Supportive Care in Cancer (2019) 27:2237–2245
https://doi.org/10.1007/s00520-018-4491-8

ORIGINAL ARTICLE

Effect of gastrectomy on blood pressure in early gastric cancer survivors with hypertension

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Received: 26 February 2018 / Accepted: 2 October 2018 / Published online: 13 October 2018

Abstract

Purpose We investigated the effect of gastrectomy on blood pressure (BP) in early gastric cancer survivors with hypertension and whether well-controlled BP was due solely to surgery-induced weight loss.

Methods The study enrolled 66 early gastric cancer patients with hypertension, undergoing endoscopic submucosal dissection (ESD), or gastrectomy. Blood analyses, 24-h ambulatory BP monitoring, brachial ankle pulse wave velocity (baPWV), and echocardiography were measured prior to, 3 months after, and 1 year after ESD or gastrectomy. The primary endpoint was remission of hypertension at 1 year.

Results The remission rate of hypertension was significantly higher in the gastrectomy group than in the ESD group ($p = 0.006$). Those with remission of hypertension had a significant weight loss ($p < 0.001$), decrease in body mass index ($p < 0.001$), 24-h total systolic BP ($p = 0.047$), baPWV ($p = 0.042$), triglycerides ($p = 0.049$) and apolipoprotein B/apolipoprotein A1 ($p = 0.004$), and an increase in high-density lipoprotein cholesterol ($p < 0.001$) at 1 year. Upon multivariate logistic regression analysis, gastrectomy [odds ratio (OR) = 7.77, 95% confidence interval (CI) = 2.05–35.89], diuretic use (OR = 3.76, 95% CI = 1.14–13.98), and lower 24-h total diastolic BP before treatment (OR = 0.90, 95% CI = 0.82–0.96) were predictive of remission of hypertension after adjusting for percent weight.

Conclusions In early gastric cancer survivors with hypertension, gastrectomy resulted in better BP control than did ESD, which may be due to the gastrectomy itself, beyond weight loss. Therefore, it should be remembered that the adequate reduction of antihypertensives may be necessary in early gastric cancer survivors after gastrectomy.

Keywords Early gastric cancer · Gastrectomy · Hypertension · Weight loss

Introduction

Gastric cancer is the fourth most common malignancy in the world and the second most common malignancy in Korea [1, 2]. As the incidence of early gastric cancer continues to rise, and the 5-year overall survival rate increases by more than 97%, the quality of life of gastric cancer survivors must be considered [3, 4]. Hypertension is a typical modifiable risk factor that can affect the quality of life of cancer survivors and is the most common nationwide illness in Korea, with a prevalence of approximately 30% in those over 30 years of age. Hypertension is closely associated with cardiovascular and cerebrovascular disease [5]. Furthermore, hypertension is the most common comorbidity in patients undergoing gastrointestinal surgery [6]. As blood pressure (BP) changes are closely related to weight changes, well-controlled BP is often experienced by patients due to weight loss after surgery. In practice, the effect of surgical weight reduction has been primarily validated for bariatric surgery [7]. It may be considered in patients with a body mass index (BMI) ≥ 35 kg/m^2 who also have one or more comorbidities such as hypertension, diabetes, or obstructive sleep apnea [8]. Following bariatric surgery, the percent resolution or improvement of hypertension, diabetes, and dyslipidemia was at least 60% [9]. In patients with

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BMI of 30.0–39.9 kg/m^2 with diabetes, Roux-en-Y gastric bypass surgery provides potential benefits for controlling glucose, BP, and cholesterol, compared with lifestyle and intensive medical treatment during a 1-year follow-up. These results are primarily due to weight loss [10]. Conventional surgery in patients with gastric cancer is not significantly different from bariatric surgery. Therefore, if the beneficial effects of surgery in early gastric cancer survivors with hypertension and diabetes are observed, the possibility of metabolic surgery can be indirectly secured. However, there is little known of the effect of gastrectomy on weight reduction, hypertension, and metabolic disturbances in patients with a BMI < 30 kg/m^2 compared with bariatric surgery in patients with severe obesity.

We designed this study to examine the effects of gastrectomy on BP changes in early gastric cancer survivors with hypertension. In addition, we investigated whether well-controlled BP is simply due to weight loss after surgery or other factors beyond weight loss.

Materials and methods

Participants and protocols

Between April 2012 and December 2014, we prospectively enrolled 66 early gastric cancer patients with hypertension undergoing endoscopic submucosal dissection (ESD) or gastrectomy at the National Cancer Center in Korea. Patients were assigned to either the ESD or gastrectomy group and followed for 12 months. The inclusion criteria of the participants were as follows: (1) patients aged 20 to 80 years with hypertension and early gastric cancer at clinical stage Ia or Ib diagnosed by endoscopy, endoscopic ultrasound, and computed tomography; (2) patients with a performance status of 0 or 1 on the Eastern Cooperative Oncology Group scale; and (3) patients planning to undergo ESD or gastrectomy. The exclusion criteria were as follows: (1) high risk for operation, such as severe heart disease, severe respiratory disease, or severe uncontrolled hypertension, with a baseline systolic BP (SBP) > 180 mmHg or diastolic BP (DBP) > 110 mmHg; (2) pregnancy or planning for pregnancy; (3) previous abdominal surgery or radiation therapy; and (4) proven more advanced disease than pathological stage II requiring adjuvant chemotherapy. Outpatient follow-up was performed at 1, 3, 6, 9, and 12 months after ESD or gastrectomy. Blood tests, 24-h ambulatory blood pressure monitoring (ABPM), brachial ankle pulse wave velocity (baPWV), and echocardiography were measured prior to, 3 months after, and 1 year after ESD or gastrectomy. Patients provided written informed consent to participate in the study, and additional written informed consent was obtained before any procedure. The protocol and data were approved by the institutional review board of the National Cancer Center (NCCNCS-12-563).

BP measurements

Hospital BP was measured three times on the arm with an automated measurement system (HEM 9020, Omron Corporation, Japan) at 1-min intervals in a sitting position after the patient rested quietly for at least 5 min. The 24-h ABPM was performed using TONOPORT V (PAR Medizintechnik, Berlin, Germany). The criteria for adequate 24-h BP was defined as an average 24-h total SBP < 130 mmHg and DBP < 80 mmHg, an average 24-h daytime SBP < 135 mmHg and DBP < 85 mmHg, and an average 24-h nighttime SBP < 120 mmHg and DBP < 70 mmHg. Antihypertensive dosage was adjusted based on the mean BP of three BPs measured at an office visit and the average BP measured by 24-h ABPM.

Measurement of baPWV

The value of baPWV was obtained by two experienced technicians with an automated device (VP-2000; Colin Co. Ltd., Komaki, Japan) after at least 5 min of rest in a supine position. The baPWV value was automatically calculated using the time interval between the brachial and tibial waveforms divided by the time for the pulse wave to travel between the brachial and posterior tibial arteries.

Echocardiography

Transthoracic echocardiographic examination was performed according to recommendations of the American Society of Echocardiography and the European Association of Echocardiography [11]. Left ventricular ejection fraction (LVEF); the peak early transmitral filling velocity during early diastole (E), late diastole (A); and Tissue Doppler imaging during early diastole (E′), late diastole (A′) were measured.

Dietary assessment

Dietary intake data were obtained from a 3-day food record. Patients were asked to complete food records for two weekdays and one weekend day within a week. In order to increase the accuracy of food records, trained registered dietitians confirmed all records written by subjects with face-to-face interviews. The daily intake of energy and nutrients was calculated using CAN-Pro 3.0 (The Korean Nutrition Society, Seoul, Korea).

Endpoints and outcomes

The primary endpoint was the remission of hypertension at 1 year after ESD or gastrectomy. The secondary endpoints included the effects of ESD or gastrectomy on BP assessed

through ABPM, weight change, BMI, lipid profiles [total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and apolipoprotein B/apolipoprotein A1 (apoB/apoA1)], aPWV, and echocardiographic parameters at 1 year after treatment. Weight change is defined as the percent change from baseline. BMI is calculated as the weight in kilograms divided by the square of the height in meters.

"Remission" is defined as complete remission (sustaining normal BP in the absence of antihypertensives) or partial remission (decreasing the dosage of antihypertensives). "No remission" is defined as unchanged (sustaining the previous dosage of antihypertensives) or aggravation (adding another antihypertensive or increasing the dosage of antihypertensives).

Statistical analyses

Approximately 600 patients with stage Ia or Ib cancer (450 patients with surgery and 150 patients with ESD) are admitted to the National Cancer Center every year. Among these, approximately 200 patients have hypertension. Therefore, 40 patients per group are classified according to the four surgical methods and ESD. We estimated that approximately 12 patients would be enrolled in each group, and 120 patients would be enrolled in 2 years, considering that the rate of entry to the study was 50%, the dropout rate according to pathologic results was 20%, and the dropout rate during follow-up was 20%. Descriptive statistics were used to describe demographics and laboratory measurements. We evaluated the normality of the distributions of all continuous variables. Continuous variables were presented as the mean followed by standard deviation if normally distributed or the median followed by interquartile range if skewed. Categorical variables are expressed as percentages. Independent data were analyzed with the Student's t test for parametric data or with the Mann-Whitney U test for nonparametric data. The chi-square test or Fisher's exact test was used for categorical data. Paired data were analyzed with the paired t test for parametric data or Wilcoxon signed rank test for nonparametric data. Parameters were selected for logistic regression analysis for detection of independent risk factors for remission of hypertension. A p value of less than 0.05 (two-tailed) was used to test for statistical significance. All statistical analyses were conducted using STATA version 14 (College Station, TX, USA).

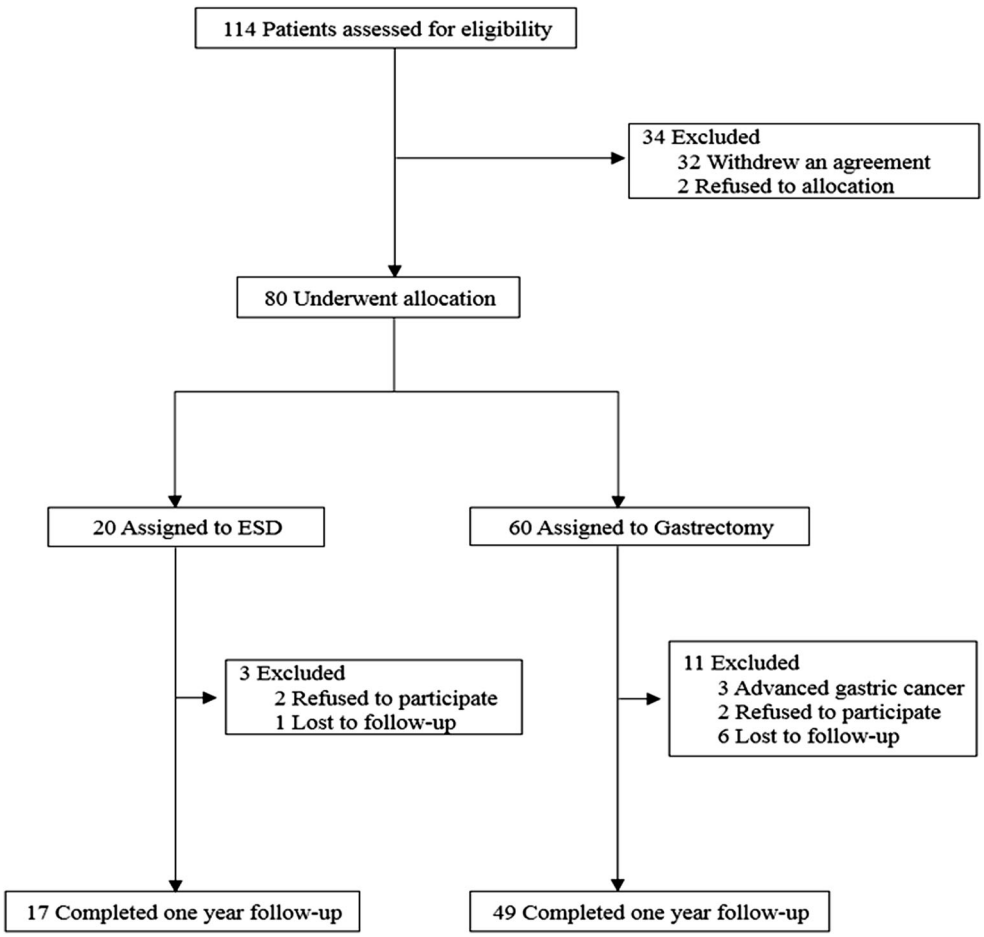

Fig. 1 Enrollment and follow-up. ESD, endoscopic submucosal dissection

Results

Characteristics of patients by treatment group

A total of 114 candidates were screened, and 80 patients were allocated to undergo ESD or gastrectomy (Fig. 1). Among the 66 patients who completed the 1-year follow-up, 17 received ESD, six received total gastrectomy with esophagojejunostomy, 11 received subtotal gastrectomy with gastroduodenostomy (Billroth type I), 23 received subtotal gastrectomy with gastrojejunostomy (Billroth type II), and nine received subtotal gastrectomy with Roux-en-Y gastrojejunostomy. The method of surgery was at the discretion of the attending surgeon. The baseline

Table 1 Baseline data and parametric changes by treatment group

	ESD			Gastrectomy			*p*
	(*n* = 17)			(*n* = 49)			
	Baseline	One year	*p*	Baseline	One year	*p*	
Age (years)	66 ± 7			62 ± 10			0.147
Female	1 (5.9)			17 (34.7)			0.027*
Smoking	14 (82.4)			27 (55.1)			0.046*
Diabetes	9 (52.9)			14 (28.6)			0.069
Dyslipidemia	6 (33.3)			12 (25.0)			0.528
Duration of hypertension(years)	8 ± 5			7 ± 7			0.650
Body weight (kg)	68.5 ± 11.4	68.1 ± 11.2	0.646	69.1 ± 12.5	62.7 ± 11.5	< 0.001*	0.854
Body mass index (kg/m^2)	24.7 ± 3.1	24.5 ± 3.2	0.647	25.5 ± 2.9	23.1 ± 2.6	< 0.001*	0.289
24-h total SBP (mmHg)	126 ± 13	125 ± 9	0.755	125 ± 12	119 ± 10	0.002*	0.928
24-h total DBP (mmHg)	80 ± 9	80 ± 6	0.732	82 ± 9	78 ± 7	0.012*	0.522
24-h day SBP (mmHg)	127 ± 13	126 ± 9	0.702	127 ± 13	121 ± 11	0.003*	0.935
24-h day DBP (mmHg)	82 ± 9	81 ± 6	0.621	84 ± 9	80 ± 7	0.009*	0.576
24-h night SBP (mmHg)	119 ± 16	120 ± 11	0.819	119 ± 15	113 ± 12	0.005*	0.922
24-h night DBP (mmHg)	75 ± 9	75 ± 7	0.876	76 ± 9	73 ± 8	0.019*	0.573
LV ejection fraction (%)	64 ± 4	64 ± 4	0.712	66 ± 4	65 ± 5	0.164	0.126
E/A	0.7 ± 0.1	0.7 ± 0.1	0.236	0.8 ± 0.2	0.9 ± 0.4	0.011*	0.186
E/E′	8.5 ± 1.9	9.1 ± 2.6	0.435	9.1 ± 2.6	9.8 ± 2.5	0.082	0.393
LA volume index (mL/m^2)	27.3 ± 5.0	26.4 ± 5.8	0.545	28.1 ± 9.5	29.3 ± 9.6	0.279	0.751
LV mass index (g/m^2)	99.9 ± 22.5	96.6 ± 15.9	0.440	92.2 ± 18.8	96.7 ± 18.7	0.084	0.170
baPWV, average (cm/s)	1513 (1455, 1995)	1559 (1454, 1643)	0.687	1588 (1388, 1693)	1454 (1299, 1716)	0.018*	0.769
Total cholesterol (mg/dL)	159 (146, 175)	161 (141, 168)	0.850	178 (152, 198)	167 (142, 190)	0.263	0.039*
Triglycerides (mg/dL)	107 (86, 135)	109 (75, 129)	0.877	110 (76, 152)	83 (61, 117)	0.012*	0.155
HDL-cholesterol (mg/dL)	50 (45, 55)	53 (45, 61)	0.468	45 (39, 54)	50 (42, 62)	< 0.001*	0.320
LDL-cholesterol (mg/dL)	97 (79, 111)	94 (74, 108)	0.959	111 (84, 136)	99 (74, 118)	0.056	0.064
ApoB/apoA1	0.6 (0.5, 0.7)	0.5 (0.4, 0.7)	0.623	0.8 (0.6, 0.9)	0.6 (0.5 0.7)	< 0.001*	0.009*
Diet Na (mg/day)	4310 (3800, 6630)	3834 (2581, 5711)	0.112	4043 (3219, 5970)	4464 (3098, 5913)	0.451	0.330
Diet K (mg/day)	2959 (2464, 3225)	2505 (2158, 3483)	0.173	2728 (2022, 3261)	2584 (2103, 3468)	0.944	0.266
Antihypertensives							
ACEi or ARB	15 (88.2)			36 (73.5)			0.318
Beta blocker	0 (0)			8 (16.3)			0.101
CCB	14 (82.4)			35 (71.4)			0.525
Diuretics	6 (35.3)			21 (42.9)			0.585

Data are presented as mean ± standard deviation, median (interquartile range) or number (%)

ESD, endoscopic submucosal dissection; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *E*, early diastolic mitral flow velocity; *A*, late diastolic mitral flow velocity; *E′*, early diastolic septal annular velocity; *LA*, left atrium; *LV*, left ventricle; *baPWV*, brachial-ankle pulse wave velocity; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *Apo*, apolipoprotein; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin II receptor blocker; *CCB*, calcium channel blocker

*$p < 0.05$

characteristics of the ESD and gastrectomy groups are presented in Table 1. There were no differences in risk factors, 24-h BP, echocardiographic findings, laboratory findings, dietary data, or antihypertensive drug composition between the two groups, except for the higher percentage of women, lower percentage of smoking, higher total cholesterol level, and the higher apoB/apoA1 value in the gastrectomy group. Table 1 also shows the parametric changes after 1 year between the ESD and gastrectomy groups. While there was no change after 1 year in the ESD group, significant weight loss ($p < 0.001$), decrease of BMI ($p < 0.001$), 24-h total SBP ($p = 0.002$), 24-h total DBP ($p = 0.012$), 24-h day SBP ($p = 0.003$), 24-h day DBP ($p = 0.009$), 24-h night SBP ($p = 0.005$), 24-h night DBP ($p = 0.019$), baPWV ($p = 0.018$), triglycerides ($p = 0.012$), apoB/apoA1 ($p < 0.001$), and increase of HDL-cholesterol ($p < 0.001$), E/A ($p = 0.011$) after 1 year were observed in the gastrectomy group.

Outcomes according to treatment

One-year outcomes of hypertension according to treatment are presented in Table 2. The remission rate of hypertension was significantly higher in the gastrectomy group than in the ESD group (67.3 vs 29.4%, $p = 0.006$). Among the gastrectomy types, the remission rate of hypertension was highest for total gastrectomy with esophagojejunostomy (83.3%), followed by Billroth type II (73.9%), Billroth type I (63.6%), and subtotal gastrectomy with Roux-en-Y anastomosis (44.4%). The percent weight change at 1-year follow-up was the largest in total gastrectomy, followed by Billroth types I and II, but subtotal gastrectomy with Roux-en-Y anastomosis was not different from ESD.

Characteristics of patients by outcome group

Table 3 shows baseline characteristics of patients with remission of hypertension compared with those with no remission at the 1-year follow-up. Patients with remission of hypertension had had a higher rate of gastrectomy ($p = 0.010$), more diuretic use ($p = 0.024$), lower 24-h total SBP ($p = 0.007$), 24-h total DBP ($p = 0.011$), 24-h day SBP ($p = 0.010$), 24-h day DBP ($p = 0.014$), 24-h night SBP ($p = 0.006$), and 24-h night DBP ($p = 0.015$) compared to patients with no remission. The parametric changes after 1 year between "remission" and "no remission" groups are also described in Table 3. Patients with remission of hypertension had significant weight change ($p < 0.001$), decrease in BMI ($p < 0.001$), 24-h total SBP ($p = 0.047$), baPWV ($p = 0.042$), triglycerides ($p = 0.049$) and apoB/apoA1 ($p = 0.004$), and an increase in HDL cholesterol ($p < 0.001$), E/A ($p = 0.035$).

Predicting factor for remission of hypertension

Multivariate logistic regression analysis revealed that gastrectomy, diuretics use, and lower 24-h total DBP before treatment were predictive of remission of hypertension after adjusting for weight loss [gastrectomy: odds ratio (OR) = 7.77, 95% confidence interval (CI) = 2.05–35.89; diuretics use: OR = 3.76, 95% CI = 1.14–13.98; 24-h total DBP: OR = 0.90, 95% CI = 0.82–0.96] (Table 4).

Discussion

Hypertension is closely related to cerebrovascular disease and cardiovascular disease [12]. Management of hypertension is recognized as an important issue in promoting

Table 2 One-year outcomes according to treatment

	No remission ($n = 28$)		Remission ($n = 38$)		p
	Aggravation ($n = 6$)	Unchanged ($n = 22$)	Partial remission ($n = 30$)	Complete remission ($n = 8$)	
Gastrectomy vs ESD					0.006*
Gastrectomy	4 (8.2%)	12 (24.5%)	25 (51.0%)	8 (16.3%)	
ESD	2 (11.8%)	10 (58.8%)	5 (29.4%)	0 (0%)	
Gastrectomy types vs ESD					0.180
Total gastrectomy	0 (0.0%)	1 (16.7%)	4 (66.6%)	1 (16.7%)	
B-I	1 (9.1%)	3 (27.3%)	4 (36.3%)	3 (27.3%)	
B-II	2 (8.7%)	4 (17.4%)	13 (56.5%)	4 (17.4%)	
STG with R-Y	1 (11.0%)	4 (44.5%)	4 (44.5%)	0 (0.0%)	
ESD	2 (11.8%)	10 (58.8%)	5 (29.4%)	0 (0.0%)	

Data are presented as number (%)

ESD, endoscopic submucosal dissection; *B-I*, distal gastrectomy with gastroduodenostomy (Billroth type I); *B-II*, distal gastrectomy with gastrojejunostomy (Billroth type II); *STG*, subtotal gastrectomy; *R-Y*, Roux-en-Y gastrojejunostomy

*$p < 0.05$

Table 3 Baseline data and parametric changes by outcome group

	No remission			Remission			*p*
	(*n* = 28)			(*n* = 38)			
	Baseline	One year	*p*	Baseline	One year	*p*	
Age (years)	63 ± 11			63 ± 8			0.954
Female	8 (28.6)			10 (26.3)			0.839
Smoking	17 (60.7)			24 (63.2)			0.840
Diabetes	12 (42.9)			11 (29.0)			0.241
Dyslipidemia	7 (25.0)			11 (29.0)			0.722
Duration of hypertension (years)	8.6 ± 6.6			6.7 ± 6.8			0.253
Gastrectomy	16 (57.1)			33 (86.8)			0.010*
Body weight (kg)	67.1 ± 11.3	64.4 ± 11.8	0.003*	70.4 ± 12.7	63.9 ± 11.6	< 0.001*	0.286
Body mass index (kg/m^2)	24.9 ± 3.1	23.8 ± 3.0	0.002*	25.7 ± 2.8	23.3 ± 2.6	< 0.001*	0.286
24-h total SBP (mmHg)	130 ± 12	124 ± 10	0.055	122 ± 12	118 ± 9	0.047*	0.007*
24-h total DBP (mmHg)	85 ± 9	81 ± 6	0.058	79 ± 8	78 ± 7	0.170	0.011*
24-h day SBP (mmHg)	132 ± 12	126 ± 11	0.061	124 ± 12	120 ± 9	0.058	0.010*
24-h day DBP (mmHg)	87 ± 10	82 ± 6	0.024*	81 ± 8	79 ± 7	0.221	0.014*
24-h night SBP (mmHg)	125 ± 14	120 ± 11	0.128	115 ± 14	111 ± 12	0.098	0.006*
24-h night DBP (mmHg)	79 ± 10	76 ± 6	0.179	74 ± 9	71 ± 9	0.102	0.015*
LV ejection fraction (%)	65 ± 4	65 ± 4	0.914	66 ± 4	65 ± 5	0.233	0.242
E/A	0.8 ± 0.2	0.8 ± 0.4	0.077	0.7 ± 0.1	0.8 ± 0.3	0.035*	0.858
E/E′	8.8 ± 2.0	9.8 ± 2.7	0.117	9.0 ± 2.8	9.5 ± 2.4	0.269	0.804
LA volume index (mL/m^2)	28.4 ± 9.8	28.7 ± 10.4	0.812	27.6 ± 7.6	28.5 ± 7.6	0.477	0.716
LV mass index (g/m^2)	95.8 ± 21.7	94.8 ± 19.9	0.676	93.0 ± 18.7	98.0 ± 16.5	0.092	0.577
baPWV, average (cm/s)	1628 (1466, 1872)	1559 (1381, 1827)	0.249	1519 (1322, 1693)	1448 (1308, 1575)	0.042*	0.149
Total cholesterol (mg/dL)	176 (149, 183)	148 (135, 170)	0.023*	176 (149, 198)	170 (153, 193)	0.567	0.772
Triglycerides (mg/dL)	109 (88, 145)	95 (71, 121)	0.249	110 (75, 156)	80 (55, 152)	0.049*	0.947
HDL-cholesterol (mg/dL)	48 ± 10	52 ± 12	0.033*	47 ± 11	54 ± 13	< 0.001*	0.689
LDL-cholesterol (mg/dL)	105 (85, 118)	77 (66, 109)	0.009*	105 (78, 129)	103 (81, 120)	1.000	0.796
ApoB/apoA1	0.7 (0.5, 0.9)	0.5 (0.4, 0.7)	0.002*	0.7 (0.5, 0.9)	0.6 (0.5, 0.7)	0.004*	0.750
Diet Na (mg/day)	4043 (3572, 5970)	3991 (2605, 6052)	0.231	4187 (3427, 6241)	4464 (3134, 5450)	0.239	0.982
Diet K (mg/day)	2391 (1987, 3308)	2400 (1882, 3168)	0.657	2968 (2306, 3261)	2892 (2413, 3468)	0.552	0.606
Antihypertensives							
ACEi or ARB	23 (82.1)			28 (73.7)			0.418
Beta blocker	5 (17.9)			3 (7.9)			0.269
CCB	22 (78.6)			27 (71.1)			0.490
Diuretics	7 (25.0)			20 (52.6)			0.024*

Data are presented as mean ± standard deviation, median (interquartile range) or number (%)

Abbreviations are shown in Table 1

*$p < 0.05$

public health among cancer survivors as well as the general population. Obesity is also one of the most important health problems worldwide and is related to hypertension, coronary heart disease, stroke, and diabetes [13]. Nearly all studies regarding the effect of gastrectomy on weight reduction and cardiovascular outcomes have been conducted on bariatric surgery in patients with severe obesity (BMI ≥ 35 kg/m^2) [8]. Although the World Health Organization (WHO) defines obesity as a BMI ≥ 30 kg/m^2, it has been re-defined as BMI ≥ 25 kg/m^2 in the Asia-Pacific region [4]. According to the Korean National Health and Nutrition Examination Survey (KNHANES), the prevalence rate of obesity (BMI > 25 kg/m^2) in Korea was 38% in men and 30% in women [14]. However, when the WHO criteria is applied to the KNHANES results, the prevalence rate of obesity in Korea is less than 5% [15]. Therefore, most

Table 4 Logistic regression analysis for predicting remission of hypertension

	Univariate model			Multivariate model		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Gastrectomy	4.95	1.49–16.5	0.009	7.77	2.05–35.89	0.004
Diuretics use	3.33	1.15–9.68	0.027	3.76	1.14–13.98	0.035
Percent weight change at 3-month follow-up	0.85	0.76–0.94	0.003	0.94	0.79–1.11	0.467
24-h total SBP	0.94	0.90–0.99	0.011	0.98	0.91–1.04	0.471
24-h total DBP	0.92	0.86–0.99	0.016	0.90	0.82–0.96	0.007

OR, odds ratio; *CI*, confidence interval; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure

patients scheduled for surgery have a BMI < 30 kg/m^2 and can be classified as patients without obesity.

This study is to investigate the effect of gastric surgery on hypertension in early gastric cancer survivors without obesity. Early gastric cancer patients were selected because they are similar to the general population and do not display cachexia, and ESD group can be used as control group.

Lifestyle modifications, such as low sodium intake, high potassium intake, weight loss, and regular physical activity, are recommended for BP control [16]. The mechanisms of the BP-lowering effect of weight loss are presumed to be a decrease of cardiac output, inhibition of the sympathetic nervous system, improvement in insulin resistance, and normalization of the renin-angiotensin-aldosterone system, regardless of salt restriction [17]. Therefore, as in the case of severe obesity, we predicted weight loss would be the most important factor for remission of hypertension after gastrectomy in patients without obesity. As expected, there were statistically significant differences in percent weight change from baseline to follow-up periods between the "remission" and "no remission" groups (− 9.0 vs − 4.4%, $p < 0.001$ at 3 months; − 9.0 vs − 4.1%, $p = 0.004$ at1 year). However, multiple logistic regression analysis showed that gastrectomy was the strongest predictor for remission of hypertension after adjusting for weight loss. Therefore, we assumed that the effect of gastrectomy on BP may be beyond weight loss and hypothesized that BP control may be associated with sodium intake after gastrectomy because high sodium intake is associated with elevated BP, and dietary sodium reduction is an important lifestyle modification for management of hypertension. For example, a 1725-mg reduction in 24-h urinary sodium was associated with a fall in SBP of 5.4 mmHg and DBP of 2.8 mmHg in patients with hypertension [18]. In our study, we used a 3-day food record instead of a 24-h urine test to measure dietary sodium and potassium changes, taking into account patient compliance. It is thought that the intake survey, using the 3-day meal recording method of food intake, is more accurate than that of the 24-h urinary sodium test. We found no difference in dietary sodium or potassium between the "remission" and "no remission" groups, or before and after gastrectomy. Therefore, we hypothesize that sodium absorption dysfunction after gastrectomy may be more important than sodium intake amount for BP control. Patients with gastrectomy suffer from diarrhea due to absorptive disorders, and in a study of mineral content in hair tissue before and after gastrectomy, the levels of sodium, but not those of most other minerals, decreased significantly after surgery [19]. This indicates that gastrectomy has an effect on sodium absorption in patients with gastric cancer.

Logistic regression analysis revealed that diuretics use is a predictor of hypertension remission after adjusting for weight loss, indicating that patients using diuretics prior to ESD or gastrectomy were better able to control BP after treatment. This result suggests that the response to diuretics is better than to other antihypertensives. In addition, logistic regression analysis demonstrated that the lower the 24-h total BP is before treatment, the higher the probability of the remission of hypertension.

Lipoproteins and lipids were measured to evaluate cardiovascular risk in patients. The higher the apoB/apoA1 ratio, the higher the risk of cardiovascular disease [20]. However, the lipid profiles were not affected by remission of hypertension in our study. Arterial stiffness is a strong predictor of cardiovascular events and all-cause mortality [21]. Measurement of baPWV is a practical, simple method to assess arterial stiffness [22]. Well-controlled BP in patients with hypertension delays PWV progression [23]. In our study, baPWV showed a statistically significant decrease in the "remission" group after 1 year. Echocardiographic left ventricular hypertrophy (LVH) is recognized as target organ damage associated with cardiovascular events such as myocardial infarction, heart failure, stroke, and cardiovascular death [24]. As shown in Table 3, left ventricular mass index as a marker of LVH, LVEF as a marker of left ventricular systolic function, and diastolic parameters (E/E′, and left atrial volume index) except E/A did not change significantly at 1 year regardless of the remission of hypertension.

The Swedish Obese Subjects study evaluated changes in cardiovascular risk factors over 2- and 10-year periods between bariatric surgery group and control group. Improvement or remission rate of hypertension was 34% at

2 years and 19% at 10 years after bariatric surgery. However, the primary preventive effect of weight loss on hypertension was not observed because the 2- and 10-year incidences of hypertension did not differ between the two groups [25]. In the surgery group, higher baseline insulin levels were significantly associated with more favorable cardiovascular outcomes, while weight reduction was not significantly related with cardiovascular events [26]. We cannot be sure at this time whether our results will continue after 1 year or whether the postoperative improvement of BP in patients without obesity will lead to improvement of cardiovascular complications and mortality. Therefore, long-term research is required to clarify these issues. Additional studies, such as hormone tests that are thought to be involved in BP control, are also needed to identify causes other than weight loss.

In conclusion, we found significant BP control after gastrectomy compared with ESD in early gastric cancer survivors with hypertension. This effect may be due to gastrectomy itself beyond weight loss. Therefore, it should be remembered that the adequate reduction of antihypertensives may be necessary in early gastric cancer survivors with hypertension.

Funding This work was supported by research grants NCC1210552-3 (PI: Keun Won Ryu) and NCC1510740-1 (PI: Mi Hyang Kwak) from the National Cancer Center, Republic of Korea.

Compliance with ethical standards

The study was approved by the institutional review board of the National Cancer Center (NCCNCS-12-563). All procedures performed were in accordance with the ethical standards of the institutional review board and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflicts of interest.

Data The authors have full control of all primary data and agree that the journal may review the data if requested.

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