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ORIGINAL SCIENTIFIC REPORT

Early Versus Delayed Source Control in Open Abdomen Management for Severe Intra-abdominal Infections: A Retrospective Analysis on 111 Cases

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Abstract

Background Time to source control plays a determinant prognostic role in patients having severe intra-abdominal infections (IAIs). Open abdomen (OA) management became an effective treatment option for peritonitis. Aim of this study was to analyze the correlation between time to source control and outcome in patients presenting with abdominal sepsis and treated by OA.

Methods We retrospectively analyzed 111 patients affected by abdominal sepsis and treated with OA from May 2007 to May 2015. Patients were classified according to time interval from first patient evaluation to source control. The end points were intra-hospital mortality and primary fascial closure rate.

Results The in-hospital mortality rate was 21.6% (24/111), and the primary fascial closure rate was 90.9% (101/111). A time to source control ≥6 h resulted significantly associated with a poor prognosis and a lower fascial closure rate (mortality 27.0 vs 9.0%, $p = 0.04$; primary fascial closure 86 vs 100%, $p = 0.02$). We observed a direct increase in mortality (and a reduction in closure rate) for each 6-h delay in surgery to source control.

Conclusion Early source control using OA management significantly improves outcome of patients with severe IAIs. This damage control approach well fits to the treatment of time-related conditions, particularly in case of critically ill patients.

Introduction

In developed countries, the incidence of severe sepsis is between 50 and 100 new cases per 100,000 persons with a wide variability [1–4]. Intra-abdominal infection (IAIs) is the second source of severe sepsis and second cause of death for infection in intensive care unit (ICU) patients [5, 6]. If not correctly treated, IAIs will develop into peritonitis, sepsis and severe sepsis [4, 7, 8]. The treatment of abdominal sepsis is based on resuscitation, antibiotic therapy and source control [9–11]. It is well known that time for treatment plays a determinant role for prognosis of patients affected by sepsis from IAIs [9, 12–17]. It has been well demonstrated, by Rivers et al., that early diagnosis and prompt introduction of a goal-directed therapy reduce mortality in case of severe sepsis; however, it should be noticed that patients who required immediate surgery for source control were excluded from original study [18].

The sepsis six, a care bundle based on this evidence, was introduced for managing patients with severe sepsis. These standards, included in Surviving Sepsis Campaign (SSC)

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[19], have been approved by several professional organizations [16, 20, 21], and the literature showed a one-third reduction in mortality for sepsis after their application, even if these results are not so clear in the context of surgical patients [22, 23]. Although source control is a cornerstone in the treatment of sepsis [15], the definition of "early" source control is still not clear [14]. In septic patients, after onset of hypotension, a delay to source control greater than 12 h could be expected to increase mortality from 25% to more than 60% when compared with a delay of less than 3 h [24]. According to damage control surgery (DCS) principles, in the setting of critically ill patients with abdominal sepsis, outcomes could be improved by early source control and OA management could be useful to achieve an effective source control limiting surgical trauma (in terms of duration of operation and weight of surgical maneuvers) [25, 26].

The present study aims to analyze the correlation between time to source control and outcome in patients presenting with abdominal sepsis treated by OA.

Materials and methods

We conducted a retrospective analysis including all patients affected by abdominal sepsis and treated by OA from May 2007 to May 2015 (from 2011 we prospectively collected database). End points of this study were intra-hospital mortality and primary fascial closure. To calculate the time to source control, we considered the time interval between first patient evaluation and surgery. Additionally, in order to detect if diagnostic phase was determinant for treatment delay, we also calculated the time intervals between first evaluation and CT and between CT and surgery. We established the "time zero" as follows: in emergency department, it was defined as the time of triage and as the onset of the first sign of sepsis for surgical ward patients. Preoperative variables related to patient (gender, age, BMI, comorbidities) and disease (contamination source, hemodynamic conditions, laboratory tests, CT findings, APACHE II and SOFA score) were evaluated. When available, all clinical variables have been considered at the first patient evaluation in emergency department or, in case of postoperative complication, at the onset of symptoms/signs. We analyzed the relationship between time to source control and these variables. Further, we analyzed the changes in outcomes (intra-hospital mortality and primary fascial closure) associated with each 6-h delay in source control. The 6-h time interval was chosen after an analysis of the literature [9, 16, 24, 27–29], and patients were classified, according to time to source control, in 7 different groups: ≤6, 6–12, 12–18, 18–24, 24–30, 30–36 and ≥36 h.

Statistical analysis

All categorical variables were expressed both as a number and percentage, while continuous variables were expressed as median and range. For analysis, the continuous variables have been categorized around median value or well-known cutoff. The statistical differences between the different groups were evaluated by nonparametric tests (Chi-square and Mann–Whitney test). The level of significance was established at $p < 0.05$ (two-tailed model for unpaired data). Statistical analyses were performed using the SPSS software for Windows OS.

Results

In the 8-year observation period, 197 patients were treated with OA: 111 (56.3%) for severe IAIs (most of them—56 patients—for a postoperative complication, whom only 6 for trauma). As reported in Table 1, in 75 cases (67.5%) the source of peritoneal contamination was bowel (in most of the cases, a colonic lesion). The in-hospital mortality rate was 21.6% (24/111), and the primary fascial closure rate was 90.9% (101/111) for a median OA duration of 5 days (range 1–46; <8 days in 88.3% of patients, 98/111). The median elapsed time from first patient evaluation to source control was 16 h (50 min–306 h): It was subdivided in a median time from first evaluation to CT of 4 h (10 min–107 h) and a median time from CT to source control of 6 h (11 min–224 h).

Table 2 shows the distribution of each variable for all the patients. Table 3 report the distribution of variables significantly associated with in-hospital mortality (Table 3a) and the primary fascial closure (Table 3b). A time to source control ≥6 h resulted significantly associated with a poor prognosis and a low closure rate (mortality 27.0 vs 9.0%, $p = 0.04$; primary fascial closure 86 vs 100%, $p = 0.02$).

Table 1 Abdominal contamination sources

Contamination source	No. (%)
Large bowel	46 (41.4)
Small bowel	29 (26.1)
Postoperative fluid collection	12 (10.8)
Gallbladder	11 (9.9)
Stomach	4 (3.6)
Duodenum	4 (3.6)
Cecal appendix	3 (2.7)
Pancreas	2 (1.8)

Table 2 Distribution of each variable for all the patients

Variable	No. (%)–median (range)
Sex	
M	57 (51)
F	54 (49)
Age	68 (17–90)
BMI	25.3 (16.6–33.2)
Comorbidity	
Yes	79 (71)
No	32 (29)
Septic shock	
Yes	31 (28)
No	80 (72)
Hgb (g/dl)	11.8 (7.3–25.8)
WBC (10^3/mm^3)	12.34 (1.7–77.8)
PLT (10^3/mm^3)	287.5 (33–972)
INR	1.14 (0.8–5.3)
Creatinine (mg/dl)	1.055 (0.3–9.3)
Lactate (mmol/l)	1.5 (0.3–8.4)
SBE (mmol/l)	−2.65 (−17.2–12.9)
CT free air	
Yes	48 (43)
No	43 (39)
CT fluid collection	
Yes	71 (64)
No	24 (22)
CT free fluid	
Yes	21 (19)
No	48 (43)
APACHE II score	8 (1–22)
SOFA score	5 (1–11)

Except for patients who underwent source control 6–12 h after first evaluation, the analysis shows a direct increase in mortality for each 6-h delay in surgery (Fig. 1). It should be noticed that most of the patients included in 6–12 h delay group had septic shock with the highest prognostic scores (Table 4). Similarly, in the 6–12 h delay group we found a low fascial closure rate (81.1%), but the lowest value (78.2%) was observed in the group with a ≥36 h delay (100% for ≤6 h group, 81.1% for 6–12 h group, 100% for 12–18, 18–24, 24–30, 30–36 h groups and 78.2% for ≥36 h group).

Table 3 Patients distribution according to factors significantly associated with (a) in-hospital mortality and (b) definitive fascial closure

Variable	Deaths # (%)	*p*
(a)		
Lactate (mmol/l)		
≥2	9/15 (60)	0.040
<2	8/40 (20)	
APACHE II score		
≥5	16/54 (30)	0.029
<5	8/56 (14)	
SOFA score		
≥9	13/39 (33)	0.035
<9	11/67 (16)	
Timing (h)		
≥6	14/51 (27)	0.040
<6	2/23 (9)	
Variable	Closure # (%)	*p*
(b)		
SOFA score		
≥9	34/40 (85)	0.031
<9	63/66 (95)	
Timing (h)		
≥6	44/51 (86)	0.022
<6	23/23 (100)	

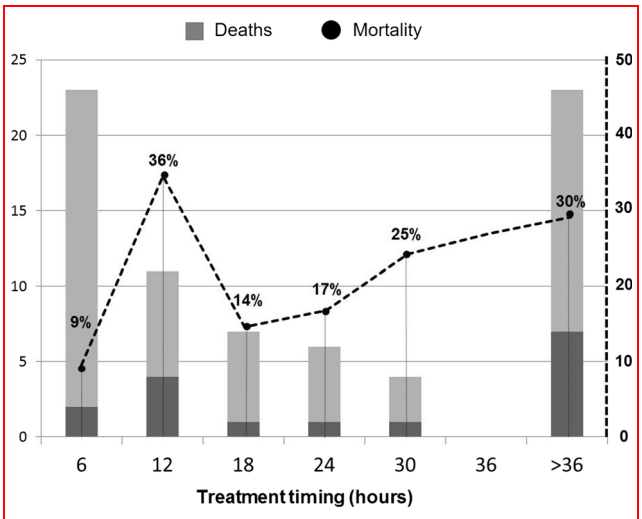

Fig. 1 Distribution of mortality rate according to treatment timing

Table 4 Distribution of prognostic scores according to treatment timing

Treatment timing (h)	APACHE score		SOFA score	
	<5 # (%)	≥5 # (%)	<9 # (%)	≥9 # (%)
<6	16 (69.6)	7 (30.4)	16 (69.6)	7 (30.4)
6–12	4 (36.4)	7 (63.6)	6 (54.5)	5 (45.5)
12–18	6 (75.0)	2 (25.0)	4 (57.1)	3 (42.9)
18–24	2 (33.3)	4 (66.7)	6 (100)	0 (0)
24–30	2 (50.0)	2 (50.0)	3 (75.0)	1 (25.0)
30–36	–	–	–	–
>36	8 (34.8)	15 (65.2)	13 (59.1)	9 (40.9)

Discussion

Complicated IAIs remain a relevant issue for surgeon and healthcare system due to the high overall mortality rate (about 30%) with peaks up to 50% in patients presenting with septic shock [30]. Even if sepsis is a well-known time-related condition [13, 27, 31, 32], it is difficult to determine the best time to initiate surgery, particularly in the setting of patients with diffuse peritonitis. Given the possibility of septic shock occurrence, source control is mandatory, but in clinical practice, many factors might influence delay in surgery: the accurate medical evaluation (often by most specialists), the attempts to reach a diagnosis (that usually requires radiological imaging as CT scan) as well as the stabilization of hemodynamics before surgery, are among these factors. Furthermore, it is well known that source control failure is more likely to occur in case of delayed intervention [33]. Interestingly, in our series the time calculated from CT to source control was longer than the time interval between first evaluation and CT (median of 6 vs 4 h): it suggests that in the preoperative phase even a forced diagnostic attempt could not be worthy. So, the determination of the optimal time for surgical source control is a decision mostly based on common sense rather than strong scientific evidence. In fact, even if time to source control has been evaluated as a critical determinant of survival in IAIs patients, the definition of "early" ranges from 2 h up to 5 days in the literature [17, 29]. Anyway, the recent changes in international guidelines reflect the importance of treating the source of infection earlier. The first SSC edition (2009) [19] suggested to start source control only after a successful initial resuscitation, and the 2012 [34] release advised to achieve it within the first 12 h after the diagnosis; finally, the last edition (SSC 2016) recommends that any required source control procedure must be done as soon as possible [9].

Moreover, the recent history of intensive care medicine has taught us that overly long and aggressive attempts to "normalize physiology" may be harmful in septic patients [35]. These findings highlight the importance of shifting the focus from definitive diagnosis and stabilization toward timely treatment of septic foci.

Some authors questioned whether, in patients with severe IAIs, surgery should be performed even if hemodynamics is not entirely stabilized. In a recent prospective observational study involving 154 patients affected by abdominal sepsis from gastro-intestinal perforation [29], Azuhata et al. analyzed the relationship between time to surgical source control and mortality. In this study, a newly developed resuscitation protocol allowed patients to go straight to surgery, even in case of poor hemodynamic status. They did not perform DCS reporting a satisfactory mortality rate (22%). They found two independent factors associated with survival: SOFA score and time from admission to source control. Authors also reported an inverse linear correlation between time to source control and mortality, but surprisingly, the survival rate showed a dramatic decrease of up to zero just after 6 h from admission. Conversely, we believe that a resuscitation protocol for early source control has to be improved by DCS because OA management allows to achieve an effective control of infection foci reducing surgical trauma. In fact, according to institutional guidelines, we do not close abdomen at first surgery in case of a severe IAIs: in our clinical practice, this attitude is valid for patients in hemodynamically stable status as well as for those in septic shock, aiming to an early definitive fascial closure (<8 days). Despite the retrospective design, our study appears fully consistent with DCS principles. Analyzing 111 severe IAIs patients (of which 31, 27.9%, with poor hemodynamic conditions, Table 2), we observed an overall mortality rate of 21.6%; also in our series, a delay in source control ≥6 h negatively affected the patients' prognosis (mortality 27.0 vs 9.0%, $p = 0.04$). As Azuhata et al., a linear correlation between time to source control and mortality was demonstrated in our study once again (Fig. 1). The aggressive approach of OA did not seem to modify this relationship, but differently from experience of Japanese group we did not find such an extreme effect of surgical delay on mortality after 6 h to source control. Actually, we reported a peak of mortality in the 6–12 h group (4/11, 36%, Fig. 1) associated with a relevant reduction in fascial closure rate: in this sample of patients, treated by the same surgery at the same timing, this effect was most probably due to the highest prognostic scores (Table 4). In fact, consistently with the literature data [9, 16, 36, 37] and our previous experience [38], we demonstrated that outcomes (survival and fascial closure rate) of patients affected by abdominal sepsis and treated with OA are strongly associated with clinical status and comorbidities rather than time to source control (Table 3).

Ultimately, we concluded that OA management for severe IAIs seems to extend the time window of source control without worsening outcomes.

Undoubtedly, our results are weakened by some unavoidable limitations. The critical conditions of patients and the emergency context make it impossible to achieve a prospective methodology; so the retrospective nature of this study limits its conclusions. Because the delay in treatment is very difficult to be estimated, our results are not sufficient to suggest substantial changes in clinical practice. There might have been some inaccuracy in calculating the timing; for example, in emergency department, definition of "first observation" did not consider time before triage.

Finally, it should be pointed out that our sample is inhomogeneous because it includes patients with postoperative complications together with severe IAIs patients presenting in emergency department and benign disease as well as malignant tumor.

Conclusion

The ideal management for severe IAIs, which allows to reduce morbidity and mortality to zero through early and effective source control, cannot be fully practiced for each case; this because diseases presentations are heterogeneous and individual patient response is extremely variable.

Any required source control intervention in sepsis and septic shock from IAIs should ideally be implemented as soon as medically and logistically possible after diagnosis. With traditional techniques, not implementing the principles of DCS, resuscitation and early source control may conflict with each other. Conversely, DCS and a correct OA management (possibly implying an early definitive fascial closure) well fit to the treatment of time-related conditions as abdominal sepsis, particularly in case of critically ill patients.

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Compliance with ethical standards

Conflict of interest Authors declare that they have no potential conflicts of interest, including financial interests, activities, relationships and sources of funding.

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