Immunological reaction and oxidative stress after light or heavy polypropylene mesh implantation in inguinal hernioplasty

A CONSORT-prospective, randomized, clinical trial

Marcello Donati (MD, PhD)a, Giovanni Brancato (MD, PhD)a, Giuseppe Grosso (MD, PhD)b, Giovanni Li Volti (MD, PhD)c,d, Giuseppina La Camera (PhD)a, Francesco Cardì (MD)a, Francesco Basile (MD)b, Angelo Donati (MD)e

Department of Surgical Sciences, Organ Transplants and New Technologies, University of Catania, Catania, Italy.

Abstract

The relationship between mesh weight and host tissue reaction has, so far, not been fully investigated. Lightweight meshes (LWM) are thought to give less inflammatory response compared with heavyweight meshes (HWM). The present study is a randomized, controlled, double-blind clinical trial performed in 61 patients who underwent an elective inguinal hernioplasty. The primary outcome of the study was to investigate the relationship between total amount of prosthetic material (polypropylene), immunological reaction, and oxidative stress. The study was double-blinded. Sixty-one patients were recruited for the study and randomly assigned to 2 groups (groups A and B). Levels of inflammation markers (interleukin-6 [IL-6] and tumor necrosis factor-α [TNF-α]) and oxidative stress markers [reduced glutathione (GSH)] and lipid hydroperoxides [LOOH)] were determined preoperatively and after undergoing inguinal hernioplasty (after 6, 72, and 288 hours), respectively, with LWM and HWM. There was no significant difference in IL-6 levels between HWM and LWM (P = 0.3, 0.7, 0.8 after 6, 72, and 288 hours, respectively). A statistically significant difference was found after 72 hours for TNF-α (P < 0.01), for GSH after 6 hours (P < 0.01), and after 6 and 72 hours for LOOH (P = 0.05, 0.01, respectively). Oxidative stress occurred at earlier time points and was more accentuated HWM versus LWM and prodromal to TNF-α increase.

Also, in randomized clinical trial, the use of LWM gives advantages in terms of less inflammatory response when compared with HWM. Moreover, there is a significant higher oxidative stress after implantation of HWM. The intensity of oxidative stress seems to be strongly related to the amount of implanted polypropylene. (Trial registration number: NCT01090294).

Abbreviations: BMI = body mass index, GSH = reduced glutathione, HWM = heavyweight mesh, IL = interleukin, LOOH = lipid hydroperoxides, LWM = lightweight mesh, TNF-α = tumor necrosis factor-α.

Keywords: cytokines, immunologic reaction, inguinal hernia repair, oxidative stress, prosthetic repair

1. Introduction

The notable development and diffusion of prosthetic surgery of the abdominal wall over the last few years has led to the introduction of lightweight meshes (LWM).[1] The efficacy of inguinal hernia repair with lightweight prostheses, as well as the better or worse biotolerability with respect to those of lightweight, remains questionable in literature,[2] where a clear answer still remains to be given.[3,4] If there exists a connection between the quantity of material implanted, the immunological reaction to the mesh,[5] the induced oxidative stress and the degree of cicatrization,[6–8] and consequently the long-term result of the efficacy of the operation remains to be demonstrated,[9] and is still a matter of debate.[10] The impressive development of prosthetic hernia repair over the last 20 years has led industry and surgeons to research on new kinds of meshes. In the last 6 to 7 years, LWM have been introduced in clinical practice on the assumption that a lightweight prosthesis could reduce local complications, such as discomfort and chronic pain, or inguinal impairment, that had been referred to heavyweight meshes (HWM).[11,12] However, published studies have succeeded in demonstrating a lower incidence of discomfort and pain using LWM, but some studies have indicated a higher incidence of hernia recurrence.[13] Despite these results, some controversies[27] still remain and the general interest for LWM has remained.[14,15]

Immunological response seems to play a major role in the complex mechanisms of repair following mesh implantation. To
the polypropylene prostheses, which are more frequently used, induce a rapid and useful acute inflammatory response followed by an incorporation of them into the area of implant, with a limited fibroblastic response and a strong scar tissue. The inflammatory response seems to be characterized by increased levels of interleukin (IL)-6 and C-reactive protein associated with other modifications of inflammatory serum markers (fibrinogen, alpha-1 antitrypsin). The immunologic reaction to polypropylene was already studied in previous published reports. However, in the present study we studied different cytokines such as IL-6 and tumor necrosis factor-α (TNF-α) compared with the previously studied types (IL-1, interferon-γ, IL-10, fibroblast growth factor, and vascular endothelial growth factor) and how these variables are related to oxidative stress. IL-6 and TNF-α were separately studied in different groups and in a smaller cohort of patients, comparing traditional surgery with prosthesis repair for inguinal hernia. The main conclusion of these studies was that polypropylene mesh induces an inflammatory response that was quantitatively relevant with respect to traditional techniques. In some other reports, Di Vita et al. stated that such an immunologic response was proportional to the quantity of polypropylene inserted and additionally postulated that such an increase of cytokines (IL-6, TNF-α, IL-1, etc.) could be correlated to the incidence of local complications due to mesh. IL-6 is often induced together with TNF-α in many inflammatory conditions. However, whether IL-6 plays a pro- or anti-inflammatory role in local inflammation is not clear. Although it is commonly believed that IL-6 acts as an inducer of inflammatory genes, a recent report about IL-6 (−/−) mice indicates a crucial anti-inflammatory role by controlling the level of proinflammatory cytokines.

There are few studies on the immunological reaction to polypropylene meshes, few on the comparison between lightweight and heavyweight, and to the best of our knowledge, none on the oxidative stress induced by the mesh. Moreover, only one study has been published that clearly correlates the immunological reaction to the amount of prosthetic material. Whether the immunologic reaction depends on pore size and texture instead of materials remains questionable and controversial data have been published in the literature.

The aim of this research was to evaluate a possible relationship between the amount of implanted polypropylene and immunological reactions as well as postoperative oxidative stress, and thus to evaluate, if present, the differences in the biological reaction and biotolerability between LWM and HWM on a statistically significant number of patients with a randomized prospective clinical trial.

2. Materials and methods

2.1. Patients

Between March 2010 and December 2011, 64 patients were prospectively recruited and randomized in a double blind manner for the present study. Three patients (dropout rate 4.68%) were excluded from the study (lost to follow-up, postoperative discovery of multiple sclerosis, and a previous mesh implant). The recruitment of patients took place following the random order in which they were referred to the hernia service of the General Surgery and Week Surgery Unit of the University Hospital of Catania which is a large, high complexity university hospital. After physical examination confirming the diagnosis of inguinal hernia and once surgery had been indicated, informed consent was obtained from the patient by means of a standardized form. Hernia type was registered for each patient according to Rutkow classification. Regarding inclusion and exclusion criteria for the study, all patients affected by primary inguinal hernia between 18 and 90 years, not previously operated with implantation of a prosthetic mesh, were enrolled. Patients affected by diabetes, cirrhosis, any chronic inflammatory disease or under corticosteroids, and/or immunosuppressive therapies (neoplastic patients) were excluded from the study. A total of 61 patients were recruited. Two patients were, after being enrolled, excluded due to the discovery of previous operations with mesh implants and an anamnestic positivity for immunological disorders (multiple sclerosis), one patient did not return after the operation to complete the requested protocol of blood analyses. These 3 patients had previously been randomly assigned to LWM. Therefore, in the end 29 patients were enrolled in LWM, whereas there were 32 in HWM. This study was carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. The patients were not informed as to which prosthesis was implanted. The ethics committee of Policlinico-Vittorio Emanuele University Hospital of Catania approved the study, informed consent form, and the workflow of the research on March 2010, study code CH001GENI. Then the study was registered at http://clinicaltrials.gov/show/NCT01090284 (registration number assigned NCT01090284). The study ended in December 2011.

2.2. Study design

Patients were randomly assigned to 2 groups (random criterion: i.e., patient 1 (LWM), patient 2 (HWM): in LWM inguinal hernioplasty surgery was carried out with the use of the so-called “lightweight” type (40 g/m² of polypropylene); for HWM, on the contrary, the mesh was of the “heavyweight” type (220 g/m²). Simple randomization was used by flipping a coin.

The laboratory assessments were determined by another investigator without any information about sample origin (if from an LWH or HWM patient, this investigator was also blind to the randomization criteria), as well as kind of implanted mesh. Although anamnestic data of patients were collected by surgeons, the statistical evaluation was carried out by another investigator.

2.3. Study intervention

The 2 types of meshes had the same pore size, the same texture (monofilament polypropylene meshes), and came from the same manufacturer (HERTRA, Herniameshs.r.l. Chivasso, Turin, Italy). They differed only in weight (g/m²) (content of polypropylene). They did not differ for stiffness or size. For each patient, a preoperative blood test was carried out to determine the basal levels of IL-6, TNF-α, reduced glutathione (GSH), and lipid hydroperoxides (LOOH). All these components were determined on blood samples, respectively preoperatively, 6 hours after the operation, on 3rd and 12th postoperative days. All samples were frozen for reference. No perioperative preparation (including medications) was performed in all patients as for our guidelines. All the patients underwent an open local anesthesia (solution of mepivacain 2%, 30 mL) prosthetic inguinal hernia repair as gold standard technique, published variant of Trabucco’s repair with the apposition of one or more plugs. Mesh fixation was performed by suturing mesh flaps around spermatic cord through 2/0 polypropylene (Prolene)
stitches (Ethicon, Somerville, NJ). Wound size was about 10 cm and was closed by intradermic reabsorbible suture with 3/0 polyglactin 910 (Vicryl) (Ethicon). All surgical procedures were performed by the same experienced surgeon (surgical experience >40 years). All patients received postoperatively, ceftriaxone (1 g/die for 4 days), tramadol (1 vial), when requested by the patient to control postoperative pain. Patients were monitored in an ambulatory manner for 12 days and complications were recorded.

2.4. Study endpoints
The primary endpoint of the present research was to evaluate a possible relationship between the amount of implanted polypropylene and immunological reactions as well as postoperative oxidative stress, and thus to evaluate, if present, the differences in the biological reaction and biotolerability between LWM and HWM on a statistically significant number of patients with a randomized prospective clinical trial.

2.5. Sample dimension
According to previous studies,[19–21,26–28] a comparison of the means and standard deviations of TNF-α at baseline and 72 hours between the 2 intervention arms was taken into account for the calculation of the sample size. Power analysis showed that 30 participants in each arm of the trial were adequate to evaluate 2-sided standardized differences between subgroups of the study and that the investigated parameters >0.5 achieved statistical power >0.80 at 5% probability level (P value).

2.6. IL-6 and TNF-α determination
Cytokines were measured by commercially available enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN). The assay was performed in accordance with the protocol provided by the manufacturer and as previously described.[29,30] Briefly, sample was incubated with anti-IL-6 or anti-TNF-α, anti-rabbit immunoglobulin G, and horseradish peroxidase conjugates, in successive order. Absorbance at 450 nmol/L was measured, and cytokine concentrations were calculated from a standard curve generated with purified IL-6 or TNF-α. Each measurement was performed in triplicate and averages were reported.

2.7. Determination of GSH levels
Blood levels of total thiol groups (GSH) were measured in 200 μL of blood samples using a spectrophotometric assay based on the reaction of thiol groups with 2,2-dithio-bis-nitrobenzoic acid at λ = 412 nm. The limit of detection for this assay is approximately 15 nmol/L.[29,31] The intra-assay coefficient of variation is 4%, whereas the interassay coefficient of variation is 5.6%.

2.8. Determination of LOOH levels
LOOH levels were evaluated following the oxidation of Fe2+ to Fe3+ in the presence of xylenol orange at λ=560 nm. The assay mixture contained 100 mmol/L xylene orange, 250 mmol/L ammonium ferrous sulfate, 90% methanol, 4 mmol/L butylated hydroxytoluene, and 25 mmol/L H2SO4. After a 30-minute incubation at room temperature, the absorbance was measured using a U2000 Hitachi spectrophotometer (Hitachi, Tokyo, Japan). Calibration was obtained using hydrogen peroxide (0.2–20 mmol/L).[32,33] The limit of detection for this assay is approximately 0.25 nmol/L.

2.9. Statistical analysis
Baseline characteristics are presented as mean and standard deviation. Assumption of normal distribution of cytokines and oxidative stress markers was tested by Shapiro-Wilk test and parametric tests were used. Statistical differences between groups (light vs heavy) at different time after operation (postoperative time, 6 hours, 72 hours, 12 days) were tested by the t test and ANOVA (with Bonferroni correction for multiple comparisons), as appropriate. Univariate linear regression analyses were performed to identify independent predictors of serum inflammatory marker levels as continuous dependent variables. In these models, we selected as independent variables such as age, body mass index (BMI), operative time, mesh type, and number of plugs. When more than one variable was found significant at univariate analysis (probability threshold, P ≤ 0.05), multivariate analysis was performed to assess which was independently associated with serum inflammatory marker levels. All statistical tests were 2-tailed and a P ≤ 0.05 was considered significant. Data were entered into Microsoft Excel for Windows (Microsoft Corporation, Redmond, WA). Statistical analysis was performed using SPSS for Windows release 17.0 (SPSS Inc, Chicago, IL).

3. Results
3.1. Patients
No statistically significant difference was found between groups related to age and BMI (Table 1). Hernia-type distribution in our study population is shown in Table 2. No postoperative complications, such as seroma, infection, wound dehiscence, mesh infections, fistulization, or allergic reaction to the prosthetic material, were observed. A difference was found regarding operative time and implanted plug number in favor of HWM (respectively 96.4 ± 21.4 vs 117.5 ± 38.6 minutes and 1.3 ± 0.6 vs 1.8 ± 1; P = 0.013 and P < 0.034) (see Table 1).

3.2. Evaluation of study endpoints
No statistical significance was found analyzing IL-6 levels, even if a trend of increase following amount of polypropylene could be

| Table 1 | Clinical characteristics of the study population according to mesh type. |
|-----------------|-------------------|-------------------|-------------------|
|                | Light (n = 29)    | Heavy (n = 32)    | P                 |
| Age, y, mean ± SD | 60.17 ± 13.56     | 59.06 ± 11.55     | 0.713             |
| BMI, kg/m², mean ± SD | 25.41 ± 3.03     | 25.4 ± 6.04       | 0.996             |
| Operative time, min, mean ± SD | 96.43 ± 21.47     | 117.59 ± 38.62    | 0.013             |
| Plug, numbers, mean ± SD | 1.38 ± 0.08      | 1.87 ± 1.1        | 0.034             |

BMI = body mass index, SD = standard deviation.
found in postoperative time at 6 and 288 hours after mesh insertion (respectively preoperative, after 6, 72, and 288 hours: LWM 1.38, 8.92, 10.03, 7.99 pg/mL vs HWM 1.29, 11.87, 8.86, 8.4 pg/mL). This trend was also confirmed by TNF-α data even if gaining significance only after 72 hours (3.67 vs 14.3 pg/mL, \( P = 0.016 \)) (Fig. 1).

Univariate linear regression analysis confirmed that TNF-α on the third postoperative day showed a tendency to increase with BMI (\( P = 0.06^* \)); there was also a statistical significance related to operative time (\( P = 0.013 \)), type of mesh (more on HWM; \( P = 0.019 \)), and number of plugs (\( P = 0.001 \)) (see Table 3). Adjusted linear regression strongly confirmed the significance relating to plug numbers (\( P = 0.048 \)) (see Table 4). Regarding oxidative stress, the GSH values were influenced by the kind of mesh, gaining significance (after 6 hours LWM 81.93 vs HWM 64.93 nmol/mL, \( P = 0.01 \)). On univariate linear regression, this tendency (also if without significance) was confirmed depending mainly on age (\( P = 0.08 \)) and mesh type (\( P = 0.06^* \)). Also, for LOOH we observed a higher increase after 6 and 72 hours for HWM (respectively LWM 7.16 vs HWM 13.98 nmol/mL, \( P = 0.055 \), and 6.61 vs 19.45 nmol/mL, \( P = 0.019 \)). On univariate analysis, the factor mainly responsible for this difference, also this time, was mesh type (\( P = 0.02 \)) (Table 3).

4. Discussion

Our data show a correlation between number of plugs (polypropylene content) and immunologic reaction related to TNF-α on the third postoperative day. Our data also demonstrate an increase of immunologic reaction proportional to the prolongation of operative times and patient body weight and significantly related to mesh weight (more weight, more inflammation) and even number of plugs (total amount of polypropylene). A previous work by Di Vita\(^{26}\) showed a similar tendency but with the bias of a different contact area with the human body.\(^{34}\) In fact, in the above-mentioned study the authors compared a group undergoing inguinal hernia repair with a group undergoing incisional hernia repair. Apart from the bias of comparing 2 different diseases with different cicatrization capabilities of patients, in that study the authors compared 2 different amounts of prosthesis implantation but with 2 different

---

### Table 2

Hernia-type distribution in the studied population according to Rutkow classification.

| Hernia type | Light (n = 29) | Heavy (n = 32) |
|-------------|---------------|---------------|
| I           | 5             | 5             |
| II          | 13            | 10            |
| III         | 3             | 8             |
| IV          | 1             | 1             |
| V           | 5             | 6             |
| VI          | 2             | 2             |

---

![Figure 1](image-url)

**Figure 1.** Overview of data, in blue lightweight mesh (LWM) mean values, and in red heavyweight meshes (HWM). Error bars represent standard error of the mean.
contact areas. In our study these 2 biases were eliminated. Furthermore, our study was a double blind (neither the patient, nor the investigators involved in collection and analysis of data were informed about which treatment the patient received) prospective randomized clinical trial. Our work confirmed some previously published data, showing that reaction to polypropylene correlates positively not only with contact area (number of plugs) but also with overall amount of implanted material (mesh type). Regarding the statistically significant difference in our cohort it was found only on the third postoperative day for TNF, but this was mostly due to the size of our cohort of patients. In addition, our recruitment was prospective and unlike other studies, all selection biases were preventively eliminated.

On the contrary, as regards oxidative stress, the study succeeded in finding such a correlation between increase of mesh weight and oxidative stress, indirectly measured by means of antioxidant system consumption (GSH decreases and LOOH increases). The oxidative stress, indirectly measured by means of antioxidant giving significance for number of plugs while losing it for BMI. Taking together these data can affirm that also in a prospective clinical trial the intensity of immunologic reaction such as oxidative stress seems to be positively related to increase of overall polypropylene amount and not only with the extension of the contact area. As far as we know this is the only study investigating immunologic reaction on 60 patients, testifying to the difficulties of conducting such a study on large cohorts of patients. In addition, our recruitment was prospective and unlike other studies, all selection biases were preventively eliminated.

In conclusion, the immunologic reaction to polypropylene after inguinal hernioplasty is directly related not only to the contact area with the host but mainly to the overall amount of material per cm². The oxidative stress is strongly related to the quantity of polypropylene for inguinal hernia repair and oxidative stress, considering the interest for oxidative stress and antioxidative systems in current research.

### Table 3

| Variable | LOOH 6h | LOOH 72h | GSH 6h | GSH 72h | TNF-α 72h |
|----------|---------|---------|--------|--------|-----------|
| Age      | β       | SE      | P      | β      | SE        | P      |
| BMI      | 0.008   | 0.152   | 0.958  | -0.077 | 0.239     | 0.744  |
| Operative time | 0.050   | 0.096   | 0.375  | 0.057  | 0.087     | 0.513  |
| Mesh type | 6.825   | 3.574   | 0.061  | 12.84  | 5.45      | 0.022  |
| Plug numbers | -0.645  | 2.097   | 0.760  | -0.646 | 3.14      | 0.838  |

### Table 4

| Variable | TNF-α 72h |
|----------|-----------|
| Age      | β         | SE       | P   |
| BMI      | 0.171     | 0.505    | 0.735 |
| Operative time | 0.050   | 0.096   | 0.375 |
| Mesh type | 6.825   | 3.574   | 0.061 |
| Plug numbers | -0.645  | 2.097   | 0.760 |

β = regression coefficient, BMI = body mass index, P = statistical significance as P ≤ 0.05, SE = standard error, TNF-α = tumor necrosis factor-α.

References

[1] Cobb WS, Kercher KW, Heniford BT. The argument for lightweight polypropylene mesh in hernia repair. Surg Innov 2005;12:61–9.
[2] Weise D, Schmitz I, Belyav O, et al. Experimental comparison of monofil light and heavy polypropylene meshes: less weight does not mean less biological response. World J Surg 2006;30:1586–91.
[3] Tang GJ. [Similarity and synergy of trauma and sepsis: role of tumor necrosis factor-alpha and interleukin-6]. Acta Anaesthesiol Sin 1996;34:141–9.

[4] Agarwal BB, Agarwal KA, Sahu T, et al. Traditional polypropylene and lightweight meshes in totally extraperitoneal inguinal hernioplasty. Int J Surg 2010;8:44–7.

[5] Di Vita G, Balistreri CR, Arzoco E, et al. Systemic inflammatory response in elderly patients following hernioplastical operation. Immun Ageing 2006;3:3.

[6] Di Vita G, Patti R, D’Agostino P, et al. Serum VEGF and b-FGF profiles after tension-free or conventional hernioplasty. Langenbecks Arch Surg 2005;354:528–33.

[7] Orenstein SB, Saberski ER, Kreutzer DL, et al. Comparative analysis of histopathologic effects of synthetic meshes based on material, weight, and pore size in mice. J Surg Res 2012;176:423–9.

[8] Pascual G, Hernandez-Gascon B, Rodriguez M, et al. The long-term behavior of lightweight and heavyweight meshes used to repair abdominal wall defects is determined by the host tissue repair process provoked by the mesh. Surgery 2012;152:886–95.

[9] O’Dwyer PJ, Kingsnorth AN, Mollov RG, et al. Randomized clinical trial assessing impact of a lightweight or heavyweight mesh on chronic pain after inguinal hernia repair. Br J Surg 2005;92:166–70.

[10] Pascual G, Rodriguez M, Sotomayor S, et al. Inflammatory reaction and neotissue maturation in the early host tissue incorporation of Polypropylene prostheses. Hernia 2012;16:97–707.

[11] Nikkolo C, Lepner U, Murruste M, et al. Randomised clinical trial comparing lightweight mesh with heavyweight mesh for inguinal hernioplasty. Hernia 2010;14:253–8.

[12] Post S, Weiss B, Willer M, et al. Randomized clinical trial of lightweight composite mesh for Lichtenstein inguinal hernia repair. Br J Surg 2004;91:44–8.

[13] Weyhe D, Belyaev O, Muller C, et al. Improving outcomes in hernia repair by the use of light mesh—a comparison of different implant constructions based on a critical appraisal of the literature. World J Surg 2007;31:234–44.

[14] Currie A, Andrew H, Toms A, et al. Lightweight versus heavyweight mesh in laparoscopic inguinal hernia repair: a meta-analysis. Surg Endosc 2012;26:2126–33.

[15] Uzzaman MM, Ramasingham K, Ashraf N. Meta-analysis of randomized controlled trials comparing lightweight and heavyweight mesh for Lichtenstein inguinal hernia repair. Hernia 2012;16:503–18.

[16] O’Dwyer PJ, Kingsnorth AN, Mollov RG, et al. Improved outcomes in hernia repair by the use of light mesh—a comparison of different implant constructions based on a critical appraisal of the literature. World J Surg 2007;31:234–44.

[17] Haffner RK, Muir TW, Rao A, et al. Histologic response of porcine collagen-coated and uncoated polypropylene grafts in a rabbit vagina model. Am J Obstet Gynecol 2008;198:e81–7.

[18] Krambeck AE, Dora CD, Sebo TJ, et al. Time-dependent variations in inflammation and scar formation of six different pubovaginal sling materials in the rabbit model. Urology 2006;67:1103–5.

[19] Di Vita G, Patti R, Sparacello M, et al. Impact of different texture of lightweight and heavyweight meshes used to repair abdominal wall defects is determined by the host tissue repair process provoked by the mesh. Surgery 2012;152:886–95.

[20] Gurleyik E, Gurleyik G, Cetinkaya F, et al. The impact of high density polyethylene mesh plug after inguinal hernia repair. Hernia 2012;16:505–11.

[21] Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. Hernia 2009;13:343–403.

[22] Di Vita G, D’Agostino P, Patti R, et al. Acute inflammatory response after inguinal and incisional hernia repair with implantation of polypropylene mesh of different size. Langenbecks Arch Surg 2005;390:306–11.

[23] Pereira-Lucena CG, Artigiani-Neto R, Lopes-Filho GJ, et al. Experimental study comparing meshes made of polypropylene, polypropylene + polyglactin and polypropylene + titanium: inflammatory cytokines, histological changes and morphometric analysis of collagen. Hernia 2010;14:298–304.

[24] Hill AD, Banwell PE, Darzi A, et al. Inflammatory markers following laparoscopic and open hernia repair. Surg Endosc 1995;9:695–8.

[25] Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. Hernia 2009;13:343–403.

[26] Di Vita G, D’Agostino P, Patti R, et al. Acute inflammatory response after inguinal and incisional hernia repair with implantation of polypropylene mesh of different size. Langenbecks Arch Surg 2005;390:306–11.

[27] Pereira-Lucena CG, Artigiani-Neto R, Lopes-Filho GJ, et al. Experimen-

[28] Simons MP, Aufenacker T, Bay-Nielsen M, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. Hernia 2009;13:343–403.

[29] Hill AD, Banwell PE, Darzi A, et al. Inflammatory markers following laparoscopic and open hernia repair. Surg Endosc 1995;9:695–8.

[30] Novo G, Cappello F, Rizzo M, et al. Hsp60 and heme oxygenase-1 (Hsp32) in acute myocardial infarction. Trans Res 2011;157:285–92.

[31] Campos A, Caccamo D, Li Volti G, et al. Glutamate-evoked redox state alterations are involved in tissue transglutaminase upregulation in primary astrocyte cultures. FEBS Lett 2004;578:80–5.

[32] Marrazzo G, Bosco F, Delia F, et al. Neuroprotective effect of sibutrim in diabetic mice. Neurosci Lett 2011;504:232–6.

[33] Sacerdoti D, Colombria G, Ghattas MH, et al. Heme oxygenase-1 transduction in endothelial cells causes downregulation of monocyte chemotactic protein-1 and of genes involved in inflammation and growth. Cell Mol Biol (Noisy-le-grand) 2005;51:63–70.

[34] Magalhães M, Vacante M, Giordano M, et al. Oral acetyl-L-carnitine therapy reduces fatigue in overt hepatic encephalopathy: a randomized, double-blind, placebo-controlled study. Am J Clin Nutr 2011;93:929–808.

[35] Conze J, Josch R, Klinge U, et al. Polypropylene in the intra-abdominal position: influence of pore size and surface area. Hernia 2004;8:365–72.

[36] Bone RC. Toward a theory regarding the pathogenesis of the systemic inflammatory response syndrome: what we do and do not know about cytokine regulation. Crit Care Med 1996;24:163–72.

[37] Costello CR, Bachman SL, Grant SA, et al. Characterization of heavy and lightweight polypropylene prosthetic mesh explants from a single patient. Surg Innov 2007;14:168–76.

[38] Pignatelli P, Tellan G, Marandola M, et al. Effect of L-carnitine on oxidative stress and platelet activation after major surgery. Acta Anaesthesiol Scand 2011;55:1022–8.

[39] Sternschuss G, Ostergard DR, Patel H. Post-implantation alterations of Hsp60 and heme oxygenase-1 (Hsp32) in acute myocardial infarction. Trans Res 2011;157:285–92.

[40] Kontidis E, Papavramidis T, Ioannidis K, et al. Can chronic intra-abdominal hypertension cause oxidative stress to the abdominal wall muscles? An experimental study. J Surg Res 2012;176:102–7.

[41] Kumar S, Kramer R, Sharma SB, et al. Effect of oral glutamine administration on oxidative stress, morbidity and mortality in critically ill surgical patients. Indian J Gastroenterol 2007;26:70–3.

[42] van Stijn MF, Ligthart-Melis GC, Boelens PG, et al. Antioxidant enriched enteral nutrition and oxidative stress after major gastrointestinal tract surgery. World J Gastroenterol 2008;14:960–9.