



Review Article

MANAGEMENT OF DUODENAL STUMP FISTULA FOLLOWING GASTRECTOMY FOR GASTRIC CANCER: A SYSTEMATIC REVIEW

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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. This study was designed to assess the most effective treatment of duodenal stump fistula (DSF) after gastrectomy for gastric cancer.

Methods: A systematic analysis of PubMed, MEDLINE, Current Contents, UpToDate databases, and the Cochrane Library Databases were carried out. A total of 80 manuscripts were retrieved and screened and nine studies published between 2009 and 2016 were selected. 241 cases of DSF were included in the study according to inclusion criteria. Only patients who underwent gastrectomy for gastric cancer were included in our review. Data about patient's characteristics, types of treatment, short and long-term outcomes were extracted and analyzed.

Results: Three different approaches were applied: conservative (75 cases), surgical (138 cases) and percutaneous (59 cases). The overall mortality rate was 19% and significant complications were identified in 21% cases. Significant complications included sepsis, abscesses, peritonitis, bleeding, pneumonia and multiple organ failure. The conservative approach was reported in 5 studies including 75 patients who were clinically stable and complete resolution occurred in 92.3% of patients with a mean healing time of 35 days. Surgery was carried out if the patient was haemodynamically unstable or showed signs of sepsis. Overall outcome after surgery was poor with 31.1% mortality derived from six studies and in-hospital stay ranged from 1 to 1035 days (median 19). Percutaneous approach was often associated with conservative treatment and consisted of abscess drainage, biliary drainage or biliary diversion. The median healing time in this group was 42 days.

Conclusion: Conservative approach is the first line of treatment in DSF, sometimes associated with percutaneous approach. Surgery should be reserved for severe cases or when conservative measures fail.

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Introduction

Gastric cancer is one of the most common causes of cancer death in the world. In the UK, the incidence is approximately 15 per 100000 per year, in the USA 10 per 100000 per year and in eastern Europe 40 per 100000 per year. In Japan, the incidence is approximately 70 per 100000 per year¹. A total or subtotal gastrectomy with R0 margins remains the standard of care for gastric cancer². Despite this, in low volume centers gastrectomy still remains a challenging procedure with a notable morbidity rate (33% - 43%) and mortality rate (7% - 12%)³. 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 problems⁴.

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%⁵. Different mechanisms have been proposed to explain the pathogenesis of DSF, 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^{6,7}.

However, despite the importance of this kind of complication, there are no reports indicating the correct management of this life-threatening condition in patients with gastric cancer. We reviewed the literature from 2009 to 2016 on management of duodenal stump leakage after gastrectomy for gastric cancer to identify the most appropriate treatment of duodenal stump fistula, and recent trends and approaches in its management.

Materials and Methods

Electronic literature search was performed on PubMed, MEDLINE, Current Contents, UpToDate databases, and the Cochrane Library Databases plus manual reference checks by entering the strings "duodenal stump fistula and treatment after gastrectomy" or "duodenal stump leak and treatment after gastrectomy". All articles on DSF after gastrectomy published between January 2009 and December 2016 were reviewed. A total of 80 manuscripts were retrieved. Screening was done by assessing title, abstract section, and keywords to select studies for further research. Case-control studies, cohort studies, randomized clinical trials, multicenter trials and case series on total and subtotal gastrectomies for gastric cancer and post-operative duodenal stump leakage management in the form of conservative, endoscopic,

percutaneous and surgical treatment were included in the study. Only patients with gastric cancer were included in our review. Single case reports regarding post-gastrectomy DSF were excluded. Studies reporting pediatric patients and non-surgery related fistulae were not included. A total of nine studies were considered eligible for review and total patients were 241.

Cozzaglio et al^{8,9,10} were involved in three different types of studies with different centres, cohorts of patients and study periods. Hence, all three were included in this review.

Results

Management of post-operative DSF was categorized on the basis of three different approaches: conservative (75 cases), surgical (138 cases) and percutaneous (59 cases). Percutaneous treatment was again undertaken by three ways: percutaneous transhepatic biliary diversion (PTBD) (13 cases), percutaneous drainage of abscess (31 cases) and percutaneous duodenostomy by inserting Foley catheter (15 cases).

The conservative approach was reported in 5 studies including 75 patients. Management consisted of administration of intravenous antibiotics, use of somatostatin or octetide or gabexate mesylate, total parenteral or enteral nutrition, positioning of nasogastric tube and close monitoring^{8,11}. It was considered as the first line of treatment in patients with stable general condition (without sepsis, peritonitis or abscess) and often associated or followed by percutaneous treatment. According to the reported data, complete resolution occurred in 92.3% of patients with a mean healing time of 35 days¹¹.

Surgery was carried out if the patient was haemodynamically unstable or showed signs of sepsis, accompanied by an increase in intra-abdominal free fluid or multiple collections not contained in the abdominal pelvic CT. The surgical techniques included duodenostomy with a Foley catheter, direct stump closure, stump resection and closure, stump closure with omental patch, external duodenal drainage, surgical abdominal drainage, duodeno-jejunostomy and use of rectus muscle flap. 6 studies reported this approach and presented a total of 138 cases. Overall outcome after surgery was poor with 31.1% mortality derived from six studies and in-hospital stay ranged from 1 to 1035 days (median 19)^{8,12}.

Percutaneous approach was often associated with conservative treatment and consisted of abscess drainage, biliary drainage or biliary diversion^{8,13}. The appropriate treatment methods were determined according to each patient's clinical situation and expertise available. 5 studies were labeled with this technique managing 59 patients. The median healing

Table 1: Review of the literature

Ref. (Year)	Country	Period	Patients, n	Study	Mean Healing time in days (range)	Conservative treatment	Surgical treatment	PTBD	PDA	Percutaneous duodenostomy	Re sul ts
Oh et al ^[12] (2009)	South Korea	1987-2004	5	RS	18(10-28)	0	5	0	0	0	Resolved
Cozzaglio et al ^[8] (2010)	Italy	1991-2006	68	RS MS	19(1-1035)	51	27	4	15	2	Complications 51 (75%): death 11 (16.2%) 3 resolved; 3 (50%) death
Cozzaglio et al ^[9] (2011)	Italy	2005-2010	6	PR	43(22-604)	0	0	6	0	0	Resolved
Lee et al ^[15] (2013)	South Korea	2005-2010	10	RS	28(10-58)	0	0	0	0	10	Resolved
Oresingo et al ^[6] (2014)	Italy	1987-2012	32	RS	31.2 ± 19.7 (Non surgical) 45.2 ± 57.4 (Surgical)	11	13	3	5	0	Non surgical: resolved Surgical: 10 resolved, 3 (23%) death Conservative: resolved Surgical: 8 resolved, 2 (20%) death Conservative: resolved Surgical: 2 resolved, 6 (75%) death
Kim et al ^[7] (2014)	South Korea	2002-2012	13	RS	11.7 (Conservative) 57.3 (Surgical)	3	10	0	0	0	resolved Surgical: 8 resolved, 2 (20%) death Conservative: resolved Surgical: 2 resolved, 6 (75%) death
Corne Jo et al ^[14] (2016)	Spain	1997-2014	13	RS	39.5 (Conservative) 34.3 (surgical)	5	8	0	0	0	resolved Surgical: 2 resolved, 6 (75%) death
Ali et al ^[15] (2016)	South Korea	2010-2014	19	RS	18 (conservative) 33 (PDA) 42 (duodenostomy)	5	0	0	11	3	Resolved
Cozzaglio et al ^[10] (2016)	Italy	1990-2011	75	RS MS	39 (22-68 days)	0	75	0	0	0	54 resolved; 21 (28%) death
Total, n (%)		1987-2014	241		1-1035	75(31.1)	138(57.3)	13(5.4)	31(12.9)	15(6.2)	

RS: Retrospective study; PR: Prospective study; MS: Multicenter study; PTBD: Percutaneous transhepatic biliary diversion; PDA: Percutaneous Drainage of Abscess

time in this group was 42 days¹¹. Percutaneous procedures were relatively safer options but significant mortality was shown in PTBD (50%)⁹. The overall mortality rate was 19% and significant complications were identified in 21% cases from aforementioned nine studies. Complications included sepsis, abscesses, peritonitis, bleeding, pneumonia and multiple organ failure.

Discussion

Duodenal stump fistula (DSF) is one of the most aggressive complications after gastrectomy. Despite its low incidence (around 3%), its importance lies in the association with a high morbidity and mortality (overall mortality 7-67%) and variable spontaneous cure rates (between 28-92% of cases)⁵.

In a recent Italian multi-centric retrospective analysis Cozzaglio et al¹⁰ reported that among 8,268 elective gastrectomies for gastric malignancies, 205 patients developed a DSF, 75 of whom underwent surgery for DSF and rest were managed by different non-surgical approaches. The indication for first re-operation was intra-abdominal sepsis; failure rate was over 30%. Complications were very common and occurred in 74 of 75 patients; important being abdominal abscess, sepsis, appearance of fistulas of neighboring organs, bleeding and pneumonia. Second and third reoperations required in 25 and 12 cases respectively. Fifty-four patients (72%) recovered after a median of 39 days and the mortality rate was 28% (21 patients) after a median of 32 days since DSF onset. Death was due to multiple organ failure in 20 patients and intra-abdominal bleeding in one patient. Unfortunately, the study failed to identify the best surgical strategy, probably because of the high number of surgical procedures and low number of events. The outcomes of non-surgical approaches were not clearly mentioned in this study.

Furthermore, in their study Oh et al¹² suggested 5 cases of DSF; all of them were treated surgically with relaparotomy and primary closure due to sepsis, apparently without complications. However, there aren't any further data available on the post-operative outcome of these patients. Cornejo et al¹⁴ in their work mentioned about 13 cases of DSF with an incidence of 1.95%. The average number of days from surgery to clinical debut of DSF was 5 days (range, 3-7 days). Of the 8 patients surgically treated, six patients (75%) died; with 3 deaths in the first 24 hours of postoperative care. 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).

Different non-surgical approaches were suggested by Ali et al¹⁵ in their work over 19 patients with DSF. Reports showed that all patients complained of high fever and showed signs of peritoneal irritation; hence

duodenal stump leakage was suspected. All the cases were effectively treated by indwelling pigtail catheter and Foley catheter placement supplemented with conservative management. The notable advantages of these procedures were- avoidance of unnecessary aggressive intervention, promotion of early oral intake and permittance of early hospital discharge. In addition, Cozzaglio et al⁹ suggested performing a percutaneous transhepatic biliary diversion to reduce the output of DSF in patients with severe clinical conditions, unfit for a conservative treatment or invasive approaches, such as relaparotomy, and when other approaches failed (output reduced from a median of 500 mL/d to 100 mL/d, P = 0.02).

Oresingo et al⁶ presented a retrospective study of 32 patients affected by DSF and 19 patients were treated conservatively and 13 surgically. Conservative treatments consisted in percutaneous abdominal abscess drainage/transhepatic biliary drainage, total parenteral/enteral nutrition and/or somatostatin/octreotide administration. The mean healing time for patients in nonsurgical group was 31.2 days. Surgical treatments consisted in direct stump closure (with or without external duodenal drainage) in 4 cases, duodenal stump resection and closure (with or without external bile diversion via trans-cystic drainage) in 6 cases, external duodenal drainage in 2 cases and surgical placement of abdominal drainages in 1 case, all associated with treatment with drugs (octreotide or somatostatin), TPN or EN. In this group, after stump resection and closure, 2 patients died for septic shock and 1 patient died for bleeding. However, DSF resolved in 45.2 days (on average) in 10 patients. In 2014 Kim et al⁷ mentioned about various risk factors of DSF with age being the most predictable factor.

As a matter of fact, in their work Cozzaglio et al⁸ reported that patients have been assigned to percutaneous drainage if they had a high daily DSF output (median 500 mL, range 300-1000 mL) or if a previous conservative treatment was unsuccessful (parenteral and enteral nutrition, antibiotics, octreotide and percutaneous drainage of abdominal abscesses); also patients with severe general conditions who couldn't undergo a relaparotomy were treated by percutaneous approach. Percutaneous drainage is a useful treatment not only for the fistula itself but also for the prevention of infections. Lee et al¹⁶ reported complete resolution of 10 DSF cases treated by fluoroscopy-guided percutaneous Foley catheter placement. All patients started a regular diet 1 day after the Foley catheter placement. The catheters were removed at a median of 28 days. There were frequent association and overlapping between conservative and percutaneous treatments as evidenced from higher number of reported procedures than total number of patients in table 1. Therefore some patients were included in two or more groups.

Conclusion

Duodenal stump fistula still remains one of the most challenging and life-threatening complications after total and sub-total gastrectomy for gastric cancer. Early detection and conservative approach, along with nutritional management and percutaneous drainage is the treatment of choice in most cases. In our review, conservative management has shown better results in terms of morbidity and mortality compared with surgical treatment. Therefore, surgery should be reserved only for severe cases like bleeding, sepsis or leak in adjacent organs, or when conservative and percutaneous approaches fail.

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