

ORIGINAL PAPERS

Duodenal fistula after gastrectomy: Retrospective study of 13 new cases

María de los Ángeles Cornejo, Pablo Priego, Diego Ramos, Magdalena Coll, Araceli Ballester, Julio Galindo, Francisca García-Moreno, Gloria Rodríguez, Pedro Carda and Eduardo Lobo

Division of Esophagogastric, Bariatric and Minimally Invasive Surgery. Hospital Universitario Ramón y Cajal. Madrid, Spain

ABSTRACT

Introduction: Duodenal stump fistula (DSF) after gastrectomy has a low incidence but a high morbidity and mortality, and is therefore one of the most aggressive and feared complications of this procedure.

Material and methods: We retrospectively evaluated all DSF occurred at our hospital after carrying out a gastrectomy for gastric cancer, between January 1997 and December 2014. We analyzed demographic, oncologic, and surgical variables, and the evolution in terms of morbidity, mortality and hospital stay.

Results: In the period covered in this study, we performed 666 gastrectomies and observed DSF in 13 patients (1.95%). In 8 of the 13 patients (61.5%) surgery was the treatment of choice and in 5 cases (38.5%) conservative treatment was carried out.

Postoperative mortality associated with DSF was 46.2% (6 cases). In the surgical group, 3 patients developed severe sepsis with multiple organ failure, 2 patients presented a major hematemesis which required endoscopic haemostasis, 1 patient had an evisceration and another presented a subphrenic abscess requiring percutaneous drainage. Six patients (75%) died despite surgery, with 3 deaths in the first 24 hours of postoperative care. The 2 patients who survived after the second surgical procedure had a hospital stay of 45 and 84 days respectively. In the conservative treatment group the cure rate was 100% with no significant complications and an average postoperative hospital stay of 39.5 days (range, 26-65 days).

Conclusion: FMD is an unusual complication but it is associated with a high morbidity and mortality. In our experience, conservative management has shown better results compared with surgical treatment.

Key words: Gastric cancer. Surgery. Duodenal stump fistula. Treatment. Morbidity. Mortality. Risk factors. Gastrectomy.

INTRODUCTION

Duodenal stump fistula (DSF) is one of the most aggressive complications after gastrectomy. Although the incidence reported in the literature is low, its association with

a high morbidity and mortality, as well as prolongation of hospital stay, makes it one of the surgeon's most feared postoperative problems (1).

The reported incidence of DSF is about 3%, the overall mortality ranges from 7% to 67%, and spontaneous cure rates are between 28 and 92%. There are few publications regarding this subject, and most are small series which include gastrectomies performed for different reasons (sometimes even emergency surgeries), so the dates are heterogeneous and probably not comparable (2,3).

Different mechanisms have been proposed to explain the pathogenesis, such as inappropriate duodenal stump closure, inadequate vascularization, neoplastic involvement of the resection line, inflammation/hematoma of the duodenal wall and postoperative duodenal distension, etc. However, given that most of the studies have a small number of cases, it is difficult to establish possible risk factors for DSF and, therefore, to avoid this serious complication (4,5).

The aim of this study is to retrospectively analyze our clinical management data in case of DSF post-gastric cancer gastrectomy, assessing not only the incidence but also the possible risk factors, taking into account those mentioned in previous publications.

MATERIAL AND METHODS

We retrospectively evaluated all DSF occurred at our hospital after performing a gastrectomy. Between January 1997 and December 2014, 666 gastrectomies (total or subtotal) were performed at the Hospital Universitario Ramón y Cajal (Madrid, Spain) for gastric cancer. We excluded from our study gastrectomies secondary to peptic ulcer, emergency procedures, and all DSF that were not related to elective oncological gastrectomy.

We define DSF by the presence of biliary-enteric drainage which exits through the abdominal wall, regardless of its clinical impact, confirmed by an abdominal-pelvic CT scan.

Received: 15-07-2015
Accepted: 02-09-2015

Correspondence: Pablo Priego-Jiménez. Division of Esophagogastric, Bariatric and Minimally Invasive Surgery. Hospital Universitario Ramón y Cajal. Ctra. Colmenar, km. 9,100. 28034 Madrid, Spain
e-mail: papriego@hotmail.com

Cornejo MÁ, Priego P, Ramos D, Coll M, Ballester A, Galindo J, García-Moreno F, Rodríguez G, Carda P, Lobo E. Duodenal fistula after gastrectomy: Retrospective study of 13 new cases. *Rev Esp Enferm Dig* 2016;108:20-26.

We analyzed demographic variables, such as age, sex, associated morbidities and the ASA score; cancer related variables such as histology, location and stage; surgical variables such as the type of gastrectomy and reconstruction, surgical approach, duration of surgery, cancer distal margin involvement, type of duodenum resection and if there was an associated reinforcement, intraoperative complications, etc. We also evaluated postoperative complications, re-interventions, mortality, length of stay and readmissions.

We define conservative treatment as patient maintenance on *nil per os* (NPO), nasogastric tube, parenteral nutrition, broad-spectrum antibiotics, percutaneous drainage of collections if present in the abdominal pelvic CT scan and/or treatment with somatostatin. Conservative treatment was recommended after an abdominal pelvic CT scan if the patient showed no signs of sepsis and the identified collection was small, localized and accessible to percutaneous drainage.

Surgery was carried out if the patient was hemodynamically unstable or showed signs of systemic inflammatory response, accompanied by an increase in intra-abdominal free fluid or multiple collections not contained in the abdominal pelvic CT. Moreover, we have also studied the different surgical strategies: simple suture of perforation with epiploasty, duodenostomy with a Foley catheter, surgical drainage of collection, etc.

RESULTS

In the period covered in the study, DSF was observed in 13 patients with an incidence of 1.95%. Nine were male (69.2%) and 4 were female (30.8%), with an average age of 71.3 years (range, 48-86 years). 5 cases were identified in the period 1997-2000, 2 cases in 2003-2008 and 6 cases in the period 2009-2014.

The demographic characteristics of patients were reflected in table I.

A subtotal gastrectomy was performed in ten patients (77%) and a total gastrectomy in 3 patients (23%). The reconstruction was Roux-en-Y type in 6 patients (46%) and Billroth II type in the remaining 7 patients (54%). The average duration of surgery was 208 minutes (range, 125-330 minutes). An open surgery was performed in 11 cases (84.6%) and a laparoscopic approach was carried out in 2 cases (15.4%). The average duration of the open surgery was 180 minutes (range, 125-280 minutes) and the laparoscopy had a duration of 290 minutes (range, 250-330 minutes).

Concomitantly to the gastrectomy, a ventral hernia repair, 2 cholecystectomies, an intestinal resection for gastrointestinal stromal tumor (GIST) not previously known and a distal splenopancreatectomy were performed.

The section of the duodenum was mechanical in 12 cases (92%) and with scissors in 1 case (7.7%). In 9 patients (69.23%) duodenal stump had been previously reinforced with a running suture; meanwhile, in the other case the reinforcement was carried out with fibrin adhesive. Difficulties to close the duodenal stump were described in 2 cases secondary to inflammation/fibrosis.

Assessment of the nutritional status of patients before surgery was based on the amount of total proteins and the

number of average preoperative lymphocytes. Total protein was 6.28 g/dl (range, 5.2-7 g/dl), located at the normal lower limit (6-8.3 g/dl). The average preoperative total lymphocyte count was 1,572.2/mm³ (range, 530-3,630/mm³), also in the normal lower limit (1,500-4,000/mm³).

Clinical symptoms of DSF in the conservative treatment group were abdominal pain (3 patients) and bilious-enteric drainage (2 patients); surgical patients had one of the following: hypovolemic or septic shock with or without acute abdomen (7 patients) and bilious drainage output material (in 1 patient). The average number of days from surgery to clinical debut of DSF was 5 days (range, 3-7 days).

Regarding DSF treatment strategy, in 8 cases (61.5%) we opted for a surgical approach and in 5 cases (38.5%), for a conservative treatment. The surgical approach consisted in a duodenostomy in 5 cases (38.5%) associated in 1 case with resection of about 30 cm of necrotic terminal ileum, primary closure in 2 patients (15.4%) after refreshing the wound edges and, finally, surgical scrub with placement of a drainage in 1 case (7.7%). In five patients a feeding jejunostomy was associated (38.5%).

Of the 8 patients surgically treated, 3 developed severe sepsis with multiple organ failure, 2 patients required an endoscopic hemostasis for major hematemesis, 1 had an evisceration, and 1 had a subphrenic abscess which required percutaneous drainage. Six out of the 8 patients (75%) died despite surgery, with 3 deaths in the first 24 hours of postoperative care.

The 2 patients who survived after reintervention had a hospital stay of 45 and 84 days each. However, both were readmitted 4 months later with signs of obstructive jaundice, secondary to lymphatic progression versus recurrence in the duodenal stump, and died during hospitalization.

Of the 5 patients who underwent a conservative approach, none had significant complications, with a cure rate of 100% and a mean postoperative hospital stay of 39.5 days (range 26-65 days). However, 3 patients were readmitted: 1 had a fever of unknown origin, 1 had an efferent loop obstruction that required surgery and another had an obstructive jaundice. Of these 3 patients the last 2 died.

The comparison between conservative treatment and surgical treatment of DSF was reflected in table II.

To summarize, in our series, the overall mortality rate of DSF in the post-operative of total or subtotal gastrectomy secondary to gastric cancer was 46.2% (6 cases), while the cure rate was 53.8% (5 after conservative treatment and 2 after surgery).

The comparison of our results with the 2 largest series reported in the literature on this subject was shown in table III.

DISCUSSION

Duodenal stump fistula (DSF) is one of the most aggressive complications after gastrectomy. Despite its low inci-

Table I. Demographic characteristics of patients

Variable	Number of patients (%)
Age	71.3 years (range, 48-86 years)
Gender	M: 9 (69.2%) F: 4 (30.8%)
ASA score	ASA I: 1 patient (7.7%) ASA II: 3 patients (23%) ASA III: 8 patients (61.54%) ASA IV: 1 patient (7.7%)
Comorbidities	Hypertension: 53.8% Heart disease: 46% COPD: 30% Diabetes Mellitus: 23% Dyslipidemia: 23% HCV liver disease: 7.7%
Previous surgery in 6 patients: 46%	Cholecystectomy: 2 patients Splenectomy due to traffic accident: 1 case Cholecystectomy, hysterectomy and double oophorectomy: 1 case Appendectomy: 1 case Exploratory laparotomy for abdominal trauma: 1 case
Histological type:	
Intestinal type adenocarcinoma	12 cases (92.3%)
Well differentiated	7 cases (59%)
Moderately differentiated	3 cases (23%)
Poorly differentiated	1 case (7.7%)
NA	1 case (7.7%)
Well-differentiated papillary carcinoma	1 case (7.7%)
Tumor site:	
Fundus	2 cases (15%)
Antro	8 cases (61%)
Lesser curvature	2 cases (15%)
Greater curvature	1 case (7.7%)
Tumor stage:	
Stage IA	4 cases (30.7%)
Stage IIA	5 cases (38.48%)
Stage IIIB	1 case (7.7%)
Stage IIIC	1 case (7.7%)
Stage IV	2 cases (14%)
Cancer distal margin involvement:	
R0	11 cases (84.6%)
R1	1 case (7.7%)
R2	1 case (7.7%)

ASA: American Society of Anesthesiology Scoring System; M: Male; F: Female; COPD: Chronic obstructive pulmonary disease; HCV: Hepatitis C virus; NA: Not available.

dence (around 3%), its importance lies in its association with a high morbidity and mortality (overall mortality ranges from 7-67%) and variable spontaneous cure rates (between 28-92% of cases) (2,3,7,8).

In our series, the incidence of DSF was 1.95%, which is close to the rates mentioned in the literature, such as the Italian multicenter study of Cozzaglio et al. (6), in which 3,785 neoplastic gastrectomies were reviewed and where DSF occurred with an incidence of 1.6%; the Orsenigo et

al. study (4) analyzed 1,287 gastrectomies secondary to cancer, estimating an incidence of 2.5%.

Due to the low number of cases in each study, it is very difficult to establish possible risk factors related to DSF which can be avoided (4,5,9-11). In the study of Orsenigo et al. (4), the presence of heart disease, low preoperative lymphocyte number and the absence of reinforcing duodenal stump after performing gastrectomy seem to act as specific risk factors for developing DSF.

Table II. Comparison between conservative treatment and surgical treatment of DSF

	<i>Conservative treatment (5 patients: 38.5%)</i>	<i>Surgical treatment (8 patients: 61.5%)</i>
Type of treatment	NPO, NGT, antibiotics	Duodenostomy: 5 patients (38.4%) Primary closure after refreshing edges: 2 patients (15.4%) Surgical drainage: 1 patient (7.7%) Feeding Jejunostomy associated: 5 patients (38.5%)
Drugs:		
Somatostatin	2 patients	0 patients
Nutrition:		
Parenteral	4 patients	8 patients
Enteral	1 patient	2 patients*
Evolution:		
Healing	5 patients (100%)	2 patients (25%)
Death	0 patients (0%)	6 patients (75%)
Complications	None (0%)	Sepsis with multiple organ failure: 3 patients Hematemesis: 2 patients Evisceration: 1 patient Subphrenic abscess: 1 patient
Hospital stay	39.5 days (range, 26-65 days)	34.3 days (range, 13-84 days)
Readmission	3 patients (60%)	2 patients (100%)

NGT: Nasogastric tube. *Although feeding jejunostomy was performed in 5 patients who underwent surgical treatment, enteral nutrition was used only in 2 of them, since the remaining 3 died in the first 24 hours after surgery.

Table III. Comparison between our series and the literature in relation to DSF

	<i>Orsenigo et al. (4) (2014)</i>	<i>Cozzaglio et al. (6) (2010)</i>	<i>Hospital Universitario Ramón y Cajal (2015)</i>
Number of patients	1,287	3,785	666
DSF cases	32	68	13
Incidence	2.5%	1.6%	1.95%
Surgical treatment	40.6%	39.7%	61.5%
Morbidity	84%	75%	53.8%
Mortality	9.37%	16%	46.2%

In our series, and regarding the association between comorbidities and DSF, we noted that in patients who developed this complication, heart disease was present in up to 46% of them. Another comorbidity associated with DSF, and with which some studies have found statistically significant differences for the development of medical-surgical complications (4,12,13), is the presence of some form of liver disease. However, it was present in only 8% of our patients.

A significant fact was that up to 46% of patients had previously undergone surgery. It is interesting to note, given its anatomical proximity to the duodenal stump, that in 3 patients a cholecystectomy had been previously performed. Furthermore, during surgery, 2 cholecystectomies were carried out simultaneously to the major surgery. We have not found any reference to it in literature, although it is worth taking into account that in our series nearly 40%

of patients had no gallbladder. We do not know whether this intervention could condition a decreased blood supply to the area of the duodenal stump, and therefore it could favor the development of a DSF after a gastrectomy.

Regarding nutritional status, it appears to have an influence not only in the prevention of postoperative complications, but in the early resolution of these once they have occurred (14). Most of the studies related to DSF (4,6) take into account the values of total protein and preoperative lymphocytes, as indicators of preoperative nutritional status. In our study, the values of lymphocytes and preoperative albumin in patients who developed DSF were normal, but in the lower limit. Therefore, malnutrition could have had some importance in poor healing of the duodenal stump after surgery.

Related to surgical technique, margin involvement is not only associated with worse outcomes in cancer surgery, but

it is also associated with a higher incidence of complications (1-10%) especially those related to DSF (15).

In our series, R0 resection was achieved in 84.6% (11 cases out of 13) being in the other two cases R1 and R2. This last case was an elderly patient with locally advanced obstructive gastric cancer which invaded the head of the pancreas and transverse mesocolon, and for whom a palliative gastrectomy was carried out. Therefore, in our experience, the involvement of the surgical resection margin does not appear to be the main cause of DSF.

Traditionally, some authors considered that DSF was most often associated with Billroth II reconstruction due to difficulties in emptying the afferent jejunal loop (16,17). However, other authors (4,6) have found no significant differences between the two types of reconstruction. In our series, 46% of the cases were reconstructed using a Roux-en-Y and 54% with a Billroth II procedure. Despite the low number of patients, a fact that prevents us from getting statistically significant findings, there seems to be no difference between the groups.

Regarding surgical approach, no significant differences were found in the studies in terms of morbidity and mortality between laparoscopy and open surgery (18,19). Nevertheless, our attention is focused on the increasing cases of DSF in recent years, which some authors (6) relate to the increase in laparoscopic surgeries, where there is not always a tendency to close the duodenal stump in the same way as it is done in open surgery. In our experience, of the 13 patients who developed DSF, only 2 patients (15.4%) had a laparoscopic approach. In any case, despite the significant strengthening of the duodenal stump in patients who developed DSF in the study by Orsenigo et al. (4), in our study, 76.92% of the patients who developed DSF had some reinforcement in the duodenum. Therefore, it seems necessary to conduct prospective, randomized and comparative studies to assess the real significance of these results.

Focusing now on the long term treatment of DSF, different surgical approaches have been proposed, such as duodenostomy (20), reparation with rectus abdominal muscle flap (21), closure with a duodenojejunostomy in Roux-en-Y (22) or performing a pancreaticoduodenectomy (23).

More recently, and with the development of minimal invasive techniques, it has been proposed the treatment of fistulas with percutaneous drainage (24), transparieto-hepatic drainage (25), endoscopic clips (26), fistuloscopy (27), obliterating the fistula using cyanoacrylate or prolamine (28) and even the use of a biliary transparietal hepatic occlusion balloon drainage (29).

Both in the studies of Babu et al. (7) and Aurello et al. (8), conservative management is considered to be the treatment of choice and should be extended at least 4 to 6 weeks, unless the clinical condition of the patient worsens and requires intervention.

In our opinion, the indication of a conservative or a surgical approach has previously been described. If the patient has no signs of sepsis and the collection identified

in the CT scan is small, localized and accessible to percutaneous drainage, we will choose a conservative approach; but if the patient is hemodynamically unstable or shows signs of systemic inflammatory response with an increase in intra-abdominal free fluid or multiple collections not contained in the abdominopelvic CT, we will opt for surgery. In this case, the most frequently used technique is a duodenostomy with a Foley catheter associated with an external drainage.

Recently, Aurello et al. (8) published a systematic review of the literature on the management of DSF after gastrectomy for gastric cancer. In their study, a total of 145 cases of DSF were collected between 1988 and 2014, with an overall mortality rate of 11.7%. In our series, we observed an overall mortality of 46.2%, significantly higher. The high mortality associated with surgical treatment is very striking. Of the 8 patients who received surgical treatment, six died (75%), 3 of them in the first 24 hours. However, we do not believe that this is because the surgery has no role in the treatment of DSF after gastrectomy, but probably because these were worse cases and, therefore, they did not seem likely to benefit from conservative treatment. Therefore, we believe it is crucial to make an early diagnosis in order to start treatment or to re-operate as quickly as possible, thus reducing morbidity and mortality associated with this life-threatening complication.

On the other hand, the morbidity rate (53.8%) was lower than those described by Orsenigo (4) and Cozzaglio et al. (6) (84% and 75% respectively).

In either case (surgical vs. conservative approach), DSF was devastating for all patients, because although 69.2% of them had a tumor stage I-II A, and therefore with a not poor prognosis, 10 of the 13 patients (76.92%) died, either in the immediate postoperative period or a few months after surgery due to recurrence of their disease, maybe because they were not able to receive adjuvant treatment after surgery.

In our series, the cure rate after DSF was 53.8%, rising to 100% for patients who received conservative treatment. This latter observation is consistent with that published by Aurello et al. (92.3%) (8).

Finally, despite some authors (30-33) who showed a decrease in the fistula output and shortening of the time needed to close it by applying somatostatin and/or analogs such as octreotide, we are not very optimistic regarding the use of these agents.

CONCLUSION

DSF is an unusual complication but it is associated with a high morbidity and mortality. In our experience, conservative management has shown better results in terms of morbidity and mortality compared with surgical treatment. It would be interesting to conduct further prospective studies in order to study possible risk factors associated

with this complication, and therefore be able to obtain a decrease in its incidence.

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