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ORIGINAL INVESTIGATION

Association of antimicrobial use and incidence of hospital-acquired pneumonia in critically ill trauma patients with pulmonary contusion: an observational study☆

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Abstract
Background: Pneumonia occurs in about 20% of trauma patients with pulmonary contusions. This study aims to evaluate the association between empirical antibiotic therapy and nosocomial pneumonia in this population.
Methods: Retrospective cohort of adult patients admitted to a trauma-surgical ICU. The Antibiotic Therapy Group (ATG) was defined by intravenous antibiotic use for more than 48 h starting on hospital admission, while the Conservative Group (CG) was determined by antibiotic use no longer than 48 h. Primary outcome was microbiologically documented nosocomial pneumonia within 14 days after hospital admission. Logistic regression was used to estimate the association between group allocation and primary outcome. Exploratory analyses evaluating the association between resistant strains in pneumonia and antibiotic use were performed.
Results: The study included 177 patients with chest trauma and pulmonary contusion on CT scan. ATG were more severely ill than CG, as shown by higher Injury Severity Score, SAPS3, SOFA score, higher rates, and longer duration of mechanical ventilation. In the multivariate analysis, ATG

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was associated with a lower incidence of primary outcome (OR = 0.25, 95% CI 0.09—0.64; $p < 0.01$). Similar results were found in the sensitivity analysis with another set of variables. However, each day of antibiotic use was associated with an increased risk of pneumonia by resistant bacteria (OR = 1.18 per day, 95% CI 1.05—1.36; $p < 0.01$).

Conclusions: Empiric antibiotic therapy was independently associated with lower incidence of nosocomial pneumonia in critically ill patients with pulmonary contusion. However, each day of antibiotic use was associated with increased resistant strains in infected patients.

Introduction

The incidence of Ventilator-Associated Pneumonia (VAP) in trauma patients is about 4-fold higher than in ventilated non trauma patients.[1] Pneumonia can occur in 21% of trauma patients with pulmonary contusions.[2] Therefore Hospital-Acquired Pneumonia (HAP) is a concerning complication among trauma patients and there is evidence that nosocomial pneumonia can have long-lasting effects on outcomes in this population. As an example, in patients with Traumatic Brain Injury (TBI), HAP is associated with poor outcomes in severe TBI 5 years after injury.[3]

Mechanisms of pulmonary infection in trauma can differ from those in other clinical situations. Specific risk factors for pneumonia in trauma include rib fractures, pulmonary contusion, and failed prehospital intubation.[4]

Delays in appropriate antibiotic therapy can have deleterious effects on the clinical resolution of nosocomial pneumonia. However, the emergence of drug-resistant bacteria strains, as the result of selective pressure, and serious adverse effects of antimicrobials are a major concern in the widespread use of antibiotics. While there is limited evidence suggesting that prophylactic antibiotics can decrease early-onset HAP in comatose trauma patients,[5] an observational study by Hoth et al suggests that prolonged prophylactic antibiotics can result in a delay in pneumonia diagnosis, an increase in resistant bacteria colonization, and a higher incidence of complications.[6]

The diagnosis of HAP in trauma is challenging, especially in pulmonary contusion patients. In these patients, lung trauma, alveolar hypoxia and blood in alveolar spaces activate inflammatory pathways. Blood in the alveolar space also provides a medium for bacteria growth. Radiologic findings of pulmonary contusions can mimic pneumonia, varying from irregular areas of consolidation to diffuse and extensive homogeneous consolidation.[7]

Signs of Systemic Inflammatory Response Syndrome (SIRS) occur in 91% of critically ill trauma patients in the first week following trauma. However, persistent SIRS is indeed associated with nosocomial infection, and the respiratory tract is the most common source.[8] This brings another challenge to diagnosing HAP in patients with pulmonary contusions since clinical and radiologic signs of infection are unspecific in this situation.

These characteristics make pulmonary contusion patients more prone to prolonged prophylactic or unnecessary antibiotics courses. There is little evidence to investigate the balance between the benefits and harms of early empirical antibiotic therapy in this situation. We sought to investigate if systemic antibiotics given for more than 48 h after Intensive Care Admission are associated with reduced nosocomial pneumonia in trauma patients with pulmonary contusions.

Methods

Study design and population

This is a retrospective cohort study of adult patients admitted to a surgical-trauma Intensive Care Unit (ICU) in a trauma center in São Paulo, Brazil. Between March 2012 and April 2016, we evaluated for inclusion all adult patients (> 18 years old) with thoracic trauma and available chest Computed Tomography (CT). We included in our analysis all patients with pulmonary contusions, which were diagnosed by a trained radiologist based on admission CT scan findings.

The study was approved by the institutional research ethics board (CAPPesq – 63077116600000068 CAAE). Due to the retrospective nature of the study, informed consent was waived by the ethics board.

Exclusion criteria were absence of chest trauma, absence of chest CT scan in the first 48 h after trauma and diagnosis of pneumonia at ICU admission.

All patients who fulfilled the inclusion criteria without any of the exclusion criteria during the period were included in the analysis. No specific calculation of sample size was performed.

Data collection and patient management

All patients with diagnosed pulmonary contusions underwent a chart and chest X-ray review by 2 trained data abstractors. We collected data through the hospital's Electronic Medical Records (EMR) and microbiologic data were individually checked with the hospital's microbiological laboratory.

Antibiotic Therapy Group (ATG) was defined as any systemic antibiotic started at hospital admission and maintained for more than 48 h. The Conservative Group (CG) was defined as any antibiotic use for no greater than 48 h or no antibiotics at all. Antimicrobials used and therapy duration were chosen by the treating physician. Antibiotics for pulmonary contusions and aspiration pneumonitis are not routinely prescribed in this Trauma ICU. The most common reasons for antibiotic prescriptions for more than 48 h were related to trauma severity in other body segments: open fractures, cerebrospinal fluid leakage or peritonitis. The first choice of antibiotic for each indication follows an institutional protocol,

respectively with ceftriaxone plus clindamycin, cefuroxime, or ceftriaxone plus metronidazole.

Microbiological cultures were collected at the treating physician's discretion. Cultures of tracheal aspirate or other samples of the lower respiratory tract were collected only when pulmonary infection was suspected based on these criteria: New or worsening pulmonary infiltrate plus ≥ 2 of the following: body temperature $\geq 38^{\circ}C$ or $\leq 35^{\circ}C$; White Blood Cell count (WBC) > 12000 or < 4000 cells/μL or immature granulocyte at blood sample; purulent sputum; and worsening of pulmonary oxygenation as accessed by a decline in the ratio between the Partial pressure of Oxygen (PaO_2)/Fraction of inspired Oxygen (FiO_2) — the PaO_2/FiO_2 ratio.[9]

Outcomes

The primary outcome was microbiologically documented nosocomial pneumonia in the first 14 days after intensive care admission. Microbiologically documented nosocomial pneumonia was defined using a combination of the clinical and radiological criteria as described above; the registration of diagnosis and treatment specifically for nosocomial pneumonia in chart review; and microbiological confirmation by: positive blood cultures, pleural cultures or lung specimen cultures with bacteria compatible with the site of infection; or quantitative tracheal aspirate or bronchoalveolar lavage cultures of at least 10^6 or 10^5 Colony-Forming Units (CFU) per millilitre, respectively.[9]

For patients not mechanically ventilated, the only respiratory microbiological specimen accepted was bronchoalveolar lavage culture (quantitative tracheal aspirate was not collected in these patients).

Secondary outcomes included nosocomial pneumonia based on the clinical and radiological criteria above but without the need for microbiological confirmation (nosocomial pneumonia with or without microbiological confirmation), duration of mechanical ventilation, ICU length of stay, hospital length of stay and hospital mortality.

Statistical analysis

Continuous variables were expressed as mean and Standard Deviation (SD) or median and Interquartile Range (IQR), depending on data distribution. Discrete variables were expressed as counts and percentages. Differences between groups were compared using Welch's *t*-test, irrespective of the distribution of numeric data, and chi-square or Fisher's Exact test, when appropriate.

A multivariate logistic regression model with the primary outcome as the dependent variable was built to control for potential confounders. Historical confounder definition[10] was used and risk factors for pneumonia complicating pulmonary contusion were independent variables: age, sex, aspiration, duration of mechanical ventilation and tube thoracostomy.[11,12]

A sensitivity analysis for the multivariate logistic regression model, also based on a historical confounder definition, was performed with the variables: Glasgow coma score, sex, heart rate, systolic blood pressure, use of mechanical ventilation and tube thoracostomy. We used the risk factors described by Landeen,[2] except for obesity (data not available in our sample), and the motor component of the Glasgow score (we used the total Glasgow score instead), but we did not use the specific proposed scoring point system by the authors in the present logistic regression. We also included tube thoracostomy as a relevant risk factor for infectious complications in chest trauma patients.[12]

Exploratory subgroup analyses were done to assess the association between the following variables: the duration of antibiotic treatment (days) and the primary outcome; the duration of antibiotic treatment (days) and colonization by antibiotic-resistant bacteria: meticillin-resistant *S. aureus*, *Pseudomonas aeruginosas* or *Acinetobacter baumannii* resistant to quinolones, third generation cephalosporin-resistant *Klebsiella spp.*, *Enterobacter spp.*, *Escherichia coli*, *Streptococcus pneumoniae*, *Proteus spp.* or *Serratia marcescens*; group allocation and pneumonia by drug-resistant bacteria.

Associations are expressed using the Odds Ratio (OR) with 95% Confidence Intervals (95% CI). A *p*-value < 0.05 was considered significant. All statistical analyses were performed using the free R software, version 14.1.[13]

Results

Of the 2040 ICU admissions, 273 patients had chest trauma with available CT scans, of which 172 had pulmonary contusions diagnosed by the radiologist (Fig. 1). A total of 79 patients were included in the conservative group and 98 in the antibiotic therapy group.

Although both groups were balanced regarding age and gender, there were notable differences between groups regarding other variables (Table 1). Patients in the antibiotic therapy group were more severely ill since they had higher admission Injury Severity Score (median 41 vs. 34 in CG), SAPS3 score (54 ± 13 vs. 48 ± 17), SOFA score (median 8 vs. 5), higher rates of mechanical ventilation at ICU admission (63% vs. 88%) and longer mechanical ventilation duration (median 5 vs. 2 days) than the conservative group. Tube thoracostomy insertion did not differ between

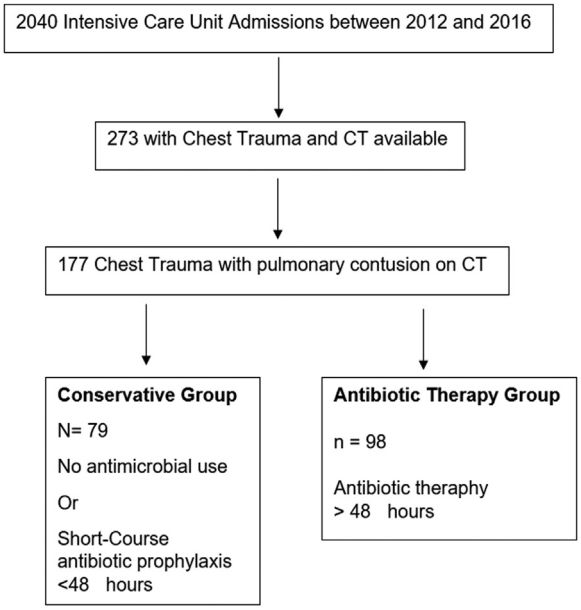

Figure 1 Flowchart.

Table 1 Baseline Variables, antibiotics, and duration of therapy in critically ill trauma patients with CT-confirmed pulmonary contusion admitted to specialized ICU.

	Conservative group	Antibiotic therapy group	*p*-value
N (% of total)	79 (45%)	98 (55%)	
Age (years)	36 ± 16	34 ± 14	0.26
Male sex	67 (84%)	75 (82%)	0.86
At least one comorbidity[a]	2 (3%)	4 (4%)	0.80
Trauma mechanism			0.22
Traffic accident	40 (50%)	34 (37%)	
Trampling	17 (21%)	26 (28%)	
Fall from height	14 (18%)	19 (21%)	
Gunshot wound	3 (4%)	9 (10%)	
Other	6 (8%)	4 (4%)	
Injury Severity Score	34 (28–42)	41 (34–46)	**0.01**
New Injury Severity Score	43 (36–57)	48 (41–57)	0.10
SAPS 3	48 ± 17	54 ± 13	**<0.01**
SOFA	5 (3–9)	8 (5–11)	**<0.01**
Mechanical Ventilation at ICU admission	50 (63%)	81 (88%)	**<0.01**
Tube thoracostomy at ICU admission	32 (40%)	32 (35%)	0,60
Prescribed antibiotics			**<0.01**
Ceftriaxone	5 (6%)	62 (67%)	
Cefuroxime	12 (15%)	16 (17%)	
Cefazolin	12 (15%)	2 (2%)	
Clyndamicin	5 (6%)	62 (67%)	
Others	2 (3%)	7 (8%)	
Duration of antibiotic therapy (days)	0 (0–1)	7 (5–7)	**<0.01**

Data are presented as mean ± standard deviation, median (interquartile range), or N of the group (%) as appropriate. Antibiotic Therapy Group: antibiotic started at hospital admission and maintained for more than 48 h; Conservative Group: antibiotic use for no greater than 48 h or no antibiotics at all; SAPS3, Simplified acute physiology score 3; SOFA, Sequential Organ Failure Assessment score.

[a] Hypertension, diabetes, coronary artery disease, heart failure, chronic pulmonary obstructive disease, chronic kidney disease, HIV, or cancer. A p-value < 0.05 was considered significant.

groups at inclusion or as duration of intervention. Ceftriaxone, cefuroxime, and clindamycin were the most commonly prescribed in both groups, with a median of 7 days (IQR 5–7) in the Antibiotic Therapy Group vs. 0 days (IQR 0–1) in the Conservative Group.

Crude rates of microbiologically documented nosocomial pneumonia did not differ significantly between groups: 25% in CG vs. 20% in ATG (p = 0.50). Rates of nosocomial pneumonia without microbiological documentation were very similar: 26% in CG vs. 21% in ATG (p = 0.59), only one patient in each group had clinical-radiological pneumonia and cultures were negative. Complications of pneumonia, such as bacteremia and empyema did not differ between groups. Although patients in the antibiotic group had higher ICU and in-hospital mortality, this difference was not statistically significant (Table 2).

We could not detect changes in bacteria species profiles between groups. S*taphylococcus aureus, Pseudomonas aeruginosas* and *Acinetobacter baumannii* were the most prevalent pathogens in infected patients in both groups. Nevertheless, the incidence of resistant bacteria to at least one class of antimicrobial was more frequent in the Antibiotic Therapy Group (50 vs. 15%, p = 0.049) (Table 3).

The multivariate analysis models showed that the major risk factor associated with the primary outcome was the duration of mechanical ventilation (OR = 1.37 per day, 95% CI 1.24—1.53; $p < 0.01$). The Antibiotic Therapy Group was associated with a significant reduction in the primary outcome in adjusted analysis (OR = 0.25, 95% CI 0.09—0.64, $p < 0.01$) (Table 4).

Sensitivity analysis with distinct variables showed very similar findings (Table 5). The most important risk factor associated with the primary outcome was the presence of mechanical ventilation at ICU admission (OR = 15.9, 95% CI 2.8–301; $p < 0.01$). Again, the Antibiotic Therapy Group was associated with a significant reduction in nosocomial pneumonia in adjusted analysis (OR = 0.33, 95% CI 0.14—0.79, p = 0.01).

In exploratory analyses, the duration of antibiotic therapy was not associated with nosocomial pneumonia (OR = 0.98 per day, 95% CI 0.88—1.09; p = 0.75); however, it was associated with resistant bacteria in samples of infected patients (OR = 1.18 per day, 95% CI 1.05—1.36; $p < 0.01$), reinforcing the aforementioned association with the Antibiotic Therapy Group (Table 3). In patients with microbiological isolates at the time of diagnosis, the previous use of an effective antibiotic against the bacteria did not decrease ICU length of stay or ICU mortality (OR = 1.2; 95% CI 0.22—6.33; p = 0.83).

Discussion

In our study, we evaluated the relationship between antibiotic therapy in patients with pulmonary contusions and the development of nosocomial pneumonia in the first 14 days

Table 2 Outcome variables of critically ill pulmonary contusion patients.

	Conservative group	Antibiotic therapy group	*p*-value
Primary Outcome: microbiologically documented nosocomial pneumonia[a]	20 (25%)	18 (20%)	0.50
Nosocomial pneumonia with or without microbiological confirmation[a]	21 (26%)	19 (21%)	0.49
Empiema[a]	3 (4%)	2 (2%)	0.87
Bacteremia[a]	4 (5%)	5 (5%)	1.00
Duration of mechanical ventilation (days)[a]	2 (0–7)	5 (3–10)	**0.02**
Duration of tube thoracostomy (days)[a]	0 (0–3)	0 (0–2)	0.65
ICU length of stay	7 (4–14)	12 (6–22)	**0.03**
ICU mortality	13 (16%)	25 (27%)	0.12
Hospital Mortality	14 (18%)	27 (29%)	0.10

Data are presented as mean ± standard deviation, median (interquartile range), or N of group (%) as appropriate.
[a] Within 14 days after ICU admission.
Conservative Group: antibiotic use for no greater than 48 h or no antibiotics at all; Antibiotic Therapy Group: antibiotic started at hospital admission and maintained for more than 48 h. A p-value < 0.05 was considered significant.

after hospital admission. Our data showed that the use of antibiotics for more than 48 h was not associated with a decrease in the incidence of nosocomial pneumonia in the crude analysis, but it was after adjusting for confounders (OR = 0.25, 95% CI 0.09—0.64, Table 4). Sensitivity analysis in a distinct logistic regression model showed very similar results, including the magnitude of effect (OR = 0.33, 95% CI 0.14—0.79, Table 5). However, exposure to antibiotics was associated with resistant strains when pneumonia developed, both when defined as allocation group (Antibiotic Therapy Group with 50% vs. Conservative Group 15%, $p = 0.0049$), and also when exposure was quantified as days of antibiotic use (OR = 1.18 per day of antibiotic use, 95% CI 1.05—1.36; $p < 0.01$).

Pulmonary contusions are both a risk factor for pneumonia and a mimicker of this disease, making it challenging for physicians to differentiate between the two pathologies. Both mechanical and inflammatory injury caused by pulmonary contusions lead to alveolar consolidation and the inflammatory response can lead to systemic inflammatory response syndrome. These characteristics increase the chances of patients receiving antibiotics, even without any confirmed infection.

Insofar, we have chosen CT scan as the diagnostic method for pulmonary contusion due to its increased sensitivity[7] when compared with chest X-rays. Also, we had strict criteria for the diagnosis of nosocomial pneumonia, with obligatory clinical and radiological criteria along with microbiological confirmation. These definitions are important because of the myriad of factors that act as risk factors or confounders in this situation. For instance, signs of SIRS are present in more than 90% of critically ill trauma patients

Table 3 Microbiological outcomes of critically ill pulmonary contusion patients according to the duration of antibiotic therapy.

Patients with pneumonia with bacteria isolated in respiratory or blood samples[a]	Conservative group	Antibiotic therapy group	*p*-value
Diference for all bacteria			0.44
Staphylococcus aureus	6 (30%)	8 (44%)	0.56
Pseudomonas aeruginosas	4 (20%)	5 (28%)	0.85
Acinetobacter baumannii	3 (15%)	6 (33%)	0.34
Klebsiella spp.	2 (10%)	3 (17%)	0.90
Enterobacter spp.	1 (5%)	4 (22%)	0.28
Haemophilus influenzae	3 (15%)	1 (6%)	0.67
Escherichia coli	3 (15%)	0 (0%)	0.27
Coagulase-negative staphylococci	2 (10%)	0 (0%)	0.51
Streptococcus pneumoniae	1 (5%)	1 (6%)	1.00
Proteus spp.	1 (5%)	1 (6%)	1.00
Serratia marcescens	1 (5%)	0 (0%)	1.00
Other (includes normal flora)	5 (25%)	1 (6%)	0.23
Resistant to antimicrobial bacteria[b]	3 (15%)	9 (50%)	**0.049**

Data are presented as N of pneumonia-positive patients in the group (%) as appropriate.
Conservative Group: antibiotic use for no greater than 48 h or no antibiotics at all; Antibiotic Therapy Group: antibiotic started at hospital admission and maintained for more than 48 h.
[a] More than one bacteria may have been isolated from each event of pneumonia, therefore the sum of % is greater than 100%.
[b] Methicillin-resistant S. aureus; *Pseudomonas aeruginosas* or *Acinetobacter baumannii* resistant to quinolones and fourth generation cephalosporins; *Acinetobacter baumannii* resistant to quinolones; third generation cephalosporin-resistant *Klebsiella spp.*, *Enterobacter spp.*, *Escherichia coli*, *Streptococcus pneumoniae*, *Proteus spp.* or *Serratia marcescens*.

Table 4 Multivariate analysis: association of antibiotic strategy and primary outcome.

	Odds Ratio	95% CI	*p*-value
Duration of mechanical ventilation, per day	1.37	1.24–1.53	<0.01
Antibiotic Therapy Group (vs. Conservative Group)	0.25	0.09–0.64	<0.01
Duration of chest thoracostomy, per day	0.94	0.85–1.03	0.23
Bronchoaspiration	0.41	0.07–1.69	0.26
Age, per year	0.99	0.95–1.02	0.38
Male Sex	1.15	0.37–3.91	0.82

Variables were selected among those available as known risk factors for pneumonia in severely injured patients with thoracic trauma, as described by Wutzler et al.[11] in addition to tube thoracostomy.[12]
Conservative Group: antibiotic use for no greater than 48 h or no antibiotics at all; Antibiotic Therapy Group: antibiotic started at hospital admission and maintained for more than 48 h.
Variance Inflation Factor varied between 1.00 and 1.36 for all variables, indicating no significant multicollinearity.

Table 5 Sensitivity analysis: multivariate analysis based on the risk factors described by Landenn et al.[2] with the addition of chest tube thoracostomy.[12] Association of antibiotic strategy and primary outcome.

	Odds Ratio	95% CI	*p*-value
Heart Rate at admission, per bpm (Highest)	0.97	0.95–0.99	<0.01
Mechanical Ventilation at ICU admission	15.9	2.8–301.9	0.01
Antibiotic Therapy Group (vs. Conservative Group)	0.33	0.14–0.79	0.01
Glasgow Coma Score at admission	0.94	0.84–1.04	0.22
Systolic Arterial Pressure at admission, per mmHg (lowest)	1.01	0.99–1.03	0.36
Duration of chest thoracostomy, per day	0.98	0.89–1.07	0.67
Age, per year	0.99	0.98–1.02	0.85

Variables were selected among those available as known risk factors for pneumonia in pulmonary contusion patients, as adapted from[2] with the addition of chest tube thoracostomy.[12]
Conservative Group: antibiotic use for no greater than 48 h or no antibiotics at all; Antibiotic Therapy Group: antibiotic started at hospital admission and maintained for more than 48 h.
Variance Inflation Factor varied between 1.00 and 1.14 for all variables, indicating no significant multicollinearity.

during the first week of ICU.[8] Also, the incidence of nosocomial pneumonia, especially VAP is higher in trauma patients than in other populations.[1] This association between VAP and trauma was highlighted in our study by the fact that only two patients in our study population had non-VAP nosocomial pneumonia. The strict criteria guaranteed that the incidence of nosocomial pneumonia in our study was similar to that reported by other authors.[2,14]

Two different sets of historical confounder variables[10] were used to mitigate differences between groups in adjusted analysis. In both main and sensitivity analysis we chose to include tube thoracostomy as a potential confounder, given its relevant role as a risk factor for pulmonary infection in trauma patients.[12]

The baseline characteristics were different between groups, and the Antibiotic Therapy Group had more severely ill patients, as suggested by higher ISS, SAPS3, SOFA, mechanical ventilation duration and ICU length of stay. The crude incidence of pneumonia was very similar between the groups. Nevertheless, due to imbalances between baseline variables, the Antibiotic Therapy Group was expected to have a higher incidence of nosocomial pneumonia. Therefore, after adjusting for confounders, this group was associated with a decreased incidence of microbiologically confirmed pneumonia.

The present findings of protective effects of antibiotics on preventing pulmonary infections in chest trauma are in line with previous studies in patients with thoracostomy,[12] while the present work focuses on pulmonary contusion.

Despite this protective association for nosocomial pneumonia incidence, antibiotic use for more than 48 hours was associated with infection by resistant bacteria both when categorized as a group (Antibiotic Therapy Group) and when quantified as days of antibiotic use. This suggests that even short periods of antibiotic exposure might affect patients' flora and lead to an increase in multi-drug resistance infection. These findings are in general agreement with other published works, showing increases in colonization and infection by resistant bacteria associated with previous antimicrobial use.[15-17]

We speculate that antibiotic therapy could be associated with reduced nosocomial pneumonia by susceptible bacteria, while the remaining episodes of infection are probably caused by a resistant pathogen.

As a quality of our study, definitions of exposures and outcomes were clear and rigorous. Sensitivity analysis showed the same results of the primary analysis, so intern validity seems strong.

Our study has several limitations. The observational nature of our data led to unbalances between groups, which were accounted for in our analysis method. Markedly, patients in the antibiotic group had more severe trauma evaluated by the ISS, more organ dysfunctions evaluated by the SOFA score, and more frequent and longer duration of mechanical ventilation. Despite the use of multivariate logistic regression,

possibly additional imbalances between groups still played a role in our findings. But all these factors could be associated with worse outcomes and higher pneumonia occurrence, therefore the direction of our findings would probably not change, since the protective association was found in more severely ill patients (Antibiotic Therapy Group).

On the other hand, the use of antibiotics in this group could have artificially decreased the primary outcome of our study: microbiologically documented nosocomial pneumonia. In patients with prior antibiotic treatment, quantitative bacterial respiratory samples have lower sensitivity in the diagnosis of nosocomial pneumonia (36—50%), when compared to patients without prior antimicrobial use (sensitivity as high as 80%).[18] In our sample, however, we could not find differences between the proportion of patients with positive cultures, and just one patient in each group fulfilled the clinical and radiological definition, but had no microbiological confirmation. So, it is not probable that the decreased accuracy of cultures with prior antibiotic exposure had any impact on our results.

Due to the high incidence of pneumonia and associated lesions (open fractures, peritonitis, cerebrospinal fluid leakage etc.), critically ill trauma patients often receive empiric antibiotics for several days, even when samples from the respiratory tract are sterile.[19] Our study suggests that this may be associated with lower pneumonia incidence, however, it may also lead to significant collateral effects, especially colonization and infection by drug-resistant bacteria.[6] Since colonization for drug-resistant bacteria can last for months,[20] a randomized powered trial in trauma patients with a high risk of nosocomial pneumonia with patient-centred outcomes and extended follow-up is necessary to assess the real benefit of this approach.

In conclusion, empiric antibiotic therapy lasting for more than 48h in critically ill patients with pulmonary contusion was associated with a lower incidence of nosocomial pneumonia. Nevertheless, it was associated with resistant strains in the respiratory samples of infected patients. A randomized trial of a short course of antibiotic therapy with patient-centred outcomes on thoracic trauma and risk factors for developing nosocomial pneumonia is warranted, to confirm these findings and assess the true benefit of this approach.

Conflicts of interest

The authors declare no conflicts of interest

CRediT authorship contribution statement

Estevão Bassi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing — original draft, Writing — review & editing. **Camila Trevizani Merighi:** Conceptualization, Data curation, Investigation, Methodology, Writing — review & editing. **Carlos Issamu Tomizuka:** Conceptualization, Data curation, Investigation, Methodology, Writing — review & editing. **Thais Guimarães:** Conceptualization, Investigation, Methodology, Writing — original draft, Writing — review & editing. **Fernando da Costa Ferreira Novo:** Conceptualization, Methodology, Supervision, Writing — original draft, Writing — review & editing. **Sergio Henrique Bastos Damous:** Supervision, Validation, Writing — review & editing. **Edivaldo Massazo Utiyama:** Project administration, Supervision, Validation, Writing — review & editing. **Luiz Marcelo Sá Malbouisson:** Conceptualization, Methodology, Project administration, Supervision, Writing — review & editing.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.bjane.2023.07.011.

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