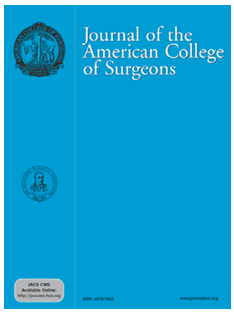
Accepted Manuscript



Patients with Complicated Intra-Abdominal Infection Presenting with Sepsis Do Not Require Longer Duration of Antimicrobial Therapy

Rishi Rattan, MD, Casey J. Allen, MD, Robert G. Sawyer, MD, Reza Askari, MD, Kaysie L. Banton, MD, Jeffrey A. Claridge, MD, MS, FACS, Christine Cocanour, MD, FACS, FCCM, Raul Coimbra, MD, PhD, FACS, Charles H. Cook, MD, FACS, FCCM, Joseph Cuschieri, MD, FACS, E Patchen Dellinger, MD, Therese M. Duane, MD, FACS, FCCM, Heather L. Evans, MD, MS, FACS, Pamela Lipsett, MD, MHPE, FACS, FCCM, John Mazuski, MD, PhD, Preston R. Miller, MD, Patrick J. O'Neill, MD, PhD, FACS, Ori D. Rotstein, MD, MSc, FRCSC, FACS, Nicholas Namias, MD, MBA, FACS, FCCM

PII: S1072-7515(16)00034-X

DOI: 10.1016/j.jamcollsurg.2015.12.050

Reference: ACS 8164

To appear in: *Journal of the American College of Surgeons*

Received Date: 23 December 2015

Accepted Date: 28 December 2015

Please cite this article as: Rattan R, Allen CJ, Sawyer RG, Askari R, Banton KL, Claridge JA, Cocanour C, Coimbra R, Cook CH, Cuschieri J, Dellinger EP, Duane TM, Evans HL, Lipsett P, Mazuski J, Miller PR, O'Neill PJ, Rotstein OD, Namias N, Patients with Complicated Intra-Abdominal Infection Presenting with Sepsis Do Not Require Longer Duration of Antimicrobial Therapy, *Journal of the American College of Surgeons* (2016), doi: 10.1016/j.jamcollsurg.2015.12.050.

Patients with Complicated Intra-Abdominal Infection Presenting with Sepsis Do Not Require Longer Duration of Antimicrobial Therapy

Rishi Rattan, MD, University of Miami Miller School of Medicine

Casey J Allen, MD, University of Miami Miller School of Medicine

Robert G Sawyer, MD, University of Virginia Health System

Reza Askari, MD, Brigham and Women's Hospital

Kaysie L Banton, MD, University of Minnesota Medical Center

Jeffrey A Claridge, MD, MS, FACS, Case Western Reserve University School of Medicine

Christine Cocanour, MD, FACS, FCCM, University of California Davis

Raul Coimbra MD, PhD, FACS, University of California San Diego

Charles H Cook, MD, FACS, FCCM, Beth Israel Deaconnness Medical Center

Joseph Cuschieri, MD, FACS, University of Washington Harborview Medical Center

E Patchen Dellinger, MD, University of Washington

Therese M Duane, MD, FACS, FCCM, Virginia Commonwealth University

Heather L Evans, MD, MS, FACS, University of Washington Harborview Medical Center

Pamela Lipsett, MD, MHPE, FACS, FCCM, Johns Hopkins University School of Medicine

John Mazuski, MD, PhD, Washington University School of Medicine

Preston R Miller, MD, Wake Forest-Baptist Health

Patrick J O'Neill, MD, PhD, FACS, Abrazo West Campus

Ori D Rotstein, MD, MSc, FRCSC, FACS, University of Toronto St Michael's Hospital

Nicholas Namias, MD, MBA, FACS, FCCM, University of Miami Miller School of Medicine

Disclosure Information: Nothing to disclose.

Presented at the Southern Surgical Association 127th Annual Meeting, Hot Springs, VA,

December 2015.

Correspondence address:
Nicholas Namias MD MBA FACS FCCM
Ryder Trauma Center T215 (D-40)
1800 NW 10th Ave
Miami, FL 33136
nnamias@miami.edu
(305)585-1822

Brief title: Antibiotic Duration in Abdominal Sepsis

Abstract

Background: A recent prospective, multicenter, randomized controlled trial found that 4 days of antibiotics after source control of complicated intra-abdominal infections (CIAI) resulted in similar outcomes when compared to longer duration. We hypothesized that the subset of patients presenting with sepsis have similar outcomes when treated with the shorter-course of antibiotics.

Study Design: Patients from the STOP-IT database meeting criteria for sepsis (temperature <36^{o} Celsius or >38^{o} Celsius and a white blood cell count <4,000 cells/mm^{3} or >12,000 cells/mm^{3}) were analyzed. Patients had been randomized to receive antibiotics until 2 days after the resolution of fever, leukocytosis, and ileus, with a maximum of 10 calendar days of therapy (n=45), or to receive a fixed short-course of antibiotics for 4±1 calendar days (n=67). Outcomes included incidence of and time to surgical site infection (SSI), recurrent intra-abdominal infection, *Clostridium difficile* infection (CDI), and extra-abdominal infections, as well as hospital days and mortality.

Results: 112 of the 588 patients in the STOPIT database met criteria for sepsis, and were adherent to the protocol. With regard to short- versus long-course therapy, SSI (11.9% vs 8.9%, p=0.759), recurrent intra-abdominal infection (11.9% vs 13.3%, p=1.00), extra-abdominal infection (11.9% vs 8.9%, p=0.759), hospital days (7.4±5.5 vs 9.0±7.5, p=0.188), days to recurrent intra-abdominal infection (12.5±6.6 vs 18.0±8.1, p=0.185), days to extra-abdominal infection (12.6±5.8 vs 17.3±3.9, p=0.194), and mortality (1.5% vs 0%, p=1.00) were similar. There were no cases of CDI. Days to SSI (6.9±3.5 vs 21.3±6.1, p<0.001) was lower in the 4-day therapy group.

Conclusions: There was no difference in outcome between short and long-course antimicrobial therapy in patients with CIAI presenting with sepsis. Our findings suggest that the presence of systemic illness does not mandate a longer antimicrobial course if source control of CIAI is obtained.

Keywords: complicated intra-abdominal infection, sepsis, septic shock, antibiotics

Abbreviations

CDI, *Clostridium difficile* infection

CIAI, complicated intra-abdominal infection

SSI, surgical site infection

WBC, white blood cell count

Introduction

Complicated intra-abdominal infections (CIAI) are an important cause of morbidity and mortality worldwide. They include a wide range of disease processes. The most common source is the appendix, accounting for approximately one-third of CIAI regardless of geographic location(1-3). Despite this diversity in organ involvement, mortality seems to be more dependent on intrinsic factors of the individual than the originating organ(3).

Nevertheless, principles of treatment remain relatively constant: resuscitation of those with sepsis, removal of the source of the inflammatory response, and systemic antimicrobial therapy. Despite this, clinically significant infectious complications arise in approximately 20% of CIAI(3). While source control has been a major foundation, management of sepsis has more recently been unified by the evidence-based Surviving Sepsis Campaign Guidelines(4). Conversely, while robust data supports the use of antimicrobial therapy in CIAI, the duration of such therapy is less well-studied. Joint guidelines from the Surgical Infection Society and the Infectious Diseases Society of America recommend 4-7 days of antimicrobial therapy(5). Data has existed for several decades, however, suggesting a shorter duration of therapy leads to acceptable outcomes in the contaminated abdomen(6). Reticence to shorten duration has been based on the notable recurrent infection rate. However, a recent prospective, observational cohort study found that there was no difference in infectious complications after appendectomy for complicated appendicitis when postoperative antibiotic therapy was reduced from 5 days to 3 days(7). Similarly, a recent prospective, randomized, multicenter trial comparing 4 days of antimicrobial therapy to a longer a course for CIAI demonstrated similar outcomes(8).

Approximately 10-15% of patients with CIAI present with severe sepsis or septic shock(1, 2). This subgroup has a significantly increased risk of mortality(1). However, the effect

of sepsis of less severe acuity on outcomes is less clear. Antimicrobial therapy is a necessary though not sufficient component of sepsis management. In addition to the underlying mortality risk of severity of presentation, the morbidity of recurrent infection in patients already compromised by severe sepsis or septic shock is a significant concern. Of equal import are the attendant risks of unnecessary antimicrobial therapy, most notably, morbidity and mortality from *Clostridium difficile* infection (CDI). In a high-risk group of patients with CIAI who present in severe sepsis or septic shock, it is unknown if shortening duration of antimicrobial therapy would change outcomes. Further, it is also unknown whether outcomes for patients with CIAI presenting with sepsis are different. We hypothesized that there is no difference in outcome between shorter and longer antimicrobial therapy in patients with CIAI presenting with sepsis.

Methods

The STOP-IT trial was a prospective, randomized, multicenter trial conducted between August 2008 and August 2013 at 23 US and Canadian academic medical centers. It was investigator-initiated and open-label. Patients were eligible to participate in the study if they were at least 16 years old and had a CIAI, which was defined as infection of any intra-abdominal tissue that met at least one of the following criteria: 1) organisms cultured from purulent intra-abdominal material, 2) abscess or other evidence of intra-abdominal infection, or 3) two of the following without recognized cause: temperature ≥38 °C, nausea, vomiting, abdominal pain, or jaundice, and at least one of the following: organisms cultured from intra-abdominal fluid or tissue or organisms cultured from blood with radiographic evidence of intra-abdominal infection.[8]

Patients must have been hospitalized and undergone an intervention to control infection. Enrolled patients must also have had either a white blood cell (WBC) count >11,000 cells/mm^3, oral temperature ≥38 °C, or gastrointestinal dysfunction preventing normal dietary intake within

24 hours of initial intervention. Exclusion criteria included: viral hepatitis, perforated gastroduodenal ulcer treated within 24 hours of symptoms, iatrogenic bowel injury treated within 12 hours of injury, non-perforated non-gangrenous appendicitis or cholecystitis, gangrenous appendicitis without organisms on culture, non-perforated intestinal ischemia, infected necrotizing pancreatitis, primary spontaneous bacterial peritonitis, infection associated with indwelling peritoneal dialysis catheter, pregnancy, primary skin closure of an open surgical incision in the setting of diffuse peritonitis, and lack of adequate source control or high likelihood of death within 72 hours of admission as determined by the local or principal investigators. Patients underwent central, block randomization in 1:1 fashion, with no more than 10% of patients per block having appendiceal disease. Following adequate source control, the control group received antibiotics until their temperature remained <38 degrees Celsius, WBC remained <11,000 cells/mm^3, or patients could tolerate oral diet for two calendar days, but for no more than 10 days. The experimental group received 4±1 calendar days of antimicrobial therapy after adequate source control. The primary outcome of the original study was a composite of surgical site or recurrent intra-abdominal infection, or mortality within 30 days of the intervention.[8]

In this post-hoc subgroup analysis, patients whose treatment adhered to the STOP-IT protocol, whose most extreme temperature was less than 36 °C or greater than 38 °C, and whose most extreme white blood cell count (WBC) was less than 4,000 cells/mm^3 or greater than 12,000 cells/mm^3 were selected. A per protocol analysis was used to reduce type 2 error. However, to ensure study quality and reduce type 1 error, an intention to treat analysis was also performed. Because analysis was performed on a de-identified database, the institutional IRB declared this study exempt under the principles of the Declaration of Helsinki.

Baseline demographics of included patients were first compared to excluded patients from the STOP-IT population to ensure difference from the non-septic STOP-IT population. Patients were then divided into short- and long-course groups. Outcome measures included incidence of and days to: surgical site infection (SSI), recurrent intra-abdominal infection, extra-abdominal infection, and CDI. For an infection to be diagnosed, the patient had to have purulent drainage from a transabdominal intraperitoneal drain, organisms present on intra-abdominal culture, evidence of an abscess, or diagnosis of an intra-abdominal SSI by a surgeon or attending physician. Extra-abdominal infections were defined as infections that neither met criteria for SSI nor intra-abdominal infection. CDI was defined as a positive toxin assay or culture. Hospital days and mortality were also measured.

Parametric data were reported as mean±standard deviation and compared using a two-tailed, independent samples t-test. Nonparametric data were reported as median [interquartile range] and compared using an independent-samples Mann-Whitney U test. Categorical variables were compared using a Fischer's exact test with significance at $p \leq 0.05$. Data were analyzed using SPSS Statistics for Windows, version 22 (IBM).

Results

The STOP-IT trial database included 518 de-identified entries, of which 399 adhered to the STOP-IT trial protocol. Of those, 112 patients met inclusion criteria for the present study. When compared to the non-septic STOP-IT population, the septic population had a higher maximum temperature (38.5±0.4 ºC vs 37.4±0.7 ºC, p<0.001) and WBC (18.1 [15.1-21.1] vs 14.2 [10.2-17.7], p<0.001). APACHE II scores were higher in the septic population (11.2±6.2 vs 9.5±5.9, p=0.01). Body mass index was higher in the septic population (30.0±7.3 vs 31.7±11.3 kg/m^2). All other baseline demographics were similar.

Of septic patients, there were 67 patients in the experimental, short-course group and 45 patients in the control, long-course group. Baseline characteristics were similar (Table 1). Patients in the short-course group received significantly shorter mean days of antibiotics (4.4±0.6 vs 7.2±2.5, p<0.001) (Table 2).

Recurrent intra-abdominal infection occurred in 13.3% of long-course patients and 11.9% of short-course patients (p=1.000). SSI occurred in 8.9% of long-course patients and 11.9% of short-course patients (p=0.759). Incidence of extra-abdominal infection (8.9% vs 11.9%, p=0.759) was not significantly different between long- and short-course patients. There were no cases of CDI in either group. The mean time to SSI was significantly shorter in the short-course group (21.3±6.1 days vs 6.9±3.5 days, p<0.001). When comparing the long-course group to the short-course groups, days to recurrent intra-abdominal infection (18.0±8.1 vs 12.5±6.6, p=0.185) and extra-abdominal infection (17.3±3.9 vs 12.6±5.8, p=0.194) were similar. There was no statistically significant difference between the two groups in hospital days (9.0±7.5 vs 7.4±5.5, p=0.188) or mortality (0% vs 1.5%, p=1.000).

Using an intention to treat approach, there were 75 patients in the long-course group and 85 patients in the short-course group. There were no difference in baseline characteristics (Table 3). The short-course group received a significantly shorter duration of antibiotics. Outcomes were similar to the per-protocol analysis (Table 4).

Discussion

Outcomes were similar in this post-hoc subgroup analysis of the STOP-IT trial, comparing patients presenting with CIAI-related sepsis but receiving a short-course of antimicrobial therapy to those receiving a longer duration after source control. While mean time to SSI was shorter in short-course group, there was no difference in hospital days or mortality. Though our data do not

allow elucidation as to why this difference was present, it is possible that prolonged antibiotic administration suppressed an inflammatory response that could be recognized clinically without actually preventing recurrent infection. The increased time to SSI in the longer-course group may result in an increased time to recognition and resolution, potentially increasing cost, length of stay, and complications as a result antibiotic exposure.

Clinicians have had to balance these concerns with the well-documented recurrent infection rate in CIAI. Given the increased mortality in severe sepsis and septic shock, many clinicians have made the assumption that increasing the duration of antimicrobial therapy may improve outcome as it relates to recurrent infection. It may seem to follow that as severity of illness increases, the duration of antimicrobial therapy necessarily increases to maintain acceptable outcome. Our findings, however, suggest otherwise in the setting of early, adequate source control.

Strengths of this study include that it was conducted at multiple institutions, it encompassed a broad array of organ sources of CIAI, and it included multiple methods of source control, including open, laparoscopic, and percutaneous drainage.

This study is limited by the fact that the set of patients presenting with sepsis were not a priori randomized as part of a planned subgroup analysis, thus introducing bias. Also, there were insufficient data to include all criteria used to diagnose sepsis, as described by the Surviving Sepsis guidelines, thus restricting our analysis to temperature and WBC(4). Limited sample size also meant difficulty in drawing conclusions on the subset of patients with severe sepsis or septic shock. Similar to the original STOP-IT trial, this study is also limited by sample size. Based on prior data suggesting a complication rate of 30% in CIAI treated with source control and antimicrobial therapy, the original investigators calculated 1010 patients were required to detect

a 10% difference between control and experimental groups with 90% power, at an alpha of 0.05, and an assumed dropout rate of 10 percent. However, after interim analysis of 518 patients, funding was discontinued for futility because outcomes appeared identical(8). Nevertheless, given the power calculation conducted, a limitation of the STOP-IT trial, and thus this subsequent study, is that results may reflect a type 2 error. However, the cumulative complication rate in the STOP-IT trial and this subset was greater than 30%, suggesting the sample size required was overestimated. An additional limitation of the external validity is that all patients were required to have source control. Source control is unable to be achieved in CIAI in up to 10% of cases(2).

The findings of this study suggest that when there is source control of CIAI, a shorter duration of antimicrobial therapy results in similar rates of infectious morbidity and mortality when compared to longer duration therapy despite the presence of sepsis. In other words, the presence of sepsis does not appear to be a valid reason to prolong antibiotic therapy duration when adequate source control has been achieved in CIAI. In other studies on CIAI, adjusting antibiotic duration, even in severe illness, does not appear to affect outcome. However, the majority of these analyses are post-hoc subgroup analysis and as such conclusions are limited. Nevertheless, implementation of these results would have significant economic and resource utilization effects. In order to determine equivalence or even superiority, for example, with regard to CDI, a larger, randomized a priori study of patients with CIAI and sepsis would be necessary. Such a study would need to perform prespecified subgroup analyses on higher risk populations, such as the elderly or immunocompromised. While it is known that patients with more severe illness related to CIAI have higher complication and mortality rates, it appears these findings are related more to pre-existing conditions(3). Nevertheless, one of the limitations of the

original STOP-IT trial was that the number of patients with severe sepsis or septic shock was limited. As such, the ability to draw conclusions about reducing antibiotic duration in this population with known increased mortality from CIAI is hindered as the average patient in the STOP-IT trial was not severely systemically ill. Building on the data presented here would entail selecting patients with severe sepsis or septic shock in order to allay concern that the current dataset cannot adequately answer the question of whether reduction of antibiotic duration in severe sepsis or septic shock is safe.

Conclusions

While more definitive findings await further studies, it appears that as long as adequate source control is achieved, 4 days of antimicrobial therapy is adequate to treat CIAI when patients present with sepsis.

References

1. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study. World J Emerg Surg 2012;7:36.
2. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW Study. World J Emerg Surg 2014;9:37.
3. Inui T, Haridas M, Claridge JA, Malangoni MA. Mortality for intra-abdominal infection is associated with intrinsic risk factors rather than the source of infection. Surgery 2009;146:654-661; discussion 661-662.
4. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41:580-637.
5. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Clin Infect Dis 2010;50:133-164.
6. Schein M, Assalia A, Bachus H. Minimal antibiotic therapy after emergency abdominal surgery: a prospective study. Br J Surg 1994;81:989-991.
7. van Rossem CC, Schreinemacher MH, van Geloven AA, et al. Antibiotic duration after laparoscopic appendectomy for acute complicated appendicitis. JAMA Surg 2015:1-7.
8. Sawyer RG, Claridge JA, Nathens AB, et al. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med 2015;372:1996-2005.

Table 1. Baseline Demographic and Clinical Characteristics, According to Study Group

			Control group (n=45)*	Experimental group (n=67)
Age, y, mean±SD			53±16	51±16
Male sex, n (%)			24 (53.3)	37 (55.2)
Race or ethnic group, n (%)[†]				
	White		37 (82.2)	54 (80.6)
	Black		8 (17.8)	11 (16.4)
	Other		0 (0)	2 (3.0)
Characteristics of index infection				
	APACHE II score, mean±SD[‡]		11.2±6.6	11.2±5.9
	Maximum white-cell count, 1,000 per mm^3, median (range)		17.1 (15.2-20.4)	18.5 (15.1-21.6)
	Maximum body temperature, °C, mean±SD		38.5±0.4	38.5±0.4
	Organ of origin, n (%)			
		Colon or rectum	18 (40.0)	21 (31.3)
		Appendix	6 (13.0)	11 (16.4)
		Small bowel	4 (8.9)	10 (14.9)
Source-control procedure, n (%)				
	Percutaneous drainage		10 (22.2)	23 (34.3)
	Resection and anastomosis or closure		13 (28.9)	11 (16.4)
	Surgical drainage only		16 (35.6)	19 (28.4)
	Resection and proximal diversion		5 (11.1)	10 (14.9)
	Simple closure		1 (2.2)	4 (6.0)
	Surgical drainage and diversion		0 (0)	0 (0)

*There were no significant differences between the groups ($p<0.05$).

[†]Race and ethnic groups were reported by the patient or surrogate.

[‡]Acute Physiology and Chronic Health Evaluation (APACHE) II scores range from 0 to 71, with higher scores indicating an increased risk of death.

Table 2. Primary and Major Secondary Outcomes. As-Treated Analysis

		Control group (n=45)	**Experimental group (n=67)**	**p Value**
Primary outcomes				
Surgical-site infection, n (%)`		4 (8.9)	8 (11.9)	0.759
Recurrent intraabdominal infection, n (%)		6 (13.3)	8 (11.9)	1.000
Death, n (%)		0 (0)	1 (1.5)	1.000
Time to event, days after index source-control procedure				
	Diagnosis of surgical-site infection, mean±SD	21.3±6.1	6.9±3.5	<0.001
	Diagnosis of recurrent intraabdominal infection, mean±SD	18.0±8.1	12.5±6.6	0.185
	Death, median (range)	--	7.0 (7.0-7.0)	--
Secondary outcomes				
Surgical-site infection with resistant pathogen, n (%)		0 (0)	2 (3.0)	0.515
Recurrent intra-abdominal infection with resistant pathogen, n (%)		1 (2.2)	0 (0)	0.402
Any extra-abdominal infection, n (%)		3 (6.7)	7 (10.4)	0.523
Clostridium difficile infection, n (%)		0 (0)	0 (0)	1.000
Duration of outcome, d, mean±SD				
	Antimicrobial therapy for index infection	7.2±2.5	4.4±0.6	<0.001
	Antimicrobial-free days at 30 d	21.3±3.9	23.6±4.9	0.009
	Hospitalization after index procedure	9.0±7.5	7.4±5.5	0.227
	Hospital-free days at 30 d	20.6±7.0	21.6±6.4	0.436

Table 3. Baseline Demographic and Clinical Characteristics, According to Study Group. Intention-to-Treat Analysis

			Control group (n=75)*	Experimental group (n=85)
Age, y, mean±SD			51±16	50±16
Male sex, n (%)			39 (52.0)	45 (52.9)
Race or ethnic group, n (%)†				
	White		62 (82.7)	70 (82.4)
	Black		11 (14.7)	13 (15.3)
	Other		2 (2.7)	2 (2.4)
Characteristics of index infection				
	APACHE II score, mean±SD‡		11.2±6.2	11.9±6.3
	Maximum white-cell count, 1,000 per mm^3, median (range)		17.8 (15.4-21.5)	19.0 (15.6-22.4)
	Maximum body temperature, °C, mean±SD		38.6±0.5	38.5±0.7
	Organ of origin, n (%)			
		Colon or rectum	27 (36.0)	28 (32.9)
		Appendix	11 (14.7)	15 (17.6)
		Small bowel	8 (10.7)	10 (11.8)
Source-control procedure, n (%)				
	Percutaneous drainage		19 (25.3)	26 (30.6)
	Resection and anastomosis or closure		19 (25.3)	14 (16.5)
	Surgical drainage only		25 (33.3)	27 (31.8)
	Resection and proximal diversion		9 (12.0)	14 (16.5)
	Simple closure		3 (4.0)	4 (5.3)
	Surgical drainage and diversion		0 (0)	0 (0)

*There were no significant differences between the groups ($p<0.05$).

†Race and ethnic groups were reported by the patient or surrogate.

‡Acute Physiology and Chronic Health Evaluation (APACHE) II scores range from 0 to 71, with higher scores indicating an increased risk of death.

Table 4. Primary and Major Secondary Outcomes. Intention-to-Treat Analysis

		Control group (n=75)	Experimental group (n=85)	p Value
Primary outcomes				
Surgical-site infection, n (%)		8 (10.6)	9 (10.6)	1.000
Recurrent intraabdominal infection, n (%)		14 (18.6)	14 (16.5)	0.835
Death, n (%)		0 (0)	2 (2.4)	0.499
Time to event, days after index source-control procedure, mean±SD				
	Diagnosis of surgical-site infection	13.6±9.4	6.7±3.4	0.055
	Diagnosis of recurrent intraabdominal infection	14.7±7.9	10.4±5.8	0.114
	Death	--	14.0±9.9	--
Secondary outcomes				
Surgical-site infection with resistant pathogen, n (%)		0 (0)	2 (2.4)	0.499
Recurrent intra-abdominal infection with resistant pathogen, n (%)		2 (2.7)	1 (1.2)	0.600
Any extra-abdominal infection, n (%)		8 (10.6)	10 (11.8)	0.835
Clostridium difficile infection, n (%)		0 (0)	0 (0)	1.000
Duration of outcome, d				
	Antimicrobial therapy for index infection, median (range)	8.0 (5.0-10.0)	5.0 (4.0-5.0)	<0.001
	Antimicrobial-free days at 30 d, mean±SD	19.4±6.5	21.7±6.8	0.034
	Hospitalization after index procedure, median (range)	7.0 (4.0-13.0)	7.0 (4.0-11.0)	0.640
	Hospital-free days at 30 d, mean±SD	19.8±7.8	19.7±8.4	0.920

Precis

There was no difference in outcomes between 4-day and longer-course antimicrobial therapy in patients with complicated intra-abdominal infection presenting with sepsis. Our findings suggest that the presence of systemic illness does not mandate a longer antimicrobial course if source control of complicated intra-abdominal infection is obtained.