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ORIGINAL ARTICLE

Retrospective Study

Novel subtype of obesity influencing the outcomes of sleeve gastrectomy: Familial aggregation of obesity

Ze-Yu Wang, Yun-Fei Qu, Tian-Ming Yu, Zeng-Lin Liu, Yu-Gang Cheng, Ming-Wei Zhong, San-Yuan Hu

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Abstract

BACKGROUND

Differences in the preoperative characteristics and weight loss outcomes after sleeve gastrectomy (SG) between patients with familial aggregation of obesity (FAO) and patients with sporadic obesity (SO) have not been elucidated.

AIM

To explore the impact of SG on weight loss and the alleviation of obesity-related comorbidities in individuals with FAO.

METHODS

A total of 193 patients with obesity who underwent SG were selected. Patients with FAO/SO were matched 1:1 by propensity score matching and were categorized into 4 groups based on the number of first-degree relatives with obesity (^{1}SO *vs* ^{1}FAO, ^{2}SO *vs* ^{2}FAO). The baseline characteristics, weight loss outcomes, prevalence of obesity-related comorbidities and incidence of major surgery-related complications were compared between groups.

RESULTS

We defined FAO as the presence of two or more first-degree relatives with obesity. Patients with FAO did not initially show significant differences in baseline data, short-term postoperative weight loss, or obesity-related comorbidities when compared to patients with SO preoperatively. However, distinctions between the two groups became evident at the two-year mark, with statistically significant differences in both percentage of total weight loss (P = 0.006) and percentage of excess weight loss (P < 0.001). The FAO group exhibited weaker remission of type 2 diabetes mellitus (T2DM) (P = 0.031), hyperlipidemia (P = 0.012), and non-alcoholic fatty liver disease (NAFLD) (P = 0.003) as well as a lower incidence of acid reflux (P = 0.038).

CONCLUSION

FAO patients is associated with decreased mid-to-long-term weight loss outcomes; the alleviation of T2DM, hyperlipidemia and NAFLD; and decreased incidence of acid reflux postoperatively.

Key Words: Obesity; Bariatric surgery; Sleeve gastrectomy; Family history; Weight loss

Core Tip: This was a retrospective study. We aimed to compare preoperative characteristics and postoperative outcomes between patients with familial aggregation of obesity (FAO) and those with sporadic obesity. The following data were examined: Baseline characteristics, weight changes at postoperative intervals (1, 3, 6, 12, 24, and 36 months), alleviation of obesity-related complications, and the occurrence of surgery-related complications. Such a comparative analysis provides valuable insights for guiding postoperative treatment and health education tailored to individuals with FAO.

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INTRODUCTION

The prevalence of overweight and obesity is steadily increasing in China[1], making it the country with the largest population of overweight and obese individuals globally. It is expected that the prevalence of overweight [body mass index (BMI) 24.0-28.0 kg/m²] and obesity (BMI ≥ 28.0 kg/m²) in adults may reach 65.3% by 2030[2], thus leading to a significant public health concern[3]. Obesity can lead to a myriad of multisystem abnormalities, encompassing cardiovascular disease, type 2 diabetes mellitus (T2DM), hyperlipidemia, hyperuricemia, nonalcoholic fatty liver disease, polycystic ovary syndrome, mental disorders, locomotor and joint disorders, and respiratory diseases, among other comorbidities.

Obesity results from the intricate interplay of genetic, environmental, lifestyle, and sociocultural factors[4]. These factors affect fat accumulation or consumption by influencing several physiologic mediators of food intake and energy expenditure[5]. An individual's family–often representing a microcosm of closely aligned genetic profiles, lifestyle behaviors, environmental exposures, and sociocultural outlooks–exerts a substantial influence on the emergence of obesity and the outcomes of weight management. Sleeve gastrectomy (SG), which accounted for 84.9% of bariatric surgical procedures[6], effectively facilitates weight loss in patients with obesity while markedly enhancing metabolic processes and ameliorating obesity-related comorbidities[7].

The familial aggregation of diseases is a focal point of research across several disciplines, including psychiatry[8], neurology[9] and oncology[10,11]. By studying the characteristics of first-degree relatives of individuals with obesity, we can gain deeper insights into the pathogenesis of obesity, thereby contributing to the search for novel treatments or prevention methods[12]. This study provides a theoretical foundation for precision prevention and treatment of obesity.

MATERIALS AND METHODS

Patients

We selected a cohort of 193 patients with obesity who met the criteria for SG and who underwent surgery at our medical center between December 2019 and April 2023 for this observational study. Following surgery, all patients received uniform postoperative guidance and health education.

Inclusion/exclusion criteria

Inclusion criteria: (1) Patients aged between 16 and 65 years; (2) patients met the surgical indications outlined in the Chinese Guidelines for the Surgical Management of Obesity and T2DM (2019 edition)[13]; and (3) patients were capable of undergoing normal follow-up after SG.

Exclusion criteria: (1) Patients lacking information about first-degree relatives; (2) patients requiring obesity-inducing medications for their medical conditions after the operation; (3) patients who became pregnant shortly after the procedure; and (4) patients on appetite suppressants (such as metformin) following surgery.

Grouping method

The familial aggregation of obesity (FAO) group and the sporadic obesity (SO) group: We divided the participants into groups according to the number of first-degree relatives (parents, children and siblings of the proband) with obesity (BMI > 28 kg/m^2). The grouping criteria for FAO were as follows.

^{1}FAO (FAO group 1): Except for the proband, the number of first-degree relatives with obesity ≥ 1. ^{1}SO (SO group 1): Except for the proband, the number of first-degree relatives with obesity = 0.

^{2}FAO (FAO group 2): Except for the proband, the number of first-degree relatives with obesity ≥ 2. ^{2}SO (SO group 2): Except for the proband, the number of first-degree relatives with obesity < 2.

Data collection

The data were collected independently by two individuals. Perioperative data for all patients, including sex, age, BMI, family history, waist circumference, hip circumference, and obesity-related comorbidities (such as hypertension, T2DM, and hyperlipidemia), were systematically recorded using the electronic case management system. Following SG, we conducted thorough postoperative follow-ups at 1, 3, 6, 12, 24, and 36 months through a combination of hospital visits and telephone interviews. These follow-ups involved evaluating postoperative weight, conducting blood tests, assessing surgery-related complications, and monitoring the improvement of preoperative obesity-related comorbidities. To assess the effectiveness of weight loss surgery, we employed the percentage of total weight loss (%TWL) and percentage of excess weight loss (%EWL) as evaluation criteria.

%TWL = (initial body weight - final body weight)/initial weight × 100%.

%EWL = [(initial body weight - final body weight)/(initial weight - ideal body weight)] × 100%.

Ideal BMI (IBMI): 23 kg/m^2 (Asian standard), ideal body weight: IBMI × (height)^2.

Statistical methods

All clinical data were analyzed using SPSS statistical software (version 26.0; SPSS, Inc., Chicago, IL, United States). Propensity score matching (PSM)[14] was employed for 1:1 matching of FAO/SO groups. Independent samples *t* tests were also conducted to compare preoperative baseline data and postoperative weight loss outcomes at each follow-up interval between patients in the FAO group and the SO group. Linear regression was employed to identify factors influencing %TWL and %EWL. To compare the prevalence of obesity-related comorbidities and surgery-related complications in patients in the FAO and SO groups, χ^2 or Fisher's exact test was employed both preoperatively and at the 6-month postoperative assessment. *P* values < 0.05 indicated statistical significance.

RESULTS

Baseline patient characteristics

This observational study included a total of 193 patients who underwent SG (male: 64, 33.2%; female: 129, 66.8%), with a mean BMI of 41.3 ± 7.0 kg/m^2. Among the obese patients, various obesity-related comorbidities were prevalent, including metabolic syndrome (88, 45.6%), hypertension (67, 34.7%), T2DM (94, 48.7%), hyperlipidemia (81, 42%), sleep apnea hypopnea syndrome (128, 66.3%), polycystic ovary syndrome (31, 24.0%, *n* = 129), nonalcoholic fatty liver disease (163, 84.5%), gout (10, 5.2%), and hyperuricemia (114, 59.1%). Additionally, 113 patients (58.5%) were in the ^{1}FAO group, while 58 (30.0%) were in the ^{2}FAO group. Specific indicators of obesity-related comorbidities are detailed in Table 1.

Comparison of preoperative information

Preoperative baseline information: We applied PSM analysis to pair patients in the ^{1}SO/^{1}FAO and ^{2}SO/^{2}FAO groups utilizing predictors of major obesity-related comorbidities (metabolic syndrome, hypertension, T2DM, hyperlipidemia, and nonalcoholic fatty liver disease). The matched groups exhibited no significant differences in patient age, height, weight, or BMI, as shown in Table 2.

Preoperative obesity-related comorbidities: We conducted PSM analysis again to compare patients within the matched ^{1}SO/^{1}FAO and ^{2}SO/^{2}FAO groups utilizing sex and BMI as predictors. The analysis revealed no significant differences in preoperative obesity-related comorbidities between patients in the matched groups, as indicated in Table 3.

Comparison of postoperative information: All 193 patients completed 1/3/6 months of postoperative follow-up, 107 patients completed 12 months of postoperative follow-up, 60 patients completed 24 months of postoperative follow-up, and 21 patients completed 36 months of postoperative follow-up (analysis at 36 months was primarily focused on trend interpretation).

Table 1 Preoperative data of all patients (*n* = 193): Baseline information and obesity-related comorbidities, *n* (%)

Baseline	Total, *n* = 193
Sex (Females)	129 (66.8)
Age (yr, mean ± SD)	31.5 ± 8.2
Height (cm, mean ± SD)	169.3 ± 8.0
Weight (kg, mean ± SD)	119.6 ± 27.7
Body mass index (kg/m^2, mean ± SD)	41.3 ± 7.0
Waistline (cm, mean ± SD)	123.2 ± 17.2
Hipline (cm, mean ± SD)	129.4 ± 15.7
^{1}FAO	113 (58.5)
^{2}FAO	58 (30.0)
Obesity-related comorbidities	
Metabolic syndrome	88 (45.6)
Hypertension	67 (34.7)
Cardiovascular disease	10 (5.2)
Type 2 diabetes mellitus	94 (48.7)
Impaired glucose tolerance	78 (40.4)
Hyperlipoidemia	81 (42.0)
Obstructive sleep apnea	128 (66.3)
Polycystic ovarian syndrome (*n* = 129)	31 (24.0)
Non-alcoholic fatty liver disease	163 (84.5)
Gout	10 (5.2)
Hyperuricemia	114 (59.1)

The data in the table are *n* (%) or mean ± SD. FAO: Familial aggregation of obesity.

Table 2 Preoperative baseline information

	^{1}SO, *n* = 75	^{1}FAO, *n* = 75	*P* value	^{2}SO, *n* = 54	^{2}FAO, *n* = 54	*P* value
Sex [female, *n* (%)]	50 (66.7)	48 (64.0)	0.731	36 (66.7)	32 (59.3)	0.425
Age (yr)	29.5 ± 6.8	31.8 ± 9.1	0.234	31.7 ± 8.6	30.7 ± 8.6	0.548
Height (cm)	170.3 ± 7.9	170.1 ± 7.7	0.884	169.9 ± 7.2	170.4 ± 8.3	0.711
Body Weight (kg)	123.5 ± 30.4	122.2 ± 29.9	0.840	120.9 ± 28.6	124.2 ± 31.3	0.562
BMI (kg/m^2)	42.2 ± 8.1	41.8 ± 7.5	0.795	41.5 ± 7.4	42.3 ± 7.9	0.591
Waistline (cm)	126.0 ± 18.3	124.1 ± 19.9	0.731	124.8 ± 19.8	124.3 ± 19.4	0.916
Hipline (cm)	128.3 ± 12.3	129.8 ± 16.5	0.744	128.0 ± 13.3	130.7 ± 17.4	0.459

The data in the table are *n* (%) or mean ± SD. SO: Sporadic obesity; FAO: Familial aggregation of obesity; BMI: Body mass index.

We conducted PSM analysis to align patients in the ^{1}SO/^{1}FAO and ^{2}SO/^{2}FAO groups. We employed sex, preoperative BMI, and major obesity-related comorbidities (metabolic syndrome, hypertension, T2DM, hyperlipidemia, and nonalcoholic fatty liver disease) as predictors to minimize differences between the groups and mitigate the impact of variations in these factors on surgical outcomes.

After PSM analysis, the patient counts were as follows:

^{1}SO *vs* ^{1}FAO = 73 *vs* 73; ^{2}SO *vs* ^{2}FAO = 53 *vs* 53 (1/3/6 months after surgery).

^{1}SO *vs* ^{1}FAO = 37 *vs* 43; ^{2}SO *vs* ^{2}FAO = 52 *vs* 31 (12 months after surgery).

Table 3 Preoperative obesity-related comorbidities, *n* (%)

		n	[1]SO, *n* = 80	[1]FAO, *n* = 80	χ^2	*P* value	*n*	[2]SO, *n* = 58	[2]FAO, *n* = 58	χ^2	*P* value
MS	Without	89	43 (53.8)	46 (57.5)	0.228	0.633	67	34 (58.6)	33 (56.9)	0.035	0.851
	With	71	37 (46.3)	34 (42.5)			49	24 (41.4)	25 (43.1)		
HTN	Without	105	54 (67.5)	51 (63.8)	0.249	0.618	75	33 (56.9)	42 (72.4)	3.056	0.080
	With	55	26 (32.5)	29 (36.3)			41	25 (43.1)	16 (27.6)		
T2DM	Without	86	43 (53.8)	43 (53.8)		> 0.999	59	31 (53.4)	28 (48.3)	0.310	0.577
	With	74	37 (46.3)	37 (46.3)			57	27 (46.6)	30 (51.7)		
IGT	Without	89	45 (56.3)	44 (55.0)	0.025	0.874	71	33 (56.9)	38 (65.5)	0.908	0.341
	With	71	35 (43.8)	36 (45.0)			45	25 (43.1)	20 (34.5)		
HLP	Without	96	51 (63.8)	45 (56.3)	0.938	0.333	68	39 (67.2)	29 (50.0)	3.554	0.059
	With	64	29 (36.3)	35 (43.8)			48	19 (32.8)	29 (50.0)		
PCOS	Without	87	41 (74.5)	46 (80.7)	0.612	0.434	52	27 (77.1)	25 (73.5)	0.157	0.924
	With	25	14 (25.5)	11 (19.3)			17	8 (22.9)	9 (26.5)		
NAFLD	Without	26	16 (20.0)	10 (12.5)	1.653	0.199	19	8 (13.8)	11 (19.0)	0.566	0.452
	With	134	64 (80.0)	70 (87.5)			97	50 (86.2)	47 (81.0)		
OSA	Without	53	27 (33.8)	26 (32.5)	0.028	0.867	37	14 (24.1)	23 (39.7)	3.215	0.073
	With	107	53 (66.3)	54 (67.5)			79	44 (75.9)	35 (60.3)		
HUA	Without	68	37 (46.3)	31 (38.8)	0.921	0.337	42	18 (31.0)	24 (41.4)	1.344	0.246
	With	92	43 (53.8)	49 (61.3)			74	40 (69.0)	34 (58.6)		

Only female participants were analyzed to compare polycystic ovarian syndrome prevalence. The number of females is 112 [[1]sporadic obesity (SO) *vs* [1] familial aggregation of obesity (FAO) = 55 *vs* 57] and 69 ([2]SO *vs* [2]FAO = 35 *vs* 34). SO: Sporadic obesity; FAO: Familial aggregation of obesity; MS: Metabolic syndrome; HTN: Hypertension; T2DM: Type 2 diabetes mellitus; IGT: Impaired glucose tolerance; HLP: Hyperlipoidemia; PCOS: Polycystic ovarian syndrome; NAFLD: Non-alcoholic fatty liver disease; OSA: Obstructive sleep apnea; HUA: Hyperuricemia.

[1]SO *vs* [1]FAO = 22 *vs* 22; [2]SO *vs* [2]FAO = 37 *vs* 17 (24 months after surgery).
[1]SO *vs* [1]FAO = 6 *vs* 7; [2]SO *vs* [2]FAO = 11 *vs* 8 (36 months after surgery).

Weight loss: (1) SG results in a substantial weight reduction in the majority of patients after the procedure, as shown in Table 4. There was no significant difference in short-term postoperative weight loss between patients in the [1]FAO group and those in the [1]SO group. Nevertheless, over time, notable differences became evident at 24 months postsurgery, with patients in the [1]FAO group experiencing less weight loss after SG than their counterparts in the [1]SO group (%TWL: P = 0.025; %EWL: P = 0.025). Comparatively, patients in the [2]FAO group exhibited similar but more pronounced differences than did those in the [2]SO group (BMI: P = 0.003, %TWL: P = 0.006, %EWL: P < 0.001). Several line graphs are shown in Figure 1. These lines of view visually illustrate the difference above. Patients with FAO regain weight to some extent at the two-year postoperative mark, while patients with SO are able to maintain a more favorable weight loss outcome.

And (2) Multiple linear regression analysis. To further explore the factors affecting weight loss outcomes and assess the impact of FAO, we conducted linear regression analyses on %TWL and %EWL at various postoperative time points (Tables 5 and 6). The %TWL, %EWL and BMI exhibited normal distributions. Factors affecting %TWL and %EWL showed no significant multicollinearity. After controlling for the effects of age and obesity-related comorbidities on surgery, we observed that the impact of [1]FAO on weight loss outcomes was not significantly different at 24 months postsurgery, whereas [2]FAO and preoperative BMI exhibited statistically significant differences in their influence on weight loss outcomes, as indicated in Tables 5 and 6 (%TWL: [2]FAO: P < 0.001, BMI: P = 0.001; %EWL: [2]FAO: P < 0.001).

Alleviation of obesity-related comorbidities: SG significantly alleviates a wide range of obesity-related comorbidities, including metabolic syndrome, hypertension, T2DM, hyperlipoidemia (HLP), non-alcoholic fatty liver disease (NAFLD), and hyperuricemia, in the majority of patients 6 months postsurgery. Nevertheless, the extent of remission varies between patients with SO or FAO. As shown in Table 7, the incidence of NAFLD was greater in the [1]FAO group than in the [1]SO group (P = 0.015). The [2]FAO group exhibited a higher prevalence of T2DM (P = 0.031), HLP (P = 0.012), and NAFLD (P = 0.003) than the [2]SO group.

Surgery-related complications: We compared major surgery-related comorbidities (acid reflux, nausea/vomiting, alopecia, and constipation) postsurgery among the different groups of patients. There was no significant difference in

Table 4 Postoperative body mass index, total weight loss percentage, excess weight loss percentage

		[1]SO, *n* = 73	[1]FAO, *n* = 73	*P* value	[2]SO, *n* = 53	[2]FAO, *n* = 53	*P* value
Baseline	Sex [female, *n* (%)]	49 (67.1)	49 (67.1)	> 0.999	36 (67.9)	33 (62.3)	0.541
	Age (yr)	30.5 ± 7.7	31.0 ± 8.5	0.706	31.6 ± 8.7	30.6 ± 8.3	0.537
	Height (cm)	169.2 ± 8.4	169.9 ± 8.1	0.617	169.8 ± 7.5	170.2 ± 8.5	0.817
	Body weight (kg)	118.8 ± 26.7	120.7 ± 27.4	0.660	123.2 ± 27.3	123.2 ± 31.3	0.995
	BMI (kg/m^2)	41.2 ± 6.9	41.5 ± 6.8	0.802	42.4 ± 6.9	42.1 ± 7.9	0.842
	Waistline (cm)	123.0 ± 16.0	123.4 ± 17.3	0.892	124.9 ± 18.4	123.4 ± 19.3	0.725
	Hipline (cm)	128.8 ± 16.3	131.0 ± 14.4	0.439	131.0 ± 18.1	129.8 ± 17.1	0.771
BMI	Pre-op (kg/m^2)	41.2 ± 6.9	41.5 ± 6.8	0.802	42.4 ± 6.9	42.1 ± 7.9	0.842
	1 month (kg/m^2)	35.5 ± 5.9	36.2 ± 6.3	0.465	36.9 ± 5.7	36.9 ± 7.6	0.974
	3 months (kg/m^2)	31.5 ± 5.4	32.4 ± 5.6	0.364	32.9 ± 5.3	33.0 ± 6.6	0.950
	6 months (kg/m^2)	28.4 ± 4.9	29.3 ± 5.0	0.246	29.6 ± 4.9	29.9 ± 5.9	0.784
	12 months (kg/m^2)	26.9 ± 4.8	27.1 ± 3.9	0.830	27.2 ± 4.4	28.6 ± 5.5	0.213
	24 months (kg/m^2)	26.3 ± 5.1	28.2 ± 4.2	0.201	26.9 ± 4.2	31.3 ± 5.7	0.003
	36 months (kg/m^2)	26.9 ± 5.1	29.3 ± 5.3	0.428	27.5 ± 4.0	32.2 ± 6.2	0.061
%TWL	1 month	13.8 ± 4.4	12.8 ± 3.2	0.116	12.7 ± 3.5	12.6 ± 3.9	0.896
	3 months	23.2 ± 5.3	21.8 ± 5.3	0.112	22.2 ± 4.2	21.6 ± 6.2	0.571
	6 months	30.9 ± 5.8	29.0 ± 6.8	0.072	29.9 ± 5.2	28.7 ± 7.2	0.323
	12 months	36.1 ± 7.5	32.7 ± 8.3	0.063	35.6 ± 6.8	32.0 ± 9.8	0.081
	24 months	37.4 ± 7.8	30.0 ± 12.6	0.025	36.6 ± 7.4	26.7 ± 12.5	0.006
	36 months	41.3 ± 11.7	27.4 ± 10.5	0.044	37.0 ± 11.6	26.4 ± 13.3	0.079
%EWL	1 month	33.2 ± 12.1	32.2 ± 16.9	0.675	29.1 ± 9.2	32.5 ± 19.9	0.262
	3 months	56.5 ± 16.5	54.4 ± 25.5	0.561	51.8 ± 12.8	54.5 ± 30.0	0.541
	6 months	74.9 ± 18.9	71.5 ± 28.9	0.399	69.8 ± 17.4	71.2 ± 32.5	0.771
	12 months	84.9 ± 24.8	79.8 ± 20.8	0.322	82.7 ± 22.4	75.2 ± 25.0	0.162
	24 months	89.1 ± 24.8	70.9 ± 27.0	0.025	83.9 ± 20.8	59.2 ± 25.2	< 0.001
	36 months	83.9 ± 25.1	66.7 ± 20.6	0.202	77.8 ± 22.8	56.9 ± 25.3	0.084

The data in the table are *n* (%) or mean ± SD. Analysis at 36 months is primarily focused on trend interpretation. SO: Sporadic obesity; FAO: Familial aggregation of obesity; BMI: Body mass index; %TWL: Total weight loss percentage; %EWL: Excess weight loss percentage; Pre-op: Pre-operation.

surgery-related complications between patients in the [1]FAO group and the [1]SO group ($P > 0.05$). However, the prevalence of acid reflux symptoms was lower in the [2]FAO group than in the [2]SO group ([2]SO:[2]FAO = 24.5%:9.4%, $P = 0.038$). There was no significant difference in nausea/vomiting, alopecia, or constipation between the two groups.

DISCUSSION

Obesity and its severity are influenced primarily by genetic, environmental, lifestyle, and sociocultural factors[5]. Families, as fundamental units in the context of obesity, often share common genetic traits, lifestyle behaviors, and sociocultural perceptions. While many studies have focused on the family history of obesity in adolescents and children [4], there is a lack of research investigating the impact of FAO on SG.

Our study examined the impact of family history on patients with obesity and introduced the novel concept of FAO. After using PSM analysis to eliminate the possible influence of sex, preoperative BMI, and major obesity-related comorbidities on surgical outcomes, we found a significant difference in the weight loss outcomes of SG between patients with FAO, defined as two or more first-degree relatives with obesity, and those with SO. Specifically, patients with FAO experienced worse weight loss outcomes as well as lower remission rates of T2DM and NAFLD after SG. These findings suggest a potential association between FAO and weight regain after SG.

Table 5 Factors affecting percentage total weight loss

		1 month	3 months	6 months	12 months	24 months
%TWL	[1]FAO	-1.036	-1.352	-1.838	-1.542	-5.123
	Sex	-0.361	-1.054	-1.798	-1.229	-1.227
	BMI	0.0280	0.096	0.250[b]	0.444[a]	0.672[a]
	MS	0.091	-0.962	-1.006	-3.808	0.829
	HTN	0.876	0.864	0.082	-0.844	-5.728
	T2DM	-0.370	-0.283	-0.087	-0.376	-3.427
	HLP	0.980	1.030	-0.817	-1.203	-4.127
	NAFLD	-0.517	-0.410	-1.568	0.065	-0.958
	OSA	-0.371	0.939	1.033	2.752	3.023
	HUA	0.506	0.028	-0.039	2.115	2.590
%TWL	[2]FAO	-0.272	-0.671	-1.385	-3.164	-9.486[b]
	Sex	1.046	0.461	1.013	2.693	2.206
	BMI	-0.039	0.054	0.156	0.285	0.618[a]
	MS	-0.891	-0.860	-1.852	-1.634	-4.611
	HTN	0.306	0.810	-0.088	-2.749	-3.853
	T2DM	-0.338	-1.478	-1.548	0.198	-1.050
	HLP	1.318	1.867	0.690	-2.605	-0.980
	NAFLD	-0.113	-0.303	0.482	0.338	2.968
	OSA	-0.483	0.747	0.288	2.558	0.332
	HUA	-0.367	-1.384	-1.298	0.120	-0.298

[a]$P < 0.01$.

[b]$P < 0.001$.

[1]SO *vs* [1]FAO: VIF^{1}_{FAO} = 1.182, VIF_{Sex} = 2.056, VIF_{BMI} = 1.783, VIF_{MS} = 3.514, $VIF_{HT}N$ = 2.561, VIF_{T2DM} = 1.854, VIF_{HLP} = 1.726, VIF_{NAFLD} = 1.244, VIF_{OSA} = 2.057, VIF_{HUA} = 2.03. [2]SO *vs* [2]FAO: VIF^{2}_{FAO} = 1.067, VIF_{Sex} = 1.683, VIF_{BMI} = 1.74, VIF_{MS} = 3.553, $VIF_{HT}N$ = 1.663, VIF_{T2DM} = 1.908, VIF_{HLP} = 2.352, VIF_{NAFLD} = 1.19, VIF_{OSA} = 1.343, VIF_{HUA} = 1.369. The data in the table are unstandardized coefficients (β-values). FAO: Familial aggregation of obesity; BMI: Body mass index; MS: Metabolic syndrome; HTN: Hypertension; T2DM: Type 2 diabetes mellitus; HLP: Hyperlipoidemia; NAFLD: Non-alcoholic fatty liver disease; OSA: Obstructive sleep apnea; HUA: Hyperuricemia; VIF: Variance inflation factor.

In terms of genetics, families of patients with FAO may share common obesity susceptibility genes. These genes included single-gene obesity genes, such as those encoding leptin (Lep) and its receptor (Lepr), the melanocortin-4 receptor, and proopiomelanocortin, and polygenic obesity genes (*FTO loci*), among others[5]. These genes influence weight by regulating the energy balance in the central nervous system, ultimately affecting body weight[15,16]. However, it is crucial to note that genetics alone cannot fully explain the differences in surgical outcomes between the two groups [17]. The disparities in surgical outcomes result from the combined influence of genetic and environmental factors.

In terms of environmental exposures, diet and lifestyle, patients who undergo SG and their family members share common obesity-inducing factors, such as similar dietary and exercise habits. All of these conditions exhibit many similarities, as both patients and their family members suffer from obesity and related comorbidities, which are often accompanied by a sedentary lifestyle[12]. In terms of cognition, similar cognitive levels within the family[18] determine the development of obesity and weight loss outcome of bariatric surgery. The combination of these factors results in weaker dietary and exercise maintenance abilities among patients with FAO[19] than in those with SO, possibly contributing to their mid-to-long-term postoperative weight regain.

SG significantly improves various metabolic processes[20], including glucose metabolism, lipid metabolism, and amino acid metabolism, in patients with obesity. Patients with FAO exhibit lower remission rates for T2DM, hyperlipidemia and NAFLD. This difference may be related to the extent of improvement in glucose and lipid metabolism. By aggregating information about patients with FAO, we aimed to investigate and identify factors influencing the postoperative remission of glucose and lipid metabolism. This research may lead to the use of novel therapeutic approaches for individuals with primary or secondary metabolic disorders.

The incidence of *de novo* gastroesophageal reflux disease (GORD) after SG is approximately 24.8%[21]. We observed a significantly lower incidence of postoperative acid reflux in patients with FAO than in those with SO. This difference may be associated with reduced intra-abdominal pressure[22]. The International Federation for the Surgery of Obesity and Metabolic Disorders recommends performing an endoscopy at 1 year after surgery, followed by subsequent screenings

Table 6 Factors affecting percentage of excess weight loss

		1 month	3 months	6 months	12 months	24 months
%EWL	[1]FAO	-0.698	-1.238	-2.329	-4.439	-14.637
	Sex	3.531	4.486	2.864	-4.092	-1.340
	BMI	-1.100 [c]	-1.751 [c]	-1.903 [c]	-1.397 [b]	-0.757
	MS	-1.272	-4.902	-6.480	-10.983	2.548
	HTN	4.388	5.435	4.388	1.123	-13.696
	T2DM	2.464	3.318	4.445	0.240	-11.171
	HLP	0.807	1.271	-2.716	-4.837	-11.703
	NAFLD	-5.720	-8.292	-11.392 [a]	0.987	1.587
	OSA	-2.937	-0.133	-0.533	5.991	6.384
	HUA	0.940	-0.329	-1.269	2.565	2.079
%EWL	[2]FAO	2.067	1.089	-0.691	-7.224	-23.513 [c]
	Sex	6.912 [a]	8.730	10.880	5.487	7.279
	BMI	-1.145 [c]	-1.806 [c]	-2.054 [c]	-1.539 [c]	-0.666
	MS	-7.068	-8.342	-12.334	-6.298	-5.596
	HTN	5.569	9.484	8.283	-2.062	-8.179
	T2DM	3.291	0.925	0.717	-0.222	-10.684
	HLP	2.784	4.219	1.786	-7.448	-5.069
	NAFLD	-3.588	-6.218	-5.107	1.598	7.874
	OSA	-5.186	-3.097	-5.148	2.368	-2.031
	HUA	-2.054	-5.344	-5.365	-2.837	-5.233

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.001$.
The data in the table are unstandardized coefficients (β-values). FAO: Familial aggregation of obesity; BMI: Body mass index; MS: Metabolic syndrome; HTN: Hypertension; T2DM: Type 2 diabetes mellitus; HLP: Hyperlipoidemia; NAFLD: Non-alcoholic fatty liver disease; OSA: Obstructive sleep apnea; HUA: Hyperuricemia; %EWL: Percentage of excess weight loss; %TWL: Percentage of total weight loss.

every 2 to 3 years based on the results of the initial examination[23]. Our findings may further contribute to the precise prevention and treatment of postoperative *de novo* GORD.

Impaired family functioning may be one of the factors influencing surgical outcomes[24]. A bidirectional relationship exists between family members and patients. Family members can play a supportive role in assisting patients in achieving and sustaining weight loss[12]. The 'halo effect'[25] of patients extends to their family members, resulting in positive changes. This includes improvements in family members' dietary and lifestyle habits[26,27] and an enhancement in their quality of life[28]. Interventions targeting obesity, by incorporating a family systems framework, can also extend the benefits of surgery to the family members of individuals with obesity[29].

The concept of familial aggregation of diseases helps in identifying groups of individuals with shared disease characteristics. For instance, individuals with a family history of type 2 diabetes are more likely to experience overweight/obesity and are susceptible to adverse metabolic consequences of fat accumulation[30]. Patients with a family history of Alzheimer's disease may experience limitations in cognitive function improvement after SG[31]. Moreover, these findings could aid in identifying susceptibility genes for related diseases and gaining deeper insights into potential pathophysiological mechanisms[32], ultimately leading to the discovery of new preventive or therapeutic strategies for obesity[5]. Currently, large-scale genome-wide association studies have identified more than 1100 obesity-associated genetic loci[33]. This study offers a novel perspective. By studying families as units of investigation rather than isolated individuals, it is possible to further discover susceptibility genes for obesity, predict the development of obesity, and enhance strategies for diagnosing and treating obesity[34].

Limitations: (1) Based on our observational study, differences in patients with FAO gradually emerge only in the mid-to-long-term postsurgery. We are actively investigating longer-term surgical outcomes as part of our ongoing research; (2) We excluded a few patients for whom it was difficult to trace first-degree relative information (*e.g.*, adopted, stepparents, or deceased first-degree relatives). These patients exhibited weight loss results equal to or below the average, possibly due to impaired family functioning[24], posing challenges for detailed analysis. We intend to increase the sample size to further explore potential underlying factors; and (3) This study was conducted at a single center, acknowledging

Table 7 Obesity-related comorbidities at 6 months postoperatively, *n* (%)

		n	[1]SO, *n* = 73	[1]FAO, *n* = 73	χ^2	*P* value	*n*	[2]SO, *n* = 53	[2]FAO, *n* = 53	χ^2	*P* value
MS	Without	133	65 (89)	68 (93.2)	0.760	0.383	100	52 (98.1)	48 (90.6)		0.205
	With	13	8 (11.0)	5 (6.8)			6	1 (1.9)	5 (9.4)		
HTN	Without	132	66 (90.4)	66 (90.4)		> 0.999	99	50 (94.3)	49 (92.5)		> 0.999
	With	14	7 (9.6)	7 (9.6)			7	3 (5.7)	4 (7.5)		
T2DM	Without	131	66 (90.4)	65 (89.0)	0.074	0.785	97	52 (98.1)	45 (84.9)		0.031
	With	15	7 (9.6)	8 (11.0)			9	1 (1.9)	8 (15.1)		
HLP	Without	118	60 (82.2)	58 (79.5)	0.177	0.674	91	50 (94.3)	41 (77.4)	6.290	0.012
	With	28	13 (17.8)	15 (20.5)			15	3 (5.7)	12 (22.6)		
NAFLD	Without	96	55 (75.3)	41 (56.2)	5.962	0.015	65	40 (75.5)	25 (47.2)	8.949	0.003
	With	50	18 (24.7)	32 (43.8)			41	13 (24.5)	28 (52.8)		
HUA	Without	98	46 (63.0)	52 (71.2)		> 0.999	78	41 (77.4)	37 (69.8)	1.603	0.205
	With	48	27 (37.0)	21 (28.8)			28	12 (22.6)	16 (30.2)		

Significant postoperative remission of obesity-related comorbidities in all patient groups ($P < 0.001$). SO: Sporadic obesity; FAO: Familial aggregation of obesity; MS: Metabolic syndrome; HTN: Hypertension; T2DM: Type 2 diabetes mellitus; HLP: Hyperlipoidemia; NAFLD: Non-alcoholic fatty liver disease; HUA: Hyperuricemia.

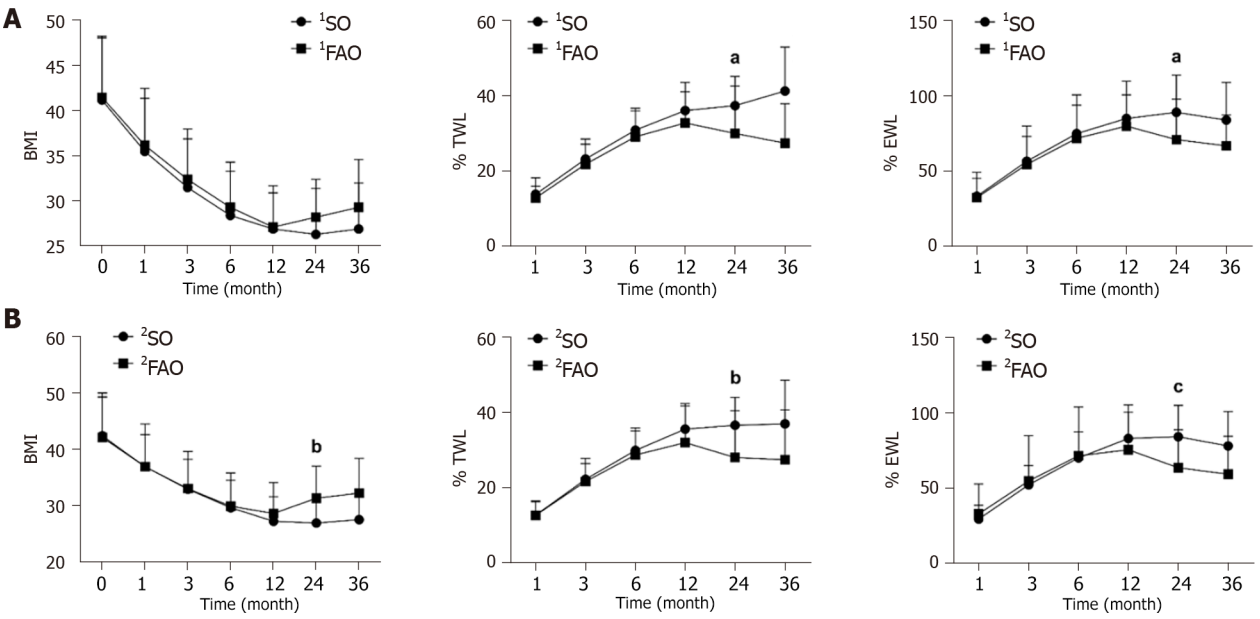

Figure 1 Line graphs depicting postoperative alterations in body mass index, total weight loss percentage, excess weight loss percentage for patients. A: In the [1]familial aggregation of obesity (FAO)/[1]sporadic obesity (SO) groups; B: In the [2]FAO/[2]SO groups. [a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$. SO: Sporadic obesity; FAO: Familial aggregation of obesity; %TWL: Total weight loss percentage; %EWL: Excess weight loss percentage; M: Month; BMI: Body mass index.

variations in familial lifestyles across countries and regions. Therefore, initiating a multicenter study involving multiple regions could provide more patients with precise treatment options.

CONCLUSION

SG can significantly reduce body weight and alleviate obesity-related comorbidities in the majority of patients. Familial aggregation in individuals with obesity impacts the mid-to-long-term weight loss outcomes of SG; affects the alleviation

of T2DM, hyperlipidemia and NAFLD; and leads to a decreased incidence of acid reflux postoperatively. By studying the familial association of obesity, we can gain further insights into the pathogenesis of obesity. Moreover, offering stratified diagnostic and treatment plans for patients with obesity, along with more personalized and targeted health education, can enhance the precision of postoperative prevention and treatment.

ARTICLE HIGHLIGHTS

Research background

Sleeve gastrectomy (SG) significantly reduces weight and improves obesity-related comorbidities in patients with obesity. However, differences in surgical outcomes between patients with familial aggregation of obesity (FAO) and those with sporadic obesity (SO) have not been elucidated.

Research motivation

To investigate whether FAO influences the surgical outcomes of SG.

Research objectives

To compare preoperative characteristics, postoperative weight loss, resolution of obesity-related comorbidities, and surgical complications between the FAO and SO groups.

Research methods

In this retrospective study, we recruited 193 patients who underwent SG and categorized them into FAO and SO groups based on the presence of obesity in their first-degree relatives. Propensity score matching analysis was used to match the patients at a 1:1 ratio to eliminate confounding factors.

Research results

The baseline data and incidence of obesity-related comorbidities did not significantly differ between FAO patients and SO patients. Two years postsurgery, the FAO group exhibited a lower total weight loss percentage ($P < 0.001$) and excess weight loss percentage ($P < 0.001$) than did the SO group. Significant differences were observed between the two groups in terms of remission rates of type 2 diabetes mellitus (T2DM) ($P = 0.031$), hyperlipidemia ($P = 0.012$), nonalcoholic fatty liver disease ($P = 0.003$), and postoperative reflux occurrence rate ($P = 0.038$).

Research conclusions

Compared to those in the SO group, the FAO patients in the SO group demonstrated slightly weaker medium-term weight loss outcomes; reduced symptoms of T2DM, hyperlipidemia, and nonalcoholic fatty liver disease; and a decreased postoperative reflux rate.

Research perspectives

This study provides a theoretical basis for the treatment, surgical method selection, and postoperative health management of patients with FAO.

FOOTNOTES

Author contributions: Wang ZY designed and performed the research and wrote the paper; Hu SY and Zhong MW designed the research and supervised the report; Qu YF contributed to the analysis; Yu TM and Liu ZL provided clinical advice; and Cheng YG supervised the report.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital (Approval No. S447).

Informed consent statement: All personal information was encrypted and all data were anonymous. Therefore, informed consent of all study subjects is waived.

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