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CLINICAL FEATURES AND THERAPEUTIC MANAGEMENT OF POSTOPERATIVE ESO-GASTRO-DUODENAL FISTULAS – A 6-YEAR RETROSPECTIVE STUDY

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Abstract: *The postoperative digestive fistula is the most feared complication of gastrointestinal surgeries. We performed a retrospective study over a period of 6 years, in which we included 28 patients who developed postoperative esophageal, gastric or duodenal fistulae in the General Surgery Department of "Bagdasar–Arseni" Emergency Hospital. We assessed the risk factors for this complication, its management and its results. Most patients were males and the mean age was 61.1 years. For 15 patients, the surgeries were required for benign lesions while the rest of 13 patients had malignant disease. Regarding the type of the fistula, 14 were duodenal stump fistulas, 13 were anastomotic leakages and one was a dehiscence of a sutured duodenal ulcer. Six cases required emergency relaparotomy for sepsis and peritonitis. Sixteen patients had a favourable outcome while death occurred in 12 cases. The mortality was higher for patients with sepsis and peritonitis as the first clinical manifestations of fistula and with the need for an emergency reoperation.*

INTRODUCTION

The digestive fistulas are the most feared postoperative complications of the upper gastro-intestinal tract surgeries. They can result from either partial or complete anastomotic failure or by dehiscence of a digestive suture (duodenal stump, suture of a perforated ulcer, pyloroplasty).

Although their incidence is relatively low (1.6 - 5%) (1-3), they produce a longer hospitalization period and grater costs, by generating complications such as wound infections, eviscerations, purulent intraperitoneal collections and hydro-electrolyte imbalances.(4,5) Their reported morbidity varies between 33 and 84% (2,6-8) and mortality can reach up to 67%.(8)

A number of factors related to the patient, the operative act and anatomical features are involved in their development. Despite a large number of studies performed on this topic, the treatment is still difficult and non-standardized, varying from patient to patient and from one medical unit to another.

AIM

This study presents an analysis of the diagnosis, risk factors and therapeutical approach of the postoperative eso-gastro-duodenal fistulas.

MATERIALS AND METHODS

We performed a retrospective study over a period of 6 years (January 2013 – December 2018), in which we included patients that developed postoperative esophageal, gastric or duodenal fistulae in the General Surgery Department of "Bagdasar – Arseni" Clinical Emergency Hospital.

The inclusion criteria were patients over 18 years old with external postoperative digestive fistulas resulted after abdominal esophagus, stomach and duodenum surgeries, both for benign and malignant pathologies. The fistulas developed either by partial or complete anastomotic failure or after digestive suture dehiscence (duodenal stump, sutured ulcer). In one case, the fistula developed after a duodenal lesion produced by an intraperitoneal drainage tube. Patients with internal fistulas, multiple fistulas or with the origin at the level of the intrathoracic esophagus were excluded. The fistulas were diagnosed either by clinical findings or by imaging studies (extravasation of contrast substance during eso-gastric fluoroscopy, CT or by endoscopy).

We analysed the patients' age and sex distribution, the type of the disease – benign or malign (and the stage of the malignant tumours according to TNM classification), and whether the surgery was performed in an emergency or elective conditions. We identified the patient-related risk factors: arterial hypertension > stage II, malnutrition – defined as a loss of more than 10% of body weight in less than 2 months, cardiac insufficiency > class II NYHA or myocardial ischemia, diabetes mellitus with HbA1c > 7,5%, history of smoking more than 10 packs – year, anaemia with a haemoglobin level less than 11g/dl, serum albumin lower than 3,5 g/dl. Also, we assessed the operative-related risk factors: the surgical procedure, the type of the suture that was performed (mechanical or manual), the operative time, the presence of intraoperative hypotension defined as a systolic arterial pressure less than 90 mmHg for more than 15 consecutive minutes, the intraoperative blood losses and presence of local sepsis. We have also studied the time between surgery and fistula onset, the therapeutic

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management and the results, with the primary endpoint being the overall survival. All data was obtained from the patients' hospital records.

RESULTS

During the 6 years, 28 patients from the General Surgery Department of "Bagdasar-Arseni" Emergency Hospital developed postoperative eso-gastric and duodenal fistulas. Most of the patients were males (75%) and the mean age was 61.1 years, ranging between 38 and 79 years (table no. 1).

The surgical procedures complicated with digestive fistulas are presented in table no. 2. For most of the patients – 12 (42.85%) gastric resection with gastro-jejunal anastomosis (GJA) was performed while total gastrectomy with eso-jejunal anastomosis (EJA) was performed 5 times (17.85%). In 3 cases (10.71%) gastro-jejunal anastomosis was chosen as a palliative procedure. Two other patients underwent a gastric resection with gastro-duodenal anastomosis (GDA). Various procedures were performed for the last 5 patients: gastric re-resection with GJA, pericyst-gastrostomy for liver hydatid cyst, partial duodenectomy with duodenal-jejunostomy, resection of the first jejunal loop and duodenal ulcer suture. One patient developed a duodenal stump fistula following a lesion produced by a peritoneal drainage tube.

The majority of the procedures were scheduled (60.71%), the rest of 39.29% being performed in emergency conditions (table no 2). For 15 patients (53.57%) the surgeries were required for benign lesions while the rest of 13 patients (46.43%) had malignant diseases, most of them – 10 (76.92%) in the end-stage.

Table no. 1. Demographic data and associated pathologies of patients with postoperative eso-gastro-duodenal fistulas

Characteristics	Value
AGE (YEARS)	
Interval	38-79
Mean	61.1
GENDER	
Male	21 (75%)
Female	7 (25%)
CO-MORBIDITIES (NO. OF PATIENTS)	
Arterial hypertension	14 (50%)
Cardiopathy	4 (14.28%)
Diabetes mellitus	5 (17.85%)
Liver cirrhosis	1 (3.57%)
BMI	
Underweight	10 (35.71%)
Normal	14 (50%)
Obesity grade 1	3 (10.71%)
Obesity grade 2	0 (0%)
Obesity grade 3	1 (3.57%)
SMOKER	
Yes	14 (50%)
No	14 (50%)
TYPE OF PATHOLOGY (NO. OF PATIENTS)	
BENIGN	15 (53.57%)
MALIGN	13 (46.43%)
Stage I	0 (%)
Stage II	2 (14.28%)
Stage III	1 (7.14%)
Stage IV	10 (76.92%)
PREOPERATIVE RADIOTHERAPY	
Yes	3 (10.71%)
No	12 (42.85%)
N/A	13 (46.42%)

Regarding the type of the fistula, 14 (50%) were duodenal stump fistulas (one resulted from a drainage tube lesion), 13 (46.42%) were anastomotic leakages and one (3.57%) was dehiscence of a sutured duodenal ulcer. Most of the digestive sutures were hand-sewed (82.14%) in a single layer fashion (81.48%). The majority of the duodenal stump fistulas developed after gastric resections with gastro-jejunal anastomosis (12/14 – 85.71%). Mechanical suture was used for duodenal stump closure in only 1/14 cases (7.14%) and the double-layer suture was performed for 3/14 patients (21.42%). The most frequent anastomotic leakage was gastro-jejunal (6 cases) (table no. 3).

Table no. 2. Particularities of the initial surgery

CHARACTERISTICS	No. of cases	%
INITIAL SURGERY		
Gastrectomy with GJA	12	42.85%
Gastrectomy with EJA	5	17.85%
GJA	3	10.71%
Gastrectomy with GDA	2	7.14%
Gastric re-resection	1	3.57%
Duodenectomy cu DJA	1	3.57%
Pericyst-gastric anastomosis	1	3.57%
First jejunal loop resection with GJA	1	3.57%
Ulcer suture	1	3.57%
Drainage tube lesion	1	3.57%
SURGICAL PROCEDURE CONDITION		
Emergency	11	39.29%
Scheduled	17	60.71%
TYPE OF SUTURE	1	
Manual	23	82.14%
Mechanical	4	14.28%
Drainage tube lesion	1	3.58%
NO. OF LAYERS		
1	22	81.48%
2	5	18.51%
UNFAVOURABLE CONDITIONS		
NO	14	50%
YES	14	50%
Carcinomatosis	7	50%
Peritonitis	6	42.85%
Peritoneal abscess	1	7.14%

Concerning the surgical-related risk factors, 8 patients (28.57%) suffered prolonged hypotension (median time 37.5 minutes). Local unfavourable conditions were identified in 14 cases: peritoneal carcinomatosis in 7 cases, 6 patients had peritonitis and one had a peritoneal abscess. The intraoperative median blood loss was 200 ml, with a higher value detected in 10 patients (35.71%). Sixteen surgical procedures (57.14%) were longer than 200 minutes (table no. 4).

Studying the patients-related risk factors for fistula development, we discovered arterial hypertension in half of the patients, diabetes mellitus in 5 (17.85%), significant cardiac pathology in 4 (14.28%) and liver cirrhosis in one case. Preoperative radiotherapy was used for three patients with malignant disease. Hypoalbuminemia was present in 23 patients (82.14%) and anemia in 15 (53.57%).

Table no. 3. Fistulas characteristics

CHARACTERISTICS	Value	%
Median time span surgery – fistula onset (days)	6.5 days	-
Start of postoperative oral feeding	4.6 days	-
TYPE OF FISTULA		
Duodenal stump	14	50%
Gastro-jejunal	6	21.42%
Esophago-jejunal	5	17.85%
Gastro-pericyst	1	3.57%
Duodeno-jejunal	1	3.57%
Ulcer suture	1	3.57%
Median fistular output (ml/24h)	425 ml	-
TYPE OF TREATMENT		

CONSERVATIVE	20	71.43%
SURGICAL	8	28.57%
Peritoneal debridement	4	50%
Gastric re-resection	2	25%
Direct suture	1	12.5%
External pericystic drainage	1	12.5%
TREATMENT OUTCOME		
Healed	16	57.14%
Died	12	42.86%

The median period between the surgical procedure and the fistula onset was 6.5 days, ranging between 2 and 21 days. Bile spillage through the surgical wound or abdominal drainage tubes was present in all of the patients. In 6 cases (21.43%) sepsis and peritoneal signs were associated. The median fistula output was 425 ml/24 h (ranging between 50 and 2000 ml). Eleven patients had high output fistula (more than 500 ml/24 h). For the patients that required emergency relaparotomy, the output could not be correctly evaluated.

Table no. 4. Intra- and perioperative features

CHARACTERISTICS	Value	%
Median time of surgery (min)	200 min	-
Intraoperative hypotension		
Yes	8	28.57%
No	20	71.43%
Median intraoperative hypotension period	37.5 min	-
Median intraoperative blood loss (ml)	200 ml	-
Median postoperative blood transfusion	1 unit	-
Median 72 hours perioperative iv fluids	7500 ml	-

A conservative approach was chosen for patients that had a good general condition, and did not have signs of sepsis or peritonitis (78.57%). Twenty patients (71.43%) were treated only by conservative treatment while 8 patients (28.57%) required a surgical procedure. Six operations were performed in emergency conditions due to peritonitis and sepsis. The other 2 patients had surgery after the fistula output did not decrease with the conservative approach and their condition worsened.

The surgical procedures were particularized for each patient. Peritoneal debridement and drainage were performed in 4 cases, gastric re-resection with gastro-jejunal anastomosis was made for 2 gastro-duodenal anastomosis leakages and a direct suture was attempted for one eso-jejunal anastomotic fistula. For the fistula that developed after internal drainage of a pericystic cavity, the anastomosis was undone, the stomach was sutured and the cavity was externally drained.

Sixteen patients (57.14%) had a favourable outcome. Fourteen of them were treated only non-operative resulting in a spontaneous fistula closer after a mean time of 41.9 days (14 - 140 days). Twelve patients died, of whom 6 were surgically treated and 6 received conservative treatment. A significantly higher mortality rate was recorded for patients for which the first signs of fistula onset were sepsis and peritoneal irritation ($p=0.0238$) as well as for the cases requiring reintervention ($p=0.0297$). Deaths from the non-operative treated group occurred after a median time of 24 days from the first clinical manifestations of fistula, varying from 2 to 180 days. In 2 cases the patients died in less than 48 hours due to the already poor general condition as they had septic shock caused by neglected peritonitis secondary to perforated ulcers at the moment of the admission. One patient had a favourable evolution but without obtaining a definitive fistula closure. She had end-stage gastric cancer and died 6 months later due to cancer evolution. All other 3 patients had terminal cancer and did not develop signs of sepsis or peritonitis, so allowing a conservative approach. Having multiple comorbidities, their condition progressively worsened and they died after a mean time of one month.

Four patients from the surgically treated group died from abdominal sepsis after less than a week. The other 2 deaths were caused by pulmonary complications that occurred after more than two weeks.

DISCUSSIONS

Digestive fistulas that develop after surgical procedures on the esophagus, stomach or duodenum can be the result of an anastomotic failure or suture dehiscence (duodenal stump, pyloroplasty, perforated ulcers). A very uncommon mechanism that was recently described is gastric or duodenal lesions generated by an intraperitoneal drainage tube.(9)

Their incidence varies by their etiology – between 0 – 40% for anastomotic dehiscence (10-14) and 1.5 – 6% for the duodenal stump fistula.(2,15) Although they are rare, these are very serious complications with mortality rates ranging between 16 – 20 % with the highest described reaching up to 67%.(2,5,8)

Several patient-related, operative and postoperative care related risk factors along with certain anatomical particularities are considered responsible for increasing the risk of digestive fistula. The anatomical particularities that favour duodenal stump fistula development are: the difficult approach to this digestive segment due to deep retroperitoneal location and close relations to the inferior vena cava, aorta, superior mesenteric vessels, bile duct and pancreas, lack of the serosa layer in the posterior wall, adequate blood supply only for 0.5 cm from the dissection margin and proteolytic action of the bile and pancreas secretions that may produce a dehiscence of an inappropriate suture.(16)

Age over 60 years represents a patient-related risk factor for fistula development.(16) In our study, more than half of the patients (53.57%) were aged over 60 years. Further studying other patient-related risk factors mentioned by literature, more precisely malignant disease (16), we found in our study group that 46.43% of patients required surgical intervention for various types of malignancies. We also noticed that most of them (76.92%) had end-stage cancers and thus surgeries were performed only as palliation. Because of the hospital's profile, a large number of procedures (39.28%) were done in emergency conditions.

Another patient-related risk factor is malnutrition (17) (defined as a recent weight loss of over 5 kg or more than 10% of body mass) which was identified in our subjects in 35.71% of cases. Also, hypoalbuminemia (18, 19) and anemia (17) were very frequent in our study group in 89.28% and 53.57% of the cases. Due to the high number of interventions performed in emergency and an important proportion of end-stage cancer patients, these deficits could not be adequately corrected preoperatively.

Conditions that can alter the blood supply and tissue oxygenation like arterial hypertension, diabetes mellitus, cardiac insufficiency or respiratory failure (20-23), along with a long history of smoking (24) are also considered risk factors for postoperative digestive fistula development. These pathologies were frequent in our study group.

Regarding the operative-related risk factors, we have identified local unfavourable conditions for digestive suturing in 14 cases: peritoneal carcinomatosis in 7 patients, general peritonitis in 6 and one peritoneal abscess.

Longer surgical procedures can favour fistula development (24, 25). Some authors consider the cut-off point at 120 minutes while others at 200 minutes. The mean operative time in our group was 218 minutes with 16 cases where the surgery was longer than 200 minutes. Intraoperative hypotension (26) also contributes to fistula development but in our study it was identified only in 8 patients.

Another operative-related risk factor is the intraoperative blood loss (25, 26) but the limit is still debatable, some authors considering it 200 ml while others 250 ml. In our

study, the median blood loss was 200 ml with higher values in 10 cases.

Although double-layer suture did not prove to be safer than the one performed in a single layer, some authors believe that the lack of a hand-sewed reinforcement of the duodenal stump might increase the chances of fistula.(15) In our study, the double layer suture was preferred for only 5 of 28 patients (17.85%) and was used only 3 times for the duodenal stump closure.

The median time between surgery and the clinical onset of the fistula was 6.5 days. However, we recorded 3 cases where the time interval was less than 72 hours, raising the suspicion of a technical flaw.

All fistulas were clinically diagnosed by a bile discharge through the surgical wound or abdominal drainage tubes. Furthermore, the site of the fistula was later revealed by contrast studies or during surgery. Six patients had peritonitis and signs of sepsis as the first clinical manifestations and required emergency reoperation. For the rest of the cases, a conservative approach was initially chosen. Two of these patients required surgery because of progressive alteration of their general status and a lack of a significant decrease in the fistula output.

The median fistula output was 425 ml/24h but 10 patients had a high-output fistula (over 500 ml/24h). We did not discover a statistical significant influence over the number of reoperations ($p = 0.3184$), spontaneous closure ($p = 0.0623$) or deaths ($p = 0.1719$). These facts could be explained by the relatively small number of patients included in our study and by the impossibility of accurate measurement of the flow in patients that required emergency relaparotomy. These patients were operated in less than 24 hours and the fistula output was only partially discharged through the wounds or drains.

We noticed that an important number of deaths occurred in patients for which conservative management was chosen. Two of these patients died after a very short period from the fistula onset, due to their already poor general condition. For another patient, the non-operative treatment was efficient, lowering the fistula output from 1500ml/24h to 100 ml/24 h, but without achieving definitive closure. This patient had end-stage gastric cancer and died 6 months later due to malignant disease. The other 3 patients had a progressive alteration of their status under the conservative treatment. They all had metastatic cancer and important co-morbidities that made less feasible an attempt to close the fistula by surgery. A possible better outcome for these patients could have been achieved if we had used the minimal-invasive non-operative therapies, but they were not available at that moment. Lately, a number of percutaneous and endoscopic procedures with very good results were published. Among them, there are the endoscopic interventions that involve the closure of the internal fistular orifice using clips, loops or fibrin glue.(27,28,29) Another endoscopic option is the metallic or plastic stents that can cover the fistula's orifice.(30-32) Percutaneous acellular fibrogenic matrix injection into the fistula tract is also an effective treatment for gastro-cutaneous fistulas.(32,33,34) The negative pressure therapy can be used either endoscopically or externally.(32,35,36)

The mortality rate from our study (42.86%) was high compared to the data obtained from the literature. This might be explained by the important number of patients that had end-stage malignant diseases and other important chronic conditions and by the large number of surgeries performed in emergency conditions, on patients with poor status.

CONCLUSIONS

Postoperative digestive fistulas are still the most feared complications of surgeries performed on the esophagus, stomach and duodenum. They have a high rate of morbidity and mortality that can reach up to 67%. In our study, the mortality rate was 42.86% and was significantly higher for patients with sepsis and peritonitis as the first clinical manifestations of fistula as well as with the need for an emergency reoperation. Also, this high rate of mortality (compared with literature data) was caused by the large number of patients with poor conditions due to either advanced neoplasia or severe acute lesions that required emergency surgeries.

The management of postoperative digestive fistulas is still debatable and is adapted for each patient. In the absence of sepsis and peritonitis, a conservative approach should always be the first option. However, when spontaneous closure cannot be obtained with the conservative management and the patient's condition is making surgery unfeasible, the minimal-invasive procedures should be considered.

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