



## Review Article

## Current progress of source control in the management of intra-abdominal infections

Xiu-Wen Wu<sup>a, b</sup>, Tao Zheng<sup>a, b</sup>, Zhi-Wu Hong<sup>a, b</sup>, Hua-Jian Ren<sup>a, b</sup>, Lei Wu<sup>a, b</sup>, Ge-Fei Wang<sup>a, b</sup>, Guo-Sheng Gu<sup>a, b</sup>, Jian-An Ren<sup>a, b, \*</sup>

<sup>a</sup> Research Institute of General Surgery, Jinling Hospital, Medical School of Nanjing University, Nanjing, China

<sup>b</sup> Lab for Trauma and Surgical Infection, Jinling Hospital, Nanjing, China

## ARTICLE INFO

## Article history:

Received 20 February 2020

Received in revised form

14 June 2020

Accepted 10 July 2020

Available online 3 August 2020

## Keywords:

Source control

Intra-abdominal infection

Open abdomen

Source control failure

## ABSTRACT

Intra-abdominal infection (IAI) is a deadly condition in which the outcome is associated with urgent diagnosis, assessment and management, including fluid resuscitation, antibiotic administration while obtaining further laboratory results, attaining precise measurements of hemodynamic status, and pursuing source control. This last item makes abdominal sepsis a unique treatment challenge. Delayed or inadequate source control is an independent predictor of poor outcomes and recognizing source control failure is often difficult or impossible. Further complicating issue in the debate is surrounding the timing, adequacy, and procedures of source control. This review evaluated and summarized the current approach and challenges in IAI management, which are the future research directions.

© 2020 Production and hosting by Elsevier B.V. on behalf of Chinese Medical Association. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

The intra-abdominal infection (IAI) remains a serious problem worldwide. Although the hospital mortality associated with IAI varies among different settings and disease entities, it can be as high as 23%–38%.<sup>1–3</sup> The mortality of severe IAI is even higher, which makes it become the second most common cause of sepsis in critically ill patients.

Achieving prompt and adequate control over the anatomic source of infection is a cornerstone in the management of IAI. Source control covers all measures undertaken to remove the source of infection, decrease the bacterial inoculum, and control or correct anatomic derangements to recover normal physiologic function.<sup>4</sup>

## Timing to source control

The most established measurement for source control would be to totally control the source of infection with the least delay possible. However, evidence regarding optimal timing of

procedures in IAI remains weak, possibly due to the ethical restriction on clinical trials. When reviewing the present national and international guidance on IAI, the only detailed recommendations regarding the timing to source control were time spans. The guideline joint issued by the Department of Health and the Royal College of Surgeons of England indicate that source control interventions must be performed as soon as possible, targeting a delay of no longer than 7–22 h from diagnosis for IAI without systemic inflammation. For severe IAI, the intervention should be conducted immediately.<sup>5</sup> As for the guidelines issued by the Surgical Infection Society (SIS) and other societies, source control should be conducted within 24 h of the IAI diagnosis.<sup>6,7</sup>

The delayed procedures in source control highly associate with an adverse outcome in IAI. A large European survey has already suggested that a delay of initial intervention (beyond 24 h) could be a predictor for the high mortality in abdominal sepsis.<sup>8</sup> In patients with septic shock originating from gastrointestinal perforation, each hour delay of intervention was correlated with decreased survival.<sup>9</sup> For reasons leading to delays, van de Groep et al.<sup>10</sup> stated that it may due to the underlying diagnostic uncertainty, hindering

\* Corresponding author.

E-mail address: [JiananR@gmail.com](mailto:JiananR@gmail.com) (J.-A. Ren).

Peer review under responsibility of Chinese Medical Association.

forthright interpretation of observed outcome relations. Furthermore, the rapid evolution of clinical symptoms also exerted a negative influence on the urgency of intervention.<sup>11</sup>

### Adequacy of source control

The crucial importance of adequate source control in the management of IAI also deserves to be a top priority. The incomplete interventions have severely adverse effects on outcomes especially in critically ill patients. In order to achieve the completeness, approximately half of patients would require more than one single procedure to eliminate their source of infection, in spite of the fact that their initial procedure was considered technically successful.<sup>10</sup>

About definitions of adequacy of source control, most studies used technical and procedural success criteria.<sup>12–14</sup> Even after an adequate source control, the physicians still need to recognize and develop a therapeutic plan for the possibility that the intervention may fail. Based on a recent report from van de Groep et al.,<sup>10</sup> more than half of IAI cases suffered persistent or recurrent infection after the initially adequate source control.

The source control failure, also known as treatment failure, is a controversial topic in the multidisciplinary management of abdominal sepsis, which encompass no clear diagnosis definitions, monitoring index, or interventions. Revised guideline from the SIS recommend to use biomarkers of ongoing or progressive systemic inflammation, or organ system dysfunction to recognize patients with likely source control failure.<sup>6</sup> But simple inflammatory markers including C-reactive protein, white blood cell count, and procalcitonin seemed non-predictive in some studies.<sup>10,15</sup> It was found that the persistence of organ failure after initial intervention highly correlated with the ultimate failure of source control.<sup>10,16</sup> Future studies incorporating both procedural findings, infection characteristics, as well as time trends of indicators related to organ failure should be conducted to investigate prediction rules for treatment failure of IAI.

Antimicrobial therapy for the management of IAI also constantly evolves. But the appropriate duration of antimicrobial therapy after adequate source control remains unclear. Practitioners may treat patients until the resolution of fever, leukocytosis, and ileus, leading to a therapy of 7–14 days. More recently, it has been suggested that with adequate source control, a fixed duration of 4 days of antibiotic treatment sufficed for cure.<sup>17</sup> The beneficial effects of systemic antimicrobial therapy were confirmed to be limited to the first few days after surgical intervention. The shorter duration of antibiotic exposure could decrease the risk of bacterial resistance to antibiotics, which is especially important in this era of escalating prevalence of antimicrobial resistance.

### Procedures of source control

Source control can be achieved either by surgical (laparotomy or laparoscopy) or non-surgical (percutaneous drainage) means. The primary objectives of these intervention were to identify the origin of peritonitis, drain fluid collections, and to control the cause of abdominal sepsis.

It is now rarely to conduct urgent surgery for intra-abdominal abscess alone. Data have shown that the number of percutaneous drainage for abdominal abscesses doubled in recent ten years.<sup>18</sup> Thanks to the progress of imaging techniques, ultrasound and CT-guided percutaneous drainage of abdominal and extraperitoneal abscesses become safe and effective.<sup>19</sup>

Although percutaneous drainage of abscesses has represented the optimal approach, surgery still remains essential for those abscesses which cannot be accessed by radiological means and infections associated with a source that requires excision. Surgical

source control procedures include resection or suture of a diseased or perforated viscus, removal of the infected organ, debridement of necrotic tissue, resection of ischemic bowel, and repair of traumatic perforations with primary anastomosis or exteriorization of the bowel.

Recent controversy in the surgical approach of IAI lies in the potential benefits and complications of open abdomen (OA) therapy. OA was initially applied to patients with severe abdominal trauma in the context of damage control surgery. Right now, its application has been extended to patients with severe IAI unrelated to trauma. Indications for OA therapy would include severe IAI or abdominal sepsis, intra-abdominal hypertension or abdominal compartment syndrome, dehiscence, and ongoing intra-abdominal bleeding. The goal of OA in patients with IAI is to achieve early source control. A retrospective analysis on 111 cases conducted by Rausei et al.<sup>20</sup> has stated that early source control using OA could significantly improve outcome the of severe IAI patients.

Although the OA management may be lifesaving, it remains a clinical challenge because of associated complications. One of the most serious complications is the development of an entero-atmospheric fistula (EAF). Spontaneous closure of EAF is very rare as the overlying tissue is poorly vascularized. Temporary abdominal closure (TAC), which is traditionally used for abdominal contents protection, infected or toxic fluid removal from the peritoneal cavity, and formation of fistulas prevention, has the potential to be improved. Routine mesh coated with hydrogels or electrospun could be used for temporary closure of the open abdomen. The modified TAC composite could significantly protect the intestines from mechanical damage and accelerate wound healing in animal studies.<sup>21,22</sup> This approach well fits to the treatment of OA, particularly in preventing EAF. Clinical trials are urgently required to confirm the efficacy.

A recent published clinical trial, the close-up study, compared the effects of immediate closure of abdominal cavity using biologic mesh with TAC of the OAs in non-trauma emergency patients.<sup>23</sup> A better result has been indicated in the closed group with significantly reduced proportions of major complications and reoperations, as well as shorter intensive care unit stays. The OA management can be prevented in these non-trauma patients in whom primary fascial closure is not deemed achievable because of visceral edema. But for abdominal sepsis, many reports are still suggesting that OA management may improve outcomes.<sup>24,25</sup> The global clinical decision as to whether the abdomen should be left open or closed after laparotomy in patients with abdominal sepsis warrants further investigation.

### Conclusion

IAI is an important cause of morbidity and mortality in contemporary healthcare. Timely and adequate source control remains a vital component for a successful management of IAI. Novel options are emerging in both surgical and non-surgical approaches for the intervention of severe infection, holding the promise of improved outcomes. But challenges still exist in the timing, adequacy, and procedures for source control. An evidence-based guideline for source control is urgently needed to facilitate earlier recognition and more timely management of IAI patients. Future research and development are required to investigate the optimal intervention with the most safety and efficacy and with the least morbidity.

### Funding

The work was supported by the National Natural Science Foundation of China (81801971), National Major Scientific and

Technological Special Project for “Significant New Drugs Development” (2017ZX09304005-002), Key Project of Science Foundation of the 12th Five-Year Plan (BNJ13J002), and Nanjing Science and Technology Development Project (201803051).

### Ethical Statement

Not applicable.

### Declaration of Competing Interest

There are no conflicts of interest to declare.

### References

- Barie PS, Hydo LJ, Eachempati SR. Longitudinal outcomes of intra-abdominal infection complicated by critical illness. *Surg Infect (Larchmt)*. 2004;5:365–373. <https://doi.org/10.1089/sur.2004.5.365>.
- Volakli E, Spies C, Michalopoulos A, et al. Infections of respiratory or abdominal origin in ICU patients: what are the differences? *Crit Care*. 2010;14:R32. <https://doi.org/10.1186/cc8909>.
- De Waele J, Lipman J, Sakr Y, et al. Abdominal infections in the intensive care unit: characteristics, treatment and determinants of outcome. *BMC Infect Dis*. 2014;14:420. <https://doi.org/10.1186/1471-2334-14-420>.
- Marshall JC. Principles of source control in the early management of sepsis. *Curr Infect Dis Rep*. 2010;12:345–353. <https://doi.org/10.1007/s11908-010-0126-z>.
- Royal College of Surgeons of England and Department of Health. *The Higher Risk General Surgical Patient: Towards Improved Care for a Forgotten Group*; 2011. <https://www.rcseng.ac.uk/library-and-publications/college-publications/docs/higher-risk-patient/>.
- Mazuski JE, Tessier JM, May AK, et al. The surgical infection society revised guidelines on the management of intra-abdominal infection. *Surg Infect (Larchmt)*. 2017;18:1–76. <https://doi.org/10.1089/sur.2016.261>.
- Lalisang TJM, Usman N, Hendrawidjaya I, et al. Clinical practice guidelines in complicated intra-abdominal infection 2018: an Indonesian perspective. *Surg Infect (Larchmt)*. 2019;20:83–90. <https://doi.org/10.1089/sur.2018.120>.
- 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. <https://doi.org/10.1186/1749-7922-7-36>.
- Azuhata T, Kinoshita K, Kawano D, et al. Time from admission to initiation of surgery for source control is a critical determinant of survival in patients with gastrointestinal perforation with associated septic shock. *Crit Care*. 2014;18:R87. <https://doi.org/10.1186/cc13854>.
- van de Groep K, Verhoeff TL, Verboom DM, et al. Epidemiology and outcomes of source control procedures in critically ill patients with intra-abdominal infection. *J Crit Care*. 2019;52:258–264. <https://doi.org/10.1016/j.jcrrc.2019.02.029>.
- Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg*. 2017;12:29. <https://doi.org/10.1186/s13017-017-0141-6>.
- Launey Y, Duteurtre B, Larmet R, et al. Risk factors for mortality in post-operative peritonitis in critically ill patients. *World J Crit Care Med*. 2017;6:48–55. <https://doi.org/10.5492/wjccm.v6.i1.48>.
- Tellor B, Skrupky LP, Symons W, et al. Inadequate source control and inappropriate antibiotics are key determinants of mortality in patients with intra-abdominal sepsis and associated bacteremia. *Surg Infect (Larchmt)*. 2015;16:785–793. <https://doi.org/10.1089/sur.2014.166>.
- Bloos F, Thomas-Ruddel D, Ruddel H, et al. Impact of compliance with infection management guidelines on outcome in patients with severe sepsis: a prospective observational multi-center study. *Crit Care*. 2014;18:R42. <https://doi.org/10.1186/cc13755>.
- Jung B, Molinari N, Nasri M, et al. Procalcitonin biomarker kinetics fails to predict treatment response in perioperative abdominal infection with septic shock. *Crit Care*. 2013;17:R255. <https://doi.org/10.1186/cc13082>.
- Paugam-Burtz C, Dupont H, Marmuse JP, et al. Daily organ-system failure for diagnosis of persistent intra-abdominal sepsis after postoperative peritonitis. *Intensive Care Med*. 2002;28:594–598. <https://doi.org/10.1007/s00134-002-1250-5>.
- 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. <https://doi.org/10.1056/NEJMoa1411162>.
- Levin DC, Eschelmann D, Parker L, et al. Trends in use of percutaneous versus open surgical drainage of abdominal abscesses. *J Am Coll Radiol*. 2015;12:1247–1250. <https://doi.org/10.1016/j.jacr.2015.06.015>.
- Azzarello G, Lanteri R, Rapisarda C, et al. Ultrasound-guided percutaneous treatment of abdominal collections. *Chir Ital*. 2009;61:337–340.
- Rausei S, Pappalardo V, Ruspi L, et al. Early versus delayed source control in open abdomen management for severe intra-abdominal infections: a retrospective analysis on 111 cases. *World J Surg*. 2018;42:707–712. <https://doi.org/10.1007/s00268-017-4233-y>.
- Deng Y, Ren J, Chen G, et al. Evaluation of polypropylene mesh coated with biological hydrogels for temporary closure of open abdomen. *J Biomater Appl*. 2016;31:302–314. <https://doi.org/10.1177/0885328216645950>.
- Zhao C, Wu X, Huang J, et al. Hybrid material for open abdomen: saving the wound from intestinal fistula. *J Mater Sci Mater Med*. 2019;30:109. <https://doi.org/10.1007/s10856-019-6311-1>.
- de Vries FEE, Claessen JJM, Atema JJ, et al. Immediate closure of abdominal cavity with biologic mesh versus temporary abdominal closure of open abdomen in non-trauma emergency patients (CLOSE-UP study). *Surg Infect (Larchmt)*. 2020 Feb 25. <https://doi.org/10.1089/sur.2019.289>.
- De Waele JJ. Abdominal sepsis. *Curr Infect Dis Rep*. 2016;18:23. <https://doi.org/10.1007/s11908-016-0531-z>.
- Bruns BR, Ahmad SA, O'Meara L, et al. Nontrauma open abdomens: a prospective observational study. *J Trauma Acute Care Surg*. 2016;80:631–636. <https://doi.org/10.1097/TA.0000000000000958>.