Author’s response to reviews

Title: Biological inflammatory markers mediate the effect of preoperative pain-related behaviours on postoperative analgesics requirements

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Author’s response to reviews:

Cover Letter – R1

Name of Corresponding Author: Patrice FORGET
Manuscript Title: Biological inflammatory markers mediate the effect of preoperative pain-related behaviours on postoperative analgesics requirements

Dear editors,

On behalf of my co-authors, I thank you for the opportunity to improve our manuscript, according to the reviewer remarks.

You will find here below a detailed point-by-point response to all his remarks.

We hope these will fulfill all the concerns.

Sincerely,

Patrice Forget, on behalf of my coauthors
Reviewer #2:

The authors evaluated the Situational Pain Scale (SPS) and the neutrophil to lymphocyte ratio (NLR) individually and in combination with other variables as predictors for the analgesic demands during the first 48 hours after laparoscopic cholecystectomy.

Introduction

Page 3
-Lines 22-25: "In this study we shall use…” . You have already done the study change to: "In this study we implemented a new questionnaire…”

Authors’ response: We agree and changed accordingly.

Reviewer #2:

-Line 39: Study hypothesis is missing. Before the aim of the study add the study hypothesis.

Authors’ response: We agree and changed accordingly.

Reviewer #2:

Methods

Page 4
-Lines 7-9: Sample size calculation is not clear. Was power analysis done to confirm the adequacy of the sample size after study completion? Please describe the sample size calculation you did in detail.

Authors’ response: We used a combined a priori and a posteriori (confirmatory) approach. We added sentences as follow: Based on preliminary observations, we expected to observe a difference of 1 ±1 (SD) units on the SPS scale between groups with low or high analgesic requirements. Using the software G*Power 3.1 (downloaded from the Website wwwpsychouni-duesseldorfaapgpower3/) with the following input parameters (one tailed t-test, alpha error probability = 0.05, power = 0.90 and equal allocation ratio), we computed a required total sample size of 46 patients.

Reviewer #2:

-Line 40: "at rest and during movement". Be specific, what movement?

Authors’ response: Walking. We added it.
Reviewer #2:

-Lines 57-60: Is the number of times the patient requested analgesic a validated method to quantify the analgesic requirements instead of recording the cumulative analgesics consumed over a certain period of time postoperatively?

Authors’ response: We agree with the reviewer that this is not a perfect method to quantify the analgesic requirements, but there is no fully satisfying alternative. As reported in the text (p. $ line $), we did not find any reliable equianalgesic charts. Moreover, the behavior linked to the “request” of the patient was the primary endpoint in our work.

Reviewer #2:

Results
Page 8
-Didn't you have dropouts? Did you collect data from the 60 patients with no missing values? In any case you must mention in the beginning of the Results section if you had missing values and patient dropouts. Otherwise make the statement that all the 60 patients completed the study and no missing values were in the collected data.

Authors’ response: Indeed, the first author (MD) was fully dedicated during this period to the care of this ward, permitting a complete assessment of all the patients. As suggested by the reviewer, we have added this information at the beginning of section Results.

Reviewer #2:

-Lines 1-25: Do not repeat in the text results shown in table 1. Just say: Population characteristics, (age, gender, etc), SPS, HADS anxiety, UD, HADS depression, VRS preoperatively at rest, VRS preoperatively during movement, N/L ratio…. (add the rest of variables) are shown in table 1.

Authors’ response: We agree with the suggestion of this reviewer and have simplified the paragraph accordingly,. However, since gender comparisons are not reported in table 1, they were maintained.

Reviewer #2:

-Line 7: In the text the number of females is 40 in table 1 is 39; which is correct?

Authors’ response: We thank the reviewer to point to this mistake; 39 is the right number. We checked all the other data without finding any other problem.

Reviewer #2:
Discussion
In a paragraph before the conclusion give the strengths and limitations of the study.

Authors’ response: Indeed, there are strengths and limitations. The exploratory way used is the main limitation of this work. The use of the SPS remains an infrequent tool to assess attitude towards painful situations, as the endpoint proposed to assess the analgesics requirements (total UD during the postoperative period). Nevertheless, the use of the SPS and the UD, as endpoints, allows to respond to the absence, or at least limitations, of available tools (for these types of status and behaviour assessments). We consider as strengths the use of the NLR as a sensitive marker of the inflammatory status, the wide use of the HADS for the assessment of the emotional status, as the clear results obtained by the mediation analysis.
We have added this paragraph as suggested.

Reviewer #2:

Table 1. Rearrange the rows in a logical order: first the patient characteristics then the variables you studied in a chronological order.

Authors’ response: We agree with this suggestion and changed accordingly.

Reviewer #2:

Patients' BMI and statistical comparisons between low and high consumers must be calculated and included in table 1. In the exclusion criteria you did not consider obesity and analgesic pharmacokinetics vary between patients with variable BMIs.

Authors’ response: We agree with this remark but did not specifically perform this analyses (not transmitted from our sources documents). We recognize that the adjusted comparisons on patient’s weight, while malnutrition and morbid obesity were exclusion criteria, would merit additional comparisons. We have added these exclusion criteria (not described) and this limitation pointed by this reviewer.

Reviewer #2:

Also in a footnote explain all the abbreviations included in table 1.

Authors’ response: We agree with this remark and have modified the footnote accordingly.