

Pathophysiological disorders, quality of life evaluation and recommendations after total resection of the stomach

Dawid MURAWA, Karol POŁOM

SUMMARY

Received: 22.08.2008
Accepted: 11.12.2008
Subject: review paper

1st Surgical Oncology and General
Surgery Department;
Wielkopolska Cancer Centre

Address for correspondence:
Dawid MURAWA
1st Surgical Oncology and General
Surgery Department;
Wielkopolska Cancer Centre,
15 Garbary Street,
61-866 Poznan, Poland.
Tel: +48618850600
Fax: +4861880601
e-mail: dmurawa@op.pl

In recent years, attention has been paid to the quality of life of patients after resection of the stomach as an additional factor of the therapeutic procedure. However, the consequences of total resection of the stomach (especially distant ones) and the influence of different methods of reconstruction of the alimentary tract on patients' quality of life are still controversial.

This article sums up the current state of knowledge of patients' quality of life after total resection of the stomach. The first part discusses the pathophysiological disorders which occur after such operations. This will allow the reader to better understand the symptoms which may possibly occur and then decide on the appropriate procedure to improve the patient's everyday function. The subsection on the evaluation of the quality of life on the basis of literature discusses the following problems: questionnaire research, laboratory investigations, endoscopic examinations, and morphological/histological examinations.

The final part of the paper is a collection of available recommendations to patients after total resection of the stomach. They refer to: optimisation of the diet, prevention of deficiencies, and follow-up examinations, all of which may influence the quality of life.

KEY WORDS: quality of life, dumping syndrome, total gastrectomy, intestinal reservoir

Pathophysiological disorders after total resection of the stomach

Total resection of the stomach, or gastrectomy, involves serious disturbances in the functional balance of the alimentary system. After total resection of the stomach the physiological mechanisms related to the function of the stomach as an organ disappear. Disorders related to the absence of the stomach can be divided into two groups:

1. Mechanical-metabolic
 - Dumping syndrome
 - Alkaline oesophagitis
2. Deficient-metabolic
 - Loss of body mass
 - Anaemia
 - Postgastrectomy bone disease

The mechanical-metabolic disorders and loss of body mass prevail in the first two years after the surgery, after which their intensity decreases gradually. However, the deficient-metabolic disorders occur and become more prominent within two years after the surgery.

Dumping syndrome – occurs with hyperosmotic food causing symptoms of the syndrome. Early and late types of the syndrome are distinguished. The average occurrence is 20%.

Early dumping syndrome results from the loss of the stomach's storage function. A sudden passage of food into the intestines causes vasomotor and abdominal symptoms – flatulence, waves of pain, diarrhoea. The symptoms occur about 20 minutes after a meal containing large amounts of sugar and starch. Such hyperosmotic food causes fluids to move into the intestinal lumen and reduce the amount of circulating blood. The effect is vasomotor symptoms – paleness of integument, sudden redness of the face, dizziness and headaches, weakness, fainting, and palpitations.

Late dumping syndrome occurs much less frequently and concerns about 2% of patients. Approximately 2–4 hours after a meal the symptoms of hypoglycaemia appear, caused by the increased level of insulin in the serum. Hyperinsulinism is a response to the tempo-

rare hyperglycaemia that occurs after a fast intake of a large amount of hyperosmotic food, which leads to a fast absorption of carbohydrates. Additionally, the osmotic stimulus induces increased secretion of intestinal hormones, e.g. enteroglucagon and serotonin, which make the pancreatic cells more sensitive to hyperglycaemia. As the sugar is absorbed rapidly, the high insulin levels caused in this manner do not act on sugar reserves in the intestine [1, 2]

Alkaline oesophagitis – is the result of intestinal contents entering the oesophagus. The highest percentage of this type of inflammation is registered after oesophagoduodenostomy and simple oesophagoenterostomy. The main cause of the occurrence of this complication is the removal of the anti-reflux gastro-oesophageal barrier. Other factors that seem to be important in the development of alkaline oesophagitis are: local cytotoxicity of the refluxed intestinal contents and the impaired ability of self-evacuation of the oesophagus [1, 3]

Loss of body mass – is another disorder occurring in patients after total resection of the stomach. In a large group of patients operated on due to gastric carcinoma, body mass deficiency is the consequence of relapse of the disease, but is also frequently seen in patients without qualities of relapse. Body mass is defined by the balance between the amount of energy ingested, its absorption, and its expenditure. After total resection of the stomach energy expenditure remains the same as before the surgery. However, there is an absorption disorder that applies especially to lipids. According to different researchers, the main cause of loss of body mass is a low-calorie diet (the amount of energy taken) resulting from the absence of the feeling of hunger, early feeling of satiety, and absence of self-discipline in meal consumption.

Also listed as a limiting factor in the consumption of meals is the patient's fear of occurrence of dumping syndrome and dysphagia related to oesophagitis.

The problem of absorption disorders after total resection of the stomach deserves more detailed discussion. These disorders may be caused by various factors: bacterial colonisation of the upper section of the alimentary tract, pancreatic juice secretion disorders,

and continued neoplastic disease if the patient underwent palliative surgery.

Bacterial colonisation of the upper section of the alimentary tract results from the absence of acidic gastric juice, disorders in intestinal motility, and generally uninvestigated changes in the local immunological response. By causing deconjugation of bile acids, bacteria reduce the emulsification ability of bile, which could lead to impaired absorption of lipids (including lipid soluble vitamins) and it cannot be ruled out that this is one of the causes of steatorrhoea observed after total gastrectomy [4,5].

Pancreatic secretion disorders – can be divided into absolute and relative. Absolute pancreatic failure occurs with a decrease in the secretion of bicarbonates (fall of about 48%) and lipase (fall of about 39%). The causes of this phenomenon include increased alkalinity, which is a direct cause of reduced secretion; pancreatic atrophy due to disuse of the organ (reduced amount of food taken); or deficiency in the agent stimulating the pancreas, i.e. gastrin.

Relative pancreatic failure involves an inappropriate use of the enzymes produced by the pancreas. There is no coordination between maximal pancreatic secretion and intestinal passage, which is accelerated after total resection of the stomach. It is also believed that there is insufficient mixing of pancreatic juice with food particles after surgeries that do not allow for passage of food through the duodenum [1]

Anaemia – is an example of a late complication after total resection of the stomach. The cause of anaemia is iron deficiency resulting from the reduced supply of iron ingested with food, iron absorption disorders (higher pH makes it impossible for Fe^{2+} to become oxidized into Fe^{+3} , which is easier to absorb) and chronic loss of small amounts of blood (e.g. oesophagitis). Anaemia resulting from vitamin B12 deficiency is the effect of absence of Castle's intrinsic factor, which is necessary for absorption of this vitamin, and the bacteria colonising the intestine. However, explicit anaemia only develops several years after the surgery. In extremely rare cases patients after resection of the stomach may develop anaemia resulting from folic acid deficiency [3].

Postgastrectomy bone disease is a group of bone disorders consisting of osteomalacia and osteoporosis. The disease is caused by a deficiency of calcium and vitamin D, which may be due to the rather unspecified role of the stomach in calcium homeostasis (hypothetical peptide hormone – gastrocalcin) [6].

Evaluation of patients' quality of life after a total resection of the stomach

Questionnaire research

In order to provide a subjective evaluation of patients' quality of life after a total gastrectomy most researchers use different types of scales. However, in some publications these are only simple questions concerning the extent of suffering given by the alimentary system. The most frequently used scales for evaluation of patients' quality of life after a total gastrectomy are: ERSS (Edinburgh Rehabilitation Status Scale), GSRS (Gastrointestinal Symptom Rating Scale), Cuschieri's index, Eypasch's quality of life index and Troidl's scale, SF 36 health survey questionnaire, 15 D health related quality of life questionnaire, and Spitzer QOL Index. All of the listed scales include questions that comprise not only an evaluation of symptoms from the alimentary tract but also a general assessment of patients' functioning in everyday life [4, 7, 8, 9]. In the evaluation of the quality of life of patients treated for cancer, the questionnaires currently used consist of two parts: a general questionnaire and one relating specifically to the neoplastic disease of the patient. Questionnaires for patients with stomach cancer are prepared similarly. A recommended questionnaire is the EORTC (European Organization for Research and Treatment) containing the general cancer questionnaires QLQ-C30 (Quality of Life Cancer 30) and the module QLQ-STO22 (Quality of Life Stomach 22) tailored to patients treated for gastric carcinoma. The QLQ-C30 is made up of 30 questions that evaluate the patient's quality of life in 5 functional scales (physical, roles, emotional, cognitive, social) and several single- or multi-item symptoms (nausea/vomiting, constipation/diarrhoea, dyspnoea, insomnia, pain, fatigue, loss of appetite). Physical function is related to the effect that somatic symptoms exert on the patient, whereas

emotional function includes such disorders as depression, suicidal ideation, feelings of loneliness or stigmatisation, and low self-esteem. The roles scale evaluates the patient's ability to continue performing their everyday tasks at home and in the workplace. The social scale is an indicator of the patient's interactions with in the community. [10]

The EORTC QLQ-STO22 uses 5 multi-item scales (dysphagia, meal restriction, pain, reflux, fear) and 4 single-item scales (dry mouth, body image, loss of hair, taste problems) to evaluate the patient's quality of life [11].

The use of the QLQ-C30 and QLQ-STO22 as modules of the EORTC questionnaire would make the results of quality-of-life studies conducted at various centres easily comparable to each other.

The American equivalent of the STO22 is called the FACT-Ga questionnaire and is composed of 27 questions evaluating the quality of life according to physical, social/family, emotional, and functional well-being.

Numerous studies on the evaluation of patients' quality of life in early post-operative periods point to a relatively frequent occurrence of various ailments of the alimentary system. Bragelmann et al. presented a study in which they evaluated a group of 17 patients one year after total resection of the stomach [7]. They found that only 10.4% of the patients complained of an unsatisfactory quality of life. The author stressed that the frequency of occurrence of adverse post-resection symptoms diminished over time after the surgery. Despite a majority of patient reports indicating a good quality of life, he noticed that 65% of the patients reported dyspeptic symptoms and 55% reported pains and a feeling of fullness after meals. As Nakane et al., Svendlund et al., Iivonen et al. and Nozoe et al. have observed, the creation of an intestinal reservoir has a positive influence on the patient's functioning and is correlated with a reduction of various abdominal ailments in early post-operative periods [12, 8, 5, 13].

By contrast, there are few such data concerning distant periods of observation. Nevertheless, the patients' very good results in psychological and social evaluations and in everyday behaviour are stressed. The biggest problem for patients, though usually much smaller than in early post-operative periods, is

suffering due to the alimentary system. Here diarrhoeas and dyspeptic symptoms become prominent. A publication by Iivonen et al. presents one of the longest periods of observation of patients, reaching eight years after total gastrectomy [5]. The authors emphasise the patients' good functioning both in the group of patients with an intestinal reservoir and in the group of patients surgically treated by the Roux-Y method. Murawa et al. quote similar results [2]. They note that the process of intestinal adaptation after reconstruction by the Roux-Y method must take several years, leading to a longer and more gradual disappearance of adverse clinical symptoms when compared to operative methods in which an intestinal reservoir is made.

Horvath et al. and Kalmar et al. present an interesting study in which they show a statistically significant increase in the quality of life of patients with an aboral pouch 15 cm intestinal reservoir (the reservoir is located distal to the oesophagojejunal anastomosis, in the duodenojejunal anastomosis) when compared to patients treated by Roux-en-Y [9,14].

Also there are not many studies indicating a positive result of reconstructive methods utilizing two intestinal reservoirs (one classically placed near the oesophagojejunal anastomosis and the second being the aboral type). Comparisons between post-gastrectomy alimentary tract reconstruction using the Roux-en-Y method with a single J pouch (10 cm) and patients treated using the Roux-en-Y method with two J pouches (10 and 8 cm) demonstrated a statistically significant increase in the quality of life of patients in whom two intestinal reservoirs were created [15]. These treatment methods require further studies, however, to determine their benefits for the quality of life of post-gastrectomy patients.

Another problem associated with post-gastrectomy reconstructive methods is the preservation of food passage through the duodenum. We can assume that we need not worry about blind loop syndrome. The oesophagoduodenal anastomosis formed after total stomach resection has been associated with technical problems having to do with duodenal motility and the head of the pancreas, as well as with symptoms relating to persistent bile reflux into the oesophagus [16].

Very few studies have evaluated the quality of life in post-gastrectomy patients in whom duodenal passage of food has been preserved. Raab et al.'s article, which compares the Roux-en-Y method to Longmire jejunal interposition without a pouch, demonstrated lack of statistical significance in the quality of life of patients treated by one or the other of these methods, using the Spitzer and Karnofsky scales [17]. The Fuchs et al. publication, based on the Viscick and Spitzer scales, also did not show a statistical increase in the quality of life in patients with preserved passage of food through the duodenum [18]. The only study demonstrating a better quality of life in patients in whom the passage of food through the duodenum was preserved is the Schwarz et al. article. The authors used their own scales in the evaluation of patients, but did not describe these scales in detail [19]. It is therefore likely that having food pass through the duodenum did not increase the quality of life of patients and did not allow the patients to gain weight, compared to not having this passage preserved.

Laboratory investigations

According to current knowledge of pathophysiology, when evaluating quality of life after total resection of the stomach, various parameters of peripheral blood should also be evaluated. Some researchers think that each of these values directly or indirectly indicates the state of nourishment of the organism (so-called immunonutritional factors) [13].

Vitamin B12. A frequently seen problem after resection of the stomach is the deficiency of vitamin B12, which, as is known, requires the presence of Castle's factor (produced in the stomach) in order to be absorbed from the alimentary system. Patients after gastrectomy must repeatedly be reminded of the need to take vitamin B12 in intramuscular injections at six-week intervals. Murawa et al. in their study presented a group of patients after gastrectomy with as many as 67% having lower than normal levels of vitamin B12 [2]. It is interesting that only 16% of these deficient patients were diagnosed with anaemia. Low levels of vitamin B12 were due to a lack of discipline in supplementation. Bae et al. suggest

that the development of anaemia due to vitamin B12 deficiency is a slow process lasting many years [4].

Iron. In many publications in which the period of observation lasted up to 2 years after the surgery, a relatively frequent occurrence of anaemia due to the deficiency of iron is seen [1,3]. However, this problem disappears in later periods, which can be explained by the adaptation of the intestinal mucosa to absorb iron under altered pH conditions. It was observed that as much as 20% of the consumed iron is used in the new altered conditions, whereas only 10% of the iron consumed with food is absorbed in healthy individuals under physiological conditions [4].

Protein. Most reports in which parameters of protein metabolism are assessed suggest absence of deficiency of protein mass and thus confirm a good state of patient nutrition. However, Sategna-Guidetti et al. indicate that, as with iron, a deficiency of proteins occurs in about 20% of cases within one year after the surgery and in successive years reaches normal values [3]. In distant periods of observation, neither Iivonen et al. nor Murawa et al. found a difference in patients' protein concentration as being dependent on the method used for surgical reconstruction of the alimentary tract [2, 5].

Lipids. Svendlund et al. indicate that the problem of body mass deficiency and qualities of anaemia in the anthropometric image are the result of a decrease in lipid reserves of up to 40% in patients after total gastrectomy [20,8]. This phenomenon is due to reduced lipid absorption and thus excessive lipid excretion with stools. Some authors report that, over long periods of observation, patients with an intestinal reservoir seem to replenish their lipid reservoirs better than patients without an intestinal reservoir [4, 6].

Calcium-phosphate metabolism. Resection of the stomach is a well-known factor for the development of osteoporosis and osteomalacia. The reason lies in mechanisms related to disordered lipid absorption and intolerance to milk, which indirectly results in a reduced uptake and absorption of vitamin D and calcium. Liedman et al. report that having observed patients in the range of 3–10 years after total resection of the stomach, they found a noticeable

increase in the value of alkaline phosphatase [6]. The increase was slightly higher in the group of patients after reconstruction with the Roux-Y method than in the group with an intestinal reservoir, and the biggest changes were observed in the first three years after the surgery. However, no differences were found in the concentrations of vitamin D. When carrying out densitometric examinations, Inoue et al. noticed that a drop in the bone mineral density observed 2–5 years after gastrectomy resolved after 6 years post-surgery [21]. It is stressed in the literature that due to the low cost and relatively sensitive signalling of bone changes, the first examination should be the measurement of alkaline phosphatase and only later, if necessary, should there be other examinations, e.g. a densitometric examination [5].

Endoscopic examinations

Additionally in the patient's neoplastic disease, endoscopic examinations are used for evaluation for the presence of alkaline oesophagitis. The state of inflammation of the oesophagus directly leads to a decreased quality of life in patients after resection of the stomach, and indirectly contributes to nutritional disorders due to reduced food consumption. Currently alkaline oesophagitis is a rarely occurring problem, as the reconstructive methods favouring its incidence have been abandoned. For example, in 1976 Morrow et al. presented a very interesting study in which they demonstrated that as many as 66% of patients after gastrectomy and omega anastomosis (oesophagoenterostomy with distal enteroenterostomy) had considerable inflammatory lesions of the oesophagus with accompanying clinical symptoms, which made patients' normal functioning impossible [22]. After surgeries that changed the above-mentioned surgery type to a reconstruction by means of the Roux-en-Y method a considerable improvement was observed in all patients. At present it is known that the Roux-en-Y loop prevents reflux of intestinal contents. In spite of this, about 18% of patients after this operation and methods with a reservoir have indices of inflammation, but usually of lesser extent (slight congestion of the mucosa) and do not cause clinical symptoms.

Morphological examinations

Pouchitis is a well-known term that refers to lesions occurring in distal intestinal reservoirs in patients after a pancolectomy. The creation of an intestinal reservoir with enteroproctostomy leads to the creation of a new rectum. Both stasis and changes in the composition of the intestinal contents lead to the occurrence of morphological lesions of an atrophying character in the reservoir, and then to reconstruction of the mucosa towards the colonic mucosa. These processes are accompanied by lesions characterised by acute and chronic inflammation and dysplasia, which later may be the cause of neoplasia. However, there are few studies dedicated to histological lesions in the oesophagoenterostomy. Murawa et al. provide the most elaborate presentation of the problem in their publication. In examinations comprising patients treated surgically 4 to over 10 years earlier, qualities of atrophy of intestinal villi or inflammatory lesions in the mucosa were not observed [2]. The ultrastructure of the oesophagoenterostomy region at the electron microscope level corresponded to the normal structure of the jejunum. This proves the absence of features which might influence the development of de novo cancer.

Table 1 presents postoperative, comprehensive recommendations for patients after total gastrectomy (own elaboration based on literature).

REFERENCES

1. Harju E: Metabolic problems after gastric surgery. *Int Surg*, 1990; 75: 27–35
2. Murawa D, Murawa P, Oszkinis G, Biczysko W: Long-term consequences of total gastrectomy: quality of life, nutritional status, bacterial overgrowth and adaptive changes in esophagojejunostomic mucosa. *Tumori*, 2006; 92(1): 26–33
3. Sategna-Guidetti C, Bianco L: Malnutrition and malabsorption after total gastrectomy. A pathophysiological approach. *J Clin Gastroenterol*, 1989; 11: 518–24
4. Bae JM, Park JW, Yang HK, Kim JP: Nutritional status of gastric cancer patients after Total gastrectomy. *World J Surg*, 1998; 22: 254–61
5. Iivonen MK, Mattila JJ, Nordback IH, Matikainen MJ: Long term follow up of patients with pouch reconstruction after total gastrectomy. *Scand J Gastroenterol*, 2000; 7: 679–85
6. Liedman B: Symptoms after total gastrectomy on food intake, body composition, bone metabolism, and quality of life in gastric cancer patients. Is reconstruction with reservoir worthwhile? *Nutrition*, 1999; 15: 677–82
7. Bragelmann R, Armbrecht U, Rosemeyer D, Volovics A, Zilly W, Stockbrugger RW: Determinants of medico-social functioning after total gastrectomy. *Disabil Rehabil*, 1999; 21: 88–95
8. Svedlund J, Sullivan M, Liedman B, Lundell L: Long term consequences of gastrectomy for patients quality of life: the impact of reconstruction techniques. *Am J Gastroenterol*, 1999; 94: 438–45
9. Horvath OP, Kalmar K, Cseke L, Poto L, Zambo K: Nutritional and life-quality consequences of

Table 1. Post-operative comprehensive recommendations in patients after total gastrectomy

Follow-up examinations	Deficiency prevention	Diet
Physical examination – every three months	Iron (e.g. ferrous gluconate 24 mg 2-3 tablets daily, especially in early post-operative period)	high-protein, high-fat with limited carbohydrates
Morphological peripheral blood test – every six months (densitometry if necessary)	Vitamin B12 (1000 µg i.m. every six weeks)	frequent small-amount meals + smorgasbord
Alkaline phosphatase level in serum – every six months	Vitamin D (1500-2000 units/day)	solid food always before fluids
Iron level in serum – every six months	calcium carbonate (about 1g/day)	avoiding hot and cold meals
Endoscopic examination – depending on ailments	pancreatic enzymes (e.g. pancreatin 10,000 3x1 tablet/day)	limited milk products depending on symptoms
	skin exposure to sunlight (vitamin D synthesis in skin)	

- Boral pouch construction after Total gastrectomy: a randomized, controlled study. *Eur J Surg Oncol*, 2001; 27: 558–63
10. Vickery CW, Blazeby JM, Conroy T, et al: Development of an EORTC disease specific quality of life module for use in patients with gastric cancer. *Eur J Cancer*, 2001; 7: 966–71
 11. Blazeby JM, Conroy T, Bottomley A, et al: Clinical and psychometric validation of a questionnaire module, the EORTC QLQ-STO 22, to assess quality of life in patients with gastric cancer. *Eur J Cancer*, 2004; 40: 2260–8
 12. Nakane Y, Okumura S, Akehira K, Okamura S, Boku T, Osuka T: Jejunal pouch reconstruction after total gastrectomy for cancer. *Ann Surg*, 1995; 222: 27–35
 13. Nozoe T, Anai H, Sugimachi K: Usefulness of reconstruction with jejuna pouch in total gastrectomy for gastric cancer in early improvement of nutritional condition. *Am J Surg*, 2001; 181: 274–8
 14. Kalmar K, Cseke L, Katalin Z, Horvath OP: Comparison of quality of life and nutritional parameters after total gastrectomy and a new type of pouch construction with simple Roux-Y reconstruction. *Dig Diseases Scien*, 2001; 46: 1791–6
 15. Gioffre'Florio MA, Bartolotta M, Miceli J, et al. Simple versus double jejuna pouch for resection after total gastrectomy. *Am J Surg*, 2000; 180: 24–8
 16. Lehnert T, Buhl K: Techniques of reconstruction after total gastrectomy for cancer. *Br J Surg*, 2004; 91: 528–39
 17. Raab M, van Maercke P, Stützer H: Lebensqualität nach Gastrektomie- Vergleich der Magenersatzmethoden nach Longmire und Roux. *Zentralbl Chir*, 1987; 112: 1140–5
 18. Fuchs KH, Thiede A, Engemann R, Deltz E, Stremme O, Hammelmann H: Reconstruction of the food passage after total gastrectomy: randomized trial. *World J Surg*, 1995; 19: 698–706
 19. Schwarz A, Büchler M, Usinger K, Rieger H, Glasbrenner B, Friess H: Importance of the duodenal passage and pouch volume after total gastrectomy and reconstruction with the Ulm pouch: prospective randomized clinical study. *World J Surg*, 1996; 20: 60–67
 20. Svedlund J, Sullivan M, Liedman B, Lundell L, Sjodin I: Quality of life after gastrectomy for gastric carcinoma: controlled study of reconstructive procedures. *World J Surg*, 1997; 21: 422–33
 21. Inoue K, Shioni K: Metabolic bone disease following gastrectomy. *Br J Surg*, 1992; 79: 321
 22. Morrow D, Pessaro E: Alkaline reflux esophagitis after total gastrectomy. *Am J Surg*, 1976; 132: 287–91