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Definitive Surgical Treatment of Enterocutaneous Fistula

Outcomes of a 23-Year Experience

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Objective: To analyze postoperative outcomes, morbidity, and mortality following enterocutaneous fistula (ECF) takedown.

Design, Setting, and Patients: Retrospective review of the complete medical records of patients who presented to a single tertiary care referral center from December 24, 1987, to June 18, 2010, and subsequently underwent definitive surgical treatment for ECF originating from the stomach, small bowel, colon, or rectum.

Main Outcome Measures: Postoperative fistula recurrence and mortality.

Results: A total of 153 patients received operative intervention for ECF. Most ECFs were referred to us from outside institutions (75.2%), high output (52.3%), originating from the small bowel (88.2%), and iatrogenic in cause (66.7%). Successful ECF closure was ultimately achieved in 128 patients (83.7%). Six patients (3.9%) died within 30 days of surgery, and overall 1-year mortality was 15.0%. Postoperative complications occurred in 134 patients, for an overall morbidity rate of 87.6%. Significant risk factors for fistula recurrence were numerous, but postoperative ventilation for longer than 48 hours, organ space surgical site infection, and blood transfusion within 72 hours of surgery carried the most considerable impact (relative risks, 4.87, 4.07, and 3.91, respectively; $P<.05$). Risk of 1-year mortality was also associated with multiple risk factors, the most substantial of which were postoperative pulmonary and infectious complications. Closure of abdominal fascia was protective against both recurrent ECF and mortality (relative risks, 0.47 and 0.38, respectively; $P<.05$).

Conclusions: Understanding risk factors both associated with and protective against ECF recurrence and postoperative morbidity and mortality is imperative for appropriate ECF management. Closure of abdominal fascia is of utmost importance, and preventing postoperative complications must be prioritized to optimize patient outcomes.

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ENTEROCUTANEOUS FISTULA (ECF) is defined as an abnormal connection between the gastrointestinal tract and the skin, and it requires labor-intensive medical management and surgical expertise. Complex wound management, severe malnutrition, frequent infectious complications, chronic pain, and depression require significant investment of health care resources and make the short-term and long-term care of these patients difficult. The subsequent operative management often requires lengthy procedures in hostile abdomens with abundant adhesions and surrounding inflammation. In addition to the significant risk of mortality, morbidity can be equally as devastating.

The first major series on ECF from Massachusetts General Hospital in 1960 reported a staggering 44% mortality rate.[1] Recent advances in nutritional and metabolic support, wound care, interventional radiology, and surgical technique have resulted in an overall decline in mortality to 5% to 15%.[2-8] Unfortunately, nonoperative closure rates continue to remain low at 5% to 20%, and definitive operative closure is successful only 75% to 85% of the time.[2-7,9,10]

Randomized studies regarding surgical management of ECF are nonexistent, and most accepted standards are based on expert opinion. Case series within the literature are limited, often

Table 1. Fistula Classifications

Fistula Classification	Description
ECF category	I: Single orifice passing through flat area of skin that is in good condition
	II: Single or multiple ECF orifices close to bony prominences, surgical scars, other stomas, or the umbilicus
	III: ECF presenting through small dehiscence within a single main wound
	IV: ECF at the base of gaping wound or large dehiscence
Daily output	Low: <200 mL
	Intermediate: 200-500 mL
	High: >500 mL
Anatomical location	Gastric, small bowel, colon, or rectum
Cause	Iatrogenic, mesh, inflammatory bowel disease, trauma, radiation, or neoplasm

Abbreviation: ECF, enterocutaneous fistula.

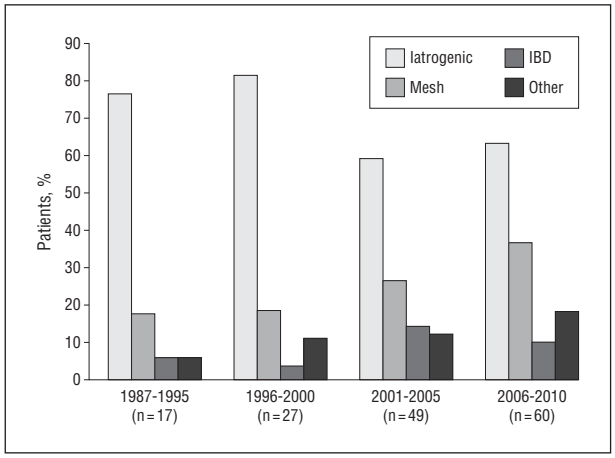

Figure 1. Causes of enterocutaneous fistula between 1987 and 2010. IBD indicates inflammatory bowel disease; other includes radiation, neoplasm, and trauma. Percentages may total more than 100% owing to the fact that some patients' enterocutaneous fistulas were secondary to multiple causes.

involving small cohorts receiving surgical intervention from multiple surgeons and multiple institutions, thus allowing for uncontrolled differences in preoperative preparation, operative technique and skill level, and postoperative care and wound management.[2-7] Additionally, many of these studies exclude certain patient populations (eg, patients with inflammatory bowel disease) or limit the cohort to specific types of ECF (eg, small-bowel fistulas only). This study aims to investigate the outcomes following surgical ECF management by a multidisciplinary team under the leadership of the same surgeon (J.R.G.) over 23 years.

METHODS

PATIENTS

Emory University Hospital is a 579-bed adult tertiary care facility where ECF treatment is orchestrated by a surgical team under the direction of a single surgeon (J.R.G.) in conjunction with enterostomal care nurses and nutritional support staff. We retrospectively reviewed medical records of patients from December 24, 1987, to June 18, 2010, who received definitive surgical treatment for ECF originating from the stomach, small bowel, colon, and rectum. Patients with esophageal, biliary, pancreatic, enterovaginal, enterovesicular, and anal fistulas were excluded from our review. Definitive surgical treatment was defined as an operative procedure in which the segment of stomach or bowel containing the ECF was either oversewn or resected in its entirety with the intention of closing a fistulous tract. Preliminary surgical procedures such as exploration and debridement of fistulous tracts, incision and drainage of associated intra-abdominal abscesses, and/or ECF exteriorization without the aforementioned definitive surgical treatment were also excluded from analysis.

Thorough preoperative, intraoperative, and postoperative data were meticulously extracted from patient records. The eAppendix (http://www.jamasurg.com) includes a complete list of all data points obtained. The data set was incomplete for some patients and is noted accordingly in results when appropriate. Approval for this study was obtained from the Emory University Institutional Review Board.

DEFINITIONS

The ECFs were classified by category, output, anatomical location, and cause (**Table 1**). Fistula categories used within this series are based on difficulty in stoma or wound care and were first described this way by Irving and Beadle[11] and Irving.[12] The ECF output was determined by patient history, clinic records, and inpatient nursing documentation. Anatomical location was diagnosed by radiographic studies and/or operative exploration. The cause of the ECF was determined from medical records. In most cases, the cause was limited to 1 factor; however, there were several cases in which the cause was multifactorial. We followed the standardized definitions of complications used by the National Surgical Quality Improvement Program.[13] All postoperative complications reported are those that occurred within 30 days of surgery.

STATISTICAL ANALYSIS

Study data were collected using research electronic data capture (REDCap)[14] tools hosted at Emory University. REDCap is a secure, web-based application designed to support data capture for research studies, providing the following: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources. All data were managed with REDCap and Microsoft Excel 2007 (Microsoft Corp). Primary study end points were postoperative fistula recurrence and/or death within 1 year of surgery. Numeric variables are presented as mean and range. Analyses of associations between independent variables and outcome were performed using χ^2 test and Fisher exact test for proportions and a 2-sample t test for continuous variables. All hypothesis testing was performed using 2-sided $\alpha = .05$.

RESULTS

OVERALL OUTCOMES

Operative intervention for ECF was undertaken in 153 patients. Trends of ECF cause and postoperative outcomes over the study period are shown in **Figure 1** and

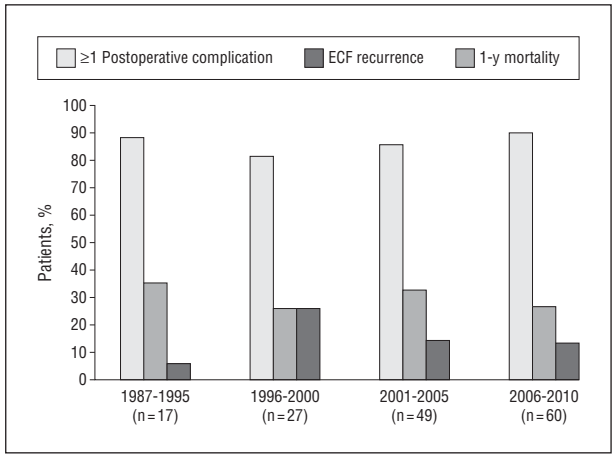

Figure 2. Outcomes of enterocutaneous fistula (ECF) between 1987 and 2010.

Figure 2, respectively. Postoperative mortality (within 30 days of surgery) occurred in 6 patients (3.9%). Overall, 14 patients (9.2%) died while in the hospital, and 1-year mortality occurred in 23 patients (15.0%).

Postoperative ECF recurrence occurred in 45 patients. Spontaneous closure of recurrent ECF occurred in 9 of these patients, leading to an initial refistulization rate of 23.5% (36 of 153 patients). Further operative interventions and their subsequent outcomes are described in **Figure 3**. Ultimately, 21 patients (58.3%) who failed their initial surgery required a second operation attempting ECF closure. Among patients who underwent a second operation, 8 (38.1%) had their fistula successfully and permanently closed. Six remaining patients returned for a third attempt at ECF closure, and 3 (50.0%) unfortunately refistulized again. The overall ECF closure rate following 1 to 3 definitive surgical procedures was 83.7% (128 of 153 patients).

The average hospital length of stay was 56 days; 125 patients (81.7%) were eventually discharged home. Nearly half of all patients (74 patients [48.4%]) were readmitted to our facility at least once within 1 year of surgery. Thirty-nine patients (25.5%) were admitted 2 or more times and 23 (15.0%) were admitted 3 or more times during the first postoperative year. The average duration of postoperative total parenteral nutrition was 86.4 days. Eighteen patients (11.8%) required permanent total parenteral nutrition for short-bowel syndrome, and 3 patients (2.0%) were referred for small-bowel transplant.

PATIENT DEMOGRAPHIC CHARACTERISTICS AND COMORBIDITIES

Patient demographic characteristics and comorbidities for the entire cohort as well as those patients who had refistulization within 30 days and/or died within 1 year of surgery are shown in **Table 2**. Most patients (75.2%) were referrals from outside our institution. The average time from development of ECF until referral was 145 days (range, 0-2190 days). The most common preoperative comorbidity was dyspnea. Seventy-three patients (47.7%) reported a history of tobacco abuse, but only 43 (28.1%) reported smoking within 1 year of surgery. The average pack-year history was 17 (range, 5-130 pack-years). More than half

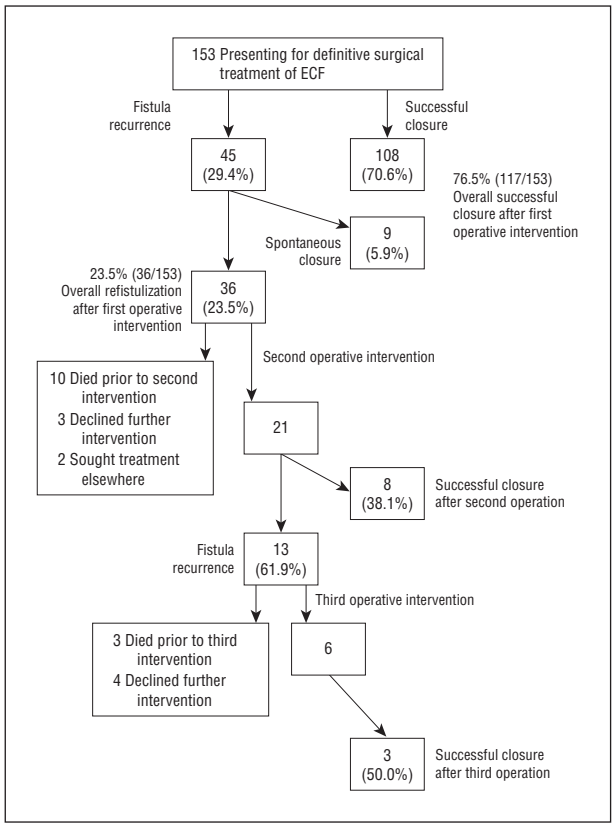

Figure 3. Overall patient outcomes, indicating rates of enterocutaneous fistula (ECF) closure and recurrence following each operative intervention.

of all patients (59.5%) were of either a partially or totally dependent functional status at the time of surgery.

On average, patients had undergone 5 or more prior abdominal operations. The average time from diagnosis of ECF to operative intervention was 267 days (range, 0-2201 days). Most patients (80.4%) required total parenteral nutrition for an average duration of 144 days (range, 0-1000 days). Among the 123 patients requiring preoperative central venous access, 77 of them (62.6%) experienced at least 1 preoperative episode of central line–associated blood stream infection.

Patients with a preoperative diagnosis of short-bowel syndrome had the highest relative risk (RR) of fistula recurrence within 30 days of surgery (RR, 2.78; 95% CI, 1.48-5.23). Other significant comorbidity-related variables for short-term refistulization included long-term steroid use, severe chronic obstructive pulmonary disease, portal hypertension, and the duration between diagnosis and surgical intervention being longer than 1 year.

Patients transferred from a long-term care facility had nearly 4 times the risk of 1-year mortality compared with patients admitted from other places (RR, 3.80; 95% CI, 1.82-7.94). Other significant risk factors associated with 1-year mortality included transfer from an outside hospital, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) lower than 20, dyspnea, portal hypertension, preoperative total parenteral nutrition–induced cholestasis, and totally dependent functional status prior to surgery. Patients admitted directly from home prior to surgery had a significantly

Table 2. Patient Demographic Characteristics and Comorbidities

Characteristic	Overall, No. (%) (N = 153)	Short-term Refistulization (n = 32)			1-y Mortality (n = 23)		
		No. (%)[a]	RR (95% CI)	*P* Value	No. (%)[b]	RR (95% CI)	*P* Value
Demographic							
Male	74 (48.4)	13 (17.6)		.32	11 (14.9)		.96
Age at surgery, mean (range), y	54.9 (19.9-84.4)						
Aged >50 y at surgery	94 (61.4)	19 (20.2)		.79	18 (19.2)		.07
BMI, mean (range)	29 (12.0-65.8)						
<20	20 (13.1)	2 (10.0)		.20	6 (30.0)	2.35 (1.05-5.24)	.04
>35	25 (16.3)	4 (16.0)		.51	1 (4.0)		.09
Prior abdominal operations, mean (range), No.	5.75 (1-43)						
>6	43 (28.1)	7 (16.3)		.38	4 (9.3)		.22
Referral source							
External referral	115 (75.2)	25 (21.7)		.66	19 (16.5)		.37
<90 d from diagnosis to OR	31 (20.3)	5 (16.1)		.46	4 (12.9)		.71
>1 y from diagnosis to OR	31 (20.3)	11 (35.5)	2.06 (1.12-3.81)	.03	6 (19.4)		.45
Admission source							
Admitted from home	97 (63.4)	19 (19.6)		.60	9 (9.3)	0.37 (0.17-0.80)	.009
Transferred from outside hospital	27 (17.6)	5 (18.5)		.74	8 (29.6)	2.49 (1.17-5.27)	.02
Admitted from ED	15 (9.8)	3 (20.0)		.93			
Transferred from long-term care facility	13 (8.5)	5 (38.5)		.10	6 (46.2)	3.80 (1.82-7.94)	.001
Comorbidity							
>10% Unintentional weight loss	33 (21.6)	8 (24.2)		.60	8 (24.2)		.09
Smoking	43 (28.1)	9 (20.9)		.66	5 (11.6)		.28
DM	35 (22.9)	7 (20.0)		.88	5 (14.3)		.89
Severe COPD	16 (10.5)	7 (43.8)	2.40 (1.24-4.63)	.02	5 (31.3)		.06
Dyspnea	54 (35.3)	13 (24.1)		.48	15 (27.8)	3.44 (1.56-7.59)	.001
Portal hypertension	15 (9.8)	6 (40.0)	2.12 (1.04-4.32)	.06	6 (40.0)	3.25 (1.51-6.96)	.004
Long-term steroid use	13 (8.5)	6 (46.2)	2.49 (1.26-4.92)	.02	3 (23.1)		.40
Anemia requiring preoperative blood transfusion	15 (9.8)	3 (20.0)		.93	5 (33.3)	2.56 (1.12-5.89)	.04
Preoperative occurrence							
Required preoperative TPN	123 (80.4)	29 (23.6)		.27	21 (17.1)		.32
TPN-induced cholestasis	15 (9.8)	3 (20.0)		.93	6 (40.0)	3.25 (1.51-6.96)	.004
Preoperative CVL infection	77 (50.3)	17 (22.1)		.72	14 (18.2)		.05
Preoperative shock	16 (10.5)	4 (25.0)		.67	3 (18.8)		.66
Preoperative diagnosis of short-bowel syndrome	14 (9.2)	7 (50.0)	2.78 (1.48-5.23)	.005	4 (28.6)		.22
Functional status at time of surgery[c]							
Independent	62 (40.5)	12 (19.4)		.70	8 (12.9)		.54
Partially dependent	77 (50.3)	17 (22.1)		.72	10 (13.0)		.48
Totally dependent	14 (9.2)	3 (21.4)		.96	5 (35.7)	2.76 (1.21-6.29)	.02

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; CVL, central venous line; DM, diabetes mellitus; ED, emergency department; OR, operating room; RR, relative risk; TPN, total parenteral nutrition.

[a] Short-term refistulization indicates within 30 days; percentage, patients with the specific variable who had short-term fistula recurrence.

[b] Percentage indicates patients with the specific variable who died within 1 year of surgery.

[c] Independent indicates that the patient does not require assistance from another person for activities of daily living; partially dependent, the patient requires some assistance from another person for activities of daily living; and totally dependent, the patient requires total assistance for activities of daily living.[13]

decreased risk of mortality compared with those admitted from elsewhere (RR, 0.37; 95% CI, 0.17-0.80).

FISTULA CHARACTERISTICS

Table 3 describes fistula characteristics. Most ECFs were category III and category IV fistulas (45.1% and 36.6%, respectively), high output (52.3%), originating from the small bowel (88.2%), and iatrogenic in cause (66.7%). Category IV ECFs were at significant risk for refistulization (RR, 1.96; 95% CI, 1.07-3.62); however, output and fistula anatomy were not associated with fistula recurrence. Inflammatory bowel disease was associated with more than 2.5 times the RR of recurrent fistula (RR, 2.58; 95% CI, 1.35-4.92). The ECFs attributed to mesh implantation were significantly less likely to recur (RR, 0.17; 95% CI, 0.04-0.68). Cause, output, and category of ECF had no significant associated risk with 1-year mortality; however, patients with gastrocutaneous fistulas had a 3-fold increased risk of death within the first year of surgery (RR, 3.13; 95% CI, 1.21-8.07).

OPERATIVE DATA

Table 4 summarizes operative data. There were no intraoperative deaths. Operative duration was often prolonged, with 56 cases (36.6%) lasting longer than 7 hours. Sixteen cases (10.5%) had an estimated blood loss greater

Table 3. Fistula Characteristics

Characteristic	Overall, No. (%) (N = 153)	Short-term Refistulization (n = 32)			1-y Mortality (n = 23)		
		No. (%)[a]	RR (95% CI)	*P* Value	No. (%)[b]	RR (95% CI)	*P* Value
Category							
I	10 (6.5)	2 (20.0)		.88	3 (30.0)		.17
II	17 (11.1)	2 (11.8)		.35	1 (5.9)		.26
III	69 (45.1)	11 (15.9)		.17	7 (10.1)		.13
IV	56 (36.6)	17 (30.4)	1.96 (1.07-3.62)	.03	12 (21.4)		.09
Output							
Low	41 (26.8)	6 (14.6)		.25	6 (14.6)		.93
Intermediate	28 (18.3)	8 (28.6)		.24	4 (14.3)		.90
High	80 (52.3)	17 (21.3)		.92	13 (16.3)		.66
Anatomical location							
Gastric	7 (4.6)	3 (42.9)		.14	3 (42.9)	3.13 (1.21-8.07)	.04
Small bowel	135 (88.2)	30 (22.2)		.28	21 (15.6)		.62
Colon	31 (20.3)	9 (29.0)		.21	3 (9.7)		.35
Rectum	3 (2.0)	1 (33.3)		.59			
Cause							
Iatrogenic	102 (66.7)	24 (23.5)		.26	18 (17.7)		.20
Mesh	43 (28.1)	2 (4.7)	0.17 (0.04-0.68)	.002	3 (7.0)		.08
IBD	15 (9.8)	7 (46.7)	2.58 (1.35-4.92)	.01	1 (6.7)		.34
Trauma	6 (3.9)	2 (33.3)		.45	1 (16.7)		.91
Radiation	3 (2.0)				1 (33.3)		.37
Neoplasm	8 (5.2)				3 (37.5)		.07

Abbreviations: IBD, inflammatory bowel disease; RR, relative risk.
[a] Short-term refistulization indicates within 30 days; percentage, patients with the specific variable who had short-term fistula recurrence.
[b] Percentage indicates patients with the specific variable who died within 1 year of surgery.

Table 4. Operative Data and Postoperative Outcomes

Outcome	Overall, No. (%) (N = 153)	Short-term Refistulization (n = 32)			1-y Mortality (n = 23)		
		No. (%)[a]	RR (95% CI)	*P* Value	No. (%)[b]	RR (95% CI)	*P* Value
Operative occurrence							
Operative duration, mean (range), h:min	6:29 (00:34-15:40)						
<8 h	114 (74.5)	19 (16.7)	0.50 (0.27-0.92)	.03	13 (11.4)	0.45 (0.21-0.93)	.03
>8 h	39 (25.5)	13 (33.3)	2.00 (1.09-3.66)	.03	10 (25.6)	2.25 (1.07-4.71)	.03
Duration of adhesiolysis, mean (range), h:min	3:45 (00:15-07:00)						
<4 h	85 (55.6)	16 (18.2)		.48	10 (11.8)		.21
≥4 h	68 (44.4)	16 (23.5)		.48	13 (19.1)		.21
EBL, mean (range), mL	551 (10-7000)						
<1000	137 (89.5)	23 (16.8)	0.30 (0.17-0.53)	<.001	16 (11.7)	0.27 (0.13-0.55)	.001
>1000	16 (10.5)	9 (56.3)	3.35 (1.89-5.93)	<.001	7 (43.8)	3.75 (1.82-7.71)	.001
Minimum temperature, mean (range), °C	35.6 (33.1-37.6)						
<35	25 (16.3)	5 (20.0)		.90	5 (20.0)		.45
>35	128 (83.7)	27 (21.1)		.90	18 (14.1)		.45
ASA class							
2	18 (11.8)	3 (16.7)		.64			
3	104 (68.0)	21 (20.2)		.75	13 (12.5)		.22
4	31 (20.3)	8 (25.8)		.45	10 (32.3)	3.02 (1.47-6.24)	.003
Type of anastomosis[c]							
Hand sewn	133 (86.9)	28 (21.1)		.76	18 (13.6)		.31
Stapled	10 (6.5)	4 (40.0)		.12			
None, ECF primarily oversewn	12 (7.8)	3 (25.0)		.72	5 (41.7)	3.26 (1.47-7.24)	.007
Abdominal wall closure							
Fascia closed[d]	108 (70.6)	17 (15.7)	0.47 (0.26-0.86)	.02	11 (10.2)	0.38 (0.18-0.80)	.009
Not closed	45 (29.4)	15 (33.3)	2.12 (1.16-3.86)	.02	12 (26.7)	2.62 (1.25-5.49)	.009

Abbreviations: ASA, American Society of Anesthesiologists; EBL, estimated blood loss; ECF, enterocutaneous fistula; RR, relative risk.
[a] Short-term refistulization indicates within 30 days; percentage, patients with the specific variable who had short-term fistula recurrence.
[b] Percentage indicates patients with the specific variable who died within 1 year of surgery.
[c] Two patients had both types of anastomosis performed during a single operation.
[d] Forty-one patients (26.8%) had component separation; 22 (14.4%) had the abdominal wall reinforced with mesh.

Table 5. Postoperative Outcomes at 30 Days

Outcome	Overall, No. (%) (N = 153)	Short-term Refistulization (n = 32)			1-y Mortality (n = 23)		
		No. (%)[a]	RR (95% CI)	*P* Value	No. (%)[b]	RR (95% CI)	*P* Value
Wound complication							
Superficial SSI	20 (13.1)	1 (5.0)		.08	1 (5.0)		.31
Deep incisional SSI	5 (3.3)	3 (60.0)		.06			
Organ space SSI	22 (14.4)	13 (59.1)	4.07 (2.37-7.01)	<.001	3 (13.6)		.84
Refistulization <30 d	32 (20.9)				10 (31.3)	2.91 (1.41-6.01)	.004
Refistulization >30 d	14 (9.2)				1 (7.1)		.39
Pulmonary complication							
Pneumonia	25 (16.3)	8 (32.0)		.14	11 (44.0)	4.69 (2.34-9.42)	<.001
Unplanned intubation	25 (16.3)	8 (32.0)		.14	8 (32.0)	2.73 (1.30-5.74)	.01
Mechanical ventilation >48 h	39 (25.5)	20 (51.3)	4.87 (2.63-9.02)	<.001	14 (35.9)	4.55 (2.14-9.67)	<.001
Cardiac complication							
Postoperative MI	2 (1.3)	1 (50.0)		.38	1 (50.0)		.28
Cardiac arrest requiring CPR	1 (0.7)				1 (100.0)		.15
Arrhythmia requiring cardioversion	9 (5.9)	1 (11.1)		.69	3 (33.3)		.11
Renal complication							
UTI	33 (21.6)	10 (30.3)		.13	5 (15.2)		.98
Progressive renal insufficiency	5 (3.3)						
Acute renal failure requiring dialysis	9 (5.9)	3 (33.3)		.40	5 (55.6)	4.44 (2.15-9.19)	.001
Other complication							
Sepsis or shock	54 (35.3)	18 (33.3)	2.35 (1.27-4.36)	.005	13 (24.1)	2.38 (1.12-5.07)	.02
CVL infection	40 (26.1)	11 (27.5)		.23	8 (20.0)		.31
DVT requiring treatment	4 (2.6)				3 (75.0)	5.59 (2.78-11.22)	.01
Blood transfusion within 72 h of surgery	109 (71.2)	29 (26.6)	3.91 (1.25-12.15)	.007	20 (18.3)		.07
Disposition							
Length of stay >30 d	55 (35.9)	26 (47.3)	7.72 (3.39-17.6)	<.001	11 (20.0)		.20
Discharged to home	125 (81.7)	21 (16.8)	0.43 (0.23-0.78)	.008	6 (4.8)	0.08 (0.03-0.18)	<.001

Abbreviations: CPR, cardiopulmonary resuscitation; CVL, central venous line; DVT, deep vein thrombosis; MI, myocardial infarction; RR, relative risk; SSI, surgical site infection; UTI, urinary tract infection.

[a] Short-term refistulization indicates within 30 days; percentage, patients with the specific variable who had short-term fistula recurrence.

[b] Percentage indicates patients with the specific variable who died within 1 year of surgery.

than 1000 mL. More than 20% of patients were classified by the American Society of Anesthesiologists as having severe, life-threatening systemic disease (American Society of Anesthesiologists class 4). Surgical repair of ECF was accomplished with resection in 141 cases (92.2%); the remaining 12 cases involved primary repair. Most cases (86.9%) were repaired with 2-layered, hand-sewn anastomoses. There were only 10 instances (6.5%) of stapled anastomoses, most of which occurred in low rectal dissections. Abdominal fascia closure was attained in more than two-thirds of cases, and only 11 patients (7.2%) exited the operating room with an open abdomen.

Cases longer than 8 hours and those with an estimated blood loss greater than 1000 mL had more than 2 and 3 times the risk of recurrent fistula formation, respectively ($P < .05$ for both). Cases in which a patient's abdominal fascia was closed intraoperatively were half as likely to have refistulization in the postoperative period ($P = .02$).

Variables associated with increased risk of 1-year mortality included American Society of Anesthesiologists class 4, cases lasting longer than 8 hours, and those with an estimated blood loss greater than 1000 mL. Closure of the abdominal fascia significantly decreased a patient's risk of 1-year mortality (RR, 0.38; 95% CI, 0.18-0.80).

POSTOPERATIVE OUTCOMES

Postoperative complications occurred in 134 patients, for an overall morbidity rate of 87.6% (**Table 5**). Numerous patients had more than 1 postoperative complication. The most common complication, blood transfusion within 72 hours of the start of surgery, occurred in 109 patients (71.2%). Fifty-four patients (35.3%) experienced an episode of sepsis or shock, and 1 in 4 patients (25.5%) required mechanical ventilation for longer than 48 hours.

Organ space surgical site infection, mechanical ventilation longer than 48 hours, blood transfusion within 72 hours of the start of surgery, and sepsis or shock were all significantly associated with an increased risk of ECF recurrence (RR, 4.07, 4.87, 3.91, and 2.35, respectively). A postoperative pulmonary complication was associated with an increased risk of mortality, ranging from 2.73 to 4.69 times the RR depending on the specific complication. Three in 4 patients with postoperative deep vein thrombosis that required treatment died within the year following surgery (RR, 5.59; 95% CI, 2.78-11.22). Postoperative sepsis or shock and acute renal failure requiring dialysis were also significantly associated with 1-year mortality.

Early refistulization correlated with a nearly 3-fold increase in the RR for mortality during the first postopera-

tive year. However, patients who were eventually discharged to home, regardless of the length of hospital stay, were more than 12 times less likely to die (RR, 0.08; 95% CI, 0.03-0.18).

COMMENT

Enterocutaneous fistulas are dreadful problems for patients to endure and are extremely challenging and onerous for the surgeon to manage and subsequently repair. Our 30-day and 1-year mortality rates (3.9% and 15.0%, respectively) are comparable with, and in some cases better than, rates reported in other series.[2-7,9,15-18] Even though the surgical community has substantially decreased the mortality rate among patients with ECF, preventing and treating the problem remain as challenging as ever. As a result, trends within both our data and other series demonstrate that successful ECF closure and the morbidity rates associated with these interventions have shown very little improvement during the past few decades.

Our 76.5% first-time definitive surgical success rate of ECF closure is on par with other series reported in the literature.[2-7,9,10,15,16] However, it was necessary to use 2 or 3 additional surgical attempts to close recurrent ECF and achieve an overall ECF closure rate of 83.7%. Unfortunately, the fact remains that expert surgical care at the best referral centers still results in a failure of ECF closure 15% to 30% of the time, with more than 80% of patients experiencing significant postoperative complications.

PATIENT SELECTION AND PREOPERATIVE MANAGEMENT

Our study reveals that patients with severe chronic obstructive pulmonary disease, portal hypertension, a history of long-term steroid use, and/or a diagnosis of short-bowel syndrome prior to surgery have double the RR for postoperative development of a recurrent fistula. Similarly, dyspnea (whether at rest or on exertion), portal hypertension, and preoperative anemia requiring a blood transfusion within 72 hours prior to surgery are preoperative indicators that a patient is at increased risk for 1-year mortality. In a series of 167 cases of surgical ECF closure, Mawdsley et al[4] reported that the presence of comorbidity was the single significant factor influencing fistula-related mortality.

Timing of operative intervention is crucial within this patient population.[5,16] Lynch et al[3] argued that delaying surgery anywhere from 12 to 36 months will improve the outcomes in patients with ECF. Our series, however, found that prolonging surgery for longer than 1 year following ECF diagnosis will double the risk of postoperative refistulization. This finding is also echoed by Brenner et al,[6] who reported that intervals from diagnosis to operation longer than 36 weeks are associated with a 5-times greater risk of fistula recurrence. Ultimately, as our data show, the high risk of central line–associated blood stream infection in patients with ECF becomes problematic with prolonged waits. Nevertheless, this concern must be balanced with the risks and difficulties in attempting ECF closure too soon before dense adhesions (ie, obliterative peritonitis) lessen, making the abdomen more amenable to exploration.[19] Our usual practice is to wait at least 4 months from any last major surgical intervention.

Within our series, BMI less than 20 and totally dependent functional status prior to surgery were each associated with more than twice the RR of 1-year mortality. Surgeons must aggressively address any signs of malnutrition and/or debilitating functional status prior to surgical intervention in efforts to maximize the chances of a successful operation and decrease the risk of refistulization or death.

Several studies within the literature attribute postoperative outcomes to the characteristics of ECFs themselves. Martinez et al[15,16] published 2 series within the literature, both concluding that high-output fistulas (>500 mL/24 hours) are more likely to recur postoperatively and be associated with higher rates of mortality. Our study demonstrates no significant association between ECF output, refistulization, and mortality. However, our results indicate that complex category IV ECFs, which make up 36.6% of our population, are almost twice as likely to refistulize following surgery. While not statistically significant, it should be noted that category III ECFs, which make up 45.1% of our population, carry a 15.9% rate of recurrence. Similarly, Mawdsley et al[4] reported that fistula complexity (>1 fistula, multiple bowel loops, and/or internal abscess cavity) is in fact the only significant factor associated with fistula recurrence following surgical repair.

Our data show that the incidence of ECF secondary to mesh implantation is on the rise. However, our results reveal that ECFs caused by mesh implantation are more than 5 times less likely to recur following surgery, probably because the offending mechanism has been removed. We also demonstrate that patients with ECF secondary to inflammatory bowel disease are 2.5 times more likely to have refistulization than those with ECF caused by other factors. Similarly, Brenner et al[6] reported that inflammatory bowel disease increases the risk of ECF recurrence by nearly 5 times (odds ratio, 4.9). Understandably, the underlying pathophysiology within this patient population both interferes with healing and promotes the formation of new ECF.

The only ECF characteristic significantly associated with mortality was anatomical location. Patients with gastrocutaneous fistulas had 1-year mortality rates 3 times higher than the rest of the cohort. Interestingly, most of these ECFs were nonhealing gastrostomy tube sites that had been previously used for feeding. Thus, it appears gastrocutaneous fistulas are rather indicators of sicker patients with poor nutritional status.

INTRAOPERATIVE TECHNIQUE

One-third of all patients within our series who were at American Society of Anesthesiologists class 4 at the time of surgery died within the first postoperative year. This is likely representative of the numerous previously mentioned comorbidities that are associated with increased risk of mortality. Additionally, our results indicate that operative duration, estimated blood loss, resection type, and abdominal wall closure each play a significant role

in patient outcomes. One-third of all cases with the operation lasting longer than 8 hours and more than half of the cases with significant blood loss (>1000 mL) were associated with a recurrent fistula and increased risk of 1-year mortality.

In multiple series, univariate and multivariate analyses demonstrate that ECF recurrence is more likely after oversewing the fistula instead of resection with primary anastomosis.[3,15] Similarly, Brenner et al[6] report that ECF recurrence is 4 times more likely in patients with stapled anastomoses compared with hand-sewn ones (odds ratio, 4.3; $P = .01$). While our series did not reveal a significant association between recurrent fistula and the type of anastamosis or resection instead of primary repair, there was a significant association between these variables and mortality. We demonstrate that patients who have a primary repair of their ECF instead of a resection have a 3-fold increased risk for 1-year mortality. We share the other authors' opinions that primary repair of ECF should be discouraged as a definitive surgical technique for closure.

Abdominal wall closure after ECF repair has a considerable effect on patient outcomes. Our study reveals that patients whose fascia we were unable to close had more than double the risk of ECF recurrence and 1-year mortality. Without appropriate fascial coverage, even the best-repaired fistulas are much less likely to heal.[20]

POSTOPERATIVE CARE

More than 35% of patients in our series developed at least 1 episode of postoperative sepsis and/or shock; among these patients, one-third developed a recurrent fistula and one-fourth died within 1 year. Martinez et al[15] similarly reported that postoperative sepsis is the most important factor associated with mortality in patients with ECF. Furthermore, patients who developed an organ space surgical site infection (eg, intra-abdominal abscess) were 4 times more likely to have refistulization. Whether the organ space surgical site infection is causative or merely an indicator of refistulization, all efforts should be made intraoperatively to minimize excessive contamination and to repair deserosalizations.

Patients who required mechanical ventilation for longer than 48 hours postoperatively had nearly 5 times the risk of refistulization. Moreover, patients requiring blood transfusion within 72 hours of the start of surgery had an almost 4-times greater risk of recurrent fistula. One might assume that anemia at any point during the healing process, whether during or after surgery, results in decreased oxygen delivery to a healing anastamosis, thus increasing its risk for breakdown.

Postoperative ECF recurrence was associated with a 3-fold increased risk of death within the first year following ECF repair. Likewise, Brenner et al[6] reported that ECF recurrence is a primary determinant for mortality. Thus, any efforts to prevent recurrence would also directly prevent mortality.

LIMITATIONS

We believe the weaknesses of our study are 3-fold. Seventeen patients (11.1%) were lost to follow-up, never having returned to our institution following surgical treatment of their ECF; it is possible that episodes of ECF recurrence were not detected in this small group of patients. Furthermore, because this is a purely descriptive analysis of outcomes following surgical repair of ECF, we do not report independent risk factors for recurrent ECF and/or mortality. It is our intent to create more in-depth predictive models in follow-up studies. Lastly, additional quality-of-life studies need to be pursued.

CONCLUSIONS

Results of our study demonstrate that careful selection of patients, aggressive preoperative management, judicious intraoperative technique, and vigilant postoperative care are essential for successful outcomes following the surgical closure of ECF. In particular, preoperative nutritional optimization, abdominal fascia closure, and prevention of postoperative complications remain paramount for preventing refistulization and postoperative mortality.

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REFERENCES

1. Edmunds LH Jr, Williams GM, Welch CE. External fistulas arising from the gastrointestinal tract. *Ann Surg.* 1960;152:445-471.
2. Hollington P, Mawdsley J, Lim W, Gabe SM, Forbes A, Windsor AJ. An 11-year experience of enterocutaneous fistula. *Br J Surg.* 2004;91(12):1646-1651.
3. Lynch AC, Delaney CP, Senagore AJ, Connor JT, Remzi FH, Fazio VW. Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery. *Ann Surg.* 2004;240(5):825-831.
4. Mawdsley JE, Hollington P, Bassett P, Windsor AJ, Forbes A, Gabe SM. An analysis of predictive factors for healing and mortality in patients with enterocutaneous fistulas. *Aliment Pharmacol Ther.* 2008;28(9):1111-1121.
5. Visschers RG, Olde Damink SW, Winkens B, Soeters PB, van Gemert WG. Treatment strategies in 135 consecutive patients with enterocutaneous fistulas. *World J Surg.* 2008;32(3):445-453.
6. Brenner M, Clayton JL, Tillou A, Hiatt JR, Cryer HG. Risk factors for recurrence after repair of enterocutaneous fistula. *Arch Surg.* 2009;144(6):500-505.
7. Datta V, Engledow A, Chan S, Forbes A, Cohen CR, Windsor A. The management

of enterocutaneous fistula in a regional unit in the United Kingdom: a prospective study. *Dis Colon Rectum*. 2010;53(2):192-199.
8. Lundy JB, Fischer JE. Historical perspectives in the care of patients with enterocutaneous fistula. *Clin Colon Rectal Surg*. 2010;23(3):133-141.
9. Draus JM Jr, Huss SA, Harty NJ, Cheadle WG, Larson GM. Enterocutaneous fistula: are treatments improving? *Surgery*. 2006;140(4):570-578.
10. Evenson AR, Fischer JE. Current management of enterocutaneous fistula. *J Gastrointest Surg*. 2006;10(3):455-464.
11. Irving M, Beadle C. External intestinal fistulas: nursing care and surgical procedures. *Clin Gastroenterol*. 1982;11(2):327-336.
12. Irving M. Gastrointestinal fistulae. In: Schwartz SI, Ellis H, eds. *Maingot's Abdominal Operations*. Vol 1. East Norwalk, CT: Appleton-Century-Crofts; 1985: 356-358.
13. American College of Surgeons National Surgical Quality Improvement Program. Data variables and definitions. http://www.acsnsqip.org. Accessed January 20, 2012.
14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap): a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.
15. Martinez JL, Luque-de-León E, Ballinas-Oseguera G, Mendez JD, Juárez-Oropeza MA, Román-Ramos R. Factors predictive of recurrence and mortality after surgical repair of enterocutaneous fistula. *J Gastrointest Surg*. 2012;16(1):156-164.
16. Martinez JL, Luque-de-Leon E, Mier J, Blanco-Benavides R, Robledo F. Systematic management of postoperative enterocutaneous fistulas: factors related to outcomes. *World J Surg*. 2008;32(3):436-444.
17. McIntyre PB, Ritchie JK, Hawley PR, Bartram CI, Lennard-Jones JE. Management of enterocutaneous fistulas: a review of 132 cases. *Br J Surg*. 1984;71(4):293-296.
18. Altomare DF, Serio G, Pannarale OC, et al. Prediction of mortality by logistic regression analysis in patients with postoperative enterocutaneous fistulae. *Br J Surg*. 1990;77(4):450-453.
19. Cohen M, Grevious M. The use of muscle flaps for the management of recalcitrant gastrointestinal fistulas. *Clin Plast Surg*. 2006;33(2):295-302.
20. Fischer JE. The importance of reconstruction of the abdominal wall after gastrointestinal fistula closure. *Am J Surg*. 2009;197(1):131-132.