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CLINICAL TRIALS STUDY

Effect of somatostatin in advanced gastric cancer after D2 radical gastrectomy

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Abstract

AIM: To study the effect of somatostatin in patients with advanced gastric cancer who received D2 lymphadenectomy and vagina vasorum dissection.

METHODS: Using a prospective, single-blind, placebo-controlled design, patients with advanced gastric cancer were randomized into a study group (n = 61) and a control group (n = 59). Patients in the study group were given somatostatin for 5-7 d starting 6 h after the operation, and patients in the control group were given normal saline. Preoperative and nonoperative complications in the perioperative period, as well as different types of postoperative drainage in the two groups were compared.

RESULTS: There was no significant difference between the study group and the control group for preoperative clinicopathological indicators. We found no significant difference between the two groups for the overall incidence of complications, but a lower percentage of peritoneal effusion was observed in the treatment group (1.6% *vs* 10.2%, $P < 0.05$). There were no significant differences between the two groups in the incidence of postoperative pancreatic dysfunction and chylous fistula. However, there were significant differences in the amylase concentration in drainage fluid, volume and duration of drainage, volume and duration of chylous fistula and peritoneal drainage, and volume and duration of gastric tube drainage. The study group did not show any increase in mean hospitalization cost and the cost reduced when the postoperative complications occurred.

CONCLUSION: Postoperative somatostatin reduces volume and duration of surgical drainage and related complications. Somatostatin may improve safety of gastric cancer surgery, reducing postoperative complications and promoting recovery.

Key words: Advanced gastric cancer; Somatostatin; Complications

Core tip: To enhance the degree of radical lymph nodes dissection for advanced gastric cancer, vagina vasorum dissection and the resection of extracapsular greater omentum was applied to D2 lymph node dissection. Vagina vasorum dissection was the complete removal of vascular adventitia and fibrous connective tissue as well as nerve tissue around the vascular sheath. But these procedure usually followed by operation-related compli-

cations. Hence It is interesting to found out the clinical effect of postoperative somatostatin treatment in the duration and amount of drain followed by gastrectomy and D2 lymphadenectomy with extra capsular epiploon resection.

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INTRODUCTION

Safety and efficacy of surgical treatment of gastric cancer are important factors to consider in selecting surgical methods. Comparison of two clinical trials reported in the literature reveals a significant difference in the safety of the same operation in different locations and with different surgeons[1-4]. Standardized and extended (D2 and even D2 plus) lymphadenectomy has been carried out extensively; extracapsular resection of the greater omentum requires removal of the capsule of the pancreas[5], and resection of the capsule of pancreas or partial resection of the pancreas is needed more for serosal infiltrative gastric cancer[4], leaving only the vascular sheath for extravascular dissection, so metastatic cancer tissue remaining in the vascular sheath cannot be thoroughly cleared to achieve radical resection[6]. Vagina vasorum dissection is emphasized in lymph node excision, and it is the complete removal of the vascular adventitia and fibrous connective tissue, as well as nerve tissue surrounding the vascular sheath. Thus, some surgeons express concern that vagina vasorum dissection and resection of the extracapsular greater omentum may increase the risk of postoperative complications[7]. Surgeons still worry that postoperative pancreatic fistula or peritoneal effusion may occur and erode vessels, and that secondary infections pose a greater risk of vascular compromise and bleeding[8,9]. Somatostatin is routinely administered after gastric cancer surgery in many clinical institutions in China and other countries, although rigorous evidence to support this practice is still lacking. This prospective, single-blind, placebo-controlled study investigated the clinical value of postoperative administration of somatostatin, with the goal of exploring surgical safety and complications.

MATERIALS AND METHODS

Patients

This clinical study was initiated in January 2010, and was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University. Selection criteria were as follows: (1) age $\geq$ 18 and $\leq$ 70 years (male or female); (2) pathologically established gastric cancer: preoperative TNM stage T2, T3 or T4a, N0-2 (by computed tomography or ultrasonic endoscopy); preoperative operation endurance score by ASA criteria meeting criteria for grades Ⅰ and Ⅱ; all recruited patients were randomized preoperatively, and patients preoperatively unable to achieve R0 resection; (3) willingness to sign informed consent; (4) absence of metabolic diseases such as diabetes mellitus or hyperthyroidism; absence of significant heart, lung, liver, or kidney failure, systemic infection or immunodeficiency disease; normal bone marrow function; and absence of history of other malignant tumors; (5) absence of other malignant tumors, diabetes mellitus, chronic liver/kidney/lung diseases, diseases of the hematopoietic or cardiovascular system that might affect treatment and observation; body mass index (BMI) < 18 and > 28 kg/m^2; and (6) no combined organ resection. Finally, 61 and 59 cases with advanced gastric cancer were included in the study group and control group, respectively (Figure 1).

Randomization and implementation

All recruited patients were clearly informed about the aims as well as the procedures of the study and gave signed informed consent. The study adopted a prospective, randomized, single-center, single-blind and placebo-controlled design. Random numbers were generated by a computer and were assigned to postoperative patients to divide them into one of two parallel groups (study and control groups) in a 1:1 ratio. The patients in the study group received a 5-d course of continuous intravenous 250 μg/h somatostatin (Stilamin; Merck Serono, China) using a micropump daily and the control group were given the equivalent amount of normal saline intravenously as a placebo control. The patients were unaware of their group assignment. The investigators were trained to allocate the patients and administering nurses and surgeons gave the interventions according to the random number. Participants were observed by two specially trained doctors who were blinded to the treatment procedure during the hospital stay and follow-up period.

Primary and secondary endpoints

The primary outcome was the overall postoperative complications in the treatment and control groups during hospitalization. Postoperative complications included abdominal hemorrhage (recent and delayed) within 2 mo, stoma fistula, chylous fistula, incision infection, dehiscence, postoperative early inflammatory bowel obstruction, pneumonia, and death. The secondary endpoint was stress status, which included peritoneal effusion. Pancreatitis and pancreatic fistula were also included as secondary endpoints. Volume and quality of postoperative drainage were assessed as follows: (1) postoperative serum amylase on days 1, 3 and 5; (2) postoperative daily volume of drainage; chyle test, duration of indwelling drainage tube; and (3) postoperative concentration of amylase in drainage on days 1, 3, 5 and 7.

Postoperative pancreatitis: A serum amylase level > 3 times the upper limit of normal (ULN) established as the

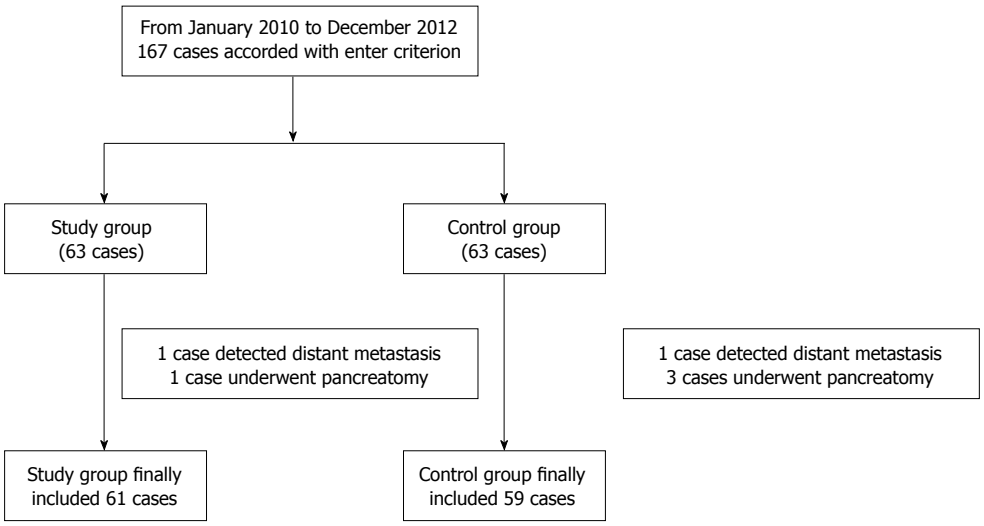

Figure 1 Flow chart of included patients.

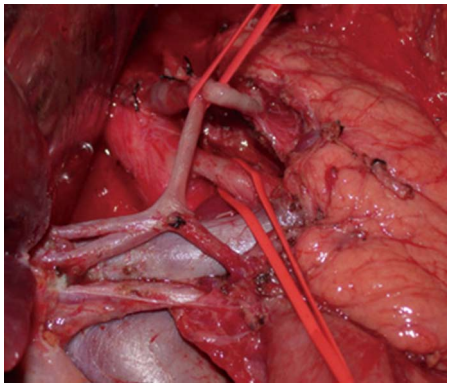

Figure 2 Overview of vagina vasorum dissection.

diagnostic criterion for postoperative pancreatitis.

Pancreatic fistula: The diagnostic criteria for postoperative pancreatic fistula proposed by Bassi *et al*[10] were used: drainage volume > 50 mL/d for ≥ 3 d postoperatively; amylase concentration in the peritoneal drainage > 3 times ULN measured values of serum amylase. Amylase in the peritoneal drainage > 600 U/L (ULN of serum amylase is 220 U/L in our hospital) was used as the diagnostic criterion for postoperative pancreatic fistula. Considering that the pancreas was not directly involved in the operation, the above diagnostic criterion was modified, and pancreatic dysfunction was diagnosed if the amylase concentration in peritoneal drainage on the postoperative day 3 was > 3 times ULN.

Chylous fistula: (1) volume of peritoneal drainage > 200 mL/d for three consecutive days after gastrectomy; (2) absence of bleeding, and normal amylase concentration in drainage; and (3) detectable chyle in drainage.

Surgical procedure and perioperative treatment

All patients accepted standard D2 or D2$^+$ surgical treatment conducted by physicians with a professional title of associate professor or above, with specific expertise in gastric cancer. All the experts were in the division of gastric cancer diagnosis and treatment and received standardized training for radical surgery for gastric cancer. Depending on the stage established according to JGCA classification (13th edition), D2 or D2$^+$ surgical lymph node dissection[11] plus extracapsular resection and vagina vasorum dissection were performed.

While dissecting the arteries, the outer vascular sheath was stripped from the hepatic artery, right gastric artery, common hepatic artery, splenic artery, left gastric artery to the origin of the celiac trunk, together with the splenic artery. The vessels were ligated at their origins outside the omentum, in order to excise all the related lymph nodes (Figure 2). Total gastrectomy, esophagojejunostomy and lymph node dissection with spleen preservation were performed in a majority of patients with proximal gastric cancer. Lymph node dissection with splenic resection was performed in patients with direct spleen invasion or splenic arteriovenous anastomosis. Billroth II anastomosis was performed in all patients with distal gastric cancer, and the reconstruction methods of middle gastric cancer patients were according to the resection margin and lymph node dissection.

Puncture of the subclavian vein with retention of a central venous catheter was performed intraoperatively in all patients. Doses of fluids and electrolytes were adjusted individually depending on the condition of the patient. Patients in both groups were given standard total parenteral nutrion (TPN) transfusion and unified antibiotics and proton pump inhibitors postoperatively. The TPN formulation was as follows: non-protein energy: 25-30 kcal/kg·d; nitrogen: 0.25-0.3 g/kg·d; energy/nitrogen ratio: 100-120 kcal/kg·d; carbohydrate/lipid ratio: 2:1; carbohydrate/insulin: 4-6:1. Half of the dose was given on the first day after the operation and the full dose thereafter, typically for 4-7 d.

Early enteral nutritional support has been included as an important consideration in the rehabilitation[12]; however, to reduce the confounding variable of differences in

Table 1 Clinical pathological indicator of patients in the trial group and the control group

	Trial group	Control group	Statistic value	*P* value
Age	56.3 ± 15.0	55.7 ± 14.7	0.209	0.835
Sex (male/female)	31:30	34:25	0.560	0.454
BMI	22.3 ± 5.0	23.0±4.7	0.861	0.391
Tumor size	4.7 ± 2.9	4.6 ± 3.1	0.325	0.746
T stage (T1/T2/T3/T4a)	0/15/28/18	0/13/29/19	0.187	0.911
Borrmann type (Ⅰ/Ⅱ/Ⅲ/Ⅳ)	6/15/31/9	7/16/29/7	1.761	0.623
Histological type (differentiated/undifferentiated)	31/30	32/29	0.033	0.856
Operation time	207.7 ± 39.8	218.0 ± 56.5	1.152	0.252
Blood loss	211.3 ± 77.6	203.7 ± 54.6	0.617	0.538
Number of lymph nodes	29.3 ± 10.5	28.5 ± 8.6	0.479	0.633
Anastomotic method (billroth Ⅰ/Ⅱ Roux-en-Y)	0/35/26	0/34/25	0.146	0.702
Gastrectomy method (proximal/distal/total)	0/35/26	0/34/25	0.146	0.702
Lymph node dissection method (D2/D2PRO)	31/20	28/21	0.082	0.775
With organ resection (yes/no)	11/50	12/47	0.103	0.748
TNM stage (1/2/3/4)	0/18/33/10	0/16/32/9	0.050	0.975

Table 2 Post-operative complications in the trial group and the control group

Complication	Trial group	Control group	*P*-value
Pancreatic fistula	2	3	0.484
Stoma fistula	1	0	0.508
Peritoneal effusion or abscess	1	6	0.046
Bowel obstruction	0	1	0.492
Pneumonia	2	0	0.256
Chylous fistula	3	3	0.644
Incision infection or dehiscence	2	1	0.513
Post-operative pancreatitis	1	2	0.487
Total	14	17	0.463

postoperative food intake, we chose to provide parenteral nutritional support. Gastric tubes were not routinely used following total gastrectomy but were routinely used for distal gastrectomy to observe postoperative drainage. Peritoneal drainage tubes were routinely used after gastric cancer surgery. For easy comparison, the indication for tube withdrawal was drainage ≤ 100 mL/d for > 3 d with normal color and quality or gastric fluid ≤ 100 mL/d for > 3 d postoperatively, irrespective of passage of gas through the anus. Drainage tubes were used in patients with pancreatic dysfunction or chylous fistula, as appropriate.

Statistical analysis

Measurement data were expressed as mean ± SD, and were analyzed using the *t* test; enumeration data were analyzed using the χ^2 test. The accepted level of significance was $P < 0.05$. SPSS version 16.0 (SPSS, Chicago, IL, United States) was used for all statistical analysis.

RESULTS

Starting in 2010, 120 patients were recruited into this study from the single site of the First Affiliated Hospital of Sun Yat-Sen University. They were randomized into a study group ($n = 61$) and a control group ($n = 59$) after the operation. Patients in the two groups presented with stable vital signs and no significant abnormality in liver/kidney function, blood lipids, or electrolytes during the period of drug administration. Intravenous infusion of nutrient fluid was well tolerated in all patients. Detailed information about patients in the two groups is given in Table 1. The differences in clinicopathological indicators were not statistically significant ($P > 0.05$). Moreover, the mean hospitalization cost in the treatment and control groups was similar (44584.51 ± 5922.57 RMB *vs* 42780.93 ± 8826.45 RMB, $t = 1.318$, $P = 0.190$).

Postoperative complications occurred in 14 patients (23%) in the study group ($n = 61$). Complications included pancreatic fistula in two (3.3%); stoma fistula, peritoneal effusion or infection, pneumonia, hemorrhage, incision complication, or post-operative pancreatitis in one each (1.6%); and chylous fistula in three (4.9%). In the control group ($n = 59$), 15 patients presented with complications (29%). Peritoneal effusion or infection occurred in six patients (10%), and the difference was statistically significant ($P < 0.05$). Other complications included pancreatic fistula in three (4.3%); pneumonia, hemorrhage, or incision complication in one each (1.7%); postoperative pancreatitis in two (3.4%); and chylous fistula in three (5%), but none of the differences was statistically significant (Table 2). We observed that when postoperative complications occurred, the treatment group cost 6372.52 ± 3391.40 yuan and the control group spent 9884.20 ± 4218.90 yuan. The cost differences were statistically significant ($t = 2.514$, P=0.017).

Gastric tubes were just routinely used for distal gastrectomy to observe postoperative drainage. Gastric tubes were routinely used in 35 patients undergoing distal gastrectomy in the study group and 34 in the control group. The mean volume of gastric fluid within 3 d after the operation was 136.1 ± 74.5 mL in the study group and 201.4 ± 81.0 mL in the control group, and the difference was statistically significant. The duration of indwelling gastric tube was 2.7 ± 1.0 d in the study group, and 3.3 ± 1.6 d in the control group. The difference was statistically significant ($P < 0.05$) (Table 3).

Peritoneal drainage tubes were used in all 61 patients in the study group and in all 59 patients in the control

Table 3 Gastric and peritoneal drainage volumes and duration in the study group and the control group

	Study group	Control group	Statistic value	*P*-value
Mean daily drainage volume of gastric fluid (mL)	*n* = 35	*n* = 34		
mean ± SD	136.1 ± 74.5	201.4 ± 81.0	4.595	< 0.001
Range	20-400	50-800		
Gastric tube indwelling duration (d)				
mean ± SD	2.7 ± 1.0	3.3 ± 1.6	2.390	0.018
Mean peritoneal drainage volume (mL)	*n* = 61	*n* = 59		
mean ± SD	165.9 ± 73.1	203.1 ± 99.2	2.395	0.018
Range	50-350	80-550		
Drainage tube indwelling duration (d)				
mean ± SD	4.1 ± 1.0	5.0 ± 1.8	3.365	0.001

Table 4 Drainage volume of chyle after the operation in the trial group and the control group

	Trial group (*n* = 61)	Control group (*n* = 59)	Statistic value	*P*-value
Peritoneal drainage volume (mL)				
mean ± SD	258.3 ± 60.1	388.9 ± 63.7	2.745	0.041
Range	210.0-360.0	330.0-510.0		
Drainage duration (d)				
mean ± SD	7.7 ± 2.5	15.8 ± 4.4	2.800	0.038
Range	5.0-10.0	11.0-20.0		

group after the operation. Within 3 d postoperatively, the mean peritoneal drainage volume was 165.9 ± 73.1 mL in the study group and 203.1 ± 99.2 mL in the control group. The duration of indwelling drainage tube was 4.1 ± 1.0 d in the study group and 5.0 ± 1.8 d in the control group. The differences were statistically significant ($P < 0.05$) (Table 3).

Three patients in the study group and three in the control group developed chylous fistula. The difference was not statistically significant ($P > 0.05$). In the three patients with chylous fistula in the study group and the three patients with chylous fistula in the control group, the mean drainage volume was 258.3 ± 60.1 and 388.9 ± 63.7 mL, respectively ($P < 0.05$). The duration of drainage was 7.7 ± 2.5 and 15.8 ± 4.4 d ($P < 0.05$), respectively, within 7 d postoperatively. These differences were statistically significant ($P < 0.05$) (Table 4).

Two patients in the study group and three in the control group met the diagnostic criteria for pancreatic fistula. Six patients in the study group and four in the control group presented with postoperative pancreatic dysfunction. No significant difference was found between the study group and the control group in terms of serum amylase concentrations on days 1, 3 and 5 after the operation ($P > 0.05$), whereas differences in drainage volumes were statistically significant ($P < 0.05$) on day 1 (191.0 ± 61.2 *vs* 281.7 ± 106.4), day 3 (171.1 ± 44.0 *vs* 224.0 ± 54.6), and day 5 (120.0 ± 64.1 *vs* 178.9 ± 47.6) postoperatively. Regarding amylase in drainage fluid, significant differences were found on day 1 (808.6 ± 133.5 *vs* 1108.6 ± 246.9) ($P < 0.05$) and day 3 (388.0 ± 154.5 *vs* 630.3 ± 215.0) ($P < 0.05$) postoperatively ($P < 0.05$), but not on day 5 (108.4 ± 72.1 *vs* 134.6 ± 92.6) ($P > 0.05$) (Table 5).

DISCUSSION

Somatostatin is a cyclic peptide hormone consisting of 14 amino acids. It mainly acts on the pituitary gland to inhibit release of growth hormone, and may also inhibit secretion of various gastrointestinal and pancreatic hormones. It even has the effect of inhibiting tumor cell growth[13]. Somatostatin also can reduce secretion of digestive juices (pancreatic juice in particular), promote absorption of water and electrolytes, maintain water-electrolyte and acid-base balances, improve blood circulation of the intestinal wall, reduce absorption of bacteria and toxins, decrease the level of toxins in plasma, accelerate resolution of inflammation, stimulate T cell proliferation, and enhance physical immunity[14]. Effects of somatostatin in treating alimentary tract hemorrhage, fistula, and obstruction have been reported frequently[15].

Some researchers believe that resection of the capsule of the pancreas does not increase the incidence of postoperative pancreatic fistula, which is associated with perioperative injury of neighboring pancreatic tissue[7]. However, according to Japanese reports, pancreatic fistula following total gastrectomy is a complication with the highest incidence (9%-19%)[16-18]. Acute pancreatitis occurring after gastrectomy also has been reported[19,20], but the incidence in this study was not high, possibly because removal of the capsule of the pancreas has only insignificant effects on the pancreas, and resultant leakage of pancreatic juice is limited and minimal. Japanese researchers believe that pancreatic complications occur rarely in patients whose amylase concentration in drainage fluid on day 1 after gastrectomy is < 1000 U[21].

In this study, postoperative pancreatic fistula occurred in five patients, but 15 patients presented with concomi-

Table 5 Post-operative amylase in blood and drainage fluid and peritoneal drainage volumes of patients with pancreatic fistula in the study group and the control group

	Day 1 post-operation		Day 3 post-operation		Day 5 post-operation	
	Study group (n = 8)	Control group (n = 7)	Study group (n = 8)	Control group (n = 7)	Study group (n = 8)	Control group (n = 7)
Serum amylase	165.1 ± 40.2 t value = 0.577	179.1 ± 64.2 P = 0.572	79.0 ± 33.4 t value = 1.590	107.8 ± 45.2 P = 0.130	49.0 ± 22 t value = 1.853	80.7 ± 48.8 P = 0.081
Drainage volume	191.0 ± 61.2 t value = 2.309	281.7 ± 106.4 P = 0.034	171.1 ± 44.0 t value = 2.308	224.0 ± 54.6 P = 0.034	120.0 ± 64.1 t value = 2.251	178.9 ± 47.6 P = 0.038
Amylase in drainage fluid	808.6 ± 133.5 t value = 2.521	1108.6 ± 246.9 P = 0.022	388.0 ± 154.5 t value = 2.532	630.3 ± 215.0 P = 0.025	108.4 ± 72.1 t value = 0.616	134.6 ± 92.6 P = 0.549

tant pancreatic dysfunction, manifested mainly as postoperative increase of amylase in drainage fluid. Postoperative use of somatostatin could significantly decrease the amylase concentration in drainage fluid, and the volume and duration of drainage. Additionally, it was found that somatostatin could decrease the volume and duration of peritoneal drainage in patients with normal amylase in drainage fluid in the study group. No explanation or report on relevant mechanisms is available, although one possibility is that somatostatin can reduce gastrointestinal hemorrhage and edema and postoperative peritoneal effusion[14,15]. It can be inferred that somatostatin is useful for preventing postoperative accumulation of pancreatic fluid and peritoneal effusion and infection secondary to fluid accumulation.

During this study, a similar incidence of lymphatic fistula was found in the two groups. In total, six patients (6/120, 5%) presented with lymphatic fistula. The incidence was higher than that previously reported[22]. Lymphatic fistula usually occurs 1-7 d postoperatively and can heal spontaneously in most patients. The operation itself and postoperative management are primary factors responsible for lymphatic fistula[23]. Most of our patients had advanced gastric cancer, therefore, the incidence of lymphatic fistula after extended lymph node dissection was greater than that after D1 operation[22]. Somatostatin is ineffective in reducing the occurrence of lymphatic fistula, but may significantly decrease the volume and duration of drainage of lymphatic fistula, and shorten the duration of indwelling drainage tubes. The mechanism of the earliest reported treatment of lymphorrhagia with somatostatin[24] was possibly associated with reduction of gastrointestinal absorption of fat. In addition, by reducing visceral blood flow, endocrine effects involving specific gastrointestinal somatostatin receptors may also reduce lymphorrhagia[25,26].

The incidence of primary operation-related complications such as stoma fistula, pancreatic fistula, and hemorrhage was similar in the two groups. The above complications correlated directly with the operation and patient factors, and the total incidence of the above complications was 4%-6%, which is not high[27]. The total number of patients in our study was not large; hence, more patients are needed to verify the clinical effects of somatostatin in reducing complications due to ascites and infection. However, somatostatin has demonstrated outstanding clinical performance in reducing peritoneal effusion, in reducing peritoneal drainage and effusion after occurrence of complications, in shortening the duration of drainage, and particularly in reducing progression and duration of diseases secondary to complications and in promoting postoperative rehabilitation of patients. It can be anticipated that more clinical case studies will reveal the important clinical benefits of somatostatin in the prevention of postoperative complications.

COMMENTS

Background

To enhance the degree of radical lymph node dissection for advanced gastric cancer, standardized D2 lymphadenectomy and vagina vasorum dissection are essential for patients with advanced gastric cancer. Vagina vasorum dissection is complete removal of vascular adventitia and fibrous connective tissue, as well as nerve tissue around the vascular sheath. However, concern has been raised by surgeons about the increase in postoperative complications, such as pancreatic fistula or peritoneal effusion. Hence, somatostatin is used after gastric cancer surgery to reduce the high risk of postoperative complications.

Research frontiers

Most of the studies about postoperative complications in gastric cancer open surgery were focused on the preoperative status and surgical quality. Fewer studies investigated drug treatment for reducing postoperative complications.

Innovations and breakthroughs

Few studies have explored the clinical effects of somatostatin in postoperative patients with advanced gastric cancer after radical surgery and standardized D2 lymphadenectomy, especially in preventing postoperative complications. The study revealed that somatostatin has an important role in reducing the volume and duration of surgical drainage and related complications.

Applications

Authors found that somatostatin had a major role in reducing the volume and duration of surgical drainage and related complications. However, there was no significant increase in hospitalization costs between the two groups. Hence, somatostatin does not increase the economic burden of patients, and it promotes postoperative recovery and reduces operation-related complications.

Terminology

Vagina vasorum dissection is complete removal of vascular adventitia and fibrous connective tissue, as well as nerve tissue around the vascular sheath.

Peer review

Postoperative administration of somatostatin can improve the safety of gastric cancer surgery, reduce postoperative complications, and promote recovery following D2 radical gastrectomy plus dissection of the vascular sheath.

REFERENCES

1 **Bonenkamp JJ**, Hermans J, Sasako M, van de Velde CJ, Welvaart K, Songun I, Meyer S, Plukker JT, Van Elk P, Obertop H, Gouma DJ, van Lanschot JJ, Taat CW, de Graaf PW, von Meyenfeldt MF, Tilanus H. Extended lymph-node dissection

for gastric cancer. *N Engl J Med* 1999; **340**: 908-914 [PMID: 10089184 DOI: 10.1056/NEJM199903253401202]
2 **Cuschieri A**, Weeden S, Fielding J, Bancewicz J, Craven J, Joypaul V, Sydes M, Fayers P. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group. *Br J Cancer* 1999; **79**: 1522-1530 [PMID: 10188901 DOI: 10.1038/sj.bjc.6690243]
3 **Sakuramoto S**, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, Furukawa H, Nakajima T, Ohashi Y, Imamura H, Higashino M, Yamamura Y, Kurita A, Arai K. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med* 2007; **357**: 1810-1820 [PMID: 17978289 DOI: 10.1056/NEJMoa072252]
4 **Wu CW**, Hsiung CA, Lo SS, Hsieh MC, Chen JH, Li AF, Lui WY, Whang-Peng J. Nodal dissection for patients with gastric cancer: a randomised controlled trial. *Lancet Oncol* 2006; **7**: 309-315 [PMID: 16574546 DOI: 10.1016/S1470-2045(06)70623-4]
5 **Hu JK**, Yang K, Zhang B, Chen XZ, Chen ZX, Chen JP. D2 plus para-aortic lymphadenectomy versus standardized D2 lymphadenectomy in gastric cancer surgery. *Surg Today* 2009; **39**: 207-213 [PMID: 19280279 DOI: 10.1007/s00595-008-3856-x]
6 **Peng JJ**, He YL, Zhan WH, Xiao P, Cai SR, Zhang CH, Wu H. Vagina vasorum dissection during D2 lymphadenectomy for gastric carcinoma. *World J Gastroenterol* 2007; **13**: 1867-1869 [PMID: 17465483]
7 **Imamura H**, Kurokawa Y, Kawada J, Tsujinaka T, Takiguchi S, Fujiwara Y, Mori M, Doki Y. Influence of bursectomy on operative morbidity and mortality after radical gastrectomy for gastric cancer: results of a randomized controlled trial. *World J Surg* 2011; **35**: 625-630 [PMID: 21161652 DOI: 10.1007/s00268-010-0914-5]
8 **Jagad RB**, Koshariya M, Kawamoto J, Chude GS, Neeraj RV, Lygidakis NJ. Postoperative hemorrhage after major pancreatobiliary surgery: an update. *Hepatogastroenterology* 2008; **55**: 729-737 [PMID: 18613444]
9 **Koukoutsis I**, Bellagamba R, Morris-Stiff G, Wickremesekera S, Coldham C, Wigmore SJ, Mayer AD, Mirza DF, Buckels JA, Bramhall SR. Haemorrhage following pancreaticoduodenectomy: risk factors and the importance of sentinel bleed. *Dig Surg* 2006; **23**: 224-228 [PMID: 16874003 DOI: 10.1159/000094754]
10 **Bassi C**, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; **138**: 8-13 [PMID: 16003309 DOI: 10.1016/j.surg.2005.05.001]
11 **Japanese Gastric Cancer Association**. Japanese Classification of Gastric Carcinoma - 2nd English Edition - *Gastric Cancer* 1998; **1**: 10-24 [PMID: 11957040]
12 **Tanguy M**, Seguin P, Mallédant Y. Bench-to-bedside review: Routine postoperative use of the nasogastric tube - utility or futility? *Crit Care* 2007; **11**: 201 [PMID: 17214909 DOI: 10.1186/cc5118]
13 **Okarvi SM**. Peptide-based radiopharmaceuticals and cytotoxic conjugates: potential tools against cancer. *Cancer Treat Rev* 2008; **34**: 13-26 [PMID: 17870245 DOI: 10.1016/j.ctrv.2007.07.017]
14 **Van Op den Bosch J**, Adriaensen D, Van Nassauw L, Timmermans JP. The role(s) of somatostatin, structurally related peptides and somatostatin receptors in the gastrointestinal tract: a review. *Regul Pept* 2009; **156**: 1-8 [PMID: 19362110 DOI: 10.1016/j.regpep.2009.04.003]
15 **Leandros E**, Antonakis PT, Albanopoulos K, Dervenis C, Konstadoulakis MM. Somatostatin versus octreotide in the treatment of patients with gastrointestinal and pancreatic fistulas. *Can J Gastroenterol* 2004; **18**: 303-306 [PMID: 15152279]
16 **Okabayashi T**, Kobayashi M, Sugimoto T, Okamoto K, Matsuura K, Araki K. Postoperative pancreatic fistula following surgery for gastric and pancreatic neoplasm; is distal pancreaticosplenectomy truly safe? *Hepatogastroenterology* 2005; **52**: 233-236 [PMID: 15783038]
17 **Sasako M**, Katai H, Sano T, Maruyama K. Management of complications after gastrectomy with extended lymphadenectomy. *Surg Oncol* 2000; **9**: 31-34 [PMID: 11525304 DOI: 10.1016/S0960-7404(00)00019-0]
18 **Nobuoka D**, Gotohda N, Konishi M, Nakagohri T, Takahashi S, Kinoshita T. Prevention of postoperative pancreatic fistula after total gastrectomy. *World J Surg* 2008; **32**: 2261-2266 [PMID: 18670802 DOI: 10.1007/s00268-008-9683-9]
19 **Testi W**, Staffieri C, Malatesti R, Macchitella Y, De Martino A, Botta G, Cirianni D, Genovese A, Bing C, Logatt M. [Postoperative acute pancreatitis: our experience and review of the literature]. *Minerva Chir* 2007; **62**: 19-24 [PMID: 17287690]
20 **Marrelli D**, Pedrazzani C, Neri A, Corso G, DeStefano A, Pinto E, Roviello F. Complications after extended (D2) and superextended (D3) lymphadenectomy for gastric cancer: analysis of potential risk factors. *Ann Surg Oncol* 2007; **14**: 25-33 [PMID: 17024558 DOI: 10.1245/s10434-006-9063-3]
21 **Iwata N**, Kodera Y, Eguchi T, Ohashi N, Nakayama G, Koike M, Fujiwara M, Nakao A. Amylase concentration of the drainage fluid as a risk factor for intra-abdominal abscess following gastrectomy for gastric cancer. *World J Surg* 2010; **34**: 1534-1539 [PMID: 20198371 DOI: 10.1007/s00268-010-0516-2]
22 **Halkic N**, Abdelmoumene A, Suardet L, Mosimann F. Postoperative chylous ascites after radical gastrectomy. A case report. *Minerva Chir* 2003; **58**: 389-391 [PMID: 12955061]
23 **Lin SZ**, Tong HF, Qin YS, Ni ZL, Zhang W. Prevention and treatment of lymphorrhoea following surgery for gastric cancer. *ANZ J Surg* 2010; **80**: 515-518 [PMID: 20795965 DOI: 10.1111/j.1445-2197.2009.05041.x]
24 **Ulíbarri JI**, Sanz Y, Fuentes C, Mancha A, Aramendia M, Sánchez S. Reduction of lymphorrhagia from ruptured thoracic duct by somatostatin. *Lancet* 1990; **336**: 258 [PMID: 1973814]
25 **Collard JM**, Laterre PF, Boemer F, Reynaert M, Ponlot R. Conservative treatment of postsurgical lymphatic leaks with somatostatin-14. *Chest* 2000; **117**: 902-905 [PMID: 10713026 DOI: 10.1378/chest.117.3.902]
26 **Reubi JC**, Horisberger U, Waser B, Gebbers JO, Laissue J. Preferential location of somatostatin receptors in germinal centers of human gut lymphoid tissue. *Gastroenterology* 1992; **103**: 1207-1214 [PMID: 1356871]
27 **Degiuli M**, Sasako M, Calgaro M, Garino M, Rebecchi F, Mineccia M, Scaglione D, Andreone D, Ponti A, Calvo F. Morbidity and mortality after D1 and D2 gastrectomy for cancer: interim analysis of the Italian Gastric Cancer Study Group (IGCSG) randomised surgical trial. *Eur J Surg Oncol* 2004; **30**: 303-308 [PMID: 15028313 DOI: 10.1016/j.ejso.2003.11.020]

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