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ORIGINAL RESEARCH

Onco-Metabolic Surgery: A Combined Approach to Gastric Cancer and Hypertension

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Purpose: The purpose of this study was to explore the changes in blood pressure in patients with concurrent gastric cancer and hypertension after gastrectomy, and to identify the factors that affect the changes in blood pressure.

Materials and Methods: Patients with concurrent gastric cancer and hypertension who underwent gastrectomy were retrospectively analyzed from January 2013 to December 2018. The pre- and 6-month postoperative medical records were compared. Predictors for the remission of hypertension were analyzed.

Results: A total of 143 patients with concurrent gastric cancer and hypertension were included in this study. The number of patients with complete remission, partial remission and no remission were 67 (46.9%), 12 (8.4%) and 64 (44.7%), respectively. The average of weight and BMI (body mass index) before gastrectomy were 63.0 ± 9.7 kg and 23.4 ± 2.9 kg/m^2, respectively, which were significantly higher than those 6-month postgastrectomy: 54.8 ± 9.8 kg and 20.4 ± 3.1 kg/m^2, respectively ($p<0.001$). The average number of antihypertensive medications before gastrectomy was 1.5 ± 0.6, while it was 0.8 ± 0.8 6-month postgastrectomy ($p<0.001$). Age ($p<0.05$) and the surgical techniques used ($p<0.05$) were significantly different between partial remission and no remission patients. Furthermore, age ($p<0.05$) and the surgical techniques used ($p<0.05$) were significantly different between complete remission and no remission patients. Age ($p<0.05$, odds ratio =0.933, 95% CI=0.890–0.978) and the surgical techniques used ($p<0.05$, odds ratio =2.749, 95% CI=1.132–6.677) are predictors for remission of hypertension.

Conclusion: Total gastrectomy is an onco-metabolic surgery that can cure younger patients with concurrent gastric cancer and hypertension. Age and the surgical techniques used can predict the remission of hypertension 6 months after gastrectomy.

Keywords: gastric cancer, age, hypertension, gastrectomy, remission

Introduction

Gastric cancer is the fifth most common cancer in the world and ranks third among cancer-related causes of death.[1] In China, the morbidity and mortality of gastric cancer are growing, and more than 400,000 newly diagnosed cases occur every year.[2] For patients with gastric cancer, gastrectomy is still the most effective treatment.[3] As the survival rate increases, the quality of life of postoperative patients is also a current concern.[4]

Hypertension is a common disease and a major risk factor for cardiovascular disease.[5] It is estimated that 40% of the world's population suffers from hypertension.[6] Hypertension is also the main global risk factor for death and accounts for 13% of deaths.[7] The number of newly-diagnosed hypertensive patients in China is

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rising every year.[8] The management of patients with hypertension also brings a corresponding financial burden.[9]

Much literature has reported the effect of bariatric surgery on blood pressure.[10] A meta-analysis reported that the blood pressure remission rate reached 75% and the complete remission rate reached 58%.[11] However, for patients with concurrent gastric cancer and hypertension, changes in blood pressure after gastrectomy have rarely been reported.[12,13]

Hence, the purpose of the current study was to retrospectively analyze the changes in blood pressure and the dosages of antihypertensive medications after gastrectomy in patients with concurrent gastric cancer and hypertension, and to explore the parameters for the remission of hypertension after gastrectomy.

Materials and Methods

Patients

A retrospective analysis of patients with gastric cancer who underwent gastrectomy from January 2013 to December 2018 at a single clinical center was conducted. The study was approved by the Institutional Ethics Committee of our hospital, and informed consent was obtained from all patients. Data from a total of 1182 patients were collected and the patients were included according to the following criteria: 1, patients who were diagnosed with gastric cancer through abdominal enhanced CT, gastroscopy and pathological biopsy; 2, patients who underwent gastrectomy; and 3, patients diagnosed with hypertension by a cardiologist and taking antihypertensive medications before gastrectomy. According to the criteria, 315 patients with concurrent gastric cancer and hypertension were included. Patients were excluded from the study according to the following exclusion criteria: 1, incomplete information before gastrectomy (n=16); 2, irregular blood pressure monitoring (n=69); 3, irregular antihypertensive medications use (n=16); 4, death within six months (n=9); 5, no consultation with a cardiologist when changing antihypertensive medications after gastrectomy (n=27); 6, irregular follow-up within 6 months (n=13); 7, presence of secondary hypertension (n=4); and 8, gastric cancer with obstruction (n=18). In total, 143 patients were determined to meet these criteria (Figure 1).

Definitions

Hypertension is defined as an average systolic blood pressure (SBP) ≥140 mmHg or an average diastolic blood pressure (DBP) ≥90 mmHg. The average BP value was based on at least two careful readings on two occasions. Hypertension is classified as Stage I, II or III: an average SBP between 140 and159 mmHg or an average DBP between 90 and 99 mmHg is regarded as Stage I, an average SBP between 160 and 179 mmHg or an average DBP between 100 and 109 mmHg is regarded as Stage II, and an average SBP ≥180 mmHg or an average DBP ≥110 mmHg is regarded as Stage III.[14] There are five types of common antihypertensive medications according to the guidelines: angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), β-blockers and diuretics.

There are three types of remission of hypertension: complete remission, partial remission and no remission. The criteria for complete remission were as follows: 1, an average SBP of <135 mmHg and an average DBP of <85 mmHg observed at least three times on different days without taking antihypertensive medications; and 2, after evaluation by a cardiologist at an outpatient visit, the blood pressure was considered to be normal. The criteria for partial remission were as follows: 1, an average SBP of <135 mmHg and an

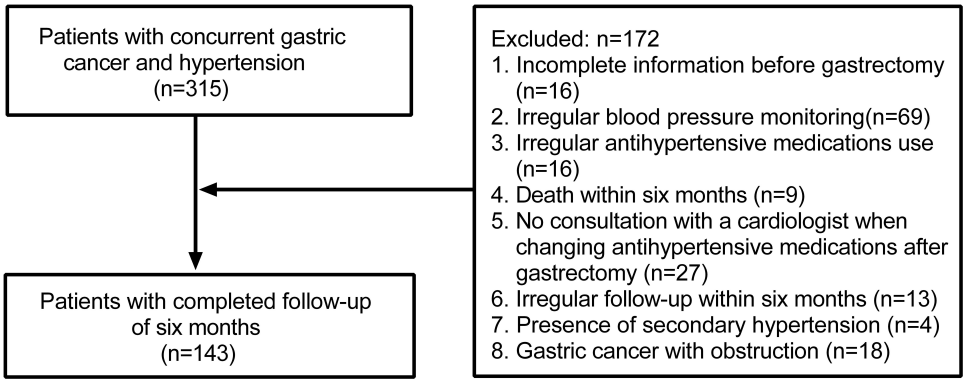

Figure 1 Inclusion criteria and exclusion criteria of patients with concurrent gastric cancer and hypertension.

average DBP of <85 mmHg observed at least three times on different days after regularly taking antihypertensive medications; and 2, after evaluation by a cardiologist at an outpatient visit, the class or dosages of antihypertensive drugs were reduced, and the blood pressure was controlled in a normal range. No remission was when the class and dosages of antihypertensive medications stayed the same or even increased when the patients consulted a cardiologist after gastrectomy.

Surgical Techniques

The surgical techniques were all standard gastrectomy procedures and the types of gastrectomy were based on the location and the size of the tumor. D2 lymph node dissection was performed according to the guideline of the Japanese gastric cancer treatment guidelines 2010 (ver. 3).[15] Billroth I, Billroth II or Roux-en-Y was performed to recover the gastrointestinal continuity.

Data Collection

Demographic data were collected by reviewing medical records from the database and through telephone interviews. The preoperative and postoperative data included age, sex, weight, preoperative BMI, comorbid diabetes mellitus (DM), hypertension classification, the class and dosages of antihypertensive medications and the surgical techniques used. Among these data, weight loss refers to the preoperative weight minus the postoperative weight 6 months after gastrectomy, and weight loss% is calculated using the following formula: weight loss/preoperative weight * 100%.

Statistical Analysis

The results are shown as the mean values ± standard deviation (SD). Categorical data were analyzed using chi-square tests or Fisher's exact test, and continuous data were analyzed using independent samples t tests. Paired t tests were also used to examine the differences in continuous variables pre- and 6-month postoperatively. Parameters were selected for multivariate regression analysis for the detection of independent risk factors for the remission of hypertension. Data were analyzed using SPSS (version 20.0) statistical software. A bilateral p value of <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 143 patients with concurrent gastric cancer and hypertension were included in this study. The baseline characteristics of sex, age, comorbid DM, preoperative BMI, preoperative weight, hypertension classification and the class and dosages of antihypertensive medications are shown in Table 1.

Table 1 Baseline Characteristics of Patients with Concurrent Gastric Cancer and Hypertension

Characteristics	No.143
Sex	
Male	91 (63.6%)
Female	52 (36.4%)
Age (mean ± SD), year	65.1 ± 8.3
DM	30 (21.0%)
BMI preoperative (mean ± SD), kg/m^2	23.4 ± 2.9
Weight preoperative (mean ± SD), kg	63.0 ± 9.7
Hypertension classification (I/II/III)	38 (26.5%)/55 (38.5%)/50 (35.0%)
Antihypertensive agent (n, %)	
ACEI	44 (30.8%)
ARB	34 (23.8%)
CCB	99 (69.2%)
Beta-blocker	17 (11.9%)
Diuretics	11 (7.7%)
Antihypertensive medications (n, %)	
1	87 (60.8%)
2	48 (33.6%)
3	8 (5.6%)

Note: Variables are expressed as the mean ± SD or n (%).
Abbreviations: DM, diabetes mellitus; BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Comparisons of Before and 6 Months After Gastrectomy

Weight, BMI and antihypertensive medication use were compared before and 6 months after gastrectomy. The average weight and BMI and the number of antihypertensive medications 6 months after gastrectomy were significantly lower than those before gastrectomy (p<0.001) (Table 2).

Table 2 Comparison Before and 6 Months After Gastrectomy

	Before	After	p
Weight (mean ± SD), kg	63.0 ± 9.7	54.8 ± 9.8	0.000*
BMI (mean ± SD), kg/m^2	23.4 ± 2.9	20.4 ± 3.1	0.000*
Antihypertensive medications (mean ± SD)	1.5 ± 0.6	0.8 ± 0.8	0.000*

Notes: Variables are expressed as the mean ± SD. *P-value <0.05.
Abbreviation: BMI, body mass index.

Differences Between Remission and No Remission Patients

Seventy-nine (55.3%) patients had hypertension remission, and 64 (44.7%) patients had no hypertension remission. Age, sex, BMI, DM, preoperative weight, weight loss, weight loss %, hypertension classification and the surgical techniques and reconstruction methods used in subtotal gastrectomy were compared between remission and no remission patients. There were significant differences in age ($p<0.05$) and the surgical techniques used ($p<0.05$) (Table 3 p^c).

Comparison of No Remission, Partial Remission and Complete Remission Patients

Sixty-seven patients (46.9%) had complete hypertension remission, 12 patients (8.4%) had partial hypertension remission, and 64 patients (44.7%) had no hypertension remission. Age, sex, BMI, DM, preoperative weight, weight loss, weight loss%, hypertension classification and the surgical techniques and reconstruction methods used in subtotal gastrectomy were compared between partial remission and no remission patients and between complete remission and no remission patients. Age ($p<0.05$) and the surgical techniques used ($p<0.05$) were significantly different between partial remission and no remission patients. Furthermore, age ($p<0.05$) and the surgical techniques used ($p<0.05$) were significantly different between complete remission and no remission patients (Table 3 p^a p^b).

Multiple Regression Analysis for Remission of Hypertension

Age, weight loss, surgical techniques, hypertension classification and BMI were included in the multiple regression. Age ($p<0.05$, odds ratio =0.933, 95% CI=0.890–0.978) and the surgical techniques ($p<0.05$, odds ratio =2.749, 95% CI=1.132–6.677) had statistical significance (Table 4).

Discussion

The remission of hypertensive in patients with concurrent gastric cancer and hypertension after gastrectomy was retrospectively analyzed in this study. The number of patients with complete remission, partial remission and no remission was 67 (46.9%), 12 (8.4%) and 64 (44.7%), respectively. It was found that the postoperative weight, BMI and antihypertensive medication use decreased compared with preoperative parameters. Age and the surgical techniques used were significantly different compared with remission and no remission patients. Furthermore, age and

Table 3 Comparison of No Remission, Remission, Partial Remission and Complete Remission

		No Remission (64)	Remission(79)			P^a	P^b	P^c
			Partial Remission (12)	Complete Remission (67)	Total (79)			
Age (mean ± SD), year		67.6 ± 7.5	62.3 ± 8.2	63.1 ± 8.5	63.0 ± 8.4	0.030*	0.001*	0.001*
Sex Male		39(27.3%)	9(6.3%)	43(30.1%)	52(36.4%)	0.518	0.721	0.602
Female		25(17.5%)	3(2.1%)	24(16.8%)	27(18.9%)			
BMI(mean± SD), kg/m^2		23.4 ± 2.9	24.2 ± 2.0	23.3 ± 3.1	23.5 ± 3.0	0.330	0.909	0.873
Weight(mean± SD), kg		62.0 ± 9.8	66.0 ± 6.1	63.4 ± 10.1	63.8 ± 9.6	0.185	0.423	0.276
Weight loss(mean ± SD), kg		7.5 ± 6.2	9.8 ± 6.6	8.3 ± 6.5	8.5 ± 6.5	0.250	0.468	0.336
Weight loss % (mean ± SD)		11.8 ± 10.0	15.0 ± 10.3	12.9 ± 9.8	13.2 ± 9.8	0.315	0.544	0.410
DM		13	1	16	13	0.447	0.623	0.860
Hypertension I or II		38	10	45	55	0.192	0.371	0.221
Classification III		26	2	22	24			
Surgical techniques						0.038*	0.008*	0.004*
Subtotal gastrectomy		55	7	44	51			
Total gastrectomy		9	5	23	28			
Reconstruction methods of subtotal gastrectomy	B-I	38	6	27	33	0.426	0.676	0.885
	B-II	11	0	12	12			
	R-Y	6	1	5	6			

Notes: Variables are expressed as the mean ± SD or n (%), *P-value <0.05, [a]No remission versus Partial remission, [b]No remission versus Complete remission, [c]No remission versus total (partial remission + complete remission).

Abbreviations: BMI, body mass index; DM, diabetes mellitus; B-I, Billroth I reconstruction; B-II, Billroth II reconstruction; R-Y, Roux-en-Y reconstruction.

Table 4 Multiple Regression Analysis for Remission of Hypertension

Individual Variable	P value	OR (95% CI)
Age	0.004*	0.933 (0.890–0.978)
Weight loss	0.763	1.010 (0.949–1.074)
Surgical techniques	0.025*	2.749 (1.132–6.677)
Hypertension classification	0.251	1.552 (0.732–3.290)
BMI	0.405	0.943 (0.890–0.987)

Note: *P-value <0.05.
Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index.

the surgical techniques used were predictors for the remission of hypertension.

Bariatric surgery is a mature and widely accepted surgical technique worldwide. Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are the main surgical techniques.[16] It has been reported that bariatric surgery can cause weight loss,[17,18] and even acquire the improvement in diabetes,[19] hyperlipidemia,[10] hypertension[11] and heart function.[20]

Radical gastrectomy plus lymphadenectomy is the currently widely accepted surgical technique for patients with resectable gastric cancer.[21] The bariatric surgery has been proven to improve metabolism-related diseases. In gastrectomy, the magnitude of the stomach incision is no less than that in bariatric surgery, so there may be some improvement in concurrent gastric cancer and metabolism-related diseases. Patients with concurrent gastric cancer and diabetes can exhibit remission of diabetes after gastrectomy.[22,23] It was thought that gastrectomy is not just a tumor resection surgery, but also an onco-metabolic surgery. However, patients with concurrent gastric cancer and hypertension after gastrectomy have rarely been reported.[17,18]

Weight loss was obtained after bariatric surgery and was a parameter for the remission of hypertension in previous studies.[24] However, in this study, weight loss seemed to be a negative parameter for the remission of hypertension. Consistent with a previous report, lifestyle modifications, such as sodium absorption dysfunction, may play an important role beyond weight loss.[13]

Age is another parameter for the remission of hypertension in patients with concurrent gastric cancer and hypertension. It was also reported that after bariatric surgery, the blood pressure of younger patients decreased more significantly than that of older patients.[25,26] A comprehensive meta-analysis reported similar conclusions.[11] Age was not a parameter for the remission of hypertension in patients with concurrent gastric cancer and hypertension in the previous literature; the possible reason is that one article did not have complete baseline information,[12] while the other article had a relatively small amount of data.[13] In this study, younger patients tended to have better rates of hypertension remission than older patients. Postoperative lifestyle and vascular elasticity may play an important role in younger patients who exhibit remission of hypertension. Furthermore, younger patients may have a short duration of hypertension, which contributes to better remission of hypertension.[25]

Different bariatric surgical techniques for metabolic diseases were compared, and some significant differences were proposed.[16–18] We compared the differences between total gastrectomy and subtotal gastrectomy in this study, and different reconstruction methods for subtotal gastrectomy were compared as well. As a result, total gastrectomy can predict remission of hypertension, and the reconstruction methods for subtotal gastrectomy had no relevance with regards to the remission of hypertension. An article reported that there was no significant difference in the amount of food consumed after different surgical techniques in patients with gastric cancer.[27] The difference between total gastrectomy and subtotal gastrectomy may be due to the volume of the residual stomach. Total gastrectomy allows less storage of food, which may cause better remission of hypertension.[13] Total gastrectomy could be a recommended surgical technique in patients with concurrent gastric cancer and hypertension.

The molecular mechanism of remission of hypertension after bariatric surgery is currently complex and unclear. It was recently proposed that multiple factors work together to cause remission of hypertension.[28] Early remission may be related to endocrine hormones,[29] and long-term remission may be related to neurohumoral.[30] Regarding the specific mechanism for the remission of hypertension after gastrectomy, a lack of endocrine hormones is important, and more experiments need to be carried out in the future.

There are some limitations to this study. First, this study was a retrospective study. Second, the follow-up time of this study was short, only 6 months, and some indicators, such as the duration of preoperative hypertension, postoperative dietary changes, and lifestyle differences, were lacking. There should be a prospective study in the future, and a long-term follow-up should be carried out. In addition, some blood measurements before and after gastrectomy should be taken into consideration in the subsequent experimental designs.

In conclusion, total gastrectomy is an onco-metabolic surgery that can cure younger patients with concurrent gastric cancer and hypertension. Age and the surgical techniques used can predict the remission of hypertension 6 months after gastrectomy.

Abbreviations

DM, diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blockers; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

Data Sharing Statement

The data of this study are available upon special request to the corresponding author(s).

Ethics Approval and Consent Statement

This study was conducted in accordance with the World Medical Association Declaration of Helsinki and was approved by the Medical Ethics Committee of the First Affiliated Hospital of Chongqing Medical University.

Consent for Publication

All patients signed the informed consent to participate in this study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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