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Epidemiology and outcome of intra-abdominal infections in intensive care unit in Italy from the Italian Register of complicated Intra-abdominal InfectionS—the IRIS study: a prospective observational nationwide study

Etrusca Brogi^{1,2*}, Camilla Cremonini^{3*}, Marco Ceresoli⁴, Fausto Catena⁵, Angela Gurrado⁶, Francesco Forfori¹, Lorenzo Ghiadoni⁷, Ettore Melai¹, IRIS study group, Massimo Sartelli⁸ and Federico Coccolini³

Abstract

Background Intra-abdominal infections are complex and potentially life-threatening conditions frequently requiring intensive care admission and are associated with highly variable mortality driven by disease severity, host response, comorbidities, and antimicrobial resistance.

Outcomes depend on timely diagnosis, effective surgical source control, appropriate antimicrobial therapy, and a coordinated multidisciplinary approach addressing both the infectious and systemic inflammatory components of the disease.

Material and method This was a prospective, observational nationwide study. We included all adult patients admitted to the hospital with complicated abdominal infections requiring ICU admission. The aim of this study was to describe the epidemiology and outcomes of patients admitted to the hospital with intra-abdominal infections (IAIs) requiring an intensive care unit (ICU) admission in 23 Italian hospitals.

Results A total of 784 patients admitted to the hospital with complicated IAIs requiring ICU admission were enrolled. Overall, in-hospital mortality among ICU patients was 23.9%. Septic shock (36.2%) and sepsis (35.9%) were the main reasons for ICU admission. Community-acquired infections accounted for 64.8% of cases, and adequate source control was achieved in 61.5% of patients. Re-operation was required in 21%.

The most frequently isolated pathogens were *Escherichia coli* (23.1%), followed by *Enterococcus* spp. (15.4%). Empiric antibiotic therapy was prescribed in more than 80% of patients (median duration ranging from 8.1 to 19.3 days). Piperacillin–tazobactam was the most commonly used antibiotic. In multivariable logistic regression analysis, increasing age (OR 1.04 per year, 95% CI 1.03–1.06), immunosuppression (OR 1.99, 95% CI 1.09–3.66), serious cardiovascular

*Correspondence:

Etrusca Brogi
etrusca.brogi@ospedaleniguarda.it
Camilla Cremonini
c.cremonini89@gmail.com

Full list of author information is available at the end of the article



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disease (OR 1.91, 95% CI 1.20–3.05), re-operation (OR 2.30, 95% CI 1.34–3.96), inadequate source control (OR 0.39, 95% CI 0.22–0.71), peritonitis (OR 0.39, 95% CI 0.23–0.66), and healthcare-associated infections (OR 1.83, 95% CI 1.10–3.04) were independently associated with in-hospital mortality. Duration of antibiotic therapy, malignancy, and delay in initial intervention were not significantly associated with mortality.

Conclusion Septic shock remains the leading cause of ICU admission in patients with IAIs. Patients with immunosuppression, serious cardiovascular comorbidities, requirement for re-operation, inadequate source control, peritonitis, and healthcare-associated infections were at significantly higher risk of in-hospital mortality. Overall, our study reinforces the multifactorial nature of mortality in critically ill patients with intra-abdominal infections, highlighting modifiable factors (source control, timely intervention) that can be targeted to improve outcomes.

Keywords Intra-abdominal infections, Antibiotic therapy, Surgery, Epidemiology, Intensive care unit, Prognosis, Outcome

Background

Intra-abdominal infection (IAIs) are complex, potentially life-threatening conditions usually requiring prompt diagnosis and appropriate management to prevent severe complications [1]. IAIs may involve several organs within the abdominal cavity, including the peritoneum, the liver, the spleen, and the gastrointestinal tract, and can be classified as uncomplicated and complicated (cIAIs) [2]. Complicated IAIs can lead to significant morbidity and mortality if not promptly and effectively managed; therefore, timely diagnosis and intervention are crucial to improve outcomes [3].

Up to 30% of patients with IAIs may necessitate admission to the intensive care unit (ICU) in severe cases [4–6]. Indeed, IAIs represent the second most common site of infection in patients admitted to the ICU, following respiratory tract infections [7]. Mortality rates range widely, from 5% to 50%. This considerable variability can be explained not only by disease severity but also by patients' clinical characteristics such as immunosuppressive therapy, cancer, prior hospitalization and colonization, frailty [8, 9].

From a pathophysiological perspective, regardless of the nature of the initial insult, infection triggers an inflammatory response that may evolve into a localized or generalized infection. The characteristics of the host inflammatory response, together with infection severity and patient comorbidities, play a pivotal role in this evolution [10].

Nevertheless, the clinical impact of multidrug resistant (MDR) bacteria on patient outcome is well known [11, 12]. The increasing prevalence of antimicrobial resistance is associated with higher morbidity and mortality in patients with IAIs, as well as rising healthcare costs [13]. Moreover, the escalating rate of antibiotic resistance highlights the urgent need for the implementation of effective antibiotic stewardship programs [14].

Early and adequate surgical source control remains the cornerstone of treatment and represents the most

important prognostic factor in IAIs [15]. However, given the central role of the systemic inflammatory response and the aforementioned microbiological factors, a multidisciplinary approach (involving surgeon, infectious specialist, and intensive care specialist) is essential for optimal management of these critically ill patients [3]. Accordingly, close collaboration among different healthcare professionals is required to improve patient care.

We previously published a prospective study on the epidemiology of intra-abdominal infections across 23 centers in Italy [16]. With the present study, we aimed to extend this analysis by focusing on the most severe cases. In this prospective, observational nationwide study, we evaluated the epidemiology and outcomes of patients admitted to the hospital with complicated abdominal infection requiring ICU admission.

Methods

This was a prospective, observational, nationwide multicentre study conducted in Italy, named “The IRIS study (Italian Register of Complicated Intra-abdominal InfectionS)”.

The study was approved by the Local Research Ethics Committee of Pisa (Prot n 56478//2019), which acted as the coordinating centre ethics committee.

Inclusion criteria

Adult patients admitted to the hospital with complicated intra-abdominal infections requiring ICU admission were included. The recruitment period extended from May 1st, 2021, to April 30th, 2023.

Data collection

Data were prospectively collected and stored in an online database (www.clinicalregisters.org).

For each patient, the following data were recorded:

- Demographic data: gender, age.
- Comorbidities, including primary or secondary immunodeficiency and severe cardiovascular disease.
- Type of infection: complicated IAIs were classified as community-acquired (CA) or healthcare-acquired (HA) [17]. Complicated IAIs were considered as HA in patients hospitalized for at least 48 h within the previous 90 days. The source of infection (stomach or duodenum, gallbladder, small bowel, colon, appendix, or other), and extent of peritonitis (generalized or localized peritonitis/abscess) were also evaluated.
- Septic status at admission; sepsis and septic shock were defined according to the Third International Consensus Definition for Sepsis and Septic Shock [18].
- Antimicrobial therapy and antifungal therapy: antimicrobial therapy administered prior to hospitalization, empiric antibiotic therapy, duration of treatment, and empiric antifungal therapy were recorded.
- Reason for ICU admission: respiratory failure, pneumonia, pulmonary embolism, septic shock, bleeding, cardiac arrhythmia.
- Radiological diagnosis: finding from ultrasound, radiography, and computer tomography.
- Source control: conservative treatment, surgical procedures, or non-operative interventional procedures, and their adequacy. Adequate source control was defined as the identification of the cause of cIAIs and effective control of the origin of peritonitis. Adequate source control involves promptly performing physical interventions to eliminate the infection source—such as draining infected collections, surgically debriding tissue, or removing infected devices or necrotic tissue—with the aim of reducing bacterial load, controlling infection, and restoring normal anatomical

and physiological function [19]. The timing (< 24 h from diagnosis) of these interventions can affect outcomes, with early source control being particularly vital for severe infections, abdominal infections, and necrotizing skin or soft tissue infections [20].

- Rate of reoperation.
- Microbiological data: cultures were performed on intraoperative samples of peritoneal fluid, purulent exudates, or discrete abscesses, as well as on blood cultures. The decision to perform cultures was left to the discretion of the treating physicians. Microbiological results identifying Gram-negative, Gram-positive, and anaerobic bacteria, and fungi were collected. Isolated microorganisms were classified according to the joint recommendations for epidemiologic studies from the European Centre for Disease Prevention and Control, and from the Centers for Disease Control and Prevention [21]. Each participating center determined antimicrobial susceptibility testing according to its own laboratory procedures. All microbiology laboratories adopted EUCAST breakpoints and guidelines [22, 23].
- Outcome: in-hospital mortality.

Statistical analysis

All analyses were performed using R Statistical Software (v4.3; R Core Team 2021). Continuous variables were summarized using mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were reported as frequencies and percentages. Bar graphs were generated using the ggplot2 R package (v3.4.4; Wickham 2016). Italy maps were obtained via the ggplot2 R package (v3.4.4; Wickham

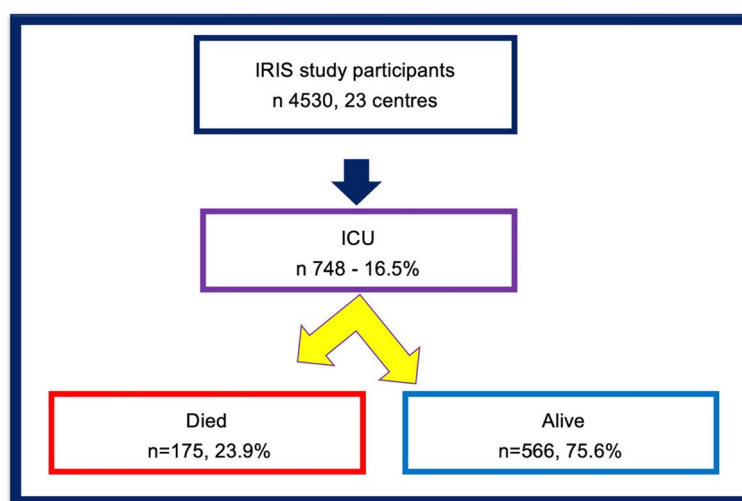


Fig. 1 Patients included from the IRIS study Database requiring ICU admission. IRIS: Italian Register of Complicated Intra-abdominal Infections; ICU: intensive care unit

2016), the tidyverse R package (v2.0.0; Wickham et al. 2019), rnatuarearth R package (v3.4; Massicotte and South 2023).

Clinical and demographic variables considered as potential predictors of in-hospital mortality were initially explored to assess data availability and distribution. Potential predictors of in-hospital mortality were selected based on clinical relevance and data availability. Candidate variables included age, duration of ICU stay, presence of malignancy, immunosuppression, severe cardiovascular comorbidities, adequate source control, re-operation, type of peritonitis, delay in initial intervention, and type of infection.

For each variable, the number and percentage of missing values were calculated. Variables with a high

proportion of missing data (>75%) were excluded from the analysis to ensure the robustness of the model. For variables with low to moderate missing data (5–30%), multiple imputation was used to handle missing values.

Handling of missing data

Multiple imputation was performed using the mice package in R (v3.13.0; van Buuren and Groothuis-Oudshoorn, 2011), generating 5 imputed datasets. The default imputation methods were applied according to variable type (continuous or categorical), while the outcome variable was excluded from the imputation procedure. Multiple imputation allowed plausible estimation of missing values while preserving variability and relationships among variables.

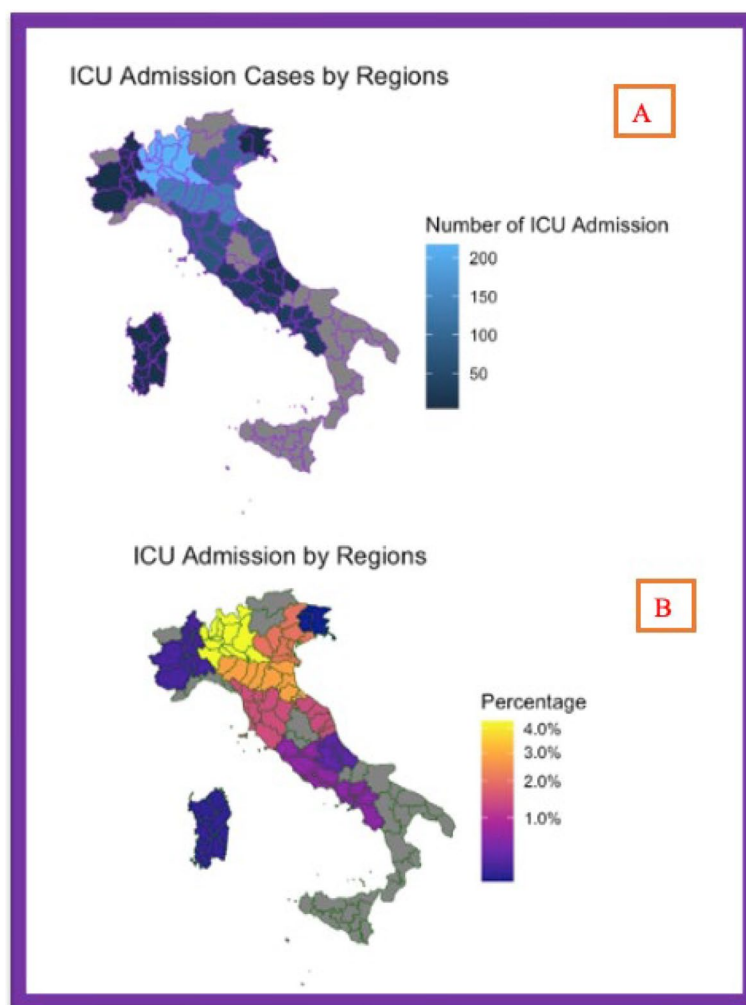


Fig. 2 Geographical distribution of Centre's contribution to IRIS study. **A** Italy map, geographical distribution of center contribution to database, number of cases for each region. **B** Italy map, geographical distribution of center contribution to database, percentage of cases for each region. All analyses were performed using R Statistical Software (v4.1.2; R Core Team 2021). Italy maps were obtained via the ggplot2 R package (v3.4.4; Wickham 2016), the tidyverse R package (v2.0.0; Wickham et al. 2019), rnatuarearth R package (v3.4; Massicotte and South 2023)

Model construction

The primary outcome was in-hospital mortality coded as a binary variable (1=deceased, 0=alive). For each imputed dataset, a multivariable logistic regression model was fitted including all candidate variables. The resulting coefficients were pooled according to Rubin's rules to obtain final estimates of odds ratios (ORs), 95% confidence intervals (CIs), and *p*-values. Variables were presented with ORs, CIs, and *p*-values. A forest plot was also generated to visualize the results, highlighting variables significantly associated with the outcome ($p < 0.05$) in purple and non-significant variables in yellow. The interpretation of effect sizes considers both *p*-values and confidence intervals. Variables with narrow CIs and ORs clearly different from 1 indicate both statistical significance and adequate precision. Variables with wide CIs, although possibly clinically relevant, may have limited power in this dataset.

Results

"The IRIS study (Italian Register of Complicated Intra-abdominal InfectionS)" enrolled a total of 4530 patients from 23 different Italian centers. Patients who were not admitted to the ICU were subsequently excluded. The final study population consisted of 784 patients hospitalized for complicated intra-abdominal infections requiring ICU admission (Fig. 1), representing 16.5% of the initial dataset.

Figure 2 illustrates the geographic distribution of participating centers across Italian regions. The regions with the highest number of enrolled patients were Lombardy, followed by Emilia-Romagna and Tuscany. No cases were reported from Liguria, Valle d'Aosta, Trentino–Alto Adige, Calabria, Molise, or Abruzzo.

Demographic and clinical characteristics

The demographic characteristics of the study population are summarized in Table 1. The main reasons for ICU admission were septic shock (271 cases, 36.2%), followed by sepsis (269 cases, 35.9%). Pneumonia accounted for 7.2% of ICU admissions, followed by bleeding (5.5%) and respiratory failure (4.3%).

Regarding comorbidities, 23.7% of patients had a history of cancer, 23.1% had cardiovascular disease, and 10.8% were receiving immunosuppressive therapy. Adequate source control was achieved in 61.5% of cases. Recent antimicrobial therapy prior to hospital admission was reported in 23% of patients.

Table 2 presents patient characteristics stratified by type of infection. Community-acquired infections accounted for 64.8% of all cases. The most frequent diagnoses were colonic perforation and diverticulitis (59.1%), followed by gastroduodenal perforation (1.9%). Figure 3A shows the number of patients admitted to the ICU or not admitted to the ICU according to diagnosis.

Table 1 Demographic characteristics and physiological status of patients admitted to ICU

Clinical characteristics			
<i>n</i> (%)	Age		Sex
748	65.9±18.7		M 390 (52.1%) F 358 (47.9%)
Recent antimicrobial therapy	Malignancy	Immunosuppression	Cardiovascular comorbidity
172 (23%)	177 (23.7%)	81 (10.8%)	173 (23.1%)
Type of infection			
CA	HA		
485 (64.8%)	263 (35.2%)		
Reason for ICU admission			
Septic shock 271 (36.2%)	Sepsis 269 (35.9%)	Pneumonia 54 (7.2%)	Bleeding 41 (5.5%)
Respiratory insufficiency 32 (4.3%)	Cardiac Arrhythmia 8 (1.1%)	Acute myocardial infarction 7 (0.9%)	
Stroke 7 (0.9%)	UTI 3 (0.4%)	Pulmonary embolism 1 (0.1%)	
Septic status at presentation			
Sepsis 320 (42.7%)	Septic shock 282 (37.7%)		No sign of sepsis 146(19.5%)
Surgical characteristics			
Adequate source control	Delay in initial intervention	Reoperation	Intra-abdominal microbiological evaluation
460(61.5%)	249 (33.3%)	157 (21%)	559 (74.7%)

Data are presented as actual number (*n*), mean ± standard deviation or percentage (%) where appropriate

F female, M male, CA community acquired vs HA healthcare-associated, NA not applicable, UTI urinary tract infection

Table 2 Demographic characteristics and physiological status of patients admitted to ICU according to the type of diagnosis

Diagnosis	Total patients (diagnosis)/ total database	ICU admission/ total patients (diagnosis)	% of ICU admission/ total database	Age	Sex n	Type of infection n (%)	Septic status at presentation	n	%
Appendicitis	1296 (28.6%)	62 (4.8%)	1.4%	40.3 ± 29.6	F 23 (37.1%) M 39 (62.9%)	CA 60 (96.7%) HA 2 (3.3%)	No sign of sepsis	11	17.7
							Sepsis	36	58.1
							Septic shock	15	24.2
Cholecystitis	683 (15.1%)	59 (8.6%)	1.3%	74 ± 11.6	F 26 (44.1%) M 33 (55.9%)	CA 44 (74.6%) HA 15 (25.4%)	No sign of sepsis	7	11.9
							Sepsis	31	52.5
							Septic shock	21	35.6
Gastro duodenal perforations	361 (7.9%)	89 (24.6%)	1.9	70.3 ± 15.5	F 44 (49.4%) M 45 (50.6%)	CA 74 (83.1%) HA 15 (16.9%)	No sign of sepsis	7	7.9
							Sepsis	50	56.2
							Septic shock	32	35.9
Bowel occlusion	166 (3.7%)	13 (7.8%)	0.3%	75.1 ± 11.2	F 5 (38.5%) M 8 (61.5%)	CA 8 (61.5%) HA 5 (38.5%)	No sign of sepsis	11	84.6
							Sepsis	1	7.7
							Septic shock	1	7.7
Small bowel perforation	168 (3.7%)	60 (35.7%)	1.3%	64.5 ± 17.9	F 38 (63.3%) M 22 (36.7%)	CA 41 (68.3%) HA 19 (31.7%)	No sign of sepsis	4	6.7
							Sepsis	31	51.7
							Septic shock	25	41.6
Colonic perforation and diverticulitis	1601 (35.3%)	442 (27.6%)	9.7%	67.1 ± 15.5	F 211 (47.7%) M 231 (52.3%)	CA 243 (55%) HA 199 (45%)	No sign of sepsis	95	21.5
							Sepsis	170	38.5
							Septic shock	177	40
Intestinal ischemia	39 (0.9%)	10 (25.6%)	0.2%	71.6 ± 15.5	F 5 (50%) M 5 (50%)	CA 6 (60%) HA 4 (40%)	No sign of sepsis	2	20
							Sepsis	1	10
							Septic shock	7	70
Gynecological emergencies	22 (0.5%)	1 (4.5%)	0.02%	69	F 1 (%)	HA 1 (100%)	Septic shock	1	100
Pancreatitis	57 (1.3%)	4 (7%)	0.08%	60.8 ± 16.4	F 2 (50%) M 2 (50%)	CA 3 (75%) HA 1 (25%)	No sign of sepsis	1	25
							Septic shock	3	75
Complicated abdominal wall hernia	135 (2.9%)	8 (5.9%)	0.2%	76 ± 8.9	F 3 (%) M 5 (%)	CA 6 (75%) HA 2 (25%)	No sign of sepsis	8	100

Data are presented as actual number (n), mean ± standard deviation or percentage (%) where appropriate

ICU intensive care unit, F female, M male, CA community acquired, HA healthcare-associated, NA not applicable

Diffuse appendicitis was observed in 55.1% of cases, and computed tomography was the primary diagnostic modality in 75.5% of patients (Table 3). A laparotomic approach was performed in 75.8% of patients, with a reoperation rate of 21%.

Figure 3B depicts the distribution of community-acquired (CA) and healthcare-associated (HA) intra-abdominal infections according to diagnosis among patients admitted to the ICU.

Microbiological sample

Microbiological samples were collected from 693 patients (94.6%) (Table 4). Of these, 648 samples (86.6%) were intra-abdominal cultures, 41 samples (5.5%) included both intra-abdominal and bloodstream cultures, and 4 samples (0.5%) were bloodstream cultures alone.

The most frequently isolated pathogens were *Escherichia coli* (160 isolates, 23.1%), followed by *Enterococcus* spp. (107 isolates, 15.4%), *Enterobacter* spp. (38 isolates,

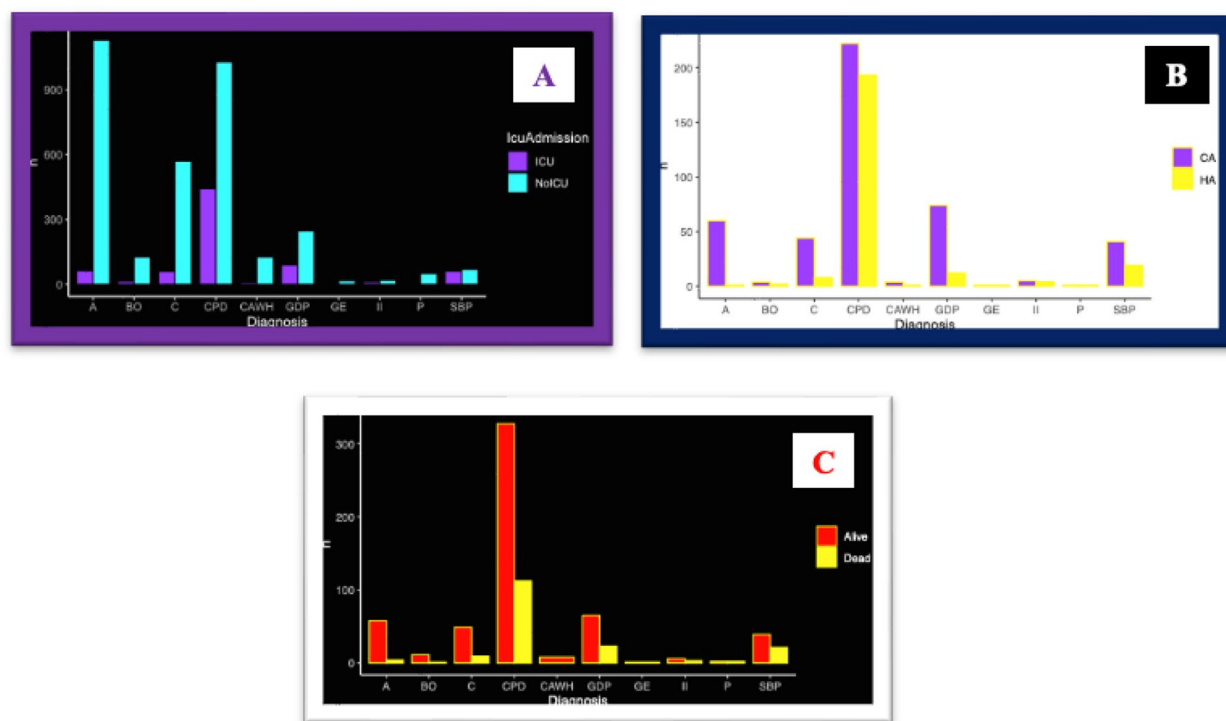


Fig. 3 Number of cases of patients admitted to intensive care unit (ICU) or not in accordance with type of diagnosis **(A)**. Number of cases of community acquired (CA) and healthcare associated (HA) Intra-abdominal infection (IAI) in accordance with type of diagnosis in patients admitted to ICU **(B)**. Outcome in accordance with type of diagnosis in patients admitted to ICU **(C)**. All analyses were performed using R Statistical Software (v4.3; R Core Team 2021). Bar graphs were obtained via the ggplot2 R package (v3.4.4; Wickham 2016). A: appendicitis; BO: bowel occlusion; C: cholecystitis; CPD: colonic perforation and diverticulitis; CAWH: complicated abdominal wall hernia; GDP: gastro duodenal perforations; GE: gynecological emergencies; II: intestinal ischemia; P: pancreatitis; SBP: small bowel perforation

5.5%), *Streptococcus* spp. (30 isolates, 4.3%), and *Klebsiella pneumoniae* (22 isolates, 3.2%) (Table 5). MDR organisms were identified in 84 samples (12.1%).

Empiric antibiotic therapy was administered in the majority of cases (>80%), with a mean duration of targeted therapy exceeding 7 days (Table 5). Piperacillin–tazobactam was the most frequently prescribed antibiotic (23%).

A total of 68 *Candida albicans* isolates and 3 fluconazole-susceptible non-resistant *Candida albicans* isolates were identified (Table 6). Additionally, 15 non-*Candida albicans* species were isolated from intra-abdominal cultures. Empiric antifungal therapy was administered to 22 patients: 3 without signs of sepsis, 10 with sepsis, and 9 with septic shock (Table 6). Azoles were used as empiric antifungal therapy in 21 patients.

Outcome

Figure 3C illustrates patient outcomes according to diagnosis among those admitted to the ICU. The overall in-hospital mortality rate in the ICU cohort was 23.9%.

When considering the entire IRIS database, overall mortality was 5.2%.

As shown in Table 7, mortality rates varied according to the underlying diagnosis: 40% of patients with intestinal ischemia, 35% with small bowel perforation, 26.9% with gastroduodenal perforation, and 25.8% with colonic perforation died during hospitalization.

Multivariable logistic regression model

A multivariable logistic regression model was constructed to assess factors associated with in-hospital mortality. Odds ratios (ORs) with 95% confidence intervals (CIs) and *p*-values were estimated from the pooled imputed datasets (Table 8 and Fig. 4).

Significant predictors of in-hospital mortality included:

- Immunosuppression (OR 1.99, 95% CI 1.09–3.66, *p*=0.025), indicating a nearly twofold increased risk.
- Serious cardiovascular disease (OR 1.91, 95% CI 1.20–3.05, *p*=0.006).
- Inadequate source control (OR 0.39, 95% CI 0.22–0.71, *p*=0.002).

Table 3 Clinical and diagnostic characteristics according to the type of diagnosis in patients admitted to ICU

Diagnosis	ICU patients <i>n</i>	Antimicrobial therapy in previous days <i>n</i> (%)	Peritonitis <i>n</i> (%)	Operative technique <i>n</i> (%)	Reoperation	Diagnostic tools	<i>n</i>	%
Total	748	Yes 39(5.21%)	Diffused 412 (55.1%) Localized 217 (29%)	Laparoscopic 73(9.8%) Laparotomic 567(75.8%)	157 (21%)	Clinical evaluation Abdomen X-ray US CT MRI	3 49 100 565 2	0.4 6.5 13.4 75.5 0.3
Appendicitis	62	2 (3.2%)	Diffused 39 (62.9%) Localized 23 (37.1%)	Laparoscopic 9 (14.5%) Laparotomic 51 (82.3%)	5 (8.1%)	Abdomen X-ray CT US	2 28 31	3.2 45.2 50
Cholecystitis	59	5 (8.5%)	Diffused 18 (30.5%) Localized 38 (64.4%)	Laparoscopic 18 (30.5%) Laparotomic 37 (62.7%)	3 (5.1%)	Abdomen X-ray CT MRI US	1 40 1 17	1.7 67.8 1.7 28.8
Gastro duodenal perforations	89	5 (5.6%)	Diffused 77 (86.5%) Localized 8 (9%)	Laparoscopic 14 (15.7%) Laparotomic 71 (79.8%)	12 (13.5%)	Abdomen X-ray CT Clinical evaluation US	10 63 1 14	11.2 70.8 1.1 15.7
Bowel occlusion	13	Yes 1 (7.7%)	None	Laparoscopic 1 (7.7%) Laparotomic 1 (7.7%)	None	CT	13	100
Small bowel perforation	60	None	Diffused 42 (70%) Localized 18 (30%)	Laparoscopic 1 (1.7%) Laparotomic 53 (88.3%)	17 (28.3%)	Abdomen X-ray CT US	5 40 9	8.3 66.7 15
Colonic perforation and diverticulitis	442	24 (5.4%)	Diffused 235 (53.2%) Localized 130 (29.4%)	Laparoscopic 28 (6.3%) Laparotomic 338 (76.5%)	120 (27.2%)	Abdomen X-ray CT Clinical evaluation US MRI	30 360 1 29 1	6.8 81.4 0.2 6.6 0.2
Intestinal ischemia	10	Yes 1 (10%)	None	Laparoscopic 1 (10%) Laparotomic 8 (80%)	None	CT	10	100
Gynecological emergencies	1	None	Diffused 1 (100%)	Laparoscopic 1 (100%)	None	CT	1	100
Pancreatitis	4	1 (25%)	None	None	None	CT	4	100
Complicated abdominal wall hernia	8	None	None	Laparotomic 8 (100%)	None	Clinical evaluation CT X-ray	1 6 1	12.5 75 12.5

Data are presented as actual number (*n*), mean $\pm$ standard deviation or percentage (%) where appropriate

ICU intensive care unit, CT computed tomography, US ultrasound, MR magnetic resonance imaging

- Re-operation (OR 2.30, 95% CI 1.34–3.96, $p=0.003$).
- Peritonitis (OR 0.39, 95% CI 0.23–0.66, $p<0.001$).
- Type of infection–healthcare-associated IAI (OR 1.83, 95% CI 1.10–3.04, $p=0.020$), showing a higher risk of mortality compared to community-acquired infections.
- Age (OR 1.04 per year, 95% CI 1.03–1.06, $p<0.001$).

Other variables, including duration of antibiotic treatment, delay in initial intervention, and malignancy, were not statistically significant in the model.

In summary, patients with immunosuppression, serious cardiovascular comorbidities, requirement for re-operation, inadequate source control, peritonitis, and healthcare-associated infections were at significantly higher risk of in-hospital mortality. Age was also a continuous

Table 4 Microbiological sample according to the type of diagnosis

Microbiological sample	Bloodstream and intra-abdominal cultures	Intra-abdominal cultures	Bloodstream cultures	Not performed
Total	41 (5.5%)	648 (86.6%)	4 (0.5%)	55 (7.4%)
Diagnosis				
Appendicitis	2 (3.2%)	58 (93.6%)	NA	2 (3.2%)
Cholecystitis	3 (5.1%)	51 (86.5%)	NA	5 (8.4%)
Gastro duodenal Perforations	18 (20.3%)	65 (73%)	NA	6 (6.7%)
Bowel occlusion	NA	2 (15.4%)	NA	11 (84.6%)
Small bowel perforation	54 (90%)	6 (10%)	NA	NA
Colonic perforation and diverticulitis	13 (2.9%)	403 (91.3%)	2 (0.4%)	24 (5.4%)
Intestinal ischemia	3 (30%)	3 (30%)	1 (10%)	3 (30%)
Gynecological emergencies	NA	1 (100%)	NA	NA
Pancreatitis	2 (50%)	1 (25%)	1 (25%)	NA
Complicated abdominal wall hernia	NA	2 (25%)	NA	6 (75%)

Data are presented as actual number (*n*), mean $\pm$ standard deviation or percentage (%) where appropriate, NA not applicable

risk factor, while other variables did not show significant associations in this cohort.

Discussion

Despite major advances in medical care, sepsis remains a leading cause of mortality worldwide, with substantial inter-individual variability in clinical presentation and outcomes, underscoring the need for integrated multi-disciplinary policies for its prevention and management [24]. Epidemiology plays a central role in the design, implementation, and evaluation of hospital-based clinical pathways by providing population-level data on disease patterns, risk stratification, and health outcomes that support evidence-based practice and targeted interventions [25, 26]. In this study, we aimed to extend our previous epidemiological analysis of intra-abdominal infections by focusing on the most severe cases, specifically patients with IAIs requiring ICU admission [16]. Our objective was to provide a comprehensive overview of the epidemiology and management of complicated IAIs in Italian ICUs. Although some regions did not enroll patients, the IRIS study covered the majority of the national territory and represents the largest cohort on this topic ever conducted in Italy.

We found that septic shock still represents the main reason for ICU admission in patients with IAIs. Notably, a substantial proportion of patients presented with significant comorbidities: 23.7% had a history of cancer, 23.1% had cardiovascular disease, and 10.8% were receiving immunosuppressive therapy. The high prevalence of pre-existing conditions is particularly relevant, as short-term survival from abdominal sepsis has improved over recent years, resulting in an increasing number of patients being

discharged from both the ICU and hospital. However, long-term outcomes remain poorly characterized. A growing population of IAI survivors experiences long-term disabilities or worsening of pre-existing conditions, a clinical condition commonly referred to as “Post-Intensive Care Syndrome”.

Timely diagnosis, effective source control, appropriate antimicrobial therapy, and rapid stabilization are essential aspects in the management of critically ill patients with AIAs. In our cohort, adequate source control was achieved in 61.5% of cases, with a reoperation rate of 21%. Microbiological samples were obtained in 94.6% of patients, and the most frequently isolated pathogens were *Escherichia coli* (23.1%), followed by *Enterococcus* species (15.4%).

The implementation of antimicrobial stewardship programs represents a major priority in this clinical setting, aiming to reduce inappropriate antibiotic use and promote responsible prescribing. In our study, empiric antibiotic therapy was administered to more than 80% of patients, with a median treatment duration ranging from 8.1 to 19.3 days. Piperacillin–tazobactam was the most commonly prescribed antibiotic. Conversely, a considerable number of patients received empiric antifungal therapy, even in clinical scenarios in which such treatment is not routinely indicated.

Overall, in-hospital mortality in our cohort reached 23.9%. In this study, we identified several independent predictors of in-hospital mortality in patients with intra-abdominal infections requiring intensive care. Immunosuppression, serious cardiovascular comorbidities, inadequate source control, peritonitis, requirement for re-operation, healthcare-associated infections, and age

Table 5 Antibiotic therapy and type of bacteria according to the type of diagnosis

Microbiological sample	Empiric antibiotic therapy administration	Duration of antibiotic therapy	Type of bacteria	n	%
Appendicitis (Total = 60)	57 (91.9%)	10 ± 8.1	E. Coli	25	41.7
			Klebsiella Pneumoniae	1	1.7
			Pseudomonas Aeruginosa	1	1.7
			Enterococcus	5	8.3
			Streptococcus	10	16.7
			MDR	6	10
			Multi	9	15
			None	3	5
Cholecystitis (Total = 54)	50 (84.7%)	10.8 ± 6.2	E. Coli	12	22.2
			Klebsiella Pneumoniae	2	3.7
			Clostridium	1	1.8
			Enterobacter	8	14.8
			Enterococcus	8	14.8
			Staphylococcus aureus	1	1.8
			MDR	1	1.8
			Multi	8	14.8
Gastro duodenal perforations (Total = 83)	85 (95.5%)	12.6 ± 8.8	None	13	24.1
			E. Coli	4	4.8
			Enterobacter	5	6
			Klebsiella Pneumoniae	7	8.4
			Pseudomonas Aeruginosa	4	4.8
			Staphylococcus aureus	4	4.8
			Streptococcus	1	10.8
			Enterococcus	9	10.1
Bowel occlusion (Total = 2)	12 (92.3%)	8.1 ± 2.3	MDR	4	4.8
			Multi	13	15.6
			None	32	38.5
			Enterobacter	1	50
			None	1	50
Small bowel perforation (Total = 60)	54 (90%)	12.3 ± 10.3	E. Coli	19	31.7
			Pseudomonas Aeruginosa	1	1.7
			Enterobacter	9	15
			Klebsiella Pneumoniae	3	5
			Proteus	1	1.7
			Enterococcus	12	20
			Streptococcus	1	1.7
			MDR	7	11.7
Colonic perforation and diverticulitis (Total = 418)	358 (80.9%)	17 ± 15.2	Multi	6	10
			None	1	1.7
			Acinetobacter baumannii	7	1.7
			Bacteroides	3	0.7
			Clostridium	4	0.9
			E. Coli	97	23.2
			Proteus	5	1.2

Table 5 (continued)

Microbiological sample	Empiric antibiotic therapy administration	Duration of antibiotic therapy	Type of bacteria	n	%
Intestinal ischemia (Total = 7)	9 (90%)	13.2 ± 6.7	Pseudomonas Aeruginosa	10	2.4
			Enterobacter	15	3.6
			Klebsiella Pneumoniae	9	2.1
			Enterococcus	69	16.5
			Staphylococcus aureus	6	1.4
			Staphylococcus epidermidis	5	1.2
			Streptococcus	18	4.3
			MDR	56	13.4
			Multi	61	14.6
			None	53	12.7
			Clostridium	1	14.3
			E. Coli	3	42.9
			Enterococcus	3	42.9
Gynecological Emergencies (Total = 0)	1 (100%)	10	Multi	1	14.3
Pancreatitis (Total = 4)	2 (50%)	19.3 ± 14.3	None	2	28.6
Complicated abdominal wall hernia (Total = 2)	8 (100%)	8.8 ± 3	NA	NA	NA
			MDR	1	25
			Enterococcus	1	25
			Multi	1	25
			None	1	25
			Multi	2	100

Data are presented as actual number (n), mean ± standard deviation or percentage (%) where appropriate. MDR multidrug resistance, Multi association of antibiotic, NA not applicable

Table 6 Microbiological samples and fungi

Microbiological samples			
Intrabdominal cultures	n	Bloodstream and intra-abdominal cultures	n
Candida albicans	61 (9.4%)	Candida albicans	7 (17.1%)
Candida albicans resistant to fluconazole	3 (0.5%)		
Non-albicans candida	10 (1.5%)		
Non-albicans candida resistant to fluconazole	5 (0.8%)		

Data are presented as actual number (n), mean ± standard deviation or percentage (%) where appropriate

were all significantly associated with higher mortality. Healthcare-associated infections emerged as a particularly important factor, showing higher odds of mortality compared to community-acquired infections. This underscores the impact of multidrug-resistant pathogens and delayed appropriate therapy in nosocomial infections, emphasizing the need for timely, targeted antimicrobial strategies and strict infection control measures. The protective effect observed for adequate source control highlights the critical role of early and effective surgical intervention. Inadequate source control not only prolongs

the infectious process but also increases systemic inflammation and organ dysfunction, explaining its strong association with mortality.

These findings align with current literature indicating that both patient-related factors (age, comorbidities, immunosuppression) and treatment-related factors (adequacy of source control, need for re-operation) strongly influence outcomes in critically ill surgical patients. The Abdominal Sepsis Study (AbSeS) is a multinational prospective abdominal study on IAIs in critically ill patients focusing on epidemiology outcomes endorsed by the

Table 7 Outcome at discharge and diagnosis

	Diagnosis	Total	Outcomes at discharge	n	%
1	Appendicitis	62	Alive	58	93.5
			Dead	4	6.5
2	Cholecystitis	59	Alive	50	84.7
			Dead	9	15.3
3	Gastro duodenal perforations	89	Alive	65	73.1
			Dead	24	26.9
4	Bowel occlusion	13	Alive	12	92.3
			Dead	1	7.7
5	Small bowel perforation	60	Alive	39	65
			Dead	21	35
6	Colonic perforation and diverticulitis	442	Alive	328	74.2
			Dead	114	25.8
7	Intestinal ischemia	10	Alive	6	60
			Dead	4	40
8	Gynecological emergencies	1	Alive	1	100
9	Pancreatitis	4	Alive	2	50
			Dead	2	50
10	Complicated abdominal wall hernia	8	Alive	8	100

Data are presented as actual number (n), mean $\pm$ standard deviation or percentage (%) where appropriate

Table 8 Multivariable logistic regression analysis for in-hospital mortality

Predictor	OR	Lower95CI	Upper95CI	p_value
Age	1.043	1.026	1.062	<0.001
Duration (antibiotic therapy)	0.988	0.969	1.008	0.230
Malignancy	0.914	0.545	1.533	0.733
Immunosuppression	1.996	1.089	3.657	0.025
Cardiovascular disease	1.914	1.201	3.049	0.006
Type of infection	1.830	1.101	3.042	0.020
Healthcare associated IAIs				
Adequate source control	0.393	0.218	0.710	0.002
Delay in the initial intervention	1.593	0.993	2.557	0.054
Re-operation	2.302	1.338	3.960	0.003
Peritonitis localized	0.392	0.234	0.656	<0.001

Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). An OR > 1 indicates increased mortality risk. *p* values < 0.05 were considered statistically significant

European Society of Intensive Care Medicine (ESICM), focusing on the epidemiology and outcomes of IAIs in critically ill patients. Published data from AbSeS demonstrated that age greater than 60 years was significantly associated with mortality, with patients aged ≥ 80 years showing the worst prognosis, reaching mortality rates of

up to 70% [27]. Comorbidities such as diabetes, chronic heart failure, liver disease, and malnutrition were also associated with poorer outcomes. Additionally, antimicrobial resistance was reported in 26.3% of cases, with an overall mortality of 29.1% [6]. Importantly, failure to achieve adequate source control was strongly associated with increased mortality [1], in line with our findings. Arvaniti and colleagues analyzed data from the multinational AbSeS cohort to describe the epidemiology and age-related mortality of critically ill patients with intra-abdominal infection [28]. In a large population of ICU patients, mortality increased progressively with advancing age and was independently associated with age greater than 60 years, with the highest risk observed in patients aged 80 years or older. Late-onset hospital-acquired infection, diffuse peritonitis, sepsis, or septic shock, source control failure, and major comorbidities further contributed to poor outcomes, emphasizing the combined impact of age, disease severity, and underlying conditions on survival in intra-abdominal infections. Interestingly, Paiva and colleagues performed a large secondary analysis of the AbSeS prospective multinational cohort to compare the epidemiology and outcomes of intra-abdominal infections in immunocompromised versus immunocompetent ICU patients and to identify mortality risk factors [29]. Among more than two thousand five hundred patients from three hundred nine ICUs worldwide, immunocompromised patients showed distinct epidemiological features, including higher rates of healthcare-associated infections, typhilitis, and septic shock at presentation, while no relevant differences were observed in disease severity, anatomical disruption, microbiology, or antimicrobial resistance patterns. Despite a more severe clinical presentation, short-term mortality was comparable between immunocompromised and immunocompetent patients, and immunocompromised status itself was not associated with increased risk of death. Septic shock at presentation and persistent inflammation due to unsuccessful source control emerged as the main independent predictors of mortality in the immunocompromised population, highlighting the central role of early recognition, effective source control, and ongoing inflammatory monitoring rather than immune status alone in determining outcomes.

Onal et al. evaluated septic shock associated with intra-abdominal infections in 390 patients at a tertiary-care hospital over nearly 9 years, focusing on epidemiology, mortality, and the impact of source control [27]. Overall, 30-day mortality was high at 71.3%, with lower mortality observed in patients who underwent surgical or percutaneous source control (52.8% vs 79.8%) and particularly when performed within the first 12 h (54.5%

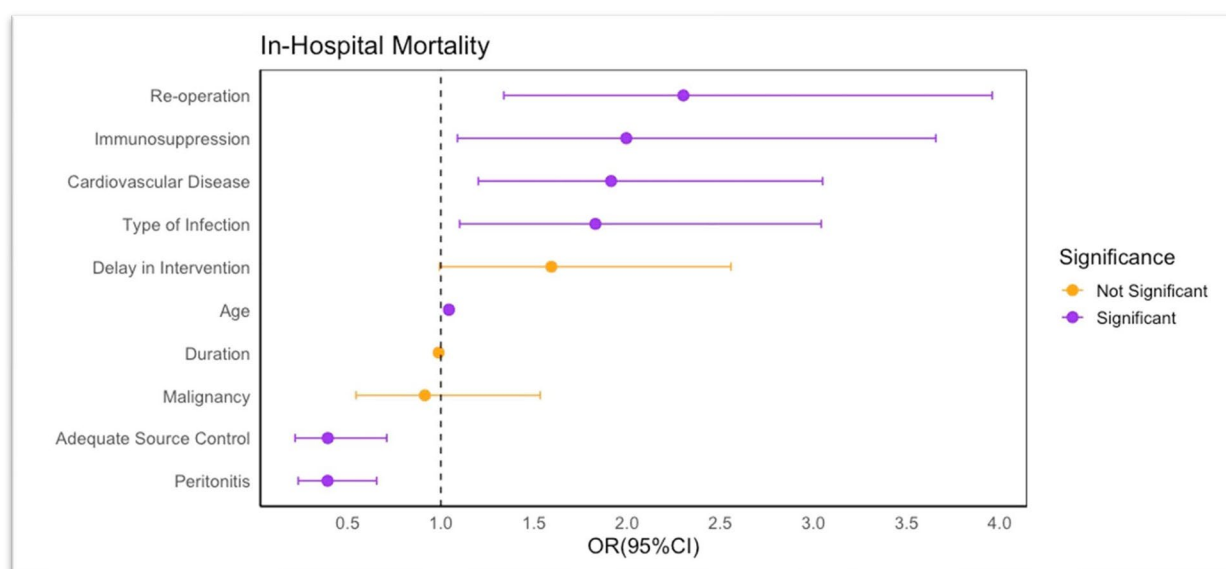


Fig. 4 Multivariable logistic regression analysis for in-hospital mortality. Odds ratios (ORs) and 95% confidence intervals (CIs) are shown for each covariate included in the multivariable model. The dashed vertical line represents the null value (OR = 1). Variables significantly associated with in-hospital mortality ($p < 0.05$) are shown in purple, whereas non-significant variables are shown in yellow. Results are derived from a multivariable logistic regression model after multiple imputation for missing data. Type of infections: healthcare acquired IAIs, peritonitis: localized

vs 73.4%). Logistic regression identified female gender, diabetes mellitus, carbapenem-resistant Gram-negative infections, SOFA score ≥ 10 , lactate > 3 mg/dl, and lack of source control as independent predictors of 30-day mortality. The study highlights the critical role of source control in reducing mortality in IAI-related septic shock and underscores the need for further research to clarify the impact of timing and other risk factors on patient outcomes.

Overall, our study reinforces the multifactorial nature of mortality in critically ill patients with intra-abdominal infections, highlighting modifiable factors (source control, timely intervention) that can be targeted to improve outcomes. These results may inform clinical decision-making, resource allocation, and future research aimed at optimizing care for high-risk surgical patients.

This study has several limitations that should be acknowledged. First, its observational design exposes the results to potential confounding factors and biases that cannot be entirely eliminated. Second, data were collected from a national registry, which may limit generalizability to healthcare systems with different patient populations, ICU admission criteria, sepsis management protocols, or resource availability. Variability in ICU practices across centers may have influenced the observed epidemiological patterns. Third, data extraction relied on electronic health records and administrative databases, which may be subject to misclassification

or incomplete documentation. Missing or inconsistently recorded data regarding comorbidities, infection sources, or severity scores could have affected the results. Fourth, long-term outcomes beyond hospital discharge were not assessed, limiting insights into post-sepsis syndrome, functional recovery, and quality of life. Future studies with extended follow-up are warranted. Finally, although standardized definitions for sepsis were applied, variability in clinical recognition, documentation, and adherence to Sepsis-3 criteria across centers may have influenced case identification. Despite these limitations, our study provides valuable insights into the epidemiology and management of severe IAIs in the ICU setting and highlights important areas for future research and quality improvement.

Conclusion

Epidemiology plays a fundamental role in improving clinical pathways by providing data to support evidence-based interventions, monitor outcomes, and address emerging healthcare challenges. Through standardized care and multidisciplinary collaboration, these strategies can improve patient outcomes, enhance quality of care, and optimize resource utilization. In patients with complicated intra-abdominal infections, septic shock remains the leading cause of ICU admission. Overall, the multivariable model highlights that immunosuppression,

serious cardiovascular comorbidities, inadequate source control, peritonitis, requirement for re-operation, health-care-associated infections, and age are independent predictors of in-hospital mortality in this ICU cohort. These results emphasize the importance of patient-specific factors—such as age, immune status, and comorbidities—alongside infection characteristics in determining outcomes in ICU patients with intra-abdominal infections. Clinically, these findings support the need for early risk stratification and aggressive management in high-risk populations to potentially reduce mortality. Our findings underscore the need for continued efforts to optimize source control strategies and to strengthen antibiotic stewardship programs in everyday clinical practice.

Abbreviations

IRIS	Italian Register of Complicated Intra-abdominal InfectionS
IAIs	Intra-abdominal infections
ICU	Intensive Care Unit
Ciai	Complicated Intra-abdominal infection
MDR	Multidrug resistant
CA	Community-acquired
HA	Healthcare-acquired
EUCAST	European Committee on Antimicrobial Susceptibility Testing
AbSeS	Abdominal Sepsis Study
ESICM	European Society of Intensive Care Medicine

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Authors' contributions

Conceptualization, E.B., C.C., M.C., F.Catena, A.G., F.F., L.G., E.M., M.S., F.Coccolini; Methodology, E.B., M.C., F.Coccolini; Validation, E.B., C.C., M.C., F.Catena, A.G., F.F., L.G., E.M., M.S., F.Coccolini; Formal Analysis, E.B., M.C., F.Coccolini; Data Curation, E.B., M.C., F.Coccolini; Writing – Original Draft Preparation, E.B., C.C., M.C., F.Catena, A.G., F.F., L.G., E.M., M.S., F.Coccolini; Writing – Review & Editing, E.B., C.C., M.C., F.Catena, A.G., F.F., L.G., E.M., M.S., F.Coccolini; Supervision, C.C., F.Catena, A.G., F.F., L.G., E.M., M.S., F.Coccolini.

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Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

IRB Information: this study was approved by the Local Research Ethics Committee of Pisa (Prot n 56478; 26/09/2019). The procedure was carried out in accordance with the Declaration of Helsinki (2000). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was not obtained in accordance with our Ethics Committee, considering the nature of the study and of the registry (prospective, observational) and that all the data collected were noted in a completely anonymous form.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Anaesthesia and Intensive Care, Pisa University Hospital, Pisa, Italy. ²Neuroscience Intensive Care Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy. ³General, Emergency and Trauma Surgery Department, Pisa University Hospital, Pisa, Italy. ⁴General Surgery Department, Milano Bicocca University Hospital, Monza, Italy. ⁵General, Emergency and Trauma Surgery Department, Bufalini Hospital, Cesena, Italy. ⁶General Surgery, Bari University Hospital, Bari, Italy. ⁷Emergency Medicine Department, Pisa University Hospital, Pisa, Italy. ⁸General Surgery Department, Macerata Hospital, Macerata, Italy.

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