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Case Control Study

Factors associated with hypertension remission after gastrectomy for gastric cancer patients

Kang B *et al*. Factors associated with hypertension remission after gastrectomy

Bing Kang, Xiao-Yu Liu, Yu-Xi Cheng, Wei Tao, Dong Peng

Abstract

BACKGROUND

Previous studies reported hypertension remission after gastrectomy for gastric cancer patients, and the remission rate was 11.1%-93.8%. We have reported the factors of hypertension remission previously, however, the follow-up time was six months. It is necessary to identify risk factors for hypertension for a relatively longer follow-up time.

AIM

The purpose of the current study is to analyze the predictive factors for hypertension remission one year after gastrectomy of gastric cancer patients and to construct a risk model for hypertension remission.

METHODS

We retrospectively collected the medical information of patients with concurrent gastric cancer and hypertension in a single clinical center from January 2013 to December 2020. Univariate and multivariate logistic regression of hypertension remission were conducted, and a nomogram model was established.

RESULTS

A total of 209 patients with concurrent gastric cancer and hypertension were included in the current study. There were 108 patients in the remission group and 101 patients in the non-remission group. The hypertension remission rate was 51.7% one year after gastrectomy. The remission group had younger aged patients (P = 0.001), larger weight loss (P = 0.001), lower portion of coronary heart disease (P = 0.017), higher portion of II-degree hypertension (P = 0.033) and higher portion of total gastrectomy (P = 0.008) than the non-remission group. Younger age (P = 0.011, odds ratio = 0.955, 95%CI = 0.922-0.990), 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 for hypertension remission. The concordance index of the model was 0.769 and the calibration curve suggested great agreement. Furthermore, decision curve analysis showed that the model was clinically useful.

CONCLUSION

Younger age, higher weight loss and total gastrectomy were independent predictors for hypertension remission after gastrectomy for gastric cancer patients. The nomogram could visually display these results.

Key Words: Gastric cancer; Hypertension; Gastrectomy; Remission; Nomogram

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Core Tip: The purpose of the current study is to analyze the predictive factors for hypertension remission one year after gastrectomy of gastric cancer patients and to construct a risk model for hypertension remission. We found that younger age, higher

weight loss and total gastrectomy were independent predictors for hypertension remission after gastrectomy for gastric cancer patients. The nomogram could visually display these results.

INTRODUCTION

Gastric cancer is the fifth most common cancer and the third most common cause of cancer-related death[1,2]. In China, gastric cancer patients account for about approximately 50% of the world's population[3]. Despite improvements in treatment strategies, radical gastrectomy remains the cornerstone of gastric cancer treatment[4-6].

Hypertension is a major risk factor for cardiovascular disease and an important cause of morbidity and mortality[7,8]. It is estimated that, in 2025, hypertensive patients will account for nearly one-third of adults worldwide[9,10]. In China, the prevalence of hypertension has increased significantly because of urbanization, economic growth, and the aging population[11]. A total of 26.6%-33.6% of the general population is diagnosed with hypertension, resulting in an estimated 23 million deaths per year[12].

Obese patients could experience hypertension remission after bariatric surgery[13,14]. Previous studies reported hypertension remission after gastrectomy for gastric cancer patients, and the remission rate was 11.1%-93.8%[15-20]. We have reported the factors of hypertension remission previously, however, the follow-up time was six months[15].

It is necessary to identify risk factors for hypertension for a relatively longer follow-up time. Therefore, the purpose of the current study was to analyze the predictive factors for hypertension remission one year after gastrectomy in gastric cancer patients; moreover, we constructed a nomogram to visually display these associated factors.

MATERIALS AND METHODS

Patients

We retrospectively collected the medical information of patients with concurrent gastric cancer and hypertension in a single clinical center from January 2013 to December 2020. This study was carried out in accordance with the World Medical Association

Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of the local hospital (2022-133-2), and informed consent was obtained from all patients.

Inclusion and exclusion criteria

The analysis of this study was restricted to patients who: (1) had concurrent gastric cancer and hypertension who underwent radical gastrectomy; and (2) had a pathology confirming R0 resection. On the other hand, those excluded had: (1) Incomplete medical records (n = 32); (2) Irregular follow-up or death within the first year after gastrectomy (n = 37); (3) Irregular hypertension monitoring (n = 77); (4) Irregular antihypertensive medications use (n = 21); (5) Secondary hypertension (n = 4); and (6) had no cardiologist when changing antihypertensive medications (n = 44). Finally, a total of 209 patients with concurrent gastric cancer and hypertension were included in this study, and the flow chart of patient selection is shown in Figure 1.

Definition

Hypertension (HTN) was defined as follows: the average systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg at least three times on different days. Hypertension was classified into I, II and III degrees. Degree I HTN was an average SBP was between 140 and159 mmHg or an average DBP between 90 and 99 mmHg; the degree II-HTN was as follows: the average SBP was between 160 and 179 mmHg or the average DBP was between 100 and 109 mmHg; and the degree III was as follows: the average SBP ≥ 180 mmHg or the average DBP ≥ 110 mmHg.

Hypertension remission was divided into two groups: the remission group and the non-remission group. The remission group was defined as follows: (1) SBP and/or DBP decreased with the same antihypertensive medications; (2) The antihypertensive medications were reduced or ceased. The non-remission group was defined as the antihypertensive medications that remained the same or increased. Weight loss was defined as: weight (one year after gastrectomy) minus preoperative weight.

Surgery management and follow-up

Subtotal gastrectomy or total gastrectomy plus D2 Lymph node dissection was conducted according to the guidelines of the 2010 Japanese gastric cancer treatment guidelines (ver. 3)[21]. The gastrectomy type was based on the location and size of the tumor and the reconstruction methods included the Billroth I, Billroth II or Roux-en-Y methods. Patients were regularly followed up every three months for the first three years and every six months for the following two years.

Data collection

Patients' information was collected through the inpatient system, outpatient system and telephone interview. The collected information was as follows: age, sex, preoperative body mass index, preoperative weight, preoperative albumin, pre-operative hemoglobin, one-year postoperative weight, weight loss, smoking, drinking, type 2 diabetes mellitus (T2DM), coronary heart disease (CHD), hypertension classification, neoadjuvant chemotherapy, surgical techniques (subtotal gastrectomy or total gastrectomy), reconstruction methods, tumor stage, tumor size, hypertension duration and hypertension remission.

Statistical analysis

The continuous data are shown as the mean ± SD and the categorical data are shown as n (%). Chi-square tests, Fisher's exact test or independent samples t tests were used to compare the difference between the remission group and the non-remission group.

Parameters were analyzed by univariate regression analysis for potential predictors of hypertension remission. Multivariate regression analysis was used to identify independent risk factors for hypertension remission. Then, a nomogram was generated. Bootstraps with 300 resamples were performed for internal validation. The predictive performance was assessed by Harrell's concordance index (C-index). A calibration

curve was plotted to evaluate the calibration of the nomogram. Decision curve analysis (DCA) was performed to evaluate the clinical usefulness of the nomogram.

Data were analyzed using SPSS (version 22.0) statistical software and R software (version 3.6.1). A bilateral *P* value of < 0.05 was considered statistically significant.

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 (Figure 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 years *vs* 67.4 ± 8.0 years, *P* = 0.001), larger weight loss (-8.2 ± 6.7 kg *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 Figure 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 (Figure 2B).

The DCA for the nomogram is shown in Figure 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.

DISCUSSION

A total of 209 patients with concurrent gastric cancer and hypertension were included in the current study and the hypertension remission rate was 51.7% one year after gastrectomy. Younger age, higher weight loss and total gastrectomy were independent predictors for hypertension remission. The C-index of the model was 0.769 and the calibration curve suggested great agreement. Furthermore, decision curve analysis showed that the model was clinically useful.

Previous studies reported that patients with concurrent colorectal cancer and hypertension and/or T2DM could experience hypertension or T2DM remission[22,23]. In gastric cancer patients, remission of T2DM and hypertension was also observed after gastrectomy[20,24-28]. Onco-metabolic surgery was proposed because of the observation of hypertension and/or T2DM remission after gastrectomy for gastric cancer patients. Based on the current findings of hypertension and/or T2DM remission after gastric

cancer and colorectal cancer surgery, we thought the onco-metabolic surgery might expand to gastrointestinal cancer surgery.

In terms of patients with concurrent gastric cancer and hypertension, the remission rate was 11.1%-93.8%[15-20]. We summarized these findings in Table 3. We previously reported that age and the surgical techniques used can predict the remission of hypertension six months after gastrectomy[15], however, the follow-up time was only 6 mo. Kim *et al*[16] reported that in early gastric cancer survivors with hypertension, gastrectomy resulted in better blood pressure control, which might be due to the gastrectomy itself, beyond weight loss. Therefore, it was necessary to identify exact risk factors for hypertension remission.

The molecular mechanism of hypertension remission after gastrectomy for gastric cancer patients is unclear, but it might be related to bariatric surgery for obese patients[29,30]. 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].

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].

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.

CONCLUSION

In conclusion, younger age, higher weight loss and total gastrectomy were independent predictors for hypertension remission after gastrectomy for gastric cancer patients one year after surgery. The nomogram could visually display these results. Our study predicted that younger hypertension patients who underwent gastrectomy for gastric cancer might decrease anti-hypertensive medication and relieve hypertension-related comorbidities.

ARTICLE HIGHLIGHTS

Research background

Previous studies reported hypertension remission after gastrectomy for gastric cancer patients, and the remission rate was 11.1%-93.8%. We have reported the factors of

hypertension remission previously, however, the follow-up time was six months. It is necessary to identify risk factors for hypertension for a relatively longer follow-up time.

Research motivation

The purpose of the current study was to analyze the predictive factors for hypertension remission one year after gastrectomy in gastric cancer patients.

Research objectives

The purpose of the current study is to analyze the predictive factors for hypertension remission one year after gastrectomy of gastric cancer patients and to construct a risk model for hypertension remission.

Research methods

Univariate and multivariate logistic regression of hypertension remission were conducted, and a nomogram model was established.

Research results

A total of 209 patients with concurrent gastric cancer and hypertension were included in the current study and the hypertension remission rate was 51.7% one year after gastrectomy. Younger age, higher weight loss and total gastrectomy were independent predictors for hypertension remission. The C-index of the model was 0.769 and the calibration curve suggested great agreement. Furthermore, decision curve analysis showed that the model was clinically useful.

Research conclusions

Younger age, higher weight loss and total gastrectomy were independent predictors for hypertension remission after gastrectomy for gastric cancer patients. The nomogram could visually display these results.

Research perspectives

Our study predicted that younger hypertension patients who underwent gastrectomy for gastric cancer might decrease anti-hypertensive medication and relieve hypertension-related comorbidities.

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