

Format for ANSWERING REVIEWERS

3th of Nov. 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (Ms. wjgs146).

Title:

Systemic inflammation and immune response after laparotomy vs laparoscopy in patients with acute cholecystitis, complicated by peritonitis

Author: Federico Sista, Mario Schietroma, Giuseppe De Santis, Antonella Mattei, Emanuela Marina Cecilia, Federica Piccione, Sergio Leardi, Francesco Carlei, Gianfranco Amicucci

Manuscript No: Ms. wjgs146

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer.

We can answer as follow point-by-point:

- (1) To illustrate study design a flow chart have been enclosed (Fig 1).
- (2) English has been reviewed
- (3) *Materials and Methods* and *Resuts* have been subdivided in subheading:
Materials and Methods: Study design (line 118) Laboratory analysis (line 206) and statistical analysis (line 277).
Results: clinical data (line 305) and Laboratory data (line 354)
- (4) The text has been shorten as reviewers suggest.
- (5) We have chose *LC group* and *OC group* to uniform the labels.
- (6) “*There is not difference....by peritonitis*” (line 163-167) and “ *three patients (8%)....LC group (p< 0.05)*” (line 192-196) has been moved in the results section. (line 306-316)
- (7) *Materials and Methods:*
 - 1 Time point of sampling for bacteria assay and endotoxin has been defined. (line 211-212)
 - 2 Because the data were not normally distributed we decided to use non parametric statistics, which are more powerful when the data shows a skewed distribution. Thus an analysis of variance non parametric Friedman’s repeated measures comparisons was performed in both groups to determine differences among post-operative values and baseline. In presence of significant difference, to compare the mean values between two groups, were made with Mann-Whitney U Test. All continuous variables were expressed as mean and standard deviation and the power of trial (1- β) of 80% was computed for the two sided null hypothesis.
 - 3 Criteria exclusion has been defined. (line 142-147)
 - 4 see point (6)
 - 5 see point (6)
- (8) *Results:*
 - 1 There is no difference between two groups examined with respect to age, as shown in Table 1, so we decided not to consider the age of analysis and subsequent sentence “*finally, the ages did not affect neutrophil elastase concentration in either group*” was removed.
 - 2 The reasons of mortality has been specified (line 351-353)
 - 3 The number of WBC has been specified (line 355-357)
 - 4 Expression of class 2 major histocompatibly complex molecules on antigen-presenting cells is a necessity for effective

antigen presentation and subsequent elimination of antigen. In phagocytosis, antigens are incorporated into cell. The lysosomal system breaks down the antigen in peptides which bind with human leucocyte antigen (HLA) class 2 within the endosomes. The HLA-II molecule with this peptide is expressed on the cell membrane. T-helper cells recognize the paired molecules and adhere to it. This leads to an activation of the T-cell. Monocyte HLA-DR expression is a reliable marker of infection. Reduced expression of major histocompatibility complex class 2 molecules, particularly HLA-DR, is associated with an impaired ability to eliminate pathogens effectively. Subsequently an increased risk of infection. Therefore dosage of HLA-DR does not coincide with that of Macrophages.*

* **Cheadle WG, Hershman MJ, Wellhausen SR, Polk HC.** HLA-DR antigen expression on peripheral blood monocytes correlates with surgical infection. *Am. J. Surg.* 1991;161(6):639-45

-5 Yes, plasma elastase concentration was higher in OC group.

-6 Fig 3 has been corrected because IL-6 levels, in LC group, increased related to baseline.

-7 As suggested by the referee we have decided to better explain this part:

“On the other hand, in the LC group patients, the increase in the serum IL-1 and IL-6 levels was delayed and the peak values were significantly lower than those in the OC group. IL-1 β and IL-6 β values the difference between baseline values and post-operative values were significant in both groups (using Friedman test, $p < 0.05$). Besides, significance was obtained by comparing values between groups at 2h, 3h, 4h, 5h, 6h and 24h after the operation using

Mann-Whitney

U test (Figure 2 and Figure 3) ($p < 0.05$).” (line 378-386)

-8 As suggested by the referee we have decided to better explain this part:

“The mean values of the serum CRP on postoperative days (1 and 3) were also lower in the LC group than those in the OC group. CRP values the difference between baseline values and post-operative values were significant in both groups (using Friedman test, $p < 0.05$). Besides significance was obtained by comparing values between groups at 1 day, 2 days and 3 days after the operation, using Mann-Whitney U test ($p < 0.05$) (Figure 4). In this case CRP concentration returned to normal values within 7 days after operation” (line 387-394)

-9 Table 4 and 5 has been omitted

-10 Fig. 4 has been corrected with the standard deviation and the correction of values pre-operative.

The values preoperative has been reported by mistake

(9) *Discussion*: the Discussion has been revised.

3 References and typesetting were corrected

Thanks so much for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



Federico SISTA, MD

Università degli Studi di L'Aquila
Facoltà di Medicina e Chirurgia
Dipartimento di Scienze Chirurgiche
Viale dell'Ospedale. Edificio Delta 6-Coppito
67100 L'Aquila-Italy
Tel:+39.34.98.50.83.08
Fax: +39.86.24.34.95.8
e-mail: silversista@gmail.com