European Hernia Society currently underscores the beneficial effect of local anesthesia for open hernia repair as it fulfils the prerequisites for day surgery and suggests that local anesthesia should be the anesthetic of choice in cases of open repair (7).

In the present study, we utilized the variations of serum albumin and CRP concentration after elective inguinal hernia repair under different types of anesthesia in our department in order to quantify the systemic immune response. Patients, after an informative discussion with the concerned surgeon, finally decided about the followed anesthetic option for open tension free inguinal hernia repair i.e. local, regional and general. The lack of randomization and the consequent selection bias represent limitations of this prospective study. However, we consider that evaluating the predetermined parameters within the context of daily clinical practice has also a significant scientific value. The fact that patient's preferences played the key role for the assignment in the study groups explains the unequal allocation among the

three groups. Generally, patients were reluctant to undergo the repair under general anesthesia. However, we consider this as a matter of less importance as statistical significance was reached regarding the study end points despite the limited number of patient in this operative category. After the predetermined number of patients (50 patients) in each group was reached, subsequent patients were still offered this anesthetic option but however they were excluded from the blood sample collection protocol of the study.

According to the study design, the repair technique was identical and strictly determined i.e. length of incision, reduction of the hernia sac, the use of a plug irrespective of the hernia type in all patients in order to neutralize bias from the comparison of different open surgical strategies. The net result was an actual comparison of the available anesthetic alternatives. In addition, the four involved surgeons were chosen on the basis of the adequate experience in the field of open tension free inguinal hernia repair. Forced by the logistics of the current medical setting, we used an e-PTFE mesh instead of the standard polypropylene for the reinforcement of the posterior inguinal canal wall. However, the common use in all patient groups of a material conformed to the universal standards for inguinal hernia

repair is a valid alternative leading to equally objective results.

According to our data, the group of patients that were submitted to open tension free hernia repair under local anesthesia was associated with the lesser activation of the systemic inflammatory response compared to the other groups. Generally, all groups experienced a significant alteration of the serum levels of either albumin or CRP following the hernia repair. However, albumin levels decline and CRP levels increase following the procedure was lesser for the open repair under local anesthesia group compared to the other groups. Conversely, the group of open repair under general anesthesia exhibited the lower recorded postoperative mean albumin levels while it was associated with the higher postoperative mean CRP levels. Certainly, carefully designed prospective randomized studies with large number of patients are needed in order to evaluate the full extent of the systemic immune response provoked after open inguinal hernia repair under different anesthetic alternative.

In conclusion, local anesthesia proved superior to regional or general anesthesia for open tension free inguinal hernia repair in the given patient sample from the standpoint of the inflammatory and the acute phase response.

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*Systemic immune response after open tension-free inguinal hernia repair under different anesthetic alternatives:
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