Nutritional and digestive effects of gastrectomy for gastric cancer

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ABSTRACT

Background: *Gastrectomy often leads to malnutrition.*

Objective: *The aim of this study was to analyze nutritional and digestive effects of gastrectomy for cancer.*

Patients and methods: *Gastrectomized patients were studied by nutritional assessment including a weekly nutritional diary exploring digestive symptoms.*

Results: *Thirty-two patients were analyzed after a mean follow-up of 41.8 months. The mean percentage of weight loss was 12.9% ± 13.5%. After total gastrectomy, mean weight loss was 22% ± 1.2%, against 7.4% ±11.9% for subtotal gastrectomy (p = 0.002). Moreover, advancing age was related to weight loss (p = 0.02), with a peak around 70 years. The most frequent postprandial symptoms were abdominal swelling (62%) and early satiety (59%). Finally, findings of the present study imply that over a long follow-up, there are no specific intolerances related to gastrectomy.*

Conclusions: *Patients who have undergone a total gastrectomy and elderly gastrectomized patients are at risk of malnutrition and need postoperative nutritional support.*

KEY WORDS: Digestive functions, Gastrectomy, Nutritional status, Weight loss

Received: December 10, 2009; Accepted: May 4, 2010

INTRODUCTION

Gastrectomy (G), subtotal or total, leads to a decrease of main gastric functions (1), but we only occasionally observe severe nutritional complications. In fact, G creates eating problems in nearly 30% of patients, but serious symptoms are present in only 1%-5% (2). The main complications of G are related to an abnormal passage of the bolus into the jejunum. In normal conditions, only food particles of less than 1 mm pass through the pylorus into the duodenum, but after G, bigger and less digested particles reach the jejunum, and the enzymes at this level cannot hydrolyze these elements; this can cause malabsorption, reduction of caloric intake, and finally weight loss (3).

The main symptoms referred by gastrectomized patients are loss of appetite, early postprandial satiety, reflux, diarrhea, dyspepsia, nausea and/or vomiting, and alteration of taste. Generally, major and subcontinuous symptoms are present after total gastrectomy (TG), while minor or episodic symptoms are present after subtotal

gastrectomy (SG). Depending on the prevalent causes leading to postgastrectomy symptoms, we can describe the following syndromes (2-7):

(i) Small stomach syndrome (only for SG): due to the smaller capacity of the gastric stump to contain the bolus. This syndrome is very frequent and is usually transitory. The principal symptoms are early postprandial satiety, nausea, vomiting, and postprandial abdominal pain even after small quantities of food.

(ii) Afferent loop syndrome (only for SG with Billroth II reconstruction) (7): due to a delayed or inefficient emptying of the biliopancreatic juice collected in the afferent loop of the gastric stump. This is characterized by nausea, postprandial fullness, and abdominal pain which results generally in bilious vomiting.

(iii) Gastric (for SG) or esophageal reflux (for TG) and bilious vomiting syndrome: caused by the reflux of alkaline liquid (bile and pancreatic juice) in the gastric stump (for SG) or in the esophagus (for TG), with gastritis or esophagitis, bilious vomiting, and dysphagia. This syndrome is due to an incorrect position of the anastomosis, with the afferent loop (containing bile and pancreatic juice) being too close to the gastric stump or to the esophagus, and is often observed in patients undergoing a Billroth II reconstruction after SG if a Braun jejunojejunal anastomosis is not performed.

(iv) Diarrhea/malabsorption (overall for TG) (8): caused by the rapid emptying of the stomach content into the small bowel, associated with a recruitment of liquids in the lumen because of the increased osmolarity. Present in about 20% of patients after a TG. The accelerated passage of the bolus in the jejunum can reduce digestive capacity, resulting in malabsorption and steatorrhea. The rapidity of the orocecal transit, bacterial overgrowth in the small bowel due to decrease of gastric acid secretion, and pancreatic insufficiency are the principal mechanisms determining steatorrhea. Diarrhea usually appears about 2 hours after a meal.

(v) Dumping syndrome (8): related to an accelerated passage of bolus or sugar in the jejunum. Its frequency varies from 5% in SG patients to more than 40% after TG; symptoms generally disappear in time, and less than 5% of cases lead to chronic disorders. There are 2 types of dumping syndrome:

- *Early dumping syndrome* appears 15 to 30 minutes after a meal and is characterized by fullness, abdominal cramps, nausea, diarrhea, and in some cases vasomotor symptoms, such as tachycardia, postural hypotension, sweating, asthenia, redness, and syncope.

- *Late dumping syndrome* appears 2 to 4 hours after a meal and is characterized by hypoglycemia caused by hyperinsulinemia; the symptoms can be perspiration, hunger, nausea, anxiety, cephalea, shaking, palpitation, and/or sweating.

(vi) Roux-en-Y stasis syndrome (9) (only for SG with Roux-en-Y reconstruction): characterized by delayed gastric emptying and vomiting. The causes of this syndrome can be functional, due to a long gastric remnant, or anatomical such as stenosis of a gastrojejunal anastomosis or jejunal loop obstruction due to adherences or kinking.

The gastrointestinal symptoms and impairment of digestive and absorption process can lead to a reduction of food intake. If these alimentary restrictions remain for a long time, very serious malnutrition can occur.

All patients suffer weight loss, ranging from 10% to 15% during the postoperative period (3-5 weeks) (1, 10, 11), due to fasting related to ileus and surgical stress during the hospital stay in addition to eating problems related to G. After hospital discharge, the principal cause of weight loss is reduced caloric intake due to lack of appetite, presence of gastrointestinal symptoms related to food ingestion (12), changes in sense of hunger, lack of personal initiative, and sometimes the abandoning of nutritional advice. Loss of appetite and alteration in sense of hunger could be caused by the drop in plasma ghrelin levels after G, overall TG (13). This hormone is principally produced by endocrine cells of the stomach, and its function consists in inducing growth hormone secretion and stimulating appetite (8). Therefore, many studies demonstrate that of weight loss is mainly due to changes in fat mass (10, 11).

The purpose of this study is to analyze changes of nutritional status and digestive functions in patients affected by gastric cancer, determined by the following possible causes: presence and growth of cancer, surgery (G), adjuvant chemotherapy, and the postoperative adaptation of the digestive process.

PATIENTS AND METHODS

The study was performed at IRCCS Istituto Clinico Humanitas of Rozzano (Milan) from September 2008 to March 2009. The patients enrolled in the study had undergone G for localized gastric cancer and were free of disease. They were independent, collaborative adults who were adequately informed by the main investigator (L.C.)

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about the purpose of this study and were reassured that the information gathered would remain totally anonymous. Informed consent was obtained from all patients enrolled in the study.

Inclusion criteria

Patients who had undergone SG or TG at least 4 months previously, and whose digestive system had been reconstructed by the Roux-en-Y technique were eligible for inclusion (14, 15).

Exclusion criteria

Patients with cancer disease still present or undergoing chemotherapy, and those who had collateral pathologies potentially influencing their nutritional status or digestive functions were excluded.

We collected anamnesis and nutritional assessment of each patient. First, for each patient, a chart was filled in, containing:
- personal data (date of birth, social and family characteristics, nutritional habits);
- clinical anamnesis (histological diagnosis, tumor location, TNM staging, grading, follow-up, presence of associated pathologies);
- surgery, date and type of operation (SG or TG);
- chemotherapy, date and duration (neoadjuvant or adjuvant);
- nutritional anthropometric parameters: height, usual weight (prepathological conditions), weight at hospital admission before surgery, weight at hospital discharge, minimum weight reached, actual weight, and the percentage of weight loss between usual and actual weight, and between the usual and minimum weight reached;
- previous food intolerance;
- biochemical nutritional parameters (serum albumin, transferrin, lymphocyte count, and cholinesterase).

Second, each patient was informed of how to fill in a nutritional diary for a week, reporting food intake, number of meals and snacks, digestive symptoms related to alimentation, nontolerated foods, and personal eating habits. The nutritional diary was completed for 7 consecutive days to explore eating habits during both working and rest days. The daily caloric intake and intake of total and simple carbohydrates were calculated on the basis of food consumed by each patient and reported in the nutritional diary. Finally, the caloric intake was compared with recommended daily allowances of the Italian Ministry of Health.

The relationship between the intake of pastry products, the percentage of simple carbohydrates, and the presence of symptoms correlated to late dumping syndrome was also investigated. The parameters considered for this analysis were (i) a percentage of simple carbohydrates more than 15% of the total caloric intake, considering that the normal daily intake should be between 10% and 15% (16); (ii) a consumption of pastry products ≥ 7 times/week, which corresponds to at least once a day; and (iii) the contemporary presence of at least 3 symptoms related to the late dumping syndrome (perspiration, hunger, nausea, anxiety, headache, shaking, palpitation, or sweating).

Those foods which always lead to the appearance of gastrointestinal symptoms were considered as not tolerated. In particular, intake of milk and dairy products, reported in the literature as common cause of intolerance in gastrectomized patients, (8) and presence of postprandial symptoms, considering consumption frequency ≥ 7 times a week and the association with at least 2 of the following disturbances: epigastric pain, early satiety, nausea, vomiting, abdominal swelling, diarrhea, and saliva overflow for 4 or more days a week, were analyzed. These arbitrary parameters were used to exclude any casual association.

Statistical analysis

All of the collected data were transferred into a database (Microsoft Access) and analyzed in collaboration with the biostatistics unit of the IRCCS Istituto Clinico Humanitas of Rozzano (Milan). Data are presented as number and percentage, or mean and standard deviation, or median and range, where appropriate. Graphics used are box-and-whisker plots, in which the central horizontal line in each box represents the median, the top and bottom borders of the boxes show the 75th and 25th percentiles, respectively, and the whiskers show the 5th and 95th percentiles. Eventual differences between the variables were explored through Student's t-test or the chi-square test with Fisher's correction when appropriate, using a p value equal to 0.05 as the significance limit. The association between age and the percentage of weight loss was explored through a linear regression. All of the analyses were performed using the Stata 10 program (http://www.stata.com/).

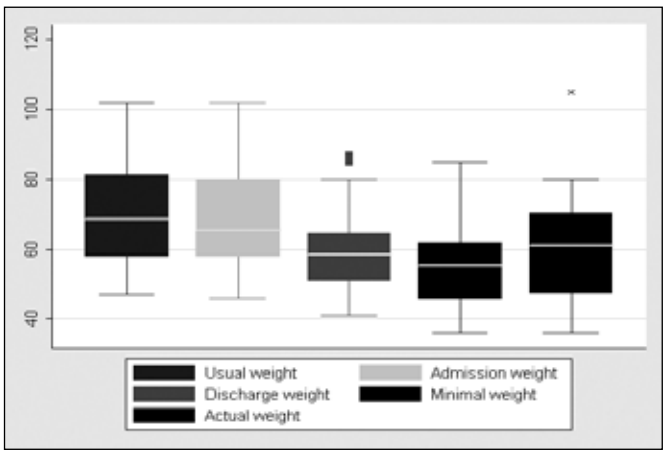

Fig. 1 - *Weight changes (in Kilograms). The central horizontal line in each box represents the median, the top and bottom borders of the boxes show the 75th and 25th percentiles, respectively, and the whiskers show the 5th and 95th percentiles.*

RESULTS

Thirty-two out of 36 patients completed the study answering all of the questions and filling in correctly all of the questionnaires. Valuations were carried out after a mean follow-up of 41.8 ± 30.8 months since G. Clinical characteristics of the series are reported in Table I. Twenty SG and 12 TG were carried out, associated with 28 lymphadenectomies of the first and second level, and 4 lymphadenectomies of the first level. Of the 32 patients, 2 underwent neoadjuvant (preoperative) and 12 adjuvant (postoperative) chemotherapy. Table II shows the nutritional characteristics of the series.

Weight changes are reported in Figure 1. We observed a mild decrease of weight before surgery (from usual to hospital admission before surgery) from a mean 70.5 ± 14.6 kg to 68.7 ±14.6 kg, and a main weight loss during hospitalization with a mean 60.1 ± 12.9 kg ($p < 0.001$) on discharge after a median hospital stay of 11.5 days (range 8-57). Unexpectedly, we did not find any statistically significant correlation between weight loss during hospitalization and length of hospital stay. For 14 patients (44%) minimum weight reached coincided with their weight on hospital discharge, whereas for the other 18 (56%) this was obtained a median of 2.5 months after surgery (range 0-96). Valuation of actual weight showed a mean increase of 1.1 ± 7.3 kg with respect to hospital discharge weight, but only 5 patients (16%) recovered to their usual weight,

TABLE I - PATIENTS' CLINICAL CHARACTERISTICS

Number of patients	32
Sex, male/female	18/14
Mean age (± SD)	66 (± 10)
Histologic type, no. of patients	
Intestinal adenocarcinoma	13
Undifferentiated diffuse adenocarcinoma	6
Signet ring cell adenocarcinoma	5
Mixed adenocarcinoma	8
Site of cancer, no. of patients	
Cardias	3
Fundus	1
Body	4
Greater curvature	2
Lesser curvature	6
Angulus	7
Antrum	8
Pylorus	1
Grading, no. of patients	
G1	1
G2	5
G3	24
GX	2
Stage T, no. of patients	
T0	1
T1	10
T2a	5
T2b	11
T3	5
Stage N, no. of patients	
N0	15
N1	12
N2	5

TABLE II - PATIENTS' NUTRITIONAL CHARACTERISTICS

	No. of patients	**Mean ± SD**
Albumin, g/dL	22	4.2 ± 0.72
Transferrin, mg/dL	13	266 ± 86.2
Lymphocyte count, no./mm^3	32	1.826 ± 538.4
Cholinesterase, kUI/L	9	21.3 ± 26.4
BMI	**No. of patients**	**Months since surgery**
Underweight (BMI < 18)	4	31.3 ± 16.6
Normal weight (BMI 18-25)	24	39.8 ± 27.4
Overweight (BMI > 25)	4	64.3 ± 54

BMI = body mass index.

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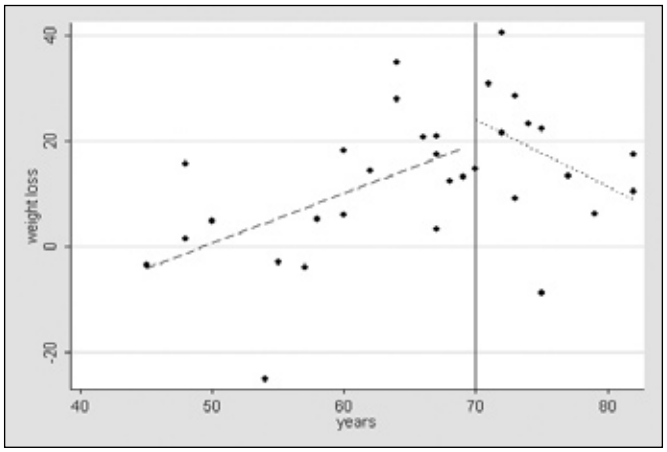

Fig. 2 - *Weight loss and years of age.*

and all of these 5 patients had undergone SG. Comparing the usual with the actual weight, we observed that the mean percentage of weight loss was 12.9% ± 13.5%.

We have considered possible factors influencing weight loss: type of G (TG vs. SG), age, and adjuvant chemotherapy. Patients who underwent TG presented a mean weight loss of 22% ± 1.2% against 7.4% ± 11.9% for SG (p = 0.002). Moreover, in patients younger than 70 years, with the rise in age there was a rise in weight loss (p = 0.02) (Fig. 2); our data had no statistical significance after this cutoff value. To estimate how adjuvant chemotherapy could influence weight loss chronically or acutely, we correlated the usual weight with the actual and minimum weight reached, both in patients who had undergone adjuvant chemotherapy and those who had not. The difference of weight loss in the 12 patients who underwent adjuvant chemotherapy versus the 20 who did not was not statistically different considering the difference between mean usual and actual weight: 14% ± 11.9% and 11% ± 16.4%, respectively. Moreover, considering the minimum weight reached, we observed a mean weight loss of 20% ± 12% in patients who underwent adjuvant chemotherapy and 19% ± 8% in the others. However, 6 out of 12 patients reached the minimum weight loss during adjuvant chemotherapy; 4 of them had undergone SG and 2 TG.

All of the patients reported 3 meals per day both before and after G and a median of 2 snacks (range 0-6) with an increase in number of snacks previously not included in daily habits. However, 17 of the 32 patients did not satisfy their estimated caloric requirement. We have also analyzed postprandial symptoms and their weekly frequency (Tab. III). The most frequent problems were abdominal swelling (20 patients), early satiety (19 patients), and sleepiness (14 patients). The most sporadic symptoms were vomiting (2 patients) and saliva overflow (2 patients), which usually appeared only after a heavy meal.

Seventeen patients (53%) reported a wide variety of food intolerances, and in 9 of these more than 1 food caused disturbances (Tab. IV). There was no association between the length of time elapsed after surgery and the presence of food intolerance.

A further investigation was also made into the relationship between diet and late dumping syndrome, considering the percentage of simple carbohydrates more than 15% of the total caloric intake, an intake of pastry products ≥ 7 times/week, and the contemporary presence of at least

TABLE III - POSTPRANDIAL SYMPTOMS AND THEIR WEEKLY FREQUENCY

Symptoms	No. of patients affected	Weekly frequency (days/week)						
		1	2	3	4	5	6	7
Epigastric pain	6	1	1	1	2	0	0	1
Early satiety	19	4	4	3	1	0	0	7
Nausea	6	4	2	0	0	0	0	0
Vomiting	2	2	0	0	0	0	0	0
Abdominal swelling	20	4	4	2	5	1	1	3
Diarrhea	6	3	3	0	0	0	0	0
Saliva overflow	2	1	0	0	0	0	1	0
Sleepiness	14	4	1	0	3	3	1	2
Weakness	7	1	4	0	1	0	1	0
Taste alteration	5	2	2	0	0	0	0	1
Anorexia	4	0	0	0	4	0	0	0

TABLE IV - NONTOLERATED FOODS

Nontolerated foods	No. of patients
Fried food	4
Pastry products	8
Oranges/juice	3
Chocolate	4
Milk/dairy product	5
Meat	1
Pork products	2
Wine/alcoholic drinks	3
Spicy food	1
Vegetables	2
Fresh fruit	2
Pulses	2
Tomatoes	3

3 symptoms related to the late dumping syndrome. Our results showed that only 3 patients presented all of the above characteristics.

We analyzed the consumption of milk and dairy products and the presence of at least 2 of the following postprandial symptoms: epigastric pain, early satiety, nausea, vomiting, abdominal swelling, diarrhea, and saliva overflow. Six patients presented at least 2 symptoms for 4 or more days/week, but only 2 of these had a milk consumption level of ≥ 7 times/week.

Finally, we evaluated the relationship between drinking liquids during meals and the presence of 2 or more symptoms (epigastric pain, early satiety, nausea, vomiting, abdominal swelling, diarrhea, saliva overflow, etc) at least 4 times a week. Even in this case, there was no significant association; in fact, in the 28 patients drinking liquids during meals, only 5 reported disturbances.

DISCUSSION

The data obtained from this study include the nutritional status, digestive effects, and eating habits in the intermediate and long-term follow-up period after G. Variations in the nutritional status will be discussed first and then the alimentary analysis. Regarding the weight variations, we have demonstrated that the presence of gastric cancer (difference between usual weight and weight at hospital admission before surgery) nowadays does not cause malnutrition, as opposed to that observed in the past and still reported in many medical books. The explanation is due to the greater attention given, both by the population and general practitioners, to initial dyspeptic symptoms and to the increased availability of endoscopy.

Two of the more important factors leading to weight loss are surgery and hospitalization. This is due to surgical stress, postsurgical fasting, and hospital food. In fact, the main weight loss occurs during hospital stay and nearly 50% (44%) of patients reach their minimum weight during hospitalization, despite this period being only a median 11.5 days (range 8-57). Data in the literature demonstrate a loss of body protein mass during the early postoperative period (10) and loss of fat mass due to fat malabsorption, later in the follow-up (1, 10). This conclusion would suggest monitoring patient nutrition during hospitalization, avoiding useless fasting, and giving more attention to dietary surveys and indications for nutritional support, because of the high risk of malnutrition. This statement is even more important because more than 50% (56%) of patients show a further weight loss after hospital discharge. Furthermore, we have identified 3 groups of patients who have a higher risk of malnutrition: those who have undergone TG; elderly people, with a peak around 70 years of age; and some of those who must undergo adjuvant chemotherapy. This leads us to suggest that these patients need postoperative nutritional support. In particular, weight loss is always associated with TG, whereas after SG there is a group of patients with weight loss and another without, despite there being no differences in surgical technique. This claim is proven by a greater weight loss with a very small SD after GT and a smaller weight loss but with a very large SD after SG (mean weight loss 22% ± 1.2% and 7.4% ± 11.9%, for GT and SG, respectively). Therefore a more attentive check of digestive problems also in SG patients is suggested in the attempt to find the risk factors related to malnutrition in this group too. No patient returns to usual weight after TG, so it is important not to consider this parameter as a reference during nutritional surveys or treatments, and to inform the patient and the practitioner regarding this new status.

Regarding the nutritional follow-up, although the majority of patients were not able to fully restore their usual weight (Fig. 1), they reach a normal body mass index with their visceral proteins within the normal range (Tab. II). Lack of return to usual weight could be explained by a low caloric intake; in fact, 17 of the 32 patients did not satisfy their estimated caloric requirement. Moreover, the calculation

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of the caloric intake could be inaccurate because of the following reasons:
- a wrong recording or a mistaken assessment of the quantity and quality of food really consumed by the patient;
- a weekly nutritional record may not be representative of usual eating habits;
- furthermore, the patient's caloric requirement may be inaccurate because the formula used for its valuation is only an estimation of resting energy expenditure (Harris-Benedict formula).

The most frequent postprandial symptoms (Tab. III) were those of reduced gastric volume: abdominal swelling (62%) and early satiety (59%), while the rapid emptying symptoms (dumping syndrome, diarrhea/malabsorption) were practically absent. This fact can be explained by the digestive type of reconstruction employed (Roux-en-Y). A possible limit of this analysis could be linked to the period of follow-up considered in the study (over 4 months after surgery). In fact the symptoms related to a rapid emptying of the stomach usually refer to the early postoperative period, whereas only 5% of the patients suffered from their chronic presence (8). Of the 17 patients suffering from at least 1 intolerance, a large variety of foods caused postprandial symptoms (Tab. IV), with 9 patients intolerant to more than 1 food at the same time. There is no relationship between the length of time elapsed after surgery and the presence of intolerance. However, we did not consider the immediate postoperative period in our analysis, so we cannot estimate whether some patients had had only an early and transient intolerance to a specific food. Our study does not confirm the responsibility of pastry products (percentage of simple carbohydrates) or milk and dairy products in the development of intolerance or symptoms. From our data, we can suppose that food intolerance depends on individual characteristics of the various patients, such as dietary habits, clinical conditions, and social and familial environment.

We usually suggest to patients undergoing G that they drink liquids 45 or 50 minutes before or after their meals; in fact, reduction of liquid intake is necessary to delay the sense of abdominal swelling, early satiety and epigastric pain, and to prevent diarrhea, nausea, and vomiting. Despite this advice, 28 out of 32 patients drank during their meals and only 5 referred symptoms. These last data confirm that symptoms tend to decrease during follow-up, and patients return to their preoperative drinking habits.

CONCLUSION

The present study has demonstrated that G with a Roux-en-Y reconstruction has an important impact on nutritional status, and it has identified 3 categories of patients who are more at risk of malnutrition and who need postoperative nutritional support: those who have undergone TG; elderly people, with a peak around 70 years of age; and in part those who must undergo adjuvant chemotherapy. Our study has also demonstrated that patients return to a normal nutritional status in the follow-up period, although this is different from their usual status, without restoring their usual weight. Furthermore, they tend to go back to their presurgery eating habits, slowly abandoning the nutritional advice (17) received after the operation. This behavior can probably be linked to the fact that the patients have few and mild symptoms associated with G. Finally, we have found that in a long-term follow-up, there are no specific food intolerances related to G.

Conflict of interest statement: none declared.
Financial support: none.

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