

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

Q1: This is a study with a specific perspective and important findings on the topic. The text is well structured and the methodology seems to be adequate. The language is satisfactory. Moreover, the subject is addressed clearly. However, some points can be improved. First, the molecular mechanisms that justify the remission of hypertension after gastrectomy for patients with gastric cancer can be described in more depth.

A1: Thanks for your carefully reading. It is our pleasure to receive your comments. We have revised the discussion part of our article as follows: There were many possible molecular mechanisms of hypertension remission for obese patients after bariatric surgery: elevated activation of the renin–angiotensin–aldosterone system in obese patients might normalize after surgery^[31] and the improvement of gastrointestinal gut hormone levels and insulin resistance after surgery^[32], a possible effect of these gut hormones on the sympathetic nervous system^[33], adipokines and other inflammatory cytokines would lead to hypertension recovery^[34]. Thus, similar to bariatric surgery, multiple factors might work together for hypertension remission after gastric cancer surgery^[35-37]. Furthermore, it was reported that early hypertension remission might be related to endocrine hormones and late hypertension remission might be related to neurohumoral regulation^[36, 37]. (Line 194-203)

Q2: Second, the usefulness of the study findings for clinical and surgical practice, as well as the implications of these findings for the future of medicine, should be presented at the conclusion of the article.

A2: We feel indebted for yours remind. We have added the study findings for clinical and surgical practice at the conclusion of the article as follows: Our study predicted that younger hypertension patients who underwent gastrectomy for gastric cancer might decrease anti-hypertensive medication and relieve hypertension-related comorbidities. (Line 229-231)

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Q1: In this paper, the authors present the predictive factor for hypertension remission one year after gastrectomy of gastric cancer patients and a risk model for hypertension remission. Overall, the data of the manuscript are clearly presented. The manuscript is interesting, and the data support the main conclusions. However, there are several concerns regarding this study that the authors need to clarify. The present manuscript represents a more limited advance than the previous paper published. Listed below are my specific comments. 1. The authors previously reported data 6 months after surgery. How much does it make sense to present data for the first year after surgery, not too long after that? The author should state a little more firmly how much the evaluation after one year, which is hard to say long-term, is meaningful. Considering the entry period of the target patients, I think there are cases where the course of several years can be observed. Are you considering cases that have been followed up for a longer period of time rather than a few months difference? Not a little, I think the word "long" is not appropriate for this paper. Also, compared to the 6-month report, I think that the novelty including the conclusion is poor.

A1: We are appreciated with your suggestion and we think that it is very helpful. The follow-up time of many articles on diabetes remission after gastric cancer surgery is one year¹⁻⁵, therefore, this study aimed to analyze the predictive factors for hypertension remission one year after gastrectomy of gastric cancer patients. This is a cross-sectional study, and some data have not been followed up, we have added this into limitation part of the article "Some limitations existed in this study. First, this was a retrospective single center study, which might cause selection bias and some detailed data were lost; Second, the follow-up time was relatively short; Third, we only established internal validation, and external validation is needed in the future; Fourth, some blood parameters including leptin, adiponectin, renin, angiotensin II and aldosterone are needed in the following experiments. Therefore, multi-center, large-sample studies with more parameters are needed in future studies to elaborately analyze the factors of hypertension remission." (Line 219-225)

Reference

1. Choi YY, Noh SH, An JY. A randomized controlled trial of Roux-en-Y gastrojejunostomy vs. gastroduodenostomy with respect to the improvement of type 2 diabetes mellitus after

- distal gastrectomy in gastric cancer patients. PLoS One. 2017;12(12):e0188904. doi:10.1371/journal.pone.0188904.*
2. *An JY, Kim YM, Yun MA, Jeon BH, Noh SH. Improvement of type 2 diabetes mellitus after gastric cancer surgery: short-term outcome analysis after gastrectomy. World J Gastroenterol. 2013;19(48):9410-7. doi:10.3748/wjg.v19.i48.9410.*
 3. *Park MJ, Kim DH, Park BJ, Kim S, Park S, Rosenthal RJ. Impact of preoperative visceral fat proportion on type 2 diabetes in patients with low body mass index after gastrectomy. Surg Obes Relat Dis. 2017;13(8):1361-8. doi:10.1016/j.soard.2017.05.012.*
 4. *Lee W, Ahn SH, Lee JH, Park DJ, Lee HJ, Kim HH et al. Comparative study of diabetes mellitus resolution according to reconstruction type after gastrectomy in gastric cancer patients with diabetes mellitus. Obes Surg. 2012;22(8):1238-43. doi:10.1007/s11695-011-0580-1.*
 5. *Wang KC, Huang KH, Lan YT, Fang WL, Lo SS, Li AF et al. Outcome after curative surgery for gastric cancer patients with type 2 diabetes. World J Surg. 2014;38(2):431-8. doi:10.1007/s00268-013-2291-3.*

Q2: In this manuscript, the decrease in blood pressure is classified into three groups and examined. The Remission group is supposed to be lower than before surgery, but how much blood pressure was actually improved? In the 6-month data report, the number of improvements in blood pressure was also defined and the effect was judged. Were there any improvements that could contribute to the onset and prognosis of complications? If possible, I think it is better to present specific values for changes in blood pressure. And if the drug has been discontinued, how often has it been discontinued? I think that the data on the drug was also examined more concretely when the 6-month data was reported.

A2: We are grateful for your recommendation. In this study, we aimed to construct a nomogram to visually display these associated factors, therefore, only the effective data were included to study for studying the predictors of blood pressure remission. The study of our previous study with six months follow-up time aimed to identify whether the blood pressure would remission in patients with concurrent gastric cancer and hypertension after gastrectomy, therefore, the study aims were different between the two studies.

Q3. What are your thoughts on specific uses as onco-metabolic surgery? What kind of surgery do you think is best if your goal is to lower blood pressure and cure stomach cancer? I don't think it is possible to perform total gastrectomy in all cases. I think it is better to show concretely how to think about adaptation of surgery. However, I do not feel strongly that the authors must respond to my comment.

A3: We are really appreciated with your suggestion. For patients with gastric cancer

and concurrent gastric cancer, the main purpose of surgery is to cure gastric cancer, the choice of surgical procedure depended on the location and TNM stages of the patients, however, the bonus of these patients was that gastrectomy is not just a tumor resection surgery, but also an onco-metabolic surgery. In gastrectomy, the magnitude of the stomach incision was no less than that in bariatric surgery, so there might be some improvement in concurrent gastric cancer and metabolism-related diseases. Patients with concurrent gastric cancer and diabetes could exhibit remission of diabetes after gastrectomy^{6,7}. Furthermore, total gastrectomy was an onco-metabolic surgery that could cure younger patients with concurrent gastric cancer and hypertension⁸.

Reference

6. *Diabetes Mellitus Remission After Gastrectomy in Patients with Gastric Cancer? A Systematic Review and Meta-Analysis. Diabetes Ther. 2020;11(12):2863-72. doi:10.1007/s13300-020-00934-7.*
7. *Kim WJ, Kwon Y, Lee CM, Lim SH, Li Y, Wang J et al. Oncometabolic surgery: Emergence and legitimacy for investigation. Chin J Cancer Res. 2020;32(2):252-62. doi:10.21147/j.issn.1000-9604.2020.02.12.*
8. *Peng D, Cheng YX, Tao W, Zou YY, Qian K, Zhang W. Onco-Metabolic Surgery: A Combined Approach to Gastric Cancer and Hypertension. Cancer Manag Res. 2020;12:7867-73. doi:10.2147/cmar.S260147.*

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Q1: Interesting study analyzing a very peculiar aspect after stomach cancer surgery. The introduction is well written. The materials and methods are exhaustive. The results paragraph is not very exhaustive. I would describe the findings obtained more carefully. The tables are explanatory.

A1: Thank you for your careful consideration of our study and we totally agreed with your suggestions. According to your suggestions, we have revised the part of results in the article as follows:

Results

Patients

A total of 209 patients with concurrent gastric cancer and hypertension were included in the current study according to the inclusion and exclusion criteria (Fig 1). There were 108 patients in the remission group and 101 patients in the non-remission group. The hypertension remission rate was 51.7%.

Characteristics of the remission group and the non-remission group

We compared the baseline information and surgical information of the two groups. The remission group had younger patients (63.6 ± 8.7 vs. 67.4 ± 8.0 years, $p=0.001$), larger weight loss (-8.2 ± 6.7 vs. -5.6 ± 4.6 kg, $p=0.001$), lower portion of CHD (8.3% vs. 19.8%, $p=0.017$), higher portion of II-degree hypertension (47.2% vs. 31.7%, $p=0.033$) and higher portion of total gastrectomy (31.5% vs. 15.8%, $p=0.008$) than the non-remission group. There was no significant difference in terms of other information ($p>0.05$). (Table 1)

Univariate and multivariate logistic regression of hypertension remission

Univariate analyses were conducted to identify potential risk factors for hypertension remission. In univariate logistic regression, younger age ($p=0.002$, odds ratio =0.947, 95% CI=0.916-0.980) and higher weight loss ($p=0.002$, odds ratio =0.922, 95% CI=0.875-0.971), CHD ($p=0.020$, odds ratio =0.368, 95% CI=0.159-0.853) and total gastrectomy ($p=0.009$, odds ratio =2.441, 95% CI=1.248-4.775) were statistically significant. (Table 2)

Multivariate logistic regression was conducted to identify independent risk factors. In multivariate logistic regression, younger age ($p=0.011$, odds ratio =0.955, 95% CI=0.922-0.990) and higher weight loss ($p=0.019$, odds ratio =0.937, 95% CI=0.887-0.989) and total gastrectomy ($p=0.039$, odds ratio =2.091, 95% CI=1.037-4.216) were independent predictors. (Table 2)

Nomogram, validation and clinical usefulness

The nomogram was built as shown in Fig 2a. The score of each variable could be calculated by drawing vertical line upward to the point scale. The risk factors for hypertension remission could be calculated by summing the total points.

The C-index value of the nomogram was 0.769. The calibration curve of the nomogram suggested great agreement. (Fig 2b)

The DCA for the nomogram is shown in Fig 2c, which indicated that when the threshold probability was larger than 0.33, the nomogram might add more benefit than the treat-all or treat-none strategies. (Line 133-167)

Q2: The discussion appears to be of adequate length with little discussion of the results obtained and comparison with the findings of the literature. Reporting the literature data in a table does not seem to me to be exhaustive. I invite the authors to review the manuscript.

A2: Thank you for your kindly suggestions. We have discussed the reporting literature comprehensively in the discussion part of the article: For younger patients, vascular elasticity might contribute to the higher rate of hypertension remission ^[15]. Total gastrectomy had a wider extent than subtotal gastrectomy, and a larger volume of residual stomach in subtotal gastrectomy allowed more food than total gastrectomy, thus total gastrectomy might be associated with higher remission of hypertension ^[16]. The purpose of this study was different from previous studies reporting the remission of hypertension after gastrectomy for gastric cancer patients. Lee et al. ^[17] found no risk factors for hypertension remission. Park et al. ^[18] focused on the comparison between long-limb R-Y reconstruction and conventional R-Y reconstruction. The information for hypertension remission was limited. Another study from China focused on the elaborate parameters of endocrine hormone change, however, the sample size was too small ^[19]. In this study, we identified three independent predictive factors including younger age, total gastrectomy and higher weight loss, which led to hypertension remission after gastrectomy. Weight loss was an important factor for hypertension control, which was related to lifestyle changes that promoted hypertension remission ^[38-40]. (Line 204-218)