

## **Our responses to the reviewers' comments for No: 23944**

**Title:** Enhanced recovery program is safe and improves postoperative insulin resistance in gastrectomy

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**Reviewer 1 (00070823):** We thank the reviewer 1 for all comments.

**Reviewer 2 (03477543):** We thank the reviewer 2 for the critical comments which have helped us to improve the manuscript. We have addressed all comments as follows.

### 1. The reviewer 2 required to describe the patient and tumor characteristics more precisely.

We thank the reviewer 1 for this valuable suggestion. We mentioned the patient selection method. Eighty patients were randomly assigned into 2 groups; 40 patients each in the conventional treatment group and the ERAS group. The assignments were made by the stratified randomization method according to age ( $<70$  or  $70 \leq$ ) and surgical approaches (abdominal surgery or laparoscopic surgery). We added the tumor characteristics, ASA and BMI. There was no differences between the conventional and ERAS groups.

These statements were described in the revised Materials and Methods (page), in the revised Results (page) and in the revised Table 1 (page 11, line 4 through line 3 from the bottom).

### 2. The reviewer 2 had mentioned that the result section is lengthy.

We apologize for the lengthy result. We used abbreviations. “the conventional group” was changed to CG, and “ERAS group” was changed to EG.

These statements were described in the revised Results (page 10, line 6 from the bottom through line 3 from the bottom).

**Reviewer 3 (01470267):** We thank the reviewer 3 for the critical comments which have helped us to improve the manuscript. We have addressed all comments as follows.

### Major 1. Reviewer 3 had a request to mention about the trial registration number and IRB number.

Exactly, we have to mention the numbers. This study was approved by the institutional review board of the study institution (Hiroshima University, Japan, No.Rin-269). This study was registered at UMIN Clinical Trial Registry (UMIN000020538).

These statements were described in the revised Materials and Methods (page 10, line 6 from the bottom through line 3 from the bottom).

Major 2. Reviewer 3 required to mention about the clinical symptoms under insulin resistance conditions.

We agree with the opinion of the reviewer 3. Poor control of glucose was the risk of wound infection (Ref 15). And some studies have suggested that the degree of insulin resistance was associated with the length of stay (LOS). In this study, there was no differences respect to complications and LOS between two groups. The attenuation of insulin resistance was observed only POD1. Maybe, the interval of fast is too short to allow assessment of benefits on insulin resistance and LOS. To clear the clinical symptoms under insulin resistance, longer fasting period will be needed. However, the trend of shortening the fast periods does not allow the trial. And so, sadly, it is hard to clear the clinical outcome of attenuating the insulin resistance.

These statements were described in the revised Discussion (page 10, line 6 from the bottom through line 3 from the bottom).

Minor 1. Reviewer 3 had a request not to use the abbreviation “ERAS” in the first appearance.

Exactly, we have not to do so.

These statements were described in the revised Abstract (page 10, line 6 from the bottom through line 3 from the bottom).

Minor 2. Reviewer 3 required to use abbreviations for readers. The conventional group as (CG), ERAS group as (EG)

We agree fully with the opinion of the reviewer 3. We changed the words to the abbreviations.

These statements were described in the revised Results (page) and in the revised Discussion (page 10, line 6 from the bottom through line 3 from the bottom).

Minor 3. Reviewer 3 required to use the “Unit”

We agree fully with the opinion of the reviewer 3. We added the several “Unit”.

These statements were described in the revised Results (page 10, line 6 from the bottom through line 3 from the bottom).