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Microbiological resistance patterns and outcomes in trauma patients

Riccardo Guelfi,[1] Camilla Cremonini,[1] Benedetta Tuvo,[2] Iacopo Franconi,[2] Dario Tartaglia,[1] Lorenzo Ghiadoni,[3] Greta Barbieri,[3] Alessandro Cipriano,[3] Ettore Melai,[4] Antonella Lupetti,[2] Riccardo Morganti,[5] Federico Coccolini,[1] Pisa Trauma Working Group

[1]General, Emergency and Trauma Surgery Department, Pisa University Hospital, Pisa; [2]Microbiology Department, Pisa University Hospital, Pisa; [3]Emergency Medicine Department, Pisa University Hospital, Pisa; [4]Intensive Care Unit, Pisa University Hospital, Pisa; [5]Section of Statistics, Pisa University Hospital, Pisa, Italy

Corresponence: Camilla Cremonini, General, Emergency and Trauma Surgery, Pisa University Hospital, Via Paradisa, 2, 56124 Pisa, Italy. Tel.: +39.050.997967. E-mail: c.cremonini89@gmail.com

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Abstract

The initial assessment and stabilization of a traumatized patient is of paramount importance. Post-traumatic infections have long been considered among the leading causes and contributing factors of outcomes such as mortality, complications, and Length Of Hospital Stay (LOHS). This is an observational study using data prospectively collected within the "trauma registry" database of the General and Emergency Surgery department of the Pisa University Hospital - Trauma Center of Cisanello (Pisa), collected from November 2019 to December 2021. Epidemiological, clinical and microbiological data have been registered for all patient. Details regarding those who developed infections were analyzed. Among the 533 patients examined, 75 people developed an infection (signs like fever, WBC count increase, infectious protein related) with at least one positive microbiological isolate during hospitalization, for a total of 234 positive isolates, among which pathogens Resistant (R) to one class of antimicrobials and pathogens resistant to more than three classes of antimicrobials (Multi-drug Resistant, MDR) were identified. Multivariate analyses were

performed to correlate trauma severity (Injury Severity Score, ISS), general population characteristics and microbiological patterns with outcomes. The presence of resistant strains identified in the second culture test together with ICU admission were found to be risk factors associated to the development of complications. Microbiological patterns were not statistically significant risk factors for mortality. A multidisciplinary team plays a pivotal role in defining the correct antibiotic stewardship program.

Introduction

Polytrauma patients require a multidisciplinary and timely approach. Patient management, focused on initial evaluation and stabilization, represents only the first step in treatment, since various complications, including infections (signs like fever, white blood cells-WBC count increase, infectious protein related to one positive microbiological isolate), can subsequently arise.
In fact, infections may result in a significant increase in late deaths due to multi-organ failure and/or sepsis; in addition to causing a worsening of the patient's outcome, they also inevitably cause a significant increase in healthcare costs.
The discontinuity of the tissue barriers caused by trauma and the medical-surgical practices performed (intubation, placement of drains, mechanical ventilation, catheters) may create colonization routes for pathogens. Furthermore, trauma itself causes a substantial alteration in patients' immune response, making them more vulnerable to the development of infections that can affect morbidity and mortality.[1]
The risk factors for Nosocomial Post-Traumatic Infections (NPI) are different and multiple as well as related both to the type of trauma (urgency of hospitalization, anatomical site of the trauma, procedures required, hospital services) and to the characteristics of the patient himself (sex, age and comorbidities).[2-4]
Over time, numerous studies have been carried out to search for potential correlations between the incidence of NPI and the various global scoring systems (Injury Severity Score-ISS, Abbreviated Injury Scale-AIS , New Injury Severity Score-NISS, Trauma and Injury Severity Score-TISS, Revised Trauma Score-RTS): in particular, a significant relationship with the NISS (New Injury Severity Score) score.[5]
Data showed that approximately half of the patients developed at least one infection during their stay in intensive care with a rate of nosocomial infections of 70%. They showed that prolonged hypo-perfusion, length of stay in intensive care units, invasive procedures (tracheostomy,

mechanical ventilation, pleural drainage and bladder catheter) and the number of surgical operations performed are significant risk factors for the development of infections. All these factors influenced mortality and length of hospital stay.[6]

A multidisciplinary approach and the consequent adequacy of antibiotic therapy are very important, therefore antibiotic prophylaxis in the polytraumatized patient is a complex topic.[7]

Lastly, the adequacy and timing of source control are essential in the management of abdominal and soft tissues infections. However, one of the main challenges in the infections management is the overwhelming increase of drug resistances of micro-organisms.[8]

The purpose of our study is to identify correlation between infections, the responsible microorganisms and their corresponding microbiological patterns with the outcomes of patients suffering of major trauma.

Materials and Methods

The study was conducted using the data prospectively collected from November 2019 to December 2021 inside the "trauma registry" database of the General and Emergency Surgery department of the Pisa University Hospital - Trauma Center of Cisanello (Pisa). Patients who were managed by the trauma team (surgeon, anesthetist, emergency room doctor) were included.

The study protocol (n.17575) was approved by the Regional Ethics Committee for Clinical Trials of Tuscany.

The data present in the trauma registry include patient demographics (in anonymized form), age, sex, presence of comorbidities, AIS score, ISS score, intubation, orthopedic surgery, general surgery, endovascular procedure, intervention neurosurgery, admission to the Intensive Care Unit, days of stay in the Intensive Care Unit, days of ventilation, positive culture, type of microorganism and antimicrobial resistance pattern. Mortality, complications (pneumonia, Acute Respiratory Distress Syndrome-ARDS, Acute Respiratory Failure-ARF, sepsis, pulmonary embolism-PE, Deep Vein Thrombosis-DVT, bleeding and anastomotic dehiscence) were identified as the study outcomes. The microbiological data were implemented with those collected by the Microbiology department.

Results were obtained on 8 different types of samples including: blood cultures, broncho aspirates, broncho washings, urine cultures, rectal swabs, balano-preputial swabs, pleural fluid, intraperitoneal fluid and wound swabs collected from individual patients; for each of them an antibiogram was carried out and, subsequently, the sensitivity and resistance were revealed for each antibiotic and/or antifungal belonging to the main classes, represented by: glycopeptides and lipoglycopeptides, cephalosporins, fluoroquinolones, macrolides, aminoglycosides, carbapenems, penicillins , sulphonamides, polypeptides, rifamycins, streptogramins and tetracycline monobactams, oxazolidinones. In addition to these classes, we have: chloramphenicol, phosfomycin, mupirocin, nitrofurantoin, lefamulin, metronidazole tigeciclyn clindamycin, daptomycin.

For the samples testing positive for fungal infections, sensitivity and resistance were evaluated for the classes of antifungals including azoles, echinocandins, amphotericin B, and flucytosine.

Multiple Drug Resistance (MDR) was defined as acquired non-susceptibility to at least one antimicrobial in three or more antimicrobial classes (e.g., tetracyclines, cephalosporins, fluoroquinolones). Extremely Drug-Resistant (XDR) bacteria were defined as non-susceptibility to at least one antimicrobial in all but two or fewer antimicrobial classes. Pandrug-Resistant (PDR) bacteria have been defined as non-susceptibility to all antimicrobial in all antimicrobial classes.[9]

International organizations such as EUCAST aim to establish to which level of susceptibility the individual microorganism belongs using two fundamental parameters: breakpoints and MIC. A percentage greater than 20% represents, in fact, the threshold for detecting the presence of resistance to a specific category of drugs.[10]

Categorical data were described by absolute and relative frequency (%), continuous data were summarized by mean and standard deviation. To compare categorical and continuous factors influencing the categorical outcomes chi-square test and t-test for independent samples were applied, respectively. To compare categorical and continuous factors influencing the continuous outcome t-test for independent samples and Pearson correlation analysis were performed, respectively. Successively, the significant factors were analyzed using multivariate binary logistic regression (with the categorical outcomes) and multiple linear regression (with the continuous outcome). Significance was set at 0.05 and all analyzes were carried out with SPSS v.29.

Results

Epidemiological and microbiological data

From all 533 patients in the "trauma registry", 487 (91.4%) are adults and 46 (76.5%) pediatric patients.

Of the patients involved, 125 (23.5%) are female, and 408 (76.5%) are male. Twenty-three (4.4%) suffered a penetrating type of trauma, 509 (95.5%) suffered a type of blunt trauma. Describing trauma, the anatomical regions involved were highlighted, including: the abdomen in 147 patients (31.7%); the chest 219 patients (47.3%); the extremities in 155 patients (33.5%); the head and neck area was affected in 188 patients (40.6%); the face in 99 patients (21.4%); the external ones in 21 patients (4.5%) (see Table 1). Based on the AIS score, the following data were obtained considering injuries with an AIS score ≥ 3: abdomen in 49 patients (10.6%); extremities in 41 patients (8.9%);

face in 7 patients (1.5%); head and neck in 91 patients (19.6%), external in 7 patients (1.5%). To evaluate the overall severity of the polytrauma patient, the ISS was used which highlighted 161 patients (34.7%) with an ISS score≥ 15. Quantifying and categorizing the different procedures to which these patients were subjected due to the trauma, we obtained: 50 patients (9.4%) underwent surgery in the general surgery department; 56 patients (10.5%) underwent neurosurgical interventions; 155 patients (29.1%) underwent orthopedic treatment; 35 patients (6.6%) underwent embolization; 6 patients (1.1%) underwent endovascular treatments; in 70 patients the data were not registered (Table 1).

Of 533 patients analyzed, 14% of patients, following the traumatic event, developed an infection, described by at least one sample positive for one or more microorganisms. The average age of the 75 patients was 47.7 years. Of these 75 patients, 18 (24%) are female and 57 are male (76%). Of the 75 patients, 2 (2.7%) suffered penetrating trauma, 73 (97.3%) were subjected to blunt trauma. Of the 75 patients with a positive isolate, 8 (10.6%) died, compared to 27 patients out of 533 (5.0%) of the total population of the study sample. Among the different types of samples collected (wound colture, broncholavage, bronchoaspiration, urine culture, blood culture, pleural fluid, rectal colture, vaginal colture, nasal colture, balano-preputial colture, intra-abdominal fluid) a total number of 234 micoorganism were identified (Supplementary materials Table 1). The data collected highlights the following cultures.

Broncho aspirate cultures

Out of a total of 149 microorganisms, 22 different microorganisms were identified and described in Supplementary materials Table 2 and Supplementary materials Figure 1.

Blood cultures

The positive blood cultures were 46 overall, with 10 different types of microorganisms identified and described in Supplementary materials Table 3 and Supplementary materials Figure 2.

Urine cultures

There were 27 positive urine culture samples, with a total of 8 types of microorganisms identified and described in Supplementary materials Table 4 and Supplementary materials Figure 3.

Wound cultures

Among the wounds cultures there were 17 positive isolates, for a total of 13 types of microorganisms identified and described in Supplementary materials Table 5 and Supplementary materials Figure 4.

For each of the 234 isolated microorganisms, the respective antibiograms/antimycograms and resistance to the main classes of antimicrobials were collected, with the corresponding percentage (Supplementary materials Table 6). Within our sample, according to EUCAST resistances stratification,[20] it was highlighted that the 20% threshold of resistance was highlighted in the following drug classes: penicillins (71.4%), b-lactams (61.5%), fluoroquinolones (56%), cephalosporins (47%), aminoglycosides (44%), carbapemens (40.6%), trimetroprim-sulfametaxazole (34.2%), phosfomycin (29.1%) (Figure 1).
Below are the 8 classes of antibiotics with a percentage of resistance greater than 20% and, for each of them, the number of samples positive for a specific microorganism (Table 2).

Multivariate analyses

Age is a statistically significant risk factor (p-value <0.01) for mortality. The ISS score is a statistically significant risk factor (p-value <0.01) for mortality. Intubation is a statistically significant risk factor (p-value <0.01) for mortality (Table 3).
General surgery is a statistically significant risk factor (p-value <0.05) for the development of complications. Admission to the Intensive Care Unit is a statistically significant risk factor (p-value <0.02) for the development of complications. Culture 2 resistant to at least one antimicrobial is a statistically significant risk factor (p-value <0.01) for the development of complications (Table 4).
Orthopedic surgery is a statistically significant risk factor (p-value <0.01) for increased length of stay. Endovascular procedures are a statistically significant risk factor (p-value <0.05) for increased length of stay. Ventilation is a statistically significant risk factor (p-value <0.01) for prolonged hospitalization (Table 5).

Discussion

Infections represent a very important topic in trauma patient management. Few data exist and they generally should be extrapolated from studies focused on other trauma topics. Investigating the local flora and its effect is of paramount importance to improve patients care and to reduce infection consequences. Present study investigated the causes and effects in a two-years period. All data derived from the trauma registry. This represents a very important tool to keep track and to constantly evaluate the management of traumatized patients.

The average age of the population of this study is 47.7 years and the most affected appears to be male, in line with the literature which highlights a predominance of the male sex and an average age of 45 years. The type of trauma prevalent in our population was blunt while penetrating traumas represented a minority. Due to the paucity of sample this last category was not included in multivariate analyses. Among the procedures most used in the treatment of patients we find orthopedic surgery, followed by neurosurgery, general surgery, embolization and endovascular procedures. The most frequent cause of surgical intervention was orthopedic surgery (39.8%), followed by general surgery (32.1%).[11]

Analyzing the respiratory district infections collected in present study, the most represented microorganism is Acinetobacter baumannii, followed by Staphylococcus aureus and Pseudomonas aeruginosa in accordance with the literature where the predominance of pathogens, in pneumonia acquired in hospital, is represented by *Acinetobacter species*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella species*, *Escherichia coli*, and *Enterobacter species*.[12]

Bloodstream infections were characterized by a prevalence of Staphylococcus epidermidis; this may be due to the fact that this microrganism penetrate through extremely serious and deep wounds, with violation of anatomical-physiological barriers caused by trauma. In the literature, however, in most cases, infections are caused by microorganisms including *Corynebacterium spp*., *Bacillus spp*., *Candida spp*, *Staphylococcus aureus*, coagulase-negative staphylococci.[11]

As regards urinary tract infections, the most common pathogen is represented by Acinetobacter baumannii, followed by *Escherichia coli* and *Pseudomonas aeruginosa*. In the literature, the data appear rather concordant with our results, in fact, the pathogens most associated with positive urine cultures are *E. coli*, *Enterococcus*, fungi, *Staphylococcus*, *Pseudomonas*.[1,14,15]

Analyzing wound infections, the most detected pathogen was *Pseudomonas aeruginosa*, followed by *Acinetobacter baumannii* and *Enterobacter cloacae*. In the literature, the main pathogens described are multi-resistant microorganisms including vancomycin-resistant enterococci, Enterobacterales producing extended-spectrum beta-lactamases and/or carbapenemases, methicillin-resistant staphylococci, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.[16]

The relevant aspect of the data obtained is the presence of *Acinetobacter baumannii* as the main pathogen present and, nevertheless, with the greatest number of resistances being found in approximately 15% of the samples examined. Hospitalized, polytraumatized and/or immunocompromised patients, in general, are at greater risk of *A. baumannii* infections given the invasion by the pathogen, not only from the airways, but also through discontinuities in the anatomical-physiological barriers caused by trauma and/or the procedures to which the patient is subjected.[17] In the literature there are analyses in line with our data, in fact, *A. baumannii* represents the main pathogen found in 21.5% of broncho aspiration samples. In blood culture, wound swab and urine culture samples, *A. baumannii* represents the pathogen mainly present although it is not considered, in the literature, as the main responsible for the colonization of these districts. Polytraumatized patients, in fact, due to trauma itself and to the consequent procedures, become compromised in their general state and exposed, on average, to long periods of hospitalization, favoring colonization.

Staphyloccocus aureus is the second most frequent and resistant pathogen, with 30 positive samples (12.8%). This significant correlation of infections with *S. Aureus* is partly due to the ability of this bacterium to penetrate and, inevitably over the years, it has developed an ever-increasing number of antibiotic resistances. In line with the results obtained from our study, it can be observed in the literature that the presence of a strong contamination of *S. Aureus* has also been highlighted in vascular prostheses and venous catheters.[18]

The third most frequently isolated pathogen within our study is *Pseudomonas Aeruginosa*, with 26 positive samples (11.1%). In agreement with the literature, we found a significant presence of culture tests of broncho aspirates positive for this microorganism; it is in fact capable of forming aggregates or biofilm-like structures mainly in patients with pulmonary comorbidities or alterations in mucus secretion.[19] Obviously, it is worth taking into consideration the fact that in polytraumatized patients there is a substantial modification of reflexes and mucociliary clearance, also due to the trauma itself, which leads to an alteration in mucus production and in biofilm growth. Mechanical ventilation must necessarily be identified as one of the causes of the onset of infections by this microorganism, favoring its growth and take root.[1,20]

In our study, 7 classes of antibiotics were found in which the percentage of resistance exceeded 20% including: cephalosporins, penicillins, fluoroquinolones, phosfomycin, trimetroprim-sulfametaxazole, aminoglycosides, carbapemens.

Multivariate analysis investigated the relationship between risk factors, the microbiological patterns and outcomes such as mortality, development of complications and length of hospital stay. As regards the mortality outcome, it was observed that microbiological resistance patterns did not represent a risk factor. This may be considered a proxy of an increasingly correct infections management which have made it possible to transform a compromised and at-risk patient (such as the patient victim of major trauma) into a patient who is vulnerable to the development of complications but without an increased risk of mortality. It is obvious that the severity of the trauma (described by the ISS score) and age are variables predictive of increased risk of mortality. Unfortunately, these variables cannot be modified by the trauma team management.[21,22]

Our analyzes show that intubation increases the risk of mortality by 8 times. The literature confirms our data indicating age, severity of trauma and pre-hospital Glasgow coma score as statistically significant risk factors for mortality.[23]

At multivariate analyzes microbiological resistance patterns represent a risk factor for complications. In fact, at the 2nd culture test the presence of resistance to at least one antimicrobial increases the risk of developing by 4 times complications.[24] Having a second culture positive, mostly resistant, in a patient already compromised in his general state such as a polytraumatized patient, can cause the development of serious and more complex infections. Its eradication may be very difficult due to a reduced availability of effective antimicrobial.[25] Being subjected to general surgery procedures appears to be a risk factor for developing complications. Patient admitted to intensive care are more at risk of developing complications. This data is consistent with the literature that describes the intensive environment as a source of multi-resistant microorganisms. The multidrug-resistant microbiological patterns are those more frequently associated with the developing nosocomial pneumonia, particularly in patients undergoing mechanical ventilation.[26]

Mechanical ventilation, orthopedic surgery and endovascular procedures are strongly related to the increase of the length of hospital stay. Orthopedic surgery increases the risk of increasing the length of hospital stay by 6 times. The literature confirms that these patients are predisposed to developing early and late outcomes resulting in long-term hospitalization.[27,28]

From a nursing perspective, the role of the nurse is central in both the early identification of infection and in the implementation of evidence-based preventive protocols. Strategies such as Ventilator-Associated Pneumonia-VAP prevention bundles, catheter care protocols, and skin integrity surveillance are essential in minimizing the risk of nosocomial infections.[29] Furthermore, active participation of nursing staff in multidisciplinary teams and in infection surveillance activities can improve clinical outcomes and reduce healthcare-associated costs.[30] Investing in nursing education and integrating nursing-sensitive indicators into trauma care pathways may strengthen the overall quality of care and promote antibiotic stewardship efforts.

The main strengths of this study are of having provided a detailed local epidemiological description of the main resistance patterns, and of having studied the relationship between the infections and the outcomes.
The main weaknesses are the observational design, the relatively small sample size due to the two years study period and the local data that may not be generalizable to other realities.

Conclusions

The presence of resistant strains identified in the second culture test together with intensive care unit admission were found to be risk factors associated to the development of complications. Microbiological patterns were not statistically significant risk factors for mortality. Focused microbial flora investigation is fundamental in implementing outcomes and in defining correct antibiotic stewardship program. A multidisciplinary team including surgeons, emergency physicians, anesthetists, nurses, infectious disease specialists, radiologists and epidemiologists plays a pivotal role in defining the correct management of the colonized and/or infected patient. Creation of multi-specialistic training networks on the topic is needed.

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Table 1. Sample characteristics (n=533) Statistics: (*) mean (SD) or frequency (%).

Characteristic	**STATISTICS N (*)**
Age	47 (21)
Gender	
F	124 (23)

M	409 (77)
ISS	12 (12)
Comorbidity	179 (34)
Intubation	124 (23)
ICU	205 (38)
Ventilation (Day)	77 (8)
General Surgery	50 (9)
Endovascular Procedures	37 (7)
Orthopedic Surgery	155 (29)
Neurosurgery	56 (10)

Table 2. Antibiotic resistence for micro-organisms.

	Acinetobacter baumannii	Staphylococcus aureus	Pseudomonas aeruginosa	Escherichia coli	Enterococcus faecalis	Klebsiella pneumoniae
Total isolated micro-organism	35	30	26	20	17	17
Class of antibiotics						
Aminoglycosides	34, 97.1	6, 20.0	7, 26.9	2, 10.0	9, 52.9	13, 76.5
B-Lactams	33, 94.3	11, 36.7	19, 73.1	11, 55.0	15, 88.2	9, 52.9
Carbapenems	32, 91.4	0	23, 88.5	1, 5.0	16, 94.1	12, 70.6
Cephalosporines	31, 88.6	3, 10.0	22, 84.6	14, 70.0	0	12, 70.6
Monobactams	0	0	20, 76.9	3, 15.0	0	15, 88.2
Penicillins	32, 91.4	16, 53.3	21, 80.8	15, 75.0	3, 17.6	13, 76.5
Fluoroquinolones	34, 97.1	26, 86.7	22, 84.6	4, 20.0	3, 17.6	0
Glycopeptides	0	1, 3.3	0	0	1, 5.9	0
Macrolides	0	11, 36.7	0	0	2, 11.8	0
Oxazolidinones	0	1, 3.3	0	0	0	2, 11.8
Polypeptides	1, 2.9	0	3, 11.5	1, 5.0	0	0
Rifamycins	0	2, 6.7	0	0	0	0
Sulphonamides	0	0	0	0	0	0
Tetracyclines	7, 20.0	1, 3.3	2, 7.7	0	0	0
Chloramphenicol	0	2, 6.7	0	0	0	0
Clindamycin	0	8, 26.7	0	0	3, 17.6	0
Daptomycin	0	0	0	0	0	0
Phosfomycin	0	1, 3.3	12, 46.2	1, 5.0	0	8, 47.1
Lefamulin	0	0	0	0	0	0
Metronidazole	0	0	0	0	0	0
Mupirocin	0	1, 3.3	0	0	0	0
Nitrofurantoin	2, 5.7	0	1, 3.8	0	0	0
Tigecycline	0	0	2, 7.7	1, 5.0	0	0
Trimetroprim-Sulfamethaxazole	29, 82.9	1, 3.3	12, 46.2	4, 20.0	3, 17.6	11, 64.7

Table 3. Multivariate analysis of mortality risk factors (step-wise method was applied). RC, regression coefficient.

Factor	RC	OR	IC 95% -	IC 95% -	p-value
Age	0.053	1.055	1.024	1.086	**<0.01**
ISS	0.078	1.081	1.038	1.126	**<0.01**
Intubation: (0) no, (1) yes	2.118	8.311	2.826	24.445	**<0.01**
Constant of the logistic	-7.998	0.001			<0.01
Comorbidity: (0) no, (1)					0.73
Neurosurgery: (0) no, (1)					0.70
ICU: (0) no, (1) yes					0.55

Table 4. Multivariate analysis of complications risk factors (step-wise method was applied). MDR, multidrug resistant; RC, regression coefficient.

Factor	RC	OR	IC 95% -	IC 95% -	p-value
General Surgery: (0) no, (1) yes	0.764	2.147	0.995	4.632	**0.05**
ICU: (0) no, (1) yes	0.939	2.558	1.406	4.656	**0.02**
2° Resistant Culture Sample: (0) no, (1)	1.539	4.660	2.158	10.060	**<0.01**
Constant of the logistic model	-2.472	0.084			<0.01
Intubation: (0) no, (1) yes					0.16
Orthopedic surgery: (0) no, (1) yes					0.30
Endovascular Procedures: (0) no, (1) yes					0.08
Positive Culture: (0) no, (1) yes					0.25
1° Resistant Culture Sample: (0) no, (1)					0.31
MDR 1: (0) no, (1) yes					0.34
MDR 2: (0) no, (1) yes					0.99
3° Resistant Culture Sample: (0) no, (1)					0.65
4° Resistant Culture Sample: (0) no, (1)					0.47

Table 5. Multivariate analysis of hospital stay length risk factors. MDR, multidrug resistant, ISS, injury severity score, ICU, intensive care unit; RC, regression coefficient; St RC, standardized RC.

Factor	RC	IC 95% -	IC 95% -	St RC	p-value

Intubation	-1.626	-7.483	4.232	-0.048	0.58
General Surgery	3.149	-4.228	10.527	0.072	0.39
Orthopedic surgery	12.313	6.282	18.344	0.351	**<0.01**
Endovascular Procedures	22.550	7.170	37.930	0.237	**0.05**
Neurosurgery	0.879	-6.189	7.947	0.021	0.80
ICU	2.249	-9.931	14.429	0.030	0.71
Positive Culture	-15.455	-32.797	1.888	-0.416	0.08
1° Resistant Culture Sample	13.935	-6.635	34.506	0.386	0.18
MDR 1	-3.679	-13.204	5.845	-0.076	0.44
2° Resistant Culture Sample	3.938	-9.073	16.949	0.102	0.54
MDR 2	3.485	-10.100	17.069	0.070	0.61
3° Resistant Culture Sample	2.291	-12.728	17.310	0.049	0.76
4° Resistant Culture Sample	4.286	-10.953	19.525	0.058	0.57
ISS	-0.042	-0.278	0.195	-0.029	0.72
Ventilation (Days)	0.925	0.517	1.334	0.432	**<0.01**
Constant of the linear model	6.519	-5.558	18.595		0.28

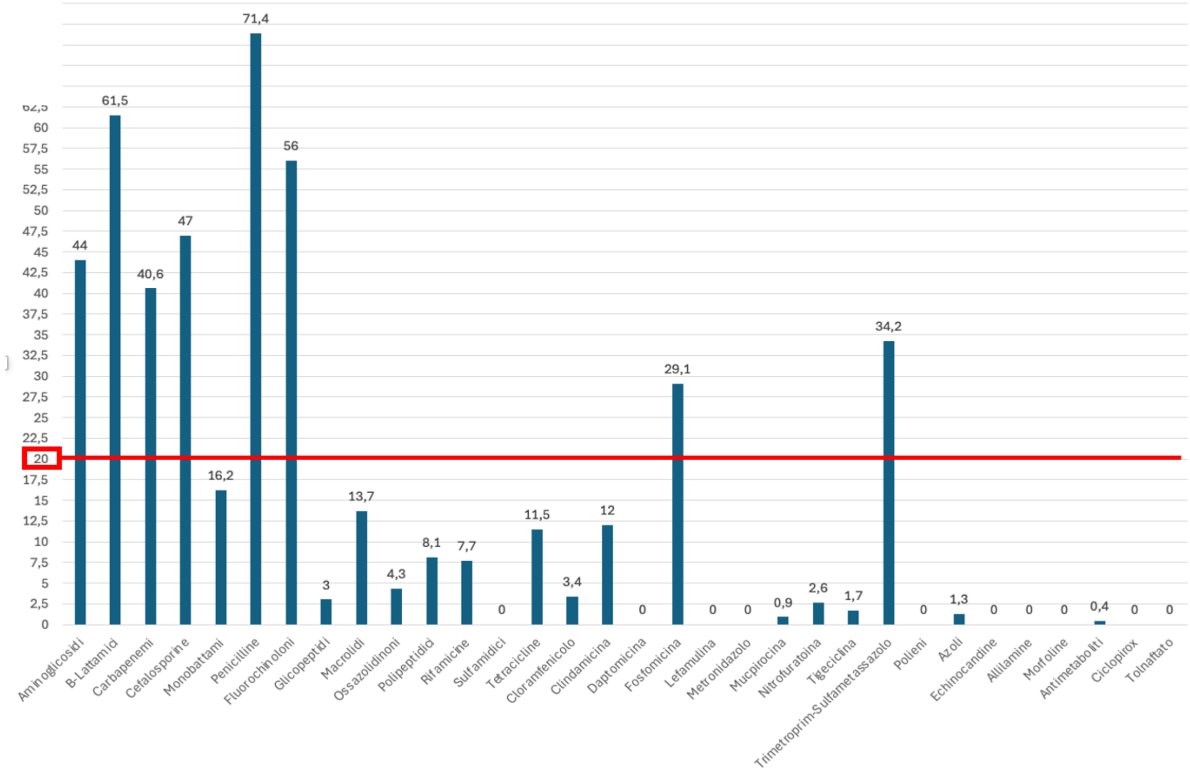

Figure 1. 20% antibiotic resistance threshold in isolated bacteria.

Pisa Trauma Working Group: Massimo Chiarugi**,** Nicola Pagnucci, Ferruccio Aquilini, Davide Antonazzo, Roberta Bertolini, Francesco Cinotti, Silvia Strambi, Serena Musetti, Giuseppe Zocco, Jacopo Giuliani, Giacomo Taddei, Filippo Vagelli, Alice Salamone, Luigi Cobuccio, Ismail Cengeli, Francesco Arces, Rachele Monetti, Rossella Facchin, Soraya Roccaforte, Gennaro D'Angelo, Chiara Del Carlo, Chiara Deri, Monica Donetti, Francesca Foltran, Matteo Filippi, Michele Tonerini, Tommaso Valentini, Silvia Pini, Diletta Dell'Agnello, Alessandro Ranalli, Massimo Santini, Silvia Trifirò.

Contributions: Federico Coccolini, Riccardo Guelfi, Antonella Lupetti, Nicola Pagnucci, conceptualization; Riccardo Guelfi, Alessandro Cipriano, Greta Barbieri, Camilla Cremonini, Riccardo Morganti, methodology; Riccardo Guelfi, Benedetta Tuvo, Iacopo Franconi, Camilla Cremonini, Greta Barbieri, data collection; Camilla Cremonini, Riccardo Morganti, formal analysis and investigation; Riccardo Guelfi, Alessandro Cipriano, Nicola Pagnucci, writing - original draft preparation; Federico Coccolini, Antonella Lupetti, Dario Tartaglia, Lorenzo Ghiadoni, Ettore Melai, writing - review and editing; Federico Coccolini, Massimo Chiarugi, Antonella Lupetti, Lorenzio Ghiadoni, supervision.

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Informed consent: all patients participating in this study signed a written informed consent form for participating in this study.

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Online supplementary materials

Table 1. Microbiological patterns of the 4 isolated micro-organisms.

Table 2. Absolute frequency of microbial species isolated in broncho-aspirate cultures.

Table 3. Absolute frequency of microbial species isolated in blood cultures.

Table 4. Absolute frequency of microbial species isolated in urine cultures.

Table 5. Absolute frequency of microbial species isolated in wound cultures.

Table 6. Cumulative antibiotic resistance.

Figure 1. distribution and frequency of broncho aspirate coltures microorganisms.

Figure 2. Distribution and frequency of blood cultures microorganisms.

Figure 3. Distribution and frequency of urine cultures microorganisms.

Figure 4. Distribution and frequency of wound cultures micro-organisms.

Figure 5. direct proportional relationship between days of ventilation and days of hospitalization.