

Surgical Management of Iatrogenic Perforation of the Gastrointestinal Tract: 15 Years of Experience in a Single Center

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Abstract

Background Gastrointestinal (GI) tract perforation during endoscopy is a rare but severe complication. The aim of this study was to determine predictors of morbidity and mortality after iatrogenic endoscopic perforation.

Materials and methods All cases with iatrogenic endoscopic perforation receiving surgery at a tertiary referral center in a 15-year period (2000–2015) were retrospectively analyzed. Demographics, type of endoscopy, site of perforation, operative procedure, morbidity and mortality were analyzed. Multiple logistic regression was used to identify parameters predicting survival.

Results A total of 106,492 endoscopies were performed, and 82 (0.08%) patients were diagnosed with GI perforation. Most perforations (63.4%) occurred in the lower GI tract, compared to 36.6% in the upper GI tract. In 21 cases (25%), perforation was noticed during endoscopy, whereas 61 perforations (75%) were diagnosed during the further clinical course. Operative care was applied within 24 h in 61%. Surgery of perforations was almost completely performed maintaining the intestinal continuity (68%), whereas diversion was performed in 32%. Mortality was associated with age above 70 (OR 4.89, $p = 0.027$), ASA class > 3 (OR 4.08, $p = 0.018$), delayed surgery later than 24 h after perforation (OR 5.9, $p = 0.015$), peritonitis/mediastinitis intraoperatively (OR 4.68, $p = 0.031$) and severe postoperative complications with a Clavien–Dindo grade \geq III (OR 5.12, $p = 0.023$).

Conclusion The prevalence of iatrogenic endoscopic perforation is low, although it is associated with a serious impact on morbidity and mortality. Delayed management worsens prognosis. To achieve successful management of endoscopic perforations, early diagnosis is essential in cases of deviation from the normal post-interventional course, especially in elderly.

Introduction

Endoscopy of the upper and lower gastrointestinal tract is a safe, fast and feasible diagnostic and therapeutic procedure [1]. The risk of intrainterventional perforation is as

low as 0.09% in esophagoscopy and 0.03% in colonoscopy. With advancing and broadening spectrum of implementation and indication of endoscopic procedures, the absolute number of adverse events is most likely to increase [2]. Perforation of the intestines due to any reason is a severe condition that can clinically present with free intraabdominal air, purulent or even fecal peritonitis and abdominal compartment syndrome [3]. It needs immediate diagnosis and treatment and it is associated with a significant morbidity and mortality rate of up to 43 and 25%, respectively [4–6]. Management of these life-threatening conditions is little standardized due to varying locations, delayed diagnosis and heterogeneous clinical findings. It

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mostly comprises drainage or surgical intervention, including Hartman's procedure and stoma in perforations of the large bowel [7, 8]. In recent years, the development of endoscopic closure procedures such as stenting and clipping promises fast and reliable alternatives to aforementioned methods [1, 9, 10]. However, these methods require trained specialists [1] and referral of outpatient with perforation into a tertiary center may delay sufficient therapy.

The aim of this study was to analyze the results of surgical management in 15-year period of a single center and to determine predictors of morbidity and mortality after gastrointestinal perforation during endoscopic procedures.

Materials and methods

In this retrospective chart review study, all cases with a perforation of the gastrointestinal tract presented to our surgical ward at a tertiary referral center (Charité, Universitätsmedizin Berlin, Campus Benjamin Franklin, Germany) within a 15-year period (2000–2015) were detected and hand-selected for those who received an endoscopic procedure within 10 days prior to symptom onset. These cases were reviewed for course, management and outcome. Variables included age, sex, endoscopic procedure, whether or not an intervention such as minimally invasive sample taking or dilatation was performed, site of the perforation and clinical signs of peritonitis. Primary endpoints were in-hospital mortality and secondary endpoints in-hospital morbidity according to the Clavien–Dindo classification [11].

Statistical analysis was performed using descriptive statistics, Student's *t* test and cross-table calculation where appropriate. All values are given as mean unless indicated otherwise. A *p* value of <0.05 was considered significant. All parameters predictive for survival which had a statistical significance of less than 0.1 (indicating a tendency toward significance) were included in a multinomial logistic regression model encompassing both forward selection and backward elimination. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 22.0, SPSS Inc., Chicago, IL, USA) statistical software. The institutional review boards of the Charité, Universitätsmedizin Berlin, do not require formal approval for retrospective archive studies; therefore, an ethical approval was not sought.

Results

Demographics

In the study period, a total of 106,492 endoscopies were performed, and 82 (0.08%) patients with a perforation of

the intestine were attributed to endoscopy. 37 (45.1%) were male, and 45 (54.9%) were female with a median age of 68.5 years. A diagnostic procedure was performed in 45 of these 82 perforation cases (54.9%), whereas a therapeutic procedure was performed in 37 perforation cases (45.1%). Perforation occurred most frequently in colonoscopy (45/82; 54.9%) followed by esophago-gastro-duodenoscopy (30/82; 36.6%), rectosigmoidoscopy (4/82; 4.9%) and double-balloon-endoscopy (3/82; 3.7%).

Sites of perforation

Perforations in colonoscopy and rectosigmoidoscopy were observed most commonly in the sigmoid colon (26/82; 31.7%) and the rest of the colon (21/82; 25.6%), more rarely in the rectum (2/82; 2.4%) and the jejunum/ileum (3/82; 3.7%). Perforations in the upper gastrointestinal tract were observed more frequently in both, the esophagus and the duodenum (each 12/82; 14.6%), whereas perforation of the stomach were observed in only 6/82 (7.3%).

Manifestation

In 21 cases (25%), perforation was noticed during endoscopy, whereas 61 patients (75%) were diagnosed to have a perforation during the further clinical course. The immediate detection rate of perforation was 30% (9/30) for the upper gastrointestinal tract, and 23.1% (12/52) for lower gastrointestinal tract (*p* > 0.05).

Surgical management

Although perforations were more rarely noticed during endoscopy, the operative management was commonly applied within 24 h (50/82; 61%) regardless of the localization of perforation. 32 patients (39%) received surgical treatment later than 24 h. Of these 32 patients, 10 patients had surgery between 24 and 48 h, 9 patients between 48 and 72 h, 8 patients 72 h and 7 days, and 5 patients later than 7 days.

Surgical treatment of perforations was performed maintaining the intestinal continuity in 70.7%, whereas resection with discontinuity (Hartmann procedure) or diversion was performed in 29.3%. Perforation was surgically treated by oversewing in 33/82 patients (40.2%), resection with anastomosis in 23/82 patients (28.1%), diversion in 15/82 patients (18.3%) or Hartmann procedure in 11/82 patients (13.4%). In 44 cases (53.7%), peritonitis/mediastinitis were detected at time of surgery. The remaining 38 patients had no sign of peritonitis/mediastinitis intraoperatively (Table 1). The mean in-hospital stay was 16.4 (range 5–78) days.

Table 1 Presence of peritonitis/mediastinitis according to time between endoscopy (perforation) and surgery

Peritonitis/mediastinitis	≤24 h post-endoscopy (n = 52)	>24 h < 48 h post-endoscopy (n = 10)	>48 h < 72 h post-endoscopy (n = 9)	>72 h ≤ 7 d post-endoscopy (n = 8)	>7 d post-endoscopy (n = 5)
Yes (n = 45)	18 (35%)	6 (60%)	9 (100%)	8 (100%)	4 (80%)
No (n = 37)	34 (65%)	4 (40%)	0	0	1 (20%)

Table 2 Univariate analysis for prognostic factors for mortality

	Death	No death	p value
<i>Sex</i>			0.083
Female	7	47	
Male	8	20	
Age, median (years)	73.2	64.3	0.163
<i>ASA class</i>			0.014
≤3	6	49	
>3	9	18	
<i>Localization of perforation</i>			0.772
Upper GI tract	5	25	
Lower GI tract	10	42	
<i>Time to surgery</i>			0.015
≤24 h	5	45	
>24 h	10	22	
<i>Surgical procedure</i>			0.702
Continuity resection or oversewing	10	48	
Discontinuity resection or ostomy	5	19	
<i>Peritonitis/mediastinitis</i>			0.031
Yes	12	33	
No	3	34	
<i>Complications</i>			0.023
Clavien–Dindo ≥3	5	7	
Clavien–Dindo <3	10	60	

Outcome and prognostic parameters

The overall postoperative in-hospital morbidity rate was 34.2% (28/82): 8 patients (9.8%) had grade I, 8 (11%) had grade II, 4 (4.9%) had grade III and 8 (8.5%) had grade IV according to the Clavien–Dindo classification. Wound infection was the most common complication ($n = 8$). Other complications were as follows: intestinal paralysis ($n = 3$), urinary tract infection ($n = 1$), pneumonia ($n = 4$), leakage ($n = 2$), intraabdominal abscess ($n = 2$) and sepsis ($n = 8$).

The mortality rate was 18.3% (15/82, Clavien–Dindo grade V). Death was caused by septic complications in 11 out of 15 patients and by pneumonia in 20% of the patients (3 of 15). One patient died due to pulmonary embolism and

Table 3 Multiple logistic regression of prognostic factors for mortality

		Odds ratio	95% CI	p value
Time to surgery	>24 h	5.9	3.636–8.607	0.015
Age	>70 y	4.89	2.743–6.645	0.027
ASA class	>3	4.08	1.273–9.635	0.018
Peritonitis/mediastinitis	Yes	4.68	2.206–6.572	0.031
Clavien–Dindo	>3	5.14	2.914–7.424	0.023

cardiogenic shock. The mortality rate of all patients who underwent endoscopy was 0.015% (15 of 106,492).

Several possible prognostic factors were examined for their influence on the risk of mortality. The results of the univariate and multivariate analyses are shown in Tables 2 and 3. Mortality was associated with age above 70 years (OR 4.89, $p = 0.027$), ASA class >3 (OR 4.08, $p = 0.018$), with surgery onset later than 24 h after the procedure that has led to the perforation (OR 5.9, $p = 0.015$), existence of peritonitis/mediastinitis intraoperatively (OR 4.68, $p = 0.031$) and severe postoperative complications with a Clavien–Dindo grade \geq III (OR 5.12, $p = 0.023$).

Discussion

In this retrospective, single-center, tertiary referral center study, we could demonstrate that iatrogenic endoscopic perforation is rare, but it has a serious impact on morbidity and mortality. Old age, peritonitis and delayed management significantly increased the risk of perforation-related mortality and emphasize a time-sensitive decision-making in the course of iatrogenic gastrointestinal perforation. Resection with discontinuity or diversion was performed in one-third of the patients with perforations due to peritonitis and advanced septic condition of the patients.

Worsening on outcome was associated with delay of definitive therapy by more than 24 h, irrespective of prior health status, endoscopic procedure or anatomic perforation site in our study. This finding concurs with several

other studies. Biancari et al. [4] calculated a risk ratio of immediate mortality of 2.279 (7.4 vs. 20.3% 95% CI 1.632–3.182) for patients treated later than 24 h versus within 24 h in a meta-analysis pooling 2791 cases of 75 studies on esophageal perforations. This is in accordance with results from other endoscopic studies on esophagogastroduodenoscopy [12–14], retrograde cholangiopancreatography [15–17], colonoscopy, sigmoidoscopy and rectoscopy related [18–23].

To date, there are only two studies comparing iatrogenic endoscopic perforation of the upper and lower gastrointestinal. Misra et al. reported 18 cases of gastrointestinal perforation after a total of 21,217 endoscopic procedures (incidence, 0.8/1000 procedures) [24] with a low overall mortality rate (incidence, 0.05/1000 procedures). Data on morbidity were not presented. Another retrospective study of 23 patients with comparable distribution of age and gender demonstrated an overall mortality rate of 13% solely after esogastric perforation [7]. In our study, 82 patients were diagnosed with a gastrointestinal perforation after a total of 106,492 endoscopic procedures (incidence, 0.8/1000 procedures) with a mortality rate of 18.3% (incidence, 0.14/1000 procedures). However, the above-mentioned studies involved significant lower numbers in participants compared to our study.

In our study, we focused on outcome after surgical treatment of iatrogenic gastrointestinal perforations. Thus, cases of successful endoscopic ad hoc closure of perforations were not included. However, recent large multicenter trials have reported no superiority of endoscopic closure of esophageal perforation on post-interventional mortality, morbidity or even in hospitalization [25] in comparison with surgical management. Our data suggest that delay of definitive treatment may lead to an increase in mortality. Endoscopic management of perforations requires high level training and appropriate medical facilities are not available area-wide. In outpatient treatment and primary care centers, where prompt surgical care is normally warranted on site, referral of iatrogenic perforations to specialized endoscopic facilities might further aggravate delay of treatment and worsen patient's prognosis. The European Society of Gastrointestinal Endoscopy (ESGE) addressed this problem in a recent position statement of diagnosis and management of iatrogenic endoscopic perforations. Paspatis et al. [1] prompted for a management team of endoscopists and surgeons resembling stroke units to select patients' for adequate treatment. Hemodynamically stable patients with no signs of sepsis may be treated by endoscopic techniques, but frequent re-evaluations based on vital signs, physical examination and laboratory values (e.g., white blood cell count) must be warranted.

Patients who present within 24 h after the perforation event have significantly improved outcomes compared with

those with delayed presentation. In this short interval, even primary endoscopic repair may be performed. Delayed presentations are associated with a greater rate of feculent peritonitis and inflammatory changes [18]. Patients who are unstable during nonoperative management should undergo immediate surgical exploration. Early definitive treatment with deprivation of inflammatory tissue, pus and underlying pathology remains the main objective in treatment of iatrogenic gastrointestinal perforation.

Aged patients do have a higher risk of complications during and after endoscopic interventions [26, 27]. In our study, age above 70 years was significantly associated with perforation-related mortality and worsening of prognosis. Therefore, indication for a nonsurgical management of iatrogenic endoscopic perforations should particularly be critical in old patients.

The main limitation of this study is its retrospective nature. While over-reporting was avoided by hand-searching, we cannot rule out under-reporting due to incorrect coding of the surgical intervention. However, there was a relatively high standardization with regard to endoscopy, diagnostic algorithm and interdisciplinary management of iatrogenic gastrointestinal perforations due to a defined number of endoscopist and surgeons in a single center. With 82 reported cases, this is the largest retrospective study on this matter, including both lower and upper gastrointestinal tract perforations. We also experienced a high quality of clinical data due to comprehensive online data acquisition.

In conclusion, delayed definitive management of iatrogenic gastrointestinal perforation worsens patient's prognosis. To control complications after perforation early diagnosis and immediate definitive treatment is crucial especially in the elderly.

Compliance with ethical standards

Conflict of interest C. Holmer and other co-authors have no conflict of interest.

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