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Pancreatic atrophy after gastric cancer surgery: influencing factors and effects on BMI and quality of life

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Abstract

Background Pancreatic atrophy can occur after gastric cancer surgery, but the influencing factors and effects of pancreatic atrophy have not been extensively studied. The aim of this study was to investigate the factors of pancreatic atrophy after gastric cancer surgery and to assess the effect of atrophy on BMI and quality of life, in order to promote postoperative management of patients with higher risk factors of pancreatic atrophy.

Methods Clinical data pertaining to 142 patients who underwent surgery for gastric cancer were retrospectively collected, and pancreatic volume was determined using abdominal computed tomography data. Influencing factors of pancreatic atrophy were analysed and the relationship of pancreatic atrophy to BMI and quality of life was measured. Correlation analysis using Pearson or Spearman rank correlation and multiple linear regression were used to analyse the risk factors influencing pancreatic atrophy.

Results Pancreatic atrophy was significant in patients with gastric cancer 1 year after surgery, regardless of the surgical procedure. T3 and T4 stages, preoperative low levels of high-density lipoprotein cholesterol(HDL-C) and smoking history were influencing factors of pancreatic atrophy. Pancreatic atrophy was associated with reduced BMI and deterioration of quality of life.

Conclusions Clinicians need to monitor pancreatic function, BMI and life quality more carefully in gastric cancer patients with T3 and T4 stages, preoperative low levels of HDL-C and smoking history.

Keywords Gastrectomy, Pancreatic atrophy, Influencing factor, Quality of life

Introduction

Gastric cancer is one of the most common malignant tumours, and according to the Global Cancer Statistics 2022, gastric cancer is currently the fifth most diagnosed malignant tumour and the fifth leading cause of cancer-related deaths in the world [1]. Patients after gastrectomy may suffer from weight loss, diarrhoea, bloating, fat malabsorption and vitamin deficiency [2–3]. Over time, these symptoms may lead to malnutrition, decreased immunity, deterioration of quality of life, prolonged postoperative recovery time, and even affect patient prognosis [4]. These side effects occur through a variety of mechanisms,

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among which pancreatic exocrine insufficiency is one of the possible causes. Pancreatic exocrine insufficiency is characterised by the inability of food and nutrition to be digested properly, and refers to the insufficient and asynchronous production or secretion of the patient's own pancreatic enzymes caused by various reasons, which in turn leads to digestion, absorption and malnutrition, etc [5]. The exocrine function of the pancreas is regulated by a combination of neural and endocrine mechanisms, and the presence of an intact gastro-pancreatic-duodenal structure is the anatomical basis for the maintenance of exocrine function of the pancreas [6]. However, after gastrectomy, disruption of endogenous stimulation occurs due to alterations in the normal anatomical structure as a result of reduced gastric volume and rerouting of the digestive tract, leading to secondary pancreatic exocrine insufficiency (PEI) [7]. Several previous studies reported residual pancreatic atrophy after pancreaticoduodenectomy and pancreatic atrophy was associated with decreased pancreatic exocrine function [8–9]. In recent years, it has also been reported that pancreatic volume atrophy also occurred after gastric cancer surgery, and pancreatic exocrine function decreased with pancreatic atrophy [10–11]. There are limited studies on pancreatic volume atrophy after gastric cancer surgery, and there are no relevant studies on the influencing factors of pancreatic atrophy and the effects of pancreatic atrophy, so this study aims to evaluate the pancreatic volume atrophy after gastric cancer surgery and to investigate the pancreatic factors and effects of pancreatic atrophy.

Materials and methods

Patient materials

We reviewed the clinical records of patients who underwent surgery for gastric cancers: total gastrectomy (TG), distal gastrectomy (DG), and proximal gastrectomy (PG) from January 2022 to October 2023 at Nanjing Drum Tower Hospital, China. In our hospital, Roux-en-Y reconstruction is usually performed after TG, Billroth II or Roux-en-Y reconstruction after DG, and oesophagogastrostomy or double-tract procedure after PG. Our study included patients aged 18 to 80 years with pathological stage I-III gastric cancer, with preoperative and 1-year postoperative enhanced CT images of the abdomen; Patients with severe cardiac, hepatic, renal dysfunction and psychiatric disorders, patients with other malignant tumours, patients with a history of oesophageal, pancreatic and other gastrointestinal surgery, patients with pancreatic-like diseases, cystic fibrosis and diabetes mellitus, patients with recurrent metastases within 1 year of surgery, patients who had received neoadjuvant therapy, patients who did not wish to be followed up, and patients for whom CT images could not be used for volumetric analysis were excluded. In addition, radiotherapy was excluded due to the small number of patients who underwent it(only one people).

Pancreas volume measurement

All patients underwent abdominal computed tomography scanning, and a deep learning based convolutional neural network [12] using upp (uAI pioneer portal, Shanghai United Imaging Intelligence Co., Ltd.) was used to automatically segment the medical image images and perform pixel volume processing to obtain the volume: the number of voxels in the region of interest multiplied by the layer spacing. Pancreatic volume was measured for each patient preoperatively and 1 year postoperatively, and the pancreatic volume measurements were performed by an experienced imaging physician. Figure 1 shows an example of PV measurement by CT volumetric method, a: a cross sectional image of the pancreas, b: a constructed 3D image of the pancreas.

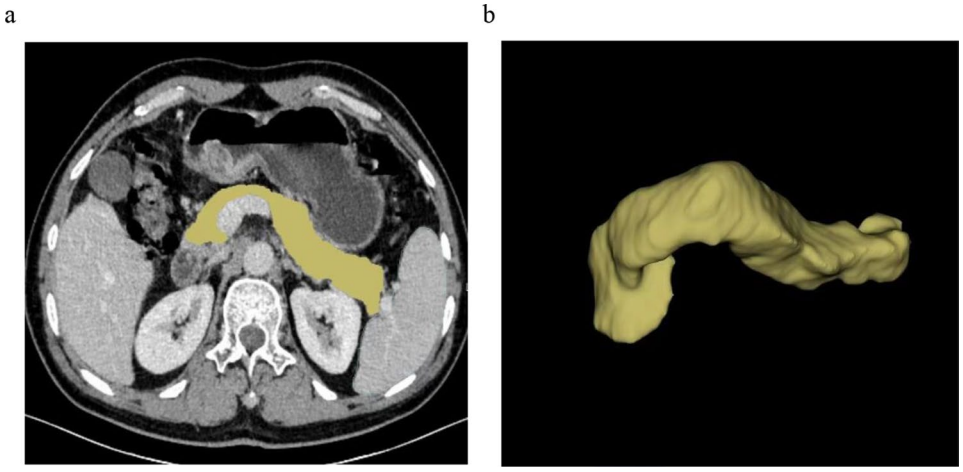

Fig. 1 An example of CT volumetry when measuring the pancreas volume. a A crosssectional image of the pancreas, b A constructed 3D image of the pancreas

Clinical data and analysis

Patients' data were extracted from the hospital medical record system, including patients' age, gender, height, weight, type of surgery, reconstruction method, tumour stage, number of lymph nodes metastasis, number of lymph nodes resected, postoperative adjuvant chemotherapy, smoking history, drinking history, postoperative complication, and preoperative blood indexes: haemoglobin, total protein, albumin, triglycerides, total cholesterol, high density lipoprotein cholesterol(HDL-C), low density lipoprotein cholesterol(LDL-C), apolipoprotein AI, and apolipoprotein B. Patients were asked to record their weight 1 year postoperatively by telephone follow-up and completed the GIQLI scale questionnaire. The GIQLI [13] is a survey consisting of 36 questions. The answers to each question were divided into five choices according to the Likert scale and scored accordingly. The GIQLI was divided into four subgroups to assess different symptoms. Includes gastrointestinal symptoms, physical condition, emotional status, and social function. The higher the total score, the better the quality of life. Patients' administration of pancreatic enzymes was recorded in detail using a combination of hospital medical record system records and telephone follow-up visits, postoperative complications according to Clavien-Dindo classification [14]. All patients with gastric cancer were pathologically staged according to the 8th edition of the TNM classification of gastric cancer of the AJCC [15], and D2 lymphadenectomy level was made according to the Japanese Gastric Carcinoma Classification [16]. Adjuvant chemotherapy was performed with a chemotherapy regimen based on fluorouracil, platinum, paclitaxel and monoclonal antibodies, which was used alone or in combination according to the patients' tumour characteristics and physical status.

The extent of pancreatic volume reduction at 1 year postoperatively was assessed in all patients, and the relative postoperative/preoperative pancreatic volume ratio (PV%) was compared in patients with TG-Roux-en-Y, DG-Billroth II, DG- Roux-en-Y, PG-Esophagogastrostomy, and PG-Double-tract. Age, gender, type of surgery, reconstruction method, tumour stage, lymph nodes metastasis, lymph nodes resected, adjuvant chemotherapy, smoking history, drinking history, took pancreatic enzymes, postoperative complication, preoperative BMI, preoperative haemoglobin, total protein, albumin, triglyceride, total cholesterol, HDL-C, LDL-C, Apolipoprotein AI, Apolipoprotein B, postoperative BMI and GIQLI score were analysed relationship between factors and postoperative/preoperative pancreatic relative volume ratio (PV%). Analysis of factors influencing pancreatic atrophy using multiple linear regression.

In accordance with the WHO standardised recommendations for smoking survey methodology, we defined a history of smoking as a person who smoked more than 1 cigarette per day for 6 consecutive or cumulative months. According to the 2007 China Chronic Disease and its Risk Factor Surveillance Report, we defined history of alcohol consumption as people who consumed more than 25 g/d (15 g/d for women).

BMI = weight (kg)/height (m) ^{2}.

Statistical analysis

SPSS 21.0 software was used for statistical processing. Descriptive statistics for continuous variables were expressed as mean ± SD or median (25–75) percentile, and categorical data were expressed as number of cases and percentage. Univariate analyses were performed using t-test, variance analysis or rank-sum test. Correlation analysis was performed using Pearson's correlation or Spearman's rank correlation analysis. Predictor variables with $P < 0.05$ on univariate and correlation analyses were included in the multiple linear regression model to analyse influence factors on pancreatic volume atrophy. Differences were considered statistically significant at $P < 0.05$.

Results

Basic clinical characteristics of the patients

A total of 142 patients were included in the analysis of this study, of whom 92(64.79%) were male and 50 (35.21%) were female, with a median age of 61 (53–68) years. There were 47 patients (33.10%) with TG-Roux-en-Y, 57 patients with DG-Billroth II (40.14%), 10 patients (7.04%) with DG-Roux-en-Y, 19 patients (13.38%) with PG-Esophagogastrostomy and 9 patients (6.34%) with PG-Double-tract; 84 cases (59.15%) with postoperative adjuvant chemotherapy, 58 cases (40.85%) without postoperative adjuvant chemotherapy, 50 cases (35.21%) with preoperative history of smoking, 92 cases (64.79%) with non-smoking, 33 cases (23.24%) with preoperative history of drinking, 109 cases (76.76%) with non-drinking, 15 cases (10.56%) with took pancreatic enzymes for at least 1 month within 1 year after surgery(Including pancreatic enzyme enteric-coated capsules, Abbott, 60000U pancreatic lipase 1 day or Compound Acinimetry Enteric-coated Tablets, 9960U or 19920U pancreatic lipase 1 day), 127 cases (89.44%) without took pancreatic enzymes for at least 1 month within 1 year after surgery, postoperative complications Clavien-Dindo grade I in 3 cases (2.11%), grade II in 16 cases (11.27%) and grade III in 2 cases (1.41%). The clinical characteristics of the study population are shown in Table 1.

Atrophy of pancreatic volume

Figure 2 shows the mean preoperative pancreatic volume of 142 patients was 67.74 ± 16.27cm^3 and decreased to 51.25 ± 14.41cm^3 at 1 year postoperatively, and the

Table 1 Clinical characteristics of the study population

	N **= 142**
Age (years)	61 (53–68)
Gender	
Male	92 (64.79%)
Female	50 (35.21%)
Type of resection and reconstruction	
Total gastrectomy, Roux-en-Y	47 (33.10%)
Distal gastrectomy, Billroth II	57 (40.14%)
Distal gastrectomy, Roux-en-Y	10 (7.04%)
Proximal gastrectomy, Esophagogastrostomy	19 (13.38%)
Proximal gastrectomy, Double-tract	9 (6.34%)
Operation method	
Open surgery	93 (65.49%)
Laparoscopic surgery	49 (34.51%)
AJCC stage (8th ed.)	
I	60 (42.25%)
II	29 (20.42%)
III	53 (37.32%)
T stage	
T1	54 (38.03%)
T2	23 (16.20%)
T3	46 (32.39%)
T4	19 (13.38%)
N stage	
N0	68 (47.89%)
N1	23 (16.20%)
N2	23 (16.20%)
N3	28 (19.72%)
Lymph nodes metastasis	1(0–4)
Lymph nodes resected	26(21–33)
Preoperative BMI(kg/m^2)	23.16(21.26–26.26)
Adjuvant Chemotherapy	
Yes	84 (59.15%)
No	58 (40.85%)
Smoking history	
Yes	50 (35.21%)
No	92 (64.79%)
Drinking history	
Yes	33 (23.24%)
No	109 (76.76%)
Took pancreatic enzymes	
Yes	15(10.56%)
No	127(89.44%)
Postoperative complications (Clavien-Dindo classification)	
I	3 (2.11%)
II	16 (11.27%)
III	2 (1.41%)
IV	0 (0.00%)

BMI: Body Mass Index

difference was statistically significant ($p < 0.001$). The mean preoperative pancreatic volume of TG-Roux-en-Y patients was $68.81 \pm 17.10 cm^3$, which decreased to $51.97 \pm 16.66 cm^3$ at 1 year postoperatively, the difference was statistically significant ($P < 0.001$); the mean preoperative pancreatic volume of DG-Billroth II patients was $65.98 \pm 17.52 cm^3$, which decreased to $48.84 \pm 13.58 cm^3$, and the difference was statistically significant ($P < 0.001$); the mean preoperative pancreatic volume of DG-Roux-en-Y patients was $67.93 \pm 10.69 cm^3$, and it decreased to $49.84 \pm 9.82 cm^3$ at 1 year after surgery, and the difference was statistically significant ($P < 0.001$)); the mean preoperative pancreatic volume of PG- Esophagogastrostomy patients had a preoperative mean pancreatic volume of $67.85 \pm 14.58 cm^3$, which decreased to $53.66 \pm 12.62 cm^3$ at 1 year postoperatively, with a statistically significant difference ($P = 0.003$); PG-Double-tract patients had a preoperative mean pancreatic volume of $72.89 \pm 12.89 cm^3$, which decreased to $59.28 \pm 13.16 cm^3$at 1 year postoperatively, with a statistically significant difference ($P = 0.04$). Figure 3 shows the percentage of postoperative PV relative to preoperative PV (PV%) for each group. At 1 year postoperatively, the PV% was 75.74% for TG-Roux-en-Y patients, 74.72% for DG-Billroth II patients, 74.17% for DG-Roux-en-Y patients, 79.55% for PG-Esophagogastrostomy patients, and 81.36% for PG-Double-tract patients, with no statistically significant difference between several procedures ($P = 0.48$).

Univariate and correlation analysis of factors influencing pancreatic atrophy

Univariate analysis showed that tumour AJCC stage ($P = 0.002$), T stage ($P < 0.001$), adjuvant chemotherapy($P = 0.008$) and smoking history ($P = 0.005$) were significantly different from PV%; correlation analysis showed that PV% was negatively correlated with lymph node metastasis (rho=-0.173, $P = 0.040$), positively correlated with total protein(rho = 0.184, $P = 0.028$), positively correlated with albumin($r = 0.166$, $P = 0.049$), and positively correlated with preoperative HDL-C (rho = 0.178, $P = 0.034$).(in Table 2).

Multiple linear regression analysis

Multiple linear regression analysis with PV% as the dependent variable and variables with $P < 0.05$ in univariate and correlation analyses as independent variables, dummy variables were also set for the covariates AJCC stage, T stage, adjuvant chemotherapy and smoking history, with stage I in AJCC stage, T1 in T stage, no chemotherapy in adjuvant chemotherapy and no smoking in smoking history as references. Table 3 shows that T3 ($P = 0.010$) and T4 ($P = 0.047$) stages, preoperative low levels of HDL-C ($P = 0.030$) and smoking history ($P = 0.039$) were influential factors for pancreatic atrophy.

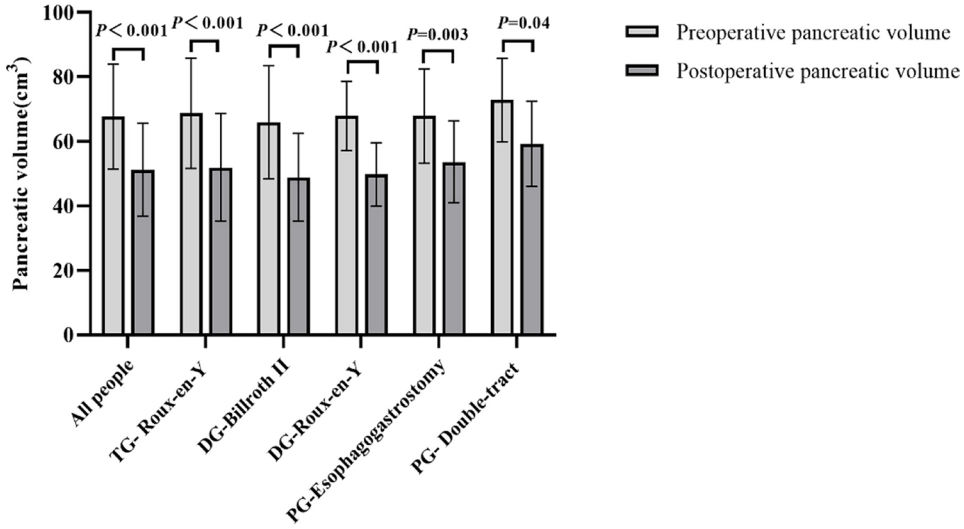

Fig. 2 Degree of reduction in pancreatic volume at 1 year postoperatively (cm^3)

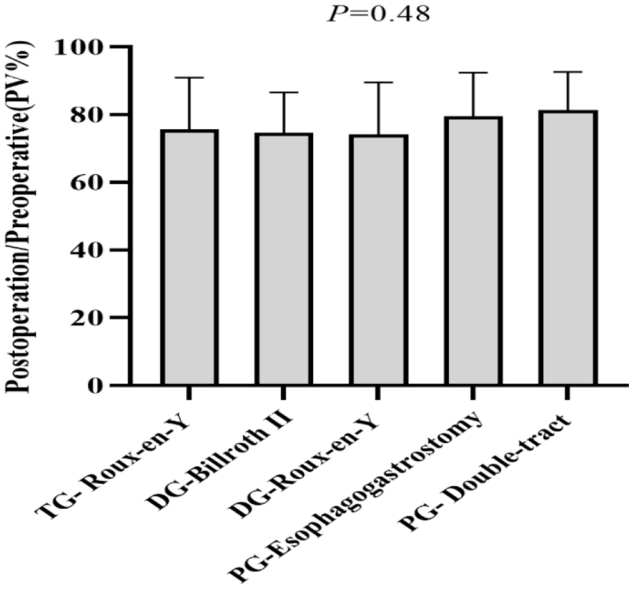

Fig. 3 Percentage of postoperative pancreatic volume (PV) relative to preoperative PV

Correlation analysis of the effects of pancreatic atrophy on BMI and quality of life

Correlation analysis showed that PV% was negatively correlated with reduced BMI (r=-0.252, P = 0.002), and positively correlated with gastrointestinal symptoms score (rho = 0.195, P = 0.020).(in Table 4).

Correlative analysis of the effect of pancreatic atrophy on Gastrointestinal symptoms

Correlation analysis showed that PV% was positively correlated with epigastric fullness score (rho = 0.208, P = 0.013), positively correlated with abdominal distension score (rho = 0.213, P = 0.011) and positively correlated with frequency of anal farting score (rho = 0.288, P = 0.001).(in Table 5).

Discussion

In this study, we confirmed pancreatic volumetric atrophy after gastric cancer surgery, assessed the factors influencing pancreatic volumetric atrophy, and evaluated the impact of atrophy on BMI reduction and quality of life. Previous studies have shown that pancreatic exocrine insufficiency occurs in patients with diabetes mellitus or chronic pancreatitis and was accompanied by a decrease in pancreatic volume [17–18], residual pancreatic volume also decreases in patients undergoing pancreaticoduodenectomy [8–9]. Although it has been reported in the literature [10–11] that pancreatic volume continues to decrease after gastric cancer surgery, and pancreatic exocrine and endocrine function decreases with pancreatic atrophy, this study further explored the factors influencing pancreatic volume atrophy after gastric cancer surgery and the effect of atrophy on BMI reduction and quality of life on this basis. It has been reported [10] that pancreatic volume decreased continuously 5 years after gastric cancer surgery, the degree of PV decrease after TG was greater than the degree of PV decrease after DG at 5 years after surgery, and the degree of PV decrease in Roux-en-Y reconstruction was greater than the degree of PV decrease in Billroth I reconstruction after DG. Our study showed that 142 patients with gastric cancer had a significant decrease in pancreatic volume one year after surgery (P < 0.001), with a preoperative pancreatic volume of 67.74 ± 16.27 cm^3, and a 1-year postoperative pancreatic volume of 51.25 ± 14.41 cm^3. Among them, the pancreatic volume of total gastrectomy, distal gastrectomy, and proximal gastrectomy also tended to be significantly reduced by each surgical procedure (P < 0.05).

Table 2 Univariate and correlation analysis of factors influencing pancreatic atrophy after gastric cancer surgery

Parameters	Postoperative/preoperative pancreatic volume(PV%)	*p*-Value
Age(years)[a]	Correlation coefficient (rho)=-0.106	0.211
Gender		0.080
Male	74.63 ± 12.94	
Female	78.76 ± 13.94	
Operation method		0.085
Open surgery	74.68 ± 13.15	
Laparoscopic surgery	78.75 ± 13.58	
AJCC stage (8th ed.)		0.002*
I	80.62 ± 13.57	
II	72.44 ± 10.39	
III	72.95 ± 13.35	
T stage		< 0.001*
T1	82.19 ± 12.04	
T2	74.82 ± 12.83	
T3	70.38 ± 12.49	
T4	74.09 ± 13.67	
N stage		0.139
N0	77.78 ± 14.18	
N1	77.85 ± 9.92	
N2	75.45 ± 14.71	
N3	71.05 ± 12.06	
Lymph nodes metastasis [a]	Correlation coefficient (rho)=-0.173	0.040*
Lymph nodes resected[a]	Correlation coefficient (rho)=-0.125	0.140
Preoperative BMI(kg/m^2)[a]	Correlation coefficient (rho)=-0.092	0.276
Hemoglobin(g/L)[a]	Correlation coefficient (rho) = 0.048	0.568
Total protein(g/L)[a]	Correlation coefficient (rho) = 0.184	0.028*
Albumin(g/L)[b]	Correlation coefficient (r) = 0.166	0.049*
Triglyceride(mmol/L)[a]	Correlation coefficient (rho)=-0.035	0.683
Total Cholesterol(mmol/L)[b]	Correlation coefficient (r) = 0.132	0.117
HDL-C (mmol/L)[a]	Correlation coefficient (rho) = 0.178	0.034*
LDL-C(mmol/L)[a]	Correlation coefficient (rho) = 0.051	0.547
Apolipoprotein AI(g/L)[a]	Correlation coefficient (rho) = 0.146	0.082
Apolipoprotein B(g/L)[b]	Correlation coefficient (r) = 0.040	0.637
Adjuvant chemotherapy		0.008*
Yes	73.61 ± 13.04	
No	79.67 ± 13.20	
Smoking history		0.005*
Yes	71.87 ± 11.23	
No	78.38 ± 13.97	
Drinking history		0.407
Yes	74.66 ± 10.08	
No	76.52 ± 14.26	
Took pancreatic enzymes		0.190
Yes	81.99 ± 18.15	
No	75.39 ± 12.63	
Postoperative complications (Clavien-Dindo classification)		0.695
I	73.92 ± 8.52	
II	74.49 ± 12.61	

Table 2 (continued)

Parameters	Postoperative/preoperative pancreatic volume(PV%)	*p*-Value
III	66.46 ± 30.21	
No	76.51 ± 13.42	

[a] Spearman's rank correlation analysis

[b] Pearson's correlation analysis

BMI: Body Mass Index, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol

*$P < 0.05$, it indicates statistically significant differences

Table 3 Multiple linear regression analysis of factors affecting pancreatic atrophy after gastric cancer surgery

Factor	B	SE	β	t	*p*
(constant)	63.190	15.262		4.140	<0.001
AJCC stage (8th ed.)					
II	-0.414	4.044	-0.013	-0.102	0.919
III	2.748	5.530	0.100	0.497	0.620
T stage					
T2	-6.071	3.556	-0.168	-1.707	0.090
T3	-11.722	4.454	-0.411	-2.632	0.010*
T4	-10.157	5.073	-0.259	-2.002	0.047*
Lymph nodes metastasis	-0.041	0.234	-0.019	-0.176	0.861
Total protein(g/L)	-0.082	0.289	-0.036	-0.284	0.777
Albumin(g/L)	0.424	0.602	0.091	0.705	0.482
HDL-C(mmol/L)	7.435	3.382	0.180	2.199	0.030*
Adjuvant chemotherapy	-0.094	3.197	-0.003	-0.029	0.977
Smoking history	-4.789	2.301	-0.171	-2.081	0.039*

HDL-C: High density lipoprotein cholesterol

*$P < 0.05$, it indicates statistically significant differences

Table 4 Correlation analysis of the effects of pancreatic atrophy on BMI and quality of life

Parameters	Postoperative/preoperative pancreatic volume(PV%)	*p*-Value
Reduced BMI(kg/m^2)[b]	Correlation coefficient (r)=-0.252	0.002*
Total GIQLI score (36 items, range 0-144)[a]	Correlation coefficient (rho) = 0.135	0.109
Gastrointestinal symptoms score (19 items, range 0–76)[a]	Correlation coefficient (rho) = 0.195	0.020*
Social function score (5 items, range 0–20)[a]	Correlation coefficient (rho) = 0.084	0.322
Emotional status score (5 items, range 0–20)[a]	Correlation coefficient (rho) = 0.085	0.316
Physical condition score (7 items, range 0–28)[a]	Correlation coefficient (rho) = 0.031	0.717

[a] Spearman's rank correlation analysis

[b] Pearson's correlation analysis

BMI: Body Mass Index

*$P < 0.05$, it indicates statistically significant differences

Table 5 Correlative analysis of the effect of pancreatic atrophy on Gastrointestinal symptoms

Parameters	Postoperative/preoperative pancreatic volume(PV%)	*p*-Value
Abdominal pain score [a]	Correlation coefficient (rho) = 0.042	0.621
Epigastric fullness score [a]	Correlation coefficient (rho) = 0.208	0.013*
Abdominal distension score [a]	Correlation coefficient (rho) = 0.213	0.011*
Frequency of anal farting score [a]	Correlation coefficient (rho) = 0.288	0.001*
Belching score [a]	Correlation coefficient (rho) = 0.021	0.803
Borborygmus score [a]	Correlation coefficient (rho) = 0.091	0.282
Excessive stool frequency score [a]	Correlation coefficient (rho) = 0.072	0.392
Have no appetite score [a]	Correlation coefficient (rho) = 0.128	0.130
Giving up a favourite food due to illness score [a]	Correlation coefficient (rho) = 0.077	0.362
Vomit score [a]	Correlation coefficient (rho)=-0.066	0.438
Restricted eating speed score [a]	Correlation coefficient (rho) = 0.072	0.397
Difficulty swallowing food score [a]	Correlation coefficient (rho) = 0.121	0.152
Urgency of stool score [a]	Correlation coefficient (rho) = 0.127	0.134
Diarrhea score [a]	Correlation coefficient (rho) = 0.094	0.268
Constipation score [a]	Correlation coefficient (rho) = 0.090	0.285
Nausea score [a]	Correlation coefficient (rho) = 0.004	0.959
Hemafecia score [a]	Correlation coefficient (rho) = 0.116	0.169
Heartburn score [a]	Correlation coefficient (rho)=-0.021	0.801
Fecal incontinence score [a]	Correlation coefficient (rho)=-0.122	0.147

[a] Spearman's rank correlation analysis

*$P < 0.05$, it indicates statistically significant differences

In addition, the relative percentage of postoperative/preoperative pancreatic volume between several surgical procedures ranged from 74.17 to 81.36%, which is consistent with the PV% reported by Satoi et al. [11]. However, probably due to the fact that we only analysed pancreatic atrophy at 1 year postoperatively, which is a short period of time, we failed to find differences in pancreatic atrophy between several surgical procedures.

The structural and functional integrity of the digestive system is essential for the normal digestion of food, and pancreatic secretion is a complex process subject to both neural and endocrine regulation. Usually, after feeding,

the dilatation of the stomach by the chyme and the diastole of the gastric fundus stimulate the vagus nerve and cause the secretion of pancreatic juice [5]. The absence of the gastric sinusogastric fundus reflex after gastrectomy leads to a reduction in nerve-stimulated pancreatic secretion [19]; the entry of chyme into the duodenum also stimulates pancreatic secretion, and reconstructive surgeries bypassing the duodenum, such as the Billroth-II and Roux-en-Y reconstructions, where chyme is unable to pass through the duodenum, lead to a reduction in the release of cholecystokinin and a reduction in the stimulation of pancreatic secretion [20]. After gastrointestinal reconstruction, accelerated gastric emptying shortens the intestinal transit time, which can be accompanied by a feedback imbalance in pancreatic enzyme secretion [5]. In addition, gastric lymph node dissection and vagotomy lead to a loss of pancreatic nerve supply [21], which further aggravates pancreatic exocrine insufficiency. Based on these results, we hypothesised that these fewer stimuli resulted in pancreatic atrophy, possibly related to decreased exocrine pancreatic function. Therefore, it seems reasonable that pancreatic volume decreases after gastrectomy. In conclusion, the mechanism of pancreatic volume atrophy after gastrectomy is complex and requires further studies.

Although postoperative pancreatic volume atrophy after gastric cancer is now gaining attention, the influencing factors of pancreatic atrophy and the effects of atrophy have not been reported. Preoperative diabetes mellitus, malignancy, surgical approach, pancreaticoenteric anastomosis approach, pancreatic duct dilatation, and adjuvant radiotherapy have been suggested as possible risk factors for residual pancreatic atrophy after pancreaticoduodenal surgery [9]. In our study, after excluding patients with diabetes mellitus and pancreatic-like diseases, possible relevant factors affecting pancreatic volume atrophy were investigated. Our findings showed that T3 and T4 stages, preoperative low levels of HDL-C and smoking history are influential factors in pancreatic atrophy. Currently,sime studeies confirmed that the later tumour stages were associated with the lower the nutritional status of the patient [22, 23, 24]. Our results concluded that T3 and T4 stages are influencing factors of pancreatic atrophy. The reason for this may be that patients with T3 and T4 stages have deeper tumour infiltration and larger tumour sizes, increased tumour consumption, and high physical exertion of the patient, leading to low nutritional status. The nutritional stability of the organism can maintain the normal metabolism of each tissue cell, when the nutritional deficiency of the organism reduces the nutrient substrate that maintains the normal proliferation of each tissue cell, it will result in the slowing down of cell proliferation, and even lead to the increase of apoptosis [25–26], which will may cause the pancreatic atrophy. In addition, we consider that it may also be due to the fact that the larger tumours in the T3 and T4 stages compress the pancreatic tissues, triggering local blood circulation disorders and promoting pancreatic cell necrosis and apoptosis, which in turn aggravates pancreatic atrophy. However, due to our small sample size, there may be bias in the data, and larger sample sizes and more in-depth studies are needed in the future to confirm and explain that late T stage can affect pancreatic atrophy. HDL is a nanoparticle with anti-atherosclerotic, anti-inflammatory and antioxidant properties associated with cardiovascular and metabolic health. Low levels of HDL-C are an important risk factor for atherosclerotic cardiovascular disease [27]. Atherosclerosis is a chronic inflammatory condition that occurs in arterial vessels throughout the body and is the pathological basis of cardiovascular diseases such as stroke and coronary heart disease, leading to narrowing of the vascular lumen, increased vascular permeability, and decreased blood flow, which triggers ischemia or hypoxia of tissues and organs in the body [28] and may cause pancreatic atrophy. This could explain our results in which low preoperative levels of HDL-C exacerbated postoperative pancreatic volume atrophy. The possible reason for exacerbation of pancreatic atrophy by smoking is that nicotine is an important component of cigarettes and may mediate the development of pancreatic disease. animal studies have demonstrated that nicotine in tobacco induces vacuolisation or swelling of pancreatic alveolar cells, leading to morphological changes in pancreatic exocrine secretion [29–30]. In addition aryl hydrocarbon receptor ligand agonists in cigarette smoke induce CD4 cells to produce IL-22, which promotes the progression of pancreatic fibrosis through the activation of pancreatic stellate cells [31]. Clinical studies have also found that cigarette smoking can increase the risk of complications associated with chronic pancreatitis, such as pancreatic calcification, pancreatic pseudocysts, and pancreatic exocrine insufficiency [32–33]. Pancreatic enzyme replacement therapy (PERT) is the cornerstone of pancreatic exocrine insufficiency treatment, aiming to improve gastrointestinal symptoms and nutritional status, to improve the quality of life of patients, and to prevent and eliminate secondary events that may result from pancreatic enzyme deficiency [34–35]. Pancreatic enzyme interventions are not routinely performed in our hospital after gastric cancer surgery, therefore only a few patients have used pancreatic enzymes. Only 15 patients in our study took pancreatic enzymes for more than 1 month within 1 year after surgery, however, probably because of the small number of people have taken pancreatic enzymes and the different specifications and quantities of pancreatin, no effect of pancreatic enzymes on pancreatic volume atrophy was found.

The final aim of this study was to assess the impact of pancreatic atrophy and we used prospectively collected patient weight and quality of life questionnaires to analyse the correlation of pancreatic atrophy with reduced BMI and quality of life. We used the GIQLI [13]scale to assess the quality of life of our patients. GIQLI is a widely accepted scale for assessing quality of life after gastrointestinal surgery, and many studies have used the GIQLI scale to assess the quality of life of patients after gastric cancer surgery [6]. The results of our study showed that BMI reduction was correlated with pancreatic atrophy severity, and low gastrointestinal symptom scores on the GIQLI scale were correlated with pancreatic atrophy severity. Low epigastric fullness scores, abdominal distension scores, and frequency of anal farting scores were associated with pancreatic atrophy severity in the gastrointestinal symptom score subgroup. It can be seen that pancreatic atrophy is associated with dyspeptic symptoms such as fullness, bloating and excessive farting. Overall, the results of our study showed that patients with severe pancreatic atrophy have a greater reduction in body mass index and a more severe deterioration in quality of life, particularly in terms of gastrointestinal symptoms such as epigastric fullness, abdominal flatulence, and more frequent anal farting.

Our study has some limitations. Firstly, it was a single-institution retrospective study. Secondly, the sample sizes of several procedures, (distal gastric Roux-en-Y, PG-Esophagogastrostomy and PG-Double-tract) were small. In addition, we only analysed pancreatic volume atrophy at 1 year postoperatively and failed to find differences in pancreatic atrophy between several surgical procedures. In the future, data on postoperative pancreatic volume at longer follow-up periods are needed to further analyse the differences in pancreatic atrophy between different surgical approaches and to further explore the factors affecting pancreatic atrophy and the impact of pancreatic atrophy.

In conclusion, this study found that pancreatic atrophy was significant in patients with gastric cancer 1 year after surgery, regardless of the surgical procedure. Clinicians need to monitor pancreatic function, BMI, and life quality more carefully in patients with T3 and T4 stages, preoperative low levels of HDL-C and smoking history, and patients found to have reduced pancreatic volume during follow-up should accept the necessary endocrine and exocrine replacement therapy.

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Author contributions
M. W. aconceptualized the study. Z. L. wrote the original draft and the data extraction. L. C. and H. C. provided the framework. F. W. and L. T. revisions were made to the draft article. Z. L. was involved in the data collection. L. C. and H. C. conducted guidance on the study. All authors read and approved the final manuscript.

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Data availability
The datasets generated and analysed during the current study are not publicly available due privacy, but can be obtained by email (wangmeng1980@nju.edu.cn) from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The entire process of this study followed the ethical standards of Declaration of Helsinki and its later amendments. This study has been approved by the Ethics Committees of Nanjing Drum Tower Hospital and informed consent was obtained from all subjects.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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