70823

This manuscript retrospectively analyzed the risk of heart diasease impact on the complication and prognosis of gastric cancer after surgery. I think that authors provided the solid cases of heart disease patients with gastric cancer for the elaborate description.

Reply) Thanks for yours reviews.

44980

This manuscript shows postoperative risk in gastrectomy with heart diseases. A lot of cases were enrolled in the multicenter, and there are several novelties. I have some of comments described as follows.

1. Authors examined the cases with heart diseases. MI or AF sometimes cause HF. Did some cases with a heart disease have another heart diseases in this study?

Reply) We created Table 2 for combined heart disease.

2. Authors should mention the follow-up period.

  Reply) We did not review and analyze the follow-up period. We analyzed postoperative complications that occurred within 30 days after surgery. (Page 7, Materials and Methods).

  We defined postoperative morbidity as a complication that occurred within 30 days after surgery that delayed the date of discharge or results in the patient who required treatment in an outpatient clinic after discharge. (Page 7, materials and methods)

3. Authors should mention approval by the institutional review board and informed consent.

Reply) The Institutional Review Board of Gyeongsang National University Hospital approved this study (GNUH 2015-1-005).

4. Did the myocardial infarction include an acute myocardial infarction in this study?

Reply) Yes, we included acute myocardial infarction. (Page 6, materials and methods)

- MI: The patient was diagnosed with I21 (acute myocardial infarction, *ICD-10*) or I25 (chronic myocardial infarction, *ICD-10*), and preoperatively evaluated using coronary angiography, treadmill test, cardiac CT, and M-SPECT.

1503696

The authors evaluated postoperative risk after radical gastrectomy underlying heart disease from a multicenter retrospective data. It is unclear whether the data is consecutive or selected one. If non-consecutive retrospective study, the result is unreliable even though the sample size was large because selection criteria are unclear.

Major comments

1. It is unclear why the authors select four heart diseases- namely, MI, Angina, HF, and AF. The authors need to describe the rational why the authors select these four heart diseases.

Reply) We added the following comments to the Discussion.

Several studies reported high cardiac risk in ischemic heart disease and congestive heart failure[17, 18]. We selected ischemic heart disease (angina, MI) and congestive heart failure to evaluate the operative risks of gastric cancer surgery. We chose AF because it is the most frequent heart rhythm abnormality. (page 12, Discussion)

2. In the method section, the author should more describe the inclusion criteria and exclusion criteria of the present study.

Reply) We added inclusion and exclusion criteria to the Material and Methods (page 6).

The following **inclusion criteria** were used in this study: histologically proven primary gastric adenocarcinoma; no evidence of other distant metastases; subtotal and total gastrectomy as the surgical method;

R0 resection; and preoperatively diagnosed underlying heart disease (Angina, AF, HF, or MI). **(Material and Methods, page 5).**

We **excluded** patients with the following conditions: active double cancer (synchronous and metachronous double cancer within 5 disease-free years), carcinoma in situ (lesions equal to intraepithelial cancer), gastric cancer recurrence, or a history of gastrectomy. **(Material and Methods, page 6).**

3. Each category of angina, AF, HF, and MI are not overlapped in the present study, according to the table. This is strange. Some of heart disease must overlap each other. How did the authors treat the patients with two or more heart disease?

Reply) We created Table 2 for associated heart disease.

4. In the method section, the authors need to describe the surgical procedures in detail, which affect the results.

Reply) We added surgical procedures to the methods.

Surgical procedure

Total or subtotal gastrectomy or total omentectomy and D1+ α or D1 + β lymph node dissection were performed in open surgery when the preoperative diagnosis using gastrofibroscopy and spiral CT scans revealed early gastric cancer (EGC). Lymph node station were identified according to the Japanese Classification of Gastric Carcinoma from 1998 [15]. Gastric resection and determination of the resection area of the lymph node stations were performed according to the Japanese Gastric Cancer Association (JGCA) guidelines from 2002 [16]. Partial omentectomy was performed using laparoscopic surgery. Reconstruction was performed based on the surgeon's preference.

Total or subtotal gastrectomy, total omentectomy and D2 lymph node dissection were performed using open surgery in cases of advanced gastric cancer.

(Materials and Methods page 7)

5. In the results section, please show the co morbidity before surgery of the present study patients. Are there any differences between the MI, Angina, HF, and AF group?

Reply) We show the co-morbidity in Table 3. We found that hypertension was rare in CHF (15.4%, 2/11) than MI (60%, 30/50), angina (42%, 42/89), and AF (44.9%, 31/69) (p=0.03). However, there were no other differences in co-morbidity between the 4 heart diseases.

6. In the discussion section, the authors should more discuss about the relation with abdominal abscess and MI.

 Reply) We added this topic to the discussion.

 We found that intra-abdominal abscess and total morbidity were significantly higher in the MI group, and postoperative cardiac problem rates were higher in the HF group. It is possible that the MI patients had larger intraabdominal abscesses because these patients had decreased wound healing with decreased circulation. (Discussion page 12)

 02537577

This is a well written manuscript with reasonable results. The authors evaluate the morbidity and mortality differences between 4 underlying heart diseases—namely, myocardial infarction (MI), angina pectoris (Angina), heart failure (HF), and atrial fibrillation (AF)—after radical surgery for gastric cancer. They conclude that MI patients had a higher risk of morbidity and HF patients had a higher risk of postoperative cardiac problems than patients with Angina and AF.

925786

1. Authors excluded many other types of heart disease. Therefore title should be changed. This study cannot show the postoperative risk of all patients with heart disease.

Reply) We agree with the reviewer's opinion. How about 'high morbidity in MI and greater cardiac problems in CHF after gastric cancer surgery: a multicenter retrospective clinical trial'

2. In this study, one patient has only one type of heart disease. This is very strange. Aren't there really any patients with more than two types of heart disease, among 15,167 cases underwent gastrectomy? If any other patients don't have more than two types of heart disease, this study group is a very specific group which doesn't reflect parent population.

Reply) We created Table 2 for associated heart disease.

3. The kinds of heart disease are important. However, there are many important factors in the patients with heart disease: severity (functional status: ejection fraction, blood pressure, heart rates etc.), the duration between events and operation, preoperative medication: necessity and kinds, cessation period of medication before operation, re-start date of medication after operation, etc. These factors (confounding variables) can affect the postoperative bleeding, cardiac problem, and postoperative recovery. These important factors should be analyzed such like the kinds of heart disease.

Reply) We fully agree with the reviewer's opinion. However, it is impossible to find and analyze this data in a retrospective and multicenter trial. These factors may be analyzed in our subsequent prospective study.

4. When high risk might be expected, surgeons sometimes reduce the extent of operation: the extent of lymph node dissection, combined resection, and so forth. What is the indication of D1 lymph node dissection? Please discuss the bias of the surgeons' decision when they expect the high risk because of patients' heart disease.

Reply) There was a mistake in the expression of D1 LN dissection. In JGCC version 2, we should have used D1 + α. We changed the expression of D1 to D1 + α. We performed the D1 + α LN dissection in small mucosa cancers with well-differentiated cancer because endoscopic submucosal dissection was not popular in 2005-2010. The indication of EMR or MG type A in JGCA guidelines is from 2002.

Total or subtotal gastrectomy or total omentectomy and D1+ α or D1 + β lymph node dissection were performed in open surgery when the preoperative diagnosis using gastrofibroscopy and spiral CT scans revealed early gastric cancer (EGC). (Materials and method 7 page)

We also agree that the extent of the operation should be reduced when high risks are expected because of a patient's heart disease.

Therefore, patients who need total gastrectomy and have more than three risk factors in the revised cardiac risk index model should be consulted about a reduced operation because these patients are expected to have a higher risk of post-operative complication than patients with no risk factors. (Discussion page 13)