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ORIGINAL ARTICLE

Long-term changes in the metabolic and nutritional parameters after gastrectomy in early gastric cancer patients with overweight

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KEYWORDS
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Summary *Background:* With the increase in the prevalence of overweight, percentage of overweight patients with gastric cancer has also increased. This 5-year retrospective cohort study was performed to investigate long-term changes in the metabolic and nutritional parameters of early gastric cancer (EGC) patients with overweight after gastrectomy.
Methods: EGC patients who underwent gastrectomy were followed up over a 5-year period. We included 393 patients (261 men, 132 women) who had an initial body mass index (BMI) of $\geq$23 kg/m^2, and analyzed the longitudinal changes in the metabolic and nutritional parameters.
Results: Body weight and random glucose, alanine aminotransferase (ALT), hemoglobin, and serum calcium levels significantly decreased, while serum protein and albumin levels increased in both men and women after gastrectomy. The odds ratios (ORs) for BMI $\geq$ 25 kg/m^2 ($P < 0.001$ for men and women), random glucose $\geq$ 126 mg/dL (men; $P = 0.001$, women; $P < 0.001$), and ALT > 40 IU/dL (men; $P < 0.001$, women; $P = 0.018$) were lower in both men and women after 5 years. The ORs for low protein and albumin levels decreased, although the ORs for anemia and hypocalcemia increased in both sexes at 5 years after gastrectomy.
Conclusion: Gastrectomy in overweight patients followed up over 5-year could lead to approximately 10% weight loss and favorable changes in the metabolic parameters in both men and women. The risk of anemia and hypocalcemia increased, and the risk of low protein and albumin levels decreased in both sexes.

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1. Introduction

Incidences of obesity-related health problems have increased not only in developing countries but also in developed countries.[1,2] In comparison with people from Western countries, Asian populations have a higher risk for cardiometabolic diseases at any given body mass index (BMI).[3] At BMIs of over 23 kg/m^2, the risks for type 2 diabetes mellitus and hypertension increase.[4,5]

Gastric cancer is the most prevalent cancer in Eastern Asia and the second leading cause of cancer-related mortality worldwide.[6] In 2013, the age-standardized incidence rate of gastric cancer was found to be the second highest, in both sexes, in Korea.[7] The prevalence and incidence of early gastric cancer (EGC) in Korea has increased due to the development of improved diagnostic methods such as esophagogastroduodenoscopy and the introduction of a national screening program.[8] With the increase in the prevalence of overweight, the percentage of overweight patients with gastric cancer has also risen. Given that the overall survival rate of EGC patients, on whom gastrectomy is performed, is more than 95%, monitoring of metabolic and nutritional parameters after gastrectomy has become an important issue.

After gastrectomy, gastric cancer patients could display effects that are similar to those of cases involving bariatric surgery, such as weight reduction and improvement in hyperlipidemia and other metabolic disorders. In one study that used data of gastric cancer patients, it was found that body weight, BMI, and the levels of total cholesterol and low density lipoprotein (LDL) were significantly decreased 1 year after radical gastrectomy, in comparison to the levels before surgery.[9]

Despite these beneficial metabolic effects, the incidences of malnutrition, osteomalacia and anemia following gastrectomy are 20–50%, 15–30%, and 30–60%, respectively.[10] In a descriptive study performed on patients undergoing total gastrectomy secondary to gastric cancer, 50% of the patients had mild anemia, 22.7% had moderate anemia, and 58% had hypoproteinemia and hypoalbuminemia at 6 months after surgery.[11]

Most studies pertaining to gastric cancer patients undergoing gastrectomy involved follow-ups around 1 year after the surgery. Data on the status of patients in the 5 years following gastrectomy is scarce, even though the survival rates and quality of life of long-term survivors of EGC have been raised as issues. In addition, previously conducted studies tended to combine the data of both sexes; however, the basic characteristics or biochemical parameters of EGC patients vary by sex or degree of obesity. Therefore, we aimed to investigate the changes in the metabolic and nutritional parameters of EGC patients with overweight, in the course of the 5 years after gastrectomy, stratified by sex, using a retrospective cohort study.

2. Materials and methods

2.1. Study participants and data collection

Patients with EGC who underwent total or subtotal gastrectomies, and were referred to the Cancer Prevention Clinic of the Asan Medical Center between September 1, 2009 and December 31, 2014 were enrolled. This cohort was examined at 1 year, and then 2, 3, 4, and 5 years after surgery. Patients were monitored through physical examinations, esophagogastroduodenoscopy, blood tests, chest radiographs, and abdominal computed tomography before and after surgery.

The inclusion criteria in this study were as follows: (1) patients who survived 5 years after gastrectomy; and (2) patients whose BMI were 23 kg/m^2 or higher. The exclusion criteria were patients with evidences of metastasis or recurrence. A total of 261 men (mean operation age $\pm$ standard deviation (SD): 53.90 $\pm$ 9.53) and 132 women (mean operation age $\pm$ SD: 52.81 $\pm$ 9.81) were enrolled. The protocol of this study was approved by the institutional review board of Asan Medical Center (ethical approval number: 2017-0138), and has been reported in line with the STROCSS criteria.[12]

2.2. Anthropometric and laboratory measurements

Data from medical records including sex, height, and weight were reviewed at the baseline as well as 1 year and 2, 3, 4, and 5 years after gastrectomy. Participants were asked to wear lightweight clothing before their weight and height were measured by well-trained examiners. BMIs were calculated by dividing the weight (kg) by the square of the height (m^2). Blood tests for random glucose, total cholesterol, aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin, calcium, protein, and albumin levels were performed at the baseline and annual follow-ups. Blood tests to measure the total iron binding capacity (TIBC), as well as ferritin and vitamin B12 levels were performed 1 year after gastrectomy and at the annual follow-ups.

2.3. Definition of metabolic and nutritional disturbances

Patients with a BMI $\geq$23 kg/m^2 were considered overweight and those with a BMI $\geq$25 kg/m^2 were considered obese, by the definition of the World Health Organization (WHO) and International Obesity Task Force, for the Western Pacific region.[13] Elevated random glucose was defined as a level of 126 mg/dL (highest quintile at the baseline) or higher. Elevated cholesterol was defined as a level of 200 mg/dL or higher.[14] Elevated ALT was defined as an alanine aminotransferase level $>$40 IU/L.[15] Anemia was defined as hemoglobin level $<$13 g/dL in men and $<$12 g/dL in women, based on the criteria of the WHO,[16] or the consumption of iron supplements or vitamin B12 supplementation, due to a deficiency. Hypocalcemia was defined as a serum calcium level $<$8.6 mg/dL.[17] A low level of serum protein was defined as a level of 6.6 g/dL or lesser (lowest quintile at the baseline in both men and women) and a low level of serum albumin was defined as a level of 3.9 g/dL or lesser in men and 3.8 g/dL or lesser in women (lowest quintile at the baseline).

2.4. Statistical analyses

Continuous variables such as body weight, BMI, and metabolic and nutritional parameters at the baseline as well as

at 1 year and 2, 3, 4, and 5 years after gastrectomy were calculated by linear mixed models and presented as estimate ± standard error. The percentage of patients with BMI ≥25 kg/m^2, random glucose level ≥126 mg/dL, total cholesterol level ≥200 mg/dL, ALT level >40 IU/L, anemia, hypocalcemia, a low protein level, and a low albumin level were presented at the baseline and 1 year and 2, 3, 4, and 5 years after gastrectomy. The odds ratios (ORs) and 95% confidence intervals (95% CI) at 1 year and 2, 3, 4, and 5 years after gastrectomy compared with baseline were calculated by generalized estimating equations. We analyzed the data using two-sided p-values; p-values < 0.05 were considered statistically significant. All the statistical analyses were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Long-term changes in the body weight, and metabolic and nutritional parameters after gastrectomy

Table 1 shows the long-term changes in the body weight, and metabolic and nutritional parameters after gastrectomy. The mean preoperative and postoperative body weights at the baseline and 1 year and 2, 3, 4, and 5 years after gastrectomy were 72.7, 65.8, 65.5, 65.2, 65.5, and 65.7 kg in men and 62.1, 55.4, 55.6, 55.4, 55.9, and 56.0 kg in women ($P < 0.001$ for both). A weight reduction of around 10% was achieved at 1 year and maintained through the 5 years after gastrectomy, in both men and women. BMI, random glucose, ALT, hemoglobin, and serum calcium levels decreased in both men and women, and serum ferritin levels decreased in men. However, serum protein and albumin levels significantly increased in both sexes, and serum cholesterol levels increased in women.

3.2. Long-term changes in the percentage of metabolic and nutritional disturbances after gastrectomy

Fig. 1 and Fig. 2 present the changes in the percentage of metabolic and nutritional disturbances after gastrectomy, at the baseline and 1 year and 2, 3, 4, and 5 years after gastrectomy, in both sexes. The incidences of BMI ≥25 kg/m^2, random glucose level ≥126 mg/dL, and ALT level >40 IU/dL were significantly decreased in both sexes, after 5 years (Fig. 1). The percentages of incidences of anemia and

Table 1 Long-term changes in the metabolic and nutritional parameters after gastrectomy in men and women.

Variables	Baseline	1 year	2 years	3 years	4 years	5 years	P (pre vs 5 yr) or (1 yr vs 5 yr)
Men							
Body weight (kg)	72.7 ± 0.3	65.8 ± 0.3	65.5 ± 0.2	65.2 ± 0.2	65.5 ± 0.2	65.7 ± 0.5	<0.001
Body mass index (kg/m^2)	25.8 ± 0.1	23.3 ± 0.1	23.2 ± 0.1	23.1 ± 0.1	23.2 ± 0.1	23.3 ± 0.1	<0.001
Random glucose (mg/dL)	112.3 ± 1.9	106.4 ± 1.5	104.6 ± 1.5	102.6 ± 1.5	103.4 ± 1.2	106.0 ± 1.5	0.001
Total cholesterol (mg/dL)	177.8 ± 2.1	168.6 ± 1.7	173.6 ± 1.6	173.6 ± 1.5	178.1 ± 1.6	176.8 ± 1.9	0.636
AST (IU/L)	25.2 ± 0.8	25.3 ± 0.6	25.7 ± 0.6	26.1 ± 0.6	27.7 ± 1.1	26.1 ± 0.6	0.259
ALT (IU/L)	28.6 ± 1.2	22.1 ± 0.7	21.4 ± 0.5	21.4 ± 0.7	21.6 ± 0.8	19.2 ± 0.6	<0.001
Hemoglobin (g/dL)	14.8 ± 0.1	14.4 ± 0.1	14.5 ± 0.1	14.4 ± 0.1	14.5 ± 0.1	14.5 ± 0.1	<0.001
TIBC (ug/dL)	–	331.1 ± 5.3	335.2 ± 3.5	337.6 ± 3.2	337.4 ± 3.4	336.5 ± 4.0	0.304
Ferritin (ng/dL)	–	54.4 ± 3.6	51.0 ± 4.2	42.5 ± 2.1	42.8 ± 2.4	42.9 ± 2.7	0.002
Vitamin B12 (pg/ml)	–	552.7 ± 29.2	591.0 ± 28.2	542.8 ± 26.6	558.2 ± 27.9	593.9 ± 29.0	0.159
Calcium (mg/dL)	9.2 ± 0.0	9.1 ± 0.0	9.0 ± 0.0	9.0 ± 0.0	8.9 ± 0.0	8.9 ± 0.0	<0.001
Protein (g/dL)	7.0 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	7.2 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	<0.001
Albumin (g/dL)	4.1 ± 0.0	4.1 ± 0.0	4.1 ± 0.0	4.2 ± 0.0	4.2 ± 0.0	4.2 ± 0.0	<0.001
Women							
Body weight (kg)	62.1 ± 0.4	55.4 ± 0.3	55.6 ± 0.3	55.4 ± 0.3	55.9 ± 0.3	56.0 ± 0.6	<0.001
Body mass index (kg/m^2)	25.6 ± 0.2	22.8 ± 0.1	22.8 ± 0.1	22.8 ± 0.1	23.0 ± 0.1	23.0 ± 0.2	<0.001
Random glucose (mg/dL)	111.1 ± 3.2	103.8 ± 3.7	98.6 ± 1.6	98.9 ± 2.0	98.1 ± 2.0	97.3 ± 1.9	<0.001
Total cholesterol (mg/dL)	186.4 ± 3.2	181.6 ± 2.4	186.8 ± 2.7	190.4 ± 2.4	194.0 ± 2.8	194.7 ± 3.2	0.010
AST (IU/L)	24.1 ± 1.0	25.9 ± 1.2	25.4 ± 0.8	24.8 ± 0.6	24.8 ± 0.7	25.8 ± 0.8	0.097
ALT (IU/L)	21.6 ± 1.4	20.6 ± 1.0	19.3 ± 0.8	19.1 ± 1.0	18.0 ± 0.7	18.1 ± 0.7	0.009
Hemoglobin (g/dL)	12.8 ± 0.1	12.2 ± 0.1	12.3 ± 0.1	12.3 ± 0.1	12.2 ± 0.1	12.4 ± 0.1	0.010
TIBC (ug/dL)	–	351.9 ± 7.0	358.4 ± 5.3	359.2 ± 6.0	364.1 ± 6.0	361.7 ± 6.2	0.167
Ferritin (ng/dL)	–	29.7 ± 3.7	26.5 ± 3.1	24.2 ± 2.4	22.8 ± 2.4	24.5 ± 3.1	0.161
Vitamin B12 (pg/ml)	–	635.3 ± 27.5	623.3 ± 26.5	626.9 ± 30.2	618.6 ± 26.8	637.0 ± 32.4	0.951
Calcium (mg/dL)	9.1 ± 0.0	9.1 ± 0.0	9.0 ± 0.0	9.0 ± 0.0	8.9 ± 0.0	8.9 ± 0.0	<0.001
Protein (g/dL)	7.0 ± 0.1	7.3 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	7.4 ± 0.0	<0.001
Albumin (g/dL)	4.0 ± 0.0	4.1 ± 0.0	4.1 ± 0.0	4.1 ± 0.0	4.2 ± 0.0	4.2 ± 0.0	<0.001

Data are calculated by linear mixed model and presented as estimate ± standard error.
AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TIBC: Total iron binding capacity.

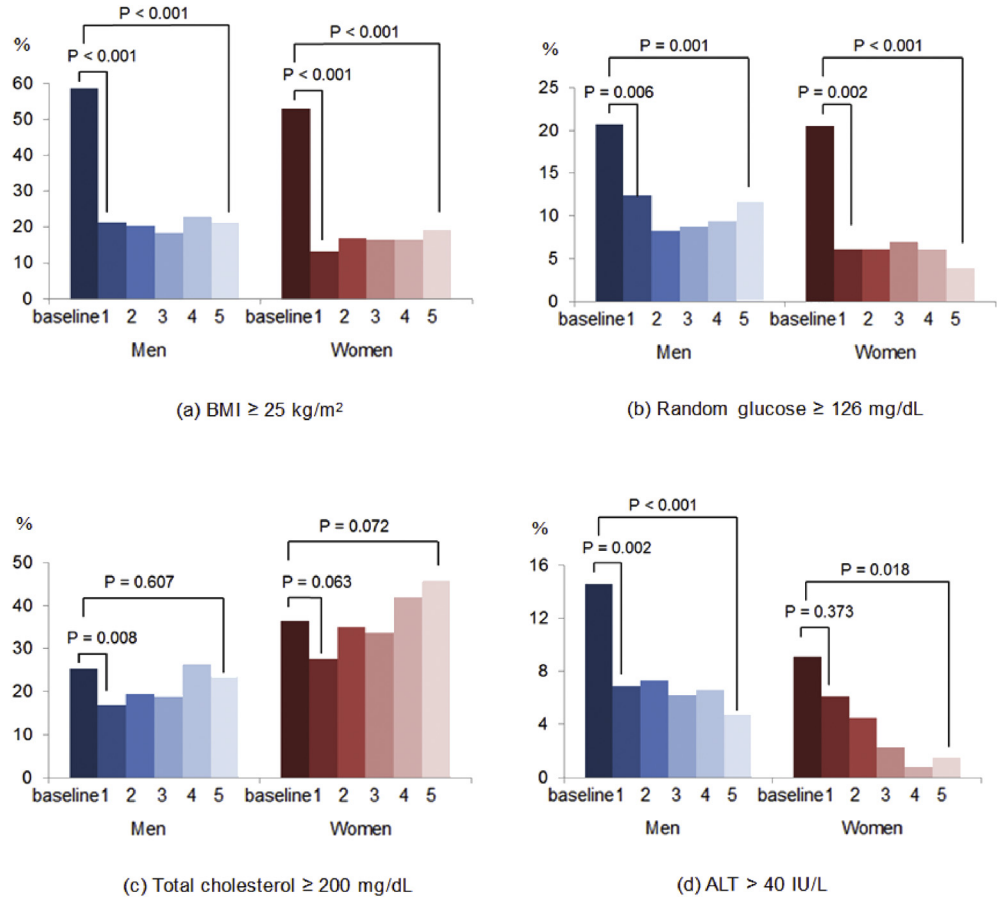

Figure 1 Frequencies of metabolic disturbances after gastrectomy in men and women.

hypocalcemia were significantly increased in both sexes. The percentages of low protein and albumin levels were significantly decreased in both sexes, at 5 years after gastrectomy (Fig. 2).

3.3. The ORs and 95% CIs for metabolic and nutritional disturbances after gastrectomy compared to the values at the baseline

Table 2 shows the ORs and 95% CIs for BMI $\geq$25 kg/m^2, random glucose level $\geq$126 mg/dL, total cholesterol level $\geq$200 mg/dL, ALT level >40 IU/L, anemia, hypocalcemia, low protein and low albumin at 1 year, and 2, 3, 4, and 5 years after gastrectomy, compared with those at the baseline. Five years after gastrectomy, the ORs and 95% CIs for BMI $\geq$25 kg/m^2 were 0.19 (0.14—0.27) in men and 0.21 (0.13—0.34) in women. The ORs for random glucose levels $\geq$126 mg/dL were 0.51 (0.34—0.77) in men and 0.16 (0.06—0.40) in women and the ORs for ALT levels > 40 IU/L were 0.29 (0.16—0.53) in men and 0.16 (0.03—0.73) in women. The ORs for anemia were 4.11 (2.10—8.05) in men and 1.93 (1.19—3.11) in women, and the ORs for hypocalcemia were 3.20 (1.65—6.21) in men and 2.99 (1.43—6.24) in women. The ORs for low protein were 0.29 (0.17—0.49) in men and 0.15 (0.07—0.35) in women, and the ORs for low albumin were 0.62 (0.41—0.94) in men and 0.25 (0.12—0.51) in women.

4. Discussion

This retrospective cohort study showed that a weight reduction of approximately 10% was achieved at 1 year and was maintained for 5 years after gastrectomy in obese Korean patients with EGC. The percentage of incidences of BMI $\geq$25 kg/m^2, random glucose level $\geq$126 mg/dL (highest quintile at the baseline), and ALT level > 40 IU/L significantly decreased at 5 years after gastrectomy, which suggests that gastrectomy in patients with overweight and obesity can lead to stable weight loss and favorable changes in the metabolic parameters. However, the incidences of anemia and hypocalcemia significantly increased in both sexes.

Gastrectomy could change the metabolic or nutritional states of EGC patients; this could be attributed to malabsorption, impaired food intake, and impaired transit time.[9,18] This leads to weight loss and even cases of underweight. However, in gastric cancer patients with overweight and obesity, gastrectomy could lead to favorable outcomes in weight loss.

Several studies on gastric cancer patients have pointed to significant weight loss following gastrectomy.[19,20] The concentration of the plasma ghrelin decreased significantly,[20] and this was thought to be the mechanism of the weight loss. Significantly, our study showed that the weight reduction observed at 1 year after gastrectomy was maintained during the 5 years of the follow-up period. In the

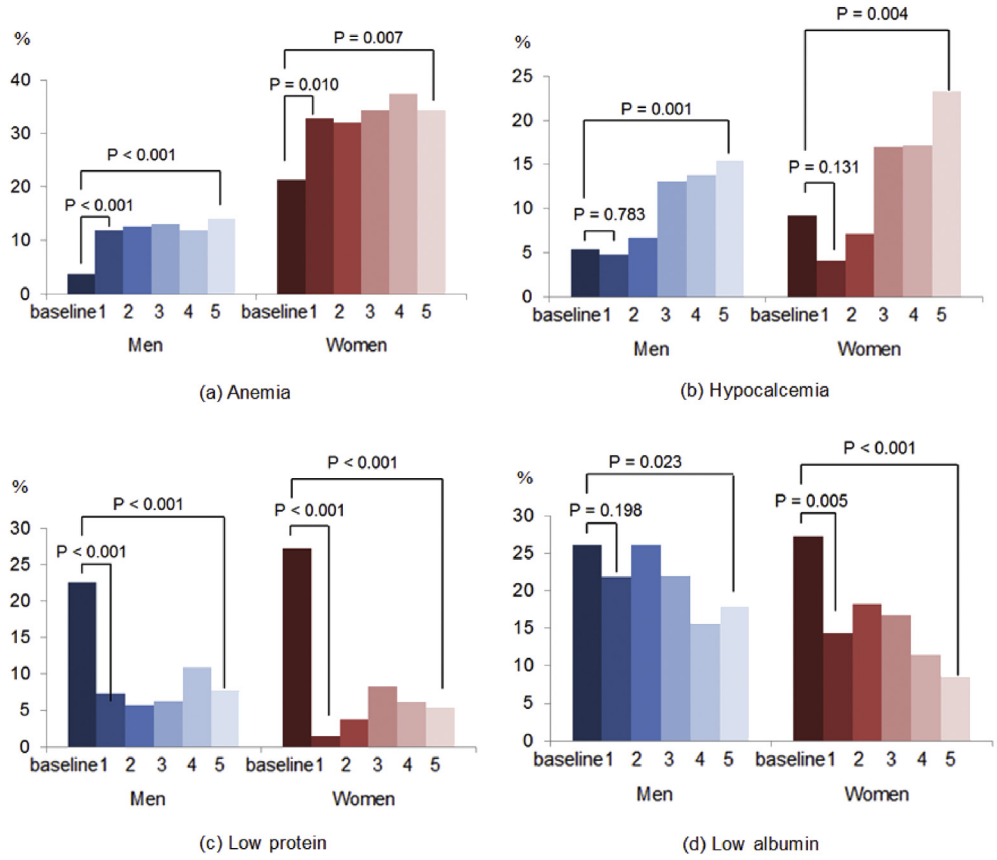

Figure 2 Frequencies of nutritional disturbances after gastrectomy in men and women.

subgroup analysis, patients who had undergone total gastrectomy displayed additional weight loss (13% weight reduction) (data not presented). The other metabolic and nutritional parameters showed similar results in the subgroup analysis.

Weight loss could lead to favorable metabolic parameters like in the case of bariatric surgeries in patients with obesity. The intentional weight loss in the severely obese patients, who are involved in the ongoing prospective Swedish Obese Subjects intervention, through bariatric surgery could lead to marked reductions in the incidences of hypertension, lipid disturbances and diabetes.[21] In that study, the adjusted odds ratio for diabetes in the surgery group was 0.02 (95% CI; 0.00—0.16) compared to the control group receiving conventional obesity treatment. In a prospective randomized controlled trial, 37% of the patients in the sleeve gastrectomy group and 42% in the gastric bypass group showed diabetes remission after 12 months, compared to the 12% of patients in the intensive medical therapy group.[22] The diabetes remission in the surgery group could be attributed to sustained weight loss and alterations in the levels of gut hormones.[23] Another study using data of EGC patients who underwent gastrectomy showed that the patients' body weight, BMI and visceral fat areas were significantly decreased 12 months after surgery, and they had lower cardiovascular-related mortality.[18] Given the similarities between the surgical procedures in the case of gastrectomy in EGC patients and bariatric surgery, our study results, which showed that the percentage of incidences of random glucose level $\geq$126 mg/dL (highest quintile at the baseline) significantly decreased at 5 years after surgery compared to the baseline, are similar to the result of diabetes remission observed in previously conducted prospective studies, among patients who underwent bariatric surgery.

Elevated serum ALT levels due to non-alcoholic fatty liver disease are associated with obesity and could be markers for metabolic syndrome and type 2 diabetes.[24—26] Sustained weight loss after bariatric surgery could reduce liver damage and prevent long-term sequelae of the liver. In the Swedish Obese Subjects study, bariatric surgery was associated with lower ALT levels at the 2 and 10-year follow-ups, compared to other standard forms of care, and the reduction was proportional to the degree of weight loss.[27] In another study involving patients with obesity who underwent bariatric surgery, both the Roux-en-Y gastric bypass surgery and laparoscopic adjustable gastric banding groups displayed significant reductions in the ALT levels at 3 months after surgery (20% and 17%, respectively, compared to the baseline, $P < 0.001$), and this reduction was parallel to the reduction in the HbA1c levels; this remained so up to 3 years after surgery, which suggests that ALT levels might be useful markers for metabolic improvement following bariatric surgery.[28] In our study results, the percentage of incidences of ALT level $>$ 40 IU/L significantly decreased at 5 years after gastrectomy compared to at the baseline; this is similar to the results of previous studies. Our results showed that hypercholesterolemia was not improved after

Table 2 The ORs and 95% CIs for metabolic and nutritional parameters after gastrectomy compared with baseline in men and women.

Variables	Baseline OR (95% CI)	1 year OR (95% CI)	2 years OR (95% CI)	3 years OR (95% CI)	4 years OR (95% CI)	5 years OR (95% CI)	P (pre vs 5 yr)
Men							
BMI $\geq$ 25 kg/m^2	1 (ref)	0.19 (0.12—0.30)	0.18 (0.11—0.29)	0.16 (0.10—0.25)	0.21 (0.14—0.31)	0.19 (0.14—0.27)	<0.001
Random glucose $\geq$ 126 mg/dL[a]	1 (ref)	0.55 (0.35—0.84)	0.34 (0.21—0.56)	0.37 (0.23—0.59)	0.40 (0.25—0.64)	0.51 (0.34—0.77)	0.001
Total cholesterol $\geq$ 200 mg/dL	1 (ref)	0.60 (0.41—0.88)	0.72 (0.50—1.03)	0.69 (0.48—0.99)	1.06 (0.74—1.51)	0.90 (0.62—1.33)	0.607
ALT > 40 IU/L	1 (ref)	0.44 (0.26—0.74)	0.46 (0.28—0.76)	0.39 (0.22—0.67)	0.41 (0.24—0.71)	0.29 (0.16—0.53)	<0.001
Anemia	1 (ref)	3.40 (1.85—6.24)	3.63 (1.89—7.00)	3.78 (1.96—7.27)	3.43 (1.78—6.60)	4.11 (2.10—8.05)	<0.001
Hypocalcemia	1 (ref)	0.89 (0.40—2.01)	1.27 (0.63—2.54)	2.65 (1.34—5.23)	2.81 (1.48—5.33)	3.20 (1.65—6.21)	0.001
Protein $\leq$6.6 g/dL[b]	1 (ref)	0.27 (0.16—0.46)	0.21 (0.12—0.35)	0.23 (0.13—0.39)	0.42 (0.27—0.66)	0.29 (0.17—0.49)	<0.001
Albumin $\leq$3.9 g/dL[b]	1 (ref)	0.79 (0.56—1.13)	1.00 (0.72—1.40)	0.80 (0.55—1.16)	0.52 (0.35—0.78)	0.62 (0.41—0.94)	0.023
Women							
BMI $\geq$ 25 kg/m^2	1 (ref)	0.13 (0.06—0.28)	0.18 (0.09—0.35)	0.17 (0.09—0.33)	0.17 (0.09—0.33)	0.21 (0.13—0.34)	<0.001
Random glucose $\geq$ 126 mg/dL[a]	1 (ref)	0.25 (0.11—0.61)	0.25 (0.11—0.58)	0.29 (0.14—0.62)	0.25 (0.11—0.55)	0.16 (0.06—0.40)	<0.001
Total cholesterol $\geq$ 200 mg/dL	1 (ref)	0.66 (0.43—1.02)	0.95 (0.62—1.44)	0.89 (0.58—1.34)	1.27 (0.84—1.91)	1.48 (0.97—2.25)	0.072
ALT > 40 IU/L	1 (ref)	0.65 (0.25—1.69)	0.48 (0.19—1.19)	0.23 (0.06—0.87)	0.08 (0.01—0.61)	0.16 (0.03—0.73)	0.018
Anemia	1 (ref)	1.80 (1.15—2.81)	1.74 (1.07—2.82)	1.93 (1.18—3.15)	2.20 (1.32—3.66)	1.93 (1.19—3.11)	0.007
Hypocalcemia	1 (ref)	0.42 (0.14—1.30)	0.75 (0.29—1.95)	2.01 (0.90—4.53)	2.04 (0.88—4.72)	2.99 (1.43—6.24)	0.004
Protein $\leq$6.6 g/dL[b]	1 (ref)	0.04 (0.01—0.17)	0.11 (0.04—0.28)	0.24 (0.13—0.47)	0.17 (0.08—0.37)	0.15 (0.07—0.35)	<0.001
Albumin $\leq$3.8 g/dL[b]	1 (ref)	0.45 (0.26—0.79)	0.59 (0.36—0.99)	0.53 (0.30—0.94)	0.34 (0.18—0.65)	0.25 (0.12—0.51)	<0.001

Data are calculated by generalized estimating equations and are presented as odds ratio (95% confidence interval).
OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; AST: ALT: Alanine aminotransferase; TIBC: Total iron binding capacity.
[a] Highest quintile at the baseline.
[b] Lowest quintile at the baseline.

gastrectomy, in both sexes. Therefore, periodic monitoring of serum cholesterol levels is required.

Despite sustained weight loss and favorable metabolic changes, the percentage of incidences of anemia and hypocalcemia was significantly increased in both sexes at 5 years after gastrectomy, in our study. In a previously conducted study that used a prospective gastric cancer database comprising EGC patients who underwent gastrectomy, the prevalence of iron deficiency anemia 3 years after gastrectomy was 31.0%.[29] In another study, that used the medical records of EGC patients who underwent gastrectomy, the incidence of anemia was 24.5% at 3 months after surgery; this increased to 37.1% at 48 months after surgery.[30] In our analysis, the prevalence of anemia was higher in women than in men; however, the ORs of anemia at 5 years after gastrectomy increased by about 4 times for men and 2 times for women, compared to at the baseline. Therefore, long-term gastric cancer survivors should be continuously monitored.

Gastrectomy is an independent risk factor for osteoporosis because nutrient deficiencies involving calcium, phosphorus and vitamin D were frequently noted in patients who underwent gastrectomy.[31] One study showed that the mean serum calcium levels were lower in the post-gastrectomy group than in the controls,[32] and another study showed that 7.3% of post-gastrectomy patients showed subnormal serum calcium levels compared to the 0.5% patients in the control group.[33] Since calcium absorption takes place in the duodenum and the upper portion of the jejunum, with the aid of gastric acid, gastrectomy could impair calcium absorption.[34] Therefore, the serum calcium levels of patients who undergo gastrectomy should be monitored and patients should be adequately supplemented.

The level of protein and albumin significantly increased, and the proportion of incidences of low protein and albumin levels significantly decreased at 5 years after gastrectomy, in both sexes. In a study which assessed the long-term nutrient status of morbidly obese patients after laparoscopic sleeve gastrectomy, the level of albumin was found to be increased at 1 year after surgery, like in our study.[35] In another cohort study of 130 patients who underwent Roux-en-Y gastric bypass and biliary pancreatic diversion, there were no significant differences in the mean albumin levels between the preoperative and postoperative (2 years after surgery) groups.[36] The levels of protein and albumin could be increased in our study because the participants were long-term survivors of EGC, with a relatively good prognosis. Additionally, serum ALT levels were found to be significantly decreased at 5 years after gastrectomy, leading to improved liver function, and thereby increased protein and albumin levels. Our results suggest that gastrectomy among EGC patients with overweight could lead to stable weight loss, by minimizing protein or albumin deficiencies, if proper nutritional education and monitoring is implemented.

This study has several limitations. First, the study population was limited to EGC patients with overweight who survived 5 years after gastrectomy and were referred to the Cancer Prevention Clinic; patients with follow-up loss were not included in this study. Therefore, the participants of this study might not represent the total EGC survivors. Second, some patients could have taken iron supplements or been treated for anemia in their local clinic, leading to the underestimation of the prevalence of anemia in our study. Third, even though we monitored the changes in body weight and BMI, we could not check the changes in lean mass and fat mass. A large-scale prospective study including the analysis of body composition is required. Fourth, the evaluation of glucose and lipid profiles was incomplete as overnight fasting blood samples were not collected. Detailed data on the levels of fasting glucose, HbA1c, triglycerides, low density lipoprotein, high density lipoprotein, and vitamin D are required in the future.

In conclusion, this study's results showed that gastrectomy in EGC survivors with overweight and obesity could lead to stable weight loss and favorable changes in the metabolic parameters. Most of these changes that were observed at 1 year after gastrectomy were sustained up to 5 years after gastrectomy. The risk of anemia and hypocalcemia increased, and the risk of low protein and albumin levels decreased. The risk of hypocalcemia continuously increased from 1 year up to 5 years after gastrectomy. Therefore, physicians should closely monitor these patients to maintain balanced nutritional and metabolic states.

Conflict of interest

The authors declare that they have no conflict of interests.

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