Open abdomen treatment for complicated intra-abdominal infection patients with gastrointestinal fistula can reduce the mortality

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Abstract

To evaluate the effect of the open abdomen (OA) and closed abdomen (CA) approaches for treating intestinal fistula with complicated intra-abdominal infection (IFWCIAI), and analyze the risk factors in OA treatment.

IFWCIAI is associated with high mortality rates and healthcare costs, as well as longer postoperative hospital stay. However, OA treatment has also been linked with increased mortality and development of secondary intestinal fistula.

A total of 195 IFWCIAI patients who were operated over a period of 7 years at our hospital were retrospectively analyzed. These patients were divided into the OA group (n=112) and CA group (n=83) accordingly, and the mortality rates, hospital costs, and hospital stay duration of both groups were compared. In addition, the risk factors in OA treatment were also analyzed.

OA resulted in significantly lower mortality rates (9.8% vs 30.1%, $P<.001$) and hospital costs ($11721.40±$9368.86 vs $20365.36±$21789.06, $P<.001$) compared with the CA group. No incidences of secondary intestinal fistula was recorded and the duration of hospital stay was similar for both groups ($P=.151$). Delayed OA was an independent risk factor of death following OA treatment (hazard ratio [HR]=1.316; 95% confidence interval [CI]=1.068–1.623, $P=.010$), whereas early enteral nutrition (EN) exceeding 666.67 mL was a protective factor (HR=0.996; 95% CI=0.993–0.999, $P=.018$). In addition, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Candida albicans* were the main pathogens responsible for the death of patients after OA treatment.

OA decreased mortality rates and hospital costs of IFWCIAI patients, and did not lead to any secondary fistulas. Early OA and EN also reduced mortality rates.

Abbreviations: CA = closed abdomen, CAD = closed abdominal drainage, EN = enteral nutrition, GI = gastrointestinal tract, IAH = intra-abdominal hypertension, IFWCIAI = intra-abdominal infection, MOD = multiple organ dysfunction, NPWT-I = negative pressure wound therapy with instillation, OA = open abdomen, PN = parenteral nutrition, SOFA = sequential organ failure assessment, SSC = Surviving Sepsis Campaign, VAC = underwent vacuum-assisted closure, WSACS = World Society of the Abdominal Compartment Syndrome.

Keywords: close abdomen, intestinal fistula, intra-abdominal infections, open abdomen, risk factors

1. Introduction

Gastrointestinal fistula may lead to intra-abdominal infection and even sepsis if not treated properly. It is associated with high mortality rates of 20% to 60%, and high medical costs.[1] Furthermore, intestinal fistula with complicated intra-abdominal infection (IFWCIAI) is often not diagnosed at the early stages, which prevents optimal treatment.[2–4] It is challenging to separate the ruptured intestine from the fistula due to severe abdominal adhesions, and swelling of the intestinal wall and mesentery. Open abdominal (OA) surgery was first successfully used to treat complicated intra-abdominal infection by Duff and Moffat in 1981,[5] but is largely limited due to high mortality rates.[6] We retrospectively analyzed 195 IFWCIAI patients to compare the outcomes of OA and closed abdominal (CA) surgery.

2. Methods

2.1. Patients

A total of 1076 patients with intra-abdominal infection were admitted to our department at the Xijing Hospital of Digestive Diseases affiliated with the Fourth Military Medical University between January 2009 and March 2016. The inclusion criteria for the patients were: intra-abdominal infection and sepsis secondary to gastrointestinal fistula,[7,16] OA grade II (clean or contaminated and developing fixation) or III (frozen abdomen) according to the World Society of the Abdominal Compartment Syndrome (WSACS) classification,[8] Acute Physiology and Chronic Health Evaluation II (APACHE-II) score ≥10, and willingness to provide informed consent. Patients without any history of abdominal surgery, presenting with intraperitoneal infection and gastrointestinal fistula caused by pancreatitis or extensive abdominal metastasis, younger than 18 years old, with APACHE II scores <10, or with incomplete clinical data were excluded. This study was approved by the Ethics Committee of Xijing Hospital, and all patients signed the consent form before surgery. The patients underwent early effective quid resuscitation and a blood pressure boost after admission, and were given broad-spectrum antibiotics that were later adjusted according to drug susceptibility results. Abdominal pus was collected on the day of admission (day 0) and thereafter on days 3 and 7, and subjected to both aerobic and anaerobic culture. APACHE II and Sequential Organ Failure Assessment (SOFA) scores and laboratory data were also collected on days 0, 3, and 7.

2.2. Definitions

Intestinal fistula is defined as an abnormal connection between the gastrointestinal tract (GI) and the skin or another organ, which results in the leakage of stomach acids and an open abdomen.

Complicated intra-abdominal infection with intestinal fistula is defined as sepsis or septic shock caused by intestinal fistula.

Open abdomen (OA) is a condition wherein the abdominal incision is either intentionally not closed (active OA) or cannot be closed (passive OA), and the abdominal cavity is temporarily exposed to drain the contaminants. Its indications are general trauma and intestinal fistula with sepsis, with clean (grade III A) or contaminated (grade III B) frozen abdomen.

Closed abdominal drainage (CAD) relies on a drainage tube or repeated percutaneous catheter drainage while keeping the abdominal cavity closed. Its indications are same as above.

Fistula secondary to OA is defined as the emergence of another fistula after OA surgery.

The time of OA is defined as the duration between the diagnosis of intestinal fistula and OA operation.

2.3. Patient treatment

For the OA surgery, the wound was kept moist with continuous saline infusion from a colostomy pouch with a suction cup. The latter was trimmed to fit the abdominal wall tear and attached to the lowest part of the wound to collect fluid from the fistula in order to prevent contamination of the abdominal bedding, which was then transfused to the distal bowel. Enteral nutrition (EN) and intestinal fluid reinfusion was started once the abdominal distension ceased and the leaking intestinal fluid could be smoothly drained from the abdominal cavity without any remnants. Glucose infusion was started at 20 mL/h, and the speed was gradually increased depending on patient tolerance. Intestinal resection or anastomosis and abdominal wall reconstruction was performed after 3 to 6 months when the abdominal incision healed to form granulomas, and the open incision contracted. For CAD operation, a peritoneal drainage tube or percutaneous catheter drainage was used under the guidance of B-ultrasound or CT (usually placed the 18th tube).

2.4. Data collection

Preoperative demographic and clinical characteristics (such as sex, age, APACHE-II scores, and SOFA scores), location of intestinal fistula, time of OA operation, surgical procedures, postoperative patient mortality, pathogen types, EN, intestinal fluid volume, and hospitalization costs data were collected. All laboratory tests were conducted according to the standard procedures of Xijing Hospital Laboratory's.

2.5. Statistical analysis

Statistical analysis was conducted using the SPSS 17.0.0 software (SPSS, Inc., Chicago, IL). Categorical data were reported as numbers with proportions, and quantitative data were reported as medians with interquartile ranges (IQRs). We used independent sample t test or Wilcoxon test. Count data expressed as a percentage. Pearson tests were used to compare proportions in the 2 groups, chi-square was replaced with the Fisher exact test when necessary. The method of multiple comparisons between multiple sample rates uses 2 partitioning. Univariate and multivariate analyses were conducted using the Logistic method. The relative risk and odds ratio for death were calculated. P values <.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 1076 patients with intra-abdominal infection and APACHE II scores ≥10 were admitted, of which 380 patients without a history of abdominal surgery, 361 with complicated abdominal infection caused by severe pancreatitis, 124 without abdominal fistula, and 16 patients younger than 18 years of age were excluded. The remaining 195 patients (148 men and 47 women, aged between 18 and 85 years) were divided into the OA (n = 112) and CA (n = 83) groups. In addition, 60 of these patients were diagnosed at our hospital and 135 were referred from other

Table 1

The baseline characteristics of enrolled patients.

Variable	OA group n = 112	CA group n = 83	P value
Age (y, n%)	57.49 ± 14.74	56.30 ± 16.20	.594
<60	59 (52.6%)	43 (51.8%)	.904
≥60	53 (47.3%)	40 (48.2%)	
Sex (male: female)	86: 26	62: 21	.736
APCAHE-II score 0th D	16 (13,18)	14 (12,15)	<.001
SOFA score 0th D	4 (3,5)	3 (2,5)	.001
Fistula location, n%			.048
Esophageal anastomoses	23 (20.5%)	15 (18.0%)	.668
Stomach	2 (1.7%)	0	.509*
Duodenal stump	5 (4.4%)	2 (2.4%)	.701*
Choledochojejunostomy	16 (14.2%)	14 (16.8%)	.621
Small bowel	29 (25.8%)	37 (44.5%)	.006
Right hemicolon	15 (13.3%)	9 (10.8%)	.592
Left hemicolon	22 (19.6%)	6 (7.2%)	.015
30-day readmission	3 (2.7%)	9 (10.8%)	.019*
90-day readmission	5 (4.5%)	7 (8.4%)	.254
ICU admission	8 (7.1%)	15 (18.1%)	.020

APACHE-II = Acute Physiology and Chronic Health Evaluation II, CA = closed abdomen, ICU = Intensive Care Unit, OA = open abdomen, SOFA = Sequential Organ Failure Assessment.
* Fisher exact probability method.

local hospitals. There are 38 cases of esophageal anastomotic fistula, 2 of gastric fistula, 7 of duodenal stump fistula after subtotal gastrectomy, 30 choledochojejunostomy fistula, 66 small bowel fistula, 24 right hemicolon fistula, and 28 left hemicolon fistula. The baseline characteristics of all patients are summarized in Table 1. There were no significant differences between both groups in terms of sex and age. The pretreatment APACHE-II and SOFA scores were significant higher in the OA group compared with the CA group (P < .001), and the fistula location also differed significantly between the 2 groups (P = .048). The incidence of small bowel fistula in the CA group (44.5%) was higher than that in the OA group (25.8%, P = .006), whereas hemicolon fistula was more frequent in the latter (P = .015).

3.2. Clinical outcomes

The patients in the OA group had lower mortality rates compared with the CA group (9.8% vs 30.1%, P < .001), as well as lower hospital costs ($11721.40 ± $9368.86 vs $20365.36 ± $21789.06, P < .001, Table 2). The presurgery APACHE-II and SOFA scores were significantly higher in the OA compared with the CA group (P < .001). While both scores decreased significantly in the OA group in the week after surgery (P < .05), neither showed any significant changes in the CA group (Table 3).

Table 2

Comparison of the results of treatment.

	OA group (n=112)	CA group (n=83)	P value
Death patients (n, %)	11 (9.8%)	25 (30.10%)	<.001
Hospital length of stay (mean, d)	26 (range: 20–34.75)	27 (range: 20–45)	.151
Hospitalization costs (mean, $)	11721.4 (range: 8537.95–17090.00)	20365.37 (range: 12120.35–29973.14)	<.001

CA = closed abdomen, OA = open abdomen.

Table 3

The change of APACHE-II score and SOFA score.

	Treatment		
	OA group n = 112	CA group n = 83	P value
APACHE-II 0th days	16 (13,18)	14 (12,15)	<.001
APACHE-II 3th days	13 (11,15)*	12 (11,14)*	.06
APACHE-II 7th days	11 (10,12)†,‡	11 (10,18)	.253
SOFA 0th days	4 (3,5)	3 (2,5)	.001
SOFA 3th days	2 (1,3)*	2 (1,3)*	.817
SOFA 7th days	1 (0,1)†,‡	1 (0,6)	.158

APACHE-II = Acute Physiology and Chronic Health Evaluation II, CA = closed abdomen, OA = open abdomen, SOFA = Sequential Organ Failure Assessment.
* 0th days versus 3th days P < .05.
† 0th days versus 7th days P < .05.
‡ 3th days versus 7th days P < .05.

3.3. Risk factors of death in OA group

The risk factors of postoperative mortality in the OA group are shown in Tables 4 and 5. Univariate analysis identified bacterial contamination of the abdominal cavity and the volume of fistuloclysis as the risk factors, and multivariate analysis showed that the delaying OA and fistuloclysis were independent risk factors. However, the volume of early EN exceeding 666.67 mL was a protective factor. *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Candida albicans* were the main pathogens responsible for death.

4. Discussion

Intestinal fistula complicated with abdominal infection or IFWCIAI is a fatal condition[3,9] that can result in an open abdomen by preventing abdominal fascial closure. The WSACS classified the open abdomen into different grades based on morphological complexity and degree of contamination (Table 6).[10] Several protocols have been developed to treat the different types of IFWCIAI, such as abdominal ostomy by pulling out the bowel, and the closed abdomen approach by replacing the peritoneal drainage tube. The former is associated with reduced mortality rates but is only suitable when there are no adhesions in the abdominal cavity or contracture in the mesentery patients. The closed abdomen drainage protocol is the preferred choice for severe abdominal adhesions, intestinal wall, and mesentery swelling despite the poor prognosis.

McCosh[11] first reported in 1897 that OA surgery can cure complicated abdominal infection. In 1940, Ogilvie[12] showed that OA is conducive to full drainage of the celiac pus and necrotic tissues, and can effectively relieve the intra-abdominal pressure. Duff and Moffat[5] applied the OA approach on 18 patients with abdominal sepsis in 1981, and found that the mortality rate was only 39% as opposed to 60% reported previously. A meta-analysis[13] of 13 retrospective observational studies and 1874 adult IFWCIAI patients showed that an active OA approach deceased the mortality rates from 70% to 40%. Similarly, a retrospective study[14] of 82 IFWCIAI patients in China found that the mortality rate decreased to 31.7% less than previously reported. An Randomized Controlled Trial (RCT) conducted in 2007 on the outcomes of active and passive OA[15] in 232 IFWCIAI patients reported no significant differences in the mortality rates. However, percutaneous drainage and the length of hospital and Intensive Care Unit (ICU) stay were significantly

Table 4

Univariate analysis of patient's risk of death in the open abdominal group.

	Cured patients	Death patients	P value
Sex			.737
Male (n, %)	78 (90.70%)	8 (9.30%)	
Female (n, %)	23 (88.46%)	3 (11.54%)	
Age			.254
<60 years (n, %)	55 (93.22%)	4 (6.78%)	
≥60 years (n, %)	46 (86.79%)	7 (13.21%)	
Fistula location			.843
Esophageal anastomoses	19 (82.61%)	4 (17.39%)	
Stomach	2 (100.0%)	0 (0.0%)	
Duodenal stump	5 (100.0%)	0 (0.0%)	
Choledochojejunostomy	14 (87.5%)	2 (12.5%)	
Small bowel	26 (89.66%)	3 (10.34%)	
Right hemicolon	14 (9.33%)	1 (6.67%)	
Left hemicolon	21 (9.55%)	1 (4.55%)	
Colony types			
A baumannii	31 (30.7%)	8 (72.7%)	.005
C albicans	35 (34.7%)	9 (81.8%)	.002
P aeruginosa	29 (28.7%)	7 (63.6%)	.019
E coli	40 (39.6%)	1 (9.1%)	.047
Enteral nutrition			.425
<666.67 mL	61 (88.41%)	8 (11.59%)	
>666.67 mL	40 (93.02%)	3 (6.98%)	
Volume of fistuloclysis (mL, range)	0.0 (0.0,122.5)	200 (0,300)	.003
Delay open abdomen			.041
≤5 days (n, %)	60 (56.25%)	3 (43.75%)	
>5 days (n, %)	41 (27.27%)	8 (72.73%)	

Table 5

Multiplicity analysis of the patient's risk of death in the OA group.

			95% CI for OR		
	β	OR	Lower	Upper	P value
Age	0.542	1.72	0.344	8.606	.509
Sex	0.228	1.256	0.221	7.135	.797
Fistula location	−0.272	0.762	0.391	1.482	.423
Colony types	0.24	1.271	0.955	1.691	.10
Delay open abdomen	0.275	1.316	1.068	1.623	.01
Volume of EN	−0.004	0.996	0.993	0.999	.018
Fistuloclysis transfusion	0.01	1.01	1.003	1.017	.006

CI = confidence interval, EN = enteral nutrition, OA = open abdomen, OR = odds ratio.

decreased. However, another RCT in the same year on 40 IFWCIAI patients from a single center found that the OA protocol increased mortality rates compared with the CAD approach. The are several possible reasons for this discrepancy: none of these studies recorded the time from diagnosis to the surgery, which made comparison of the therapeutic effects difficult, and OA has several drawbacks like enteroatmospheric fistula (EOF), massive loss of fluids, electrolytes and proteins, and spontaneous enteric fistulas which were secondary to the open abdomen. In our study, the OA protocol decreased the mortality from 30.1% to 9.8%, along with reducing the hospital costs. In addition, delaying OA and fistuloclysis were independent risk factors of death, whereas the volume of early EN was a protective factor for patients undergoing OA surgery.

The 2017 Surviving Sepsis Campaign (SSC) guidelines[16] recommended that OA surgery should be performed at the earliest on sepsis shock patients under the following conditions: substantial organ rupture, especially that of liver, intra-abdominal hypertension (IAH) >20 mmHg accompanied by multiple organ dysfunction (MOD), and abdominal trauma accompanied with severe abdominal infection. However, the definitive time to perform OA surgery has not been reported so far,[17] and some studies indicate that delaying surgery can increase the mortality

rate to almost 100%.[18–20] Since most patients included in our study had been transferred from other hospitals, their diagnosis was delayed. The median OA period was 5 days, and the mortality rates increased from 8.33% when the time from diagnosis to surgery was <5 days to 22.22% for >5 days. The APACHE II and SOFA scores also decreased rapidly and organ dysfunction improved significantly after OA operation.

Exposure of the naked bowel to air may result in EOF, defined as secondary intestinal fistula formed when the small bowel is exposed to air. To prevent air exposure, temporary abdominal closure is performed by delaying the full-thickness suture incision, closing the abdomen with patches of various materials, suturing the incised skin and closing the abdominal cavity, or delaying skin grafting. However, these methods are mainly suitable for these patients without intestinal fistula (type I or II). For those with intestinal fistula, negative-pressure wound therapy devices are used to suck the leaking intestinal fluid and thus prevent bowel exposure. Rao et al[21] reported that one-fifth of the patients with intestinal fistula that underwent vacuum-assisted closure (VAC) of abdominal wounds eventually developed small bowel fistula and 66% of these patients died from multi-organ function failure. Sibaja et al[22] reported that negative pressure wound therapy with instillation (NPWT-I) following OA achieved fascia closure in 96% of the patients, and only 8% later died from postoperative complications unrelated to NPWT-I. Another possible reason for the development of secondary fistula is the continuous friction between the surgical gauze and the bowel surface. To minimize gauze friction, reduce the frequency of gauze replacement and prevent contamination of the abdominal bed, a colostomy pouch with a suction cup trimmed to a "V" shape or an arc was fixed to the lowest part of the incision to collect abdominal fluids. None of the 112 OA patients in our study that underwent continuous saline infusion without any gauze dressing developed EAF, indicating that our wound management strategy was effective.

One of the disadvantages of OA is the extensive loss of intestinal fluids which can result in water and electrolyte balance disorders and nutritional deficiencies, and even impair tissue healing and immune responses. Picot et al[23] reported that

Table 6

Classification scheme for the complexity of the open abdomen.

	I No fixation	II Developing fixation	III Frozen abdomen
A Clean	Clean, no fixation	Clean, developing fixation	Clean, frozen abdomen
B Contaminated	Contaminated, no fixation	Contaminated, developing fixation	Contaminated, frozen abdomen
C Fistula	Enteric leak, no fixation	Enteric leak, developing fixation	

intestinal fluid reinfusion in 232 IFWCIAI patients improved their nutritional status and replaced 91% parenteral nutrition (PN). Consistent with this, Wu et al[24] found that intestinal fluid reinfusion improved liver function and nutritional status, and significantly decreased the length of hospital stay and mortality rates in 95 IFWCIAI patients. Early EN can also significantly improve the survival rates of IFWCIAI patients. Ortiz et al[3] reported that early EN decreased the mortality rates of IFWCIAI patients from 44% to 3%, and similar findings were reported by Doig et al[25] after analyzing 126 IFWCIAI patients from 3 centers. Consistent with this, we found that the early total EN exceeding 666.67 mL was a protective factor for OA patients, and each additional unit of EN (100 mL) decreased mortality risk by 1.004 times. However, EN transfusion through the oral or jejunal routes can lead to massive fluid loss in patients with intestinal fistula. Therefore, we collected the fluid or chyme from the fistula and simultaneously transfused the EN through both oral and distal intestine tube intubation. This "double mouth" transfusion promoted patient recovery by minimizing the loss of digestive juices and enabling reuse of distal bowel function.

4.1. Limitations

Our study was retrospective and conducted on a small sample derived from a single center. Therefore, our findings have to be validated with a larger, multicenter cohort.

5. Conclusion

The OA approach can reduce mortality of IFWCIAI patients without increasing the risk of secondary fistulas. Early OA and EN can also reduce the mortality rates.

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