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Original Article

Characterization of Antibiotic Use, Documented Infection and Prevalence of Multidrug-Resistant Organisms in Palliative Care Patients Admitted to a Private Hospital in Brazil: A Retrospective, **Cohort Study**

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ABSTRACT

Objectives: Antibiotic use in palliative care patients is a frequent dilemma. The benefits of their use in terms of quality of end-of-life care or survival improvement are not clear and the potential harm and futility of this practice not well established. Our aim was to characterise the prevalence of antibiotic use, documented infection and multidrug-resistant organisms (MDROs) colonisation among palliative care patients admitted to a private hospital in Brazil.

Materials and Methods: Retrospective analysis of all palliative care patients admitted to our hospital during 1 year, including demographic characteristics, diagnosis of infectious disease at admission, antibiotic use during hospital stay, infectious agents isolated in cultures, documented MDRO colonisation and hospital mortality.

Results: A total of 114 patients were included in the analysis. Forty-five (39%) were male and the median age was 83 years. About 78% of the patients had an infectious diagnosis at hospital admission and 80% of the patients not admitted with an infectious diagnosis used antibiotics during their stay, out of which a great proportion of large spectrum antibiotics. Previous MDRO colonisation and hospital mortality were similar between patients admitted with or without an infectious diagnosis.

Conclusion: Infection is the leading cause of hospital admission in palliative care patients. However, antibiotics prescription is also very prevalent during hospital stay of patients not admitted with an infectious condition. Mortality is very high regardless of the initial reason for hospital admission. Therefore, the impact of multiple large spectrum antibiotics prescription and consequent significant cost burden should be urgently confronted with the real benefit to these patients.

Keywords: Antibiotics, Infection, Mortality, Multidrug-resistant organisms, Palliative care

INTRODUCTION

Antibiotic use in palliative care patients is controversial and constitutes a frequent ethical dilemma.[1,2] Rosenberg et al. [3] argued that infections are very frequent in these patients and antibiotics administration could improve symptoms and prolong life. Givens et al.,[4] however, suggested that antibiotics should not be part of the medications used to improve end-of-life care because the increased survival is not associated with improved comfort or symptoms relief. There is also an emerging fear of an increased prevalence of multidrug-resistant organisms (MDROs) mainly as a result of frequent exposure to health-care facilities,

recurrent hospital admissions and use of broad-spectrum antibiotics.[5]

The previous studies [6,7] reported that approximately 90% of advanced cancer hospitalised patients and 25% of hospice patients receive antibiotics in their final week of life. Antibiotics are prescribed for terminal patients even without evidence of bacterial infection.^[6]

Although antibiotics administration is less aggressive than invasive procedures, their use is not innocuous, being associated with pharmacodermy, drug interaction, Clostridioides difficile infection and MDRO colonisation and/or infection.[8]

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Therefore, the primary objective of the present study was to retrospectively characterise the palliative care population admitted to a private hospital in Brazil according to an infectious or non-infectious diagnosis at hospital admission. The secondary objectives were to characterise their antibiotic use (number and type), possible source of infection (at admission or later during hospital stay) and the main causative organisms, presence of MDRO colonisation and their impact on mortality.

MATERIALS AND METHODS

This study was approved by the Local Ethics Committee of São Camilo Ipiranga Hospital (approval number 1.880.538). Because of the retrospective nature of data collection with minimal risk of harm to individual patients except a possible breach of confidentiality, informed verbal or written consent from the patients or their relatives was waived by the local ethics committee. All patients admitted during the year of 2016 who were selected for palliative care in the current or in a previous hospital stay were included. Data from subsequent admission of the same patients at the hospital were not included in the analysis. General characteristics were retrospectively retrieved from electronic medical records with no missing data and patients were divided according to a diagnosis at hospital admission of infection or not. The diagnosis that motivated current hospital internment appearing in the medical record was used for dividing patients. Information regarding culture results, infection sites and antibiotics administered were retrieved from the Infection Control Department of the hospital. The International Classification of Diseases, Tenth Revision (ICD-10) classification system was used for both infectious and non-infectious diagnosis. The following data were obtained: Age, gender, comorbidities, main reason for current hospital admission, main reason for palliation, palliative care institution before or at the current hospital admission, type of palliative care (therapeutic proportionality or exclusive comfort care), intensive care unit (ICU) admission at the current hospital stay (related to palliation or not), use of antibiotics (all types of antibiotics available at our hospital), infection source, organisms isolated in cultures, presence of MDRO colonisation, (which means the presence of vancomycin-resistant enterococci, methicillinresistant Staphylococcus aureus or multidrug-resistant Gramnegative bacilli in some part of the human body but not causing harm or symptoms, as stated by the National Healthcare Safety Network of the Centre for Disease Control USA: NHSN-CDC) and hospital mortality. We have considered a suspected infectious diagnosis a condition in which infection was not microbiologically documented but physical examination or laboratory examinations suggested its presence. A confirmed infectious diagnosis was made when there was a strong clinical and laboratory suspicion and an infectious agent isolated in culture. Large spectrum antibiotics were defined as antibiotics with action against a broad range of bacteria, frequently both

Gram-positive and Gram-negative organisms and healthcareassociated infection as infections affecting patients in a hospital or health-care facility not present or incubating at the time of admission as stated by the World Health Organisation. Community-acquired infections were those that were contracted outside of a hospital or health-care facility or diagnosed in 48 h of hospital admission without any previous health care encounter. The Clinical and Laboratory Standard Institute methodology was used for testing antimicrobial susceptibility of clinical isolates. The choice of initial antibiotic was made by the assistant physician as well as subsequent changes during hospital stay. The institution of palliative care occurred after referral from the responsible medical team, assessment of the palliative care group and family agreement.

Statistical analysis

Due to the descriptive and retrospective nature of our study, no statistical sample size was performed a priori. General characteristics of the patients were described as median and interquartile ranges for continuous variables and as percentages for categorical variables. Patients admitted with an infectious diagnosis were compared with patients admitted with a non-infectious diagnosis. Mann-Whitney rank-sum test was used for comparison of continuous variables and Fisher's or Chi-square test was used for comparison of categorical variables as appropriate. Multiple logistic regression was used to evaluate possible independent association between main reason for palliation, MDRO colonisation and infectious diagnosis at hospital admission with outcome, adjusted for other variables. The software R 4.0.2 (R Core Team, 2020) was used for the analyses. P < 0.05was considered statistically significant.

RESULTS

A total of 114 patients admitted to the hospital in 2016 were included in the analysis. General characteristics of these patients are shown in [Table 1]. Of these, 89 patients (78%) started palliative care follow-up in the current hospital stay and 25 patients (22%) were under palliative care since a previous hospital admission. One-hundred and two patients (89.5%) had some limitations of invasive procedures (mostly due to a 'do-not-intubate' order) and 12 patients (10.5%) were not candidates to any invasive lifesustaining method.

One-hundred and nine patients (95.6%) used antibiotics during the current hospital stay. Of these, 19 patients (17.4%) used only a single antibiotic, 39 patients (35.8%) used two antibiotics, 16 patients (14.7%) used three antibiotics and 35 patients (32.1%) used four or more antibiotics. Thirteen patients who used antibiotics also used antifungal agents and five patients who used antibiotics also used antiviral medications.

	Total (<i>n</i> =114)	Infectious diagnosis at admission (n=89)	Non-infectious diagnosis at admission (n=25)	P-value	
Gender (M/F)	45/69	34/55	11/14	0.647	
Age (years)	83 [74; 90]	84 [76, 91]	80 [66, 88]	0.029	
Type of palliative care $(n-\%)$, , <u>,</u>	. , .	. , ,		
Therapeutic proportionality	102 (89)	80 (90)	22 (88)	0.724	
Exclusive comfort care	12 (11)	9 (10)	3 (12)		
Decision of palliative care $(n-\%)$. ,	, ,	, ,		
Previous hospital admission	25 (22)	20 (22)	5 (20)	0.992	
Current hospital admission	89 (78)	69 (78)	20 (80)		
Main comorbidities (<i>n</i> -%)	. ,	,	, ,		
Dementia	50 (44)	41 (46)	9 (36)	0.495	
Parkinson	12 (11)	12 (13)	0 (0)	0.066	
Previous stroke	27 (24)	22 (25)	5 (20)	0.792	
Non-metastatic cancer	19 (16)	11 (12)	8 (32)	0.031	
Metastatic cancer	10 (9)	8 (9)	2 (8)	1.000	
Congestive heart failure	12 (11)	8 (9)	4 (16)	0.294	
Cirrhosis	3 (3)	3 (3)	0 (0)	1.000	
COPD	10 (9)	9 (10)	1 (4)	0.689	
Chronic renal failure	(-)	- ()	- (-)		
Without dialysis	2 (2)	12 (13)	2 (8)	0.731	
With dialysis	14 (12)	2(2)	0 (0)	1.000	
Other neurological diseases	5 (4)	2 (2)	3 (12)	0.069	
Main reason for palliation $(n-\%)$	- (-)	- (-)	- ()		
Frailty	44 (38)	36 (41)	8 (32)	0.047	
Advanced dementia	35 (31)	31 (35)	4 (16)	010 17	
Advanced non-haematologic cancer	15 (13)	10 (11)	5 (20)		
Leukaemia/lymphoma	3 (3)	2(2)	1 (4)		
Anoxic encephalopathy	1(1)	0 (0)	1 (4)		
Advanced heart failure	1(1)	0 (0)	1 (4)		
Other neurologic diseases	15 (13)	10 (11)	5 (20)		
Times admitted in the ICU (<i>n</i> -%)	()	()	- ()		
0	12 (11)	8 (9)	4 (16)	0.321	
1	74 (65)	61 (69)	13 (52)	****	
2	21 (18)	14 (16)	7 (28)		
3	7 (6)	6 (6)	1 (4)		
SAPS 3	54 [49; 61]	54 [51, 61]	50 [46, 56]	0.186	
	n=101	n=81	n=20	0.100	
Antibiotic use during hospital stay (<i>n</i> -%)	11 101	89 (100)	20 (80)	< 0.001	
Number of antibiotics used $(n-\%)$		07 (100)	20 (80)	(0.001	
0	5 (4)	0 (0)	5 (20)	0.001	
1	19 (17)	15 (17)	4 (16)	2,001	
2	39 (34)	32 (36)	7 (28)		
3	16 (14)	13 (15)	3 (12)		
4or more	35 (31)	29 (32)	6 (24)		
Previous MDRO colonisation (<i>n</i> -%)	24 (21)	20 (22)	4 (16)	0.587	
Hospital mortality $(n-\%)$	59 (52)	47 (53)	12 (48)	0.821	

Eighty-nine patients (78.1%) had at least one suspected or confirmed infectious diagnosis at hospital admission [Table 1]. They were significantly older than the patients admitted due to a non-infectious diagnosis. Of the 25 patients without a suspected or confirmed infectious diagnosis at hospital admission, 20 patients (80%) have used at least one antibiotic during hospital stay. Only 5 of these 20 patients (25%) had a subsequent confirmed infectious diagnosis.

One-hundred and two patients (89.5%) were admitted to the ICU during hospital stay: 74 patients once, 21 patients twice and 7 patients were admitted 3 times to the ICU [Table 1].

Table 2: Infection sites and types of antibiotics used by the patients included in the study. Total (n=114)Infectious diagnosis Non-infectious diagnosis P-value at admission (n=89) at admission (n=25)Infection site (n-%)52 (46) 46 (52) Respiratory tract Urinary tract 27 (24) 26 (29) 17 (15) Soft tissue 15 (17) Gastrointestinal tract 9 (8) 9 (10) Bloodstream 9(8) 8 (9) Undefined 6(5)2(2)Types of antimicrobials used: Antibiotics (*n*-%) Penicillin (amoxi/ampi) 2(2)0(0)1.000 2(2) Cephalosporin 1st generation 8 (9) 14 (12) 6 (24) 0.077 Cephalosporin 2nd generation 6(5)2(2)4(16) 0.020 Cephalosporin 3rd generation 52 (46) 50 (56) 2(8) < 0.001 Cephalosporin 3rd generation anti-Pseudomonas 1(1) 1(1) 0(0)1.000 Cephalosporin 4th generation 6(5)4(4) 2(8) 0.611 Macrolides 0(0)12 (11) 12 (13) 0.066 Clindamycin 20 (18) 20 (22) 0(0)0.006 Quinolones 11 (10) 9 (10) 2(8) 1.000 Piperacillin-tazobactam 45 (40) 34 (38) 11 (44) 0.647 Glycopeptides 36 (32) 26 (29) 10 (40) 0.336 Carbapenem 50 (44) 42 (47) 8 (32) 0.254 Aminoglycosides 0.504 14 (12) 10(11) 4(16) Linezolid 10 (9) 10(11) 0(0)0.114 Ceftaroline 4(4) 4(4) 0(0)0.575 Polymyxin B 12 (11) 11 (12) 1 (4) 0.459 Metronidazole 19 (17) 15 (17) 1.000 4(16) Sulfamethoxazole/trimethoprim 4(4) 3 (3) 1(4) 1.000 Tigecycline 5 (4) 2(2)3(12)0.069 Ampicillin-sulbactam 1(1) 1(1)0(0)1.000 Antifungal (*n*-%) Fluconazole 5(4) 3(3)2(8) 0.301 Echinocandins 6(5)6(7)0(0)0.336 Amphotericin 2(2) 1(1)1(1)0.392 Antiviral (*n*-%) Acyclovir 4(4) 4(4) 0(0)0.575 Valacyclovir 1(1) 0(0)1.000 1(1)

MDRO colonisation prevalence, healthcare-associated infections and mortality

Twenty-four patients (21%) were previously colonised by MDRO [Table 1]. All these patients used antibiotics during the current hospital stay and the majority of them (21 out of 24) used at least two antibiotics. Mortality was similar between groups with or without previous MDRO colonisation (54.2 vs. 51.1%, respectively, P = 0.971). Mortality was also very similar between patients with or without a suspected/ confirmed infectious diagnosis at hospital admission [Table 1]. Patients with an infectious diagnosis at hospital admission that subsequently had a healthcare-associated infectious (HCAI) diagnosis during the course of hospital

stay had a trend toward increased mortality in comparison to patients with an infectious diagnosis at hospital admission that did not develop additional nosocomial infection (87.5% vs. 49.4%, P = 0.061). Interestingly, mortality was significantly greater among patients palliated in the current hospital stay in comparison to the group of patients palliated in a previous hospital admission (57.3% vs. 32.0%, P = 0.044). Among the five patients with no evidence of infection during the entire hospital stay and with no use of antibiotics, 3 (60.0%) died.

Infection sites and classes of antibiotics used

Respiratory tract (including both upper and lower respiratory tract - RTI) was the main site of suspected or confirmed infection among patients admitted to the hospital [Table 2]. However, only a minority of patients admitted with an infectious diagnosis had a positive culture documenting the infection site. Of these, urinary tract and bloodstream infections were the most prevalent [Table 3].

Eight patients admitted with an infectious diagnosis had a posterior positive culture documenting a subsequent HCAI as follows: Four had central line associated bloodstream infections CLABSI, two had catheter associated urinary tract infections CAUTI and two had RTI. Out of five patients with a positive culture during hospital stay but no infectious diagnosis at hospital admission, two patients had RTI (tracheal aspirate culture), one patient had CAUTI, one patient had CLABSI and one patient had a soft-tissue infection - an infected decubitus ulcer [Table 3].

A number of antibiotics were used by the study patients, being third-generation cephalosporins, piperacillin/tazobactam, carbapenem and glycopeptides, the most frequently used in the group of patients with an infectious diagnosis at hospital admission [Table 2]. The group of patients without an infectious diagnosis at hospital admission has equally used large spectrum antibiotics during hospital stay but the first- and secondgeneration cephalosporins were more prevalent than the thirdgeneration cephalosporin in this group [Table 2].

Escherichia coli was the most common infectious agent found in cultures obtained at hospital admission, particularly from the urinary tract [Table 4] and [Table 5]. It was also, together with Klebsiella species, the most frequent colonising MDRO isolated from anal, inguinal or axilla swabs at hospital admission, being present as extended spectrum betalactamase-producing isolates.

Main reason for palliation and mortality

Considering the three main reasons for palliation (frailty, advanced dementia and advanced cancer), patients with advanced cancer (as defined by the National Cancer Institute at the National Institute of Health-USA) were 5 times as likely to die than a patient palliated due to dementia (CI_{95%} 1.11-21.22, P-value: 0.036) [Table 6]. Moreover, only one patient in each of these three main groups did not use antibiotics during hospital stay.

DISCUSSION

In the present single centre, retrospective study, we were able to characterise the population of palliative care patients admitted to a private hospital in Brazil including main diagnosis (infectious vs. non-infectious), main reason for

	Total (n=114)	Infectious diagnosis at admission (n=89)	Non-infectious diagnosis at admission (<i>n</i> =25)	P-value
Positive culture considered infection at admission (<i>n</i> -%)	25 (22)	25 (28)	-	-
Urine	13 (52)	13 (52)	-	
Peripheral blood	8 (32)	8 (32)	-	
Soft tissue	1 (4)	1 (4)	-	
Tracheal secretion	1 (4)	1 (4)	-	
Lung abscess	1 (4)	1 (4)	-	
Gallbladder empyema	1 (4)	1 (4)	-	
Positive culture considered colonisation/contamination at	19 (17)	14 (16)	5 (20)	0.561
admission (<i>n</i> -%)				
Anal/inguinal/axilla swab	14 (74)	10 (71)	4 (80)	0.566
Peripheral blood	3 (16)	3 (21)	0 (0)	
Urine	2 (11)	1 (7)	1 (20)	
No cultures collected or negative cultures at admission (<i>n</i> -%)	52 (46)	39 (44)	13 (52)	0.502
Positive cultures considered nosocomial infections during	13 (11)	8 (9)	5 (20)	0.155
hospital stay (<i>n</i> -%)				
Urine	3 (23)	2 (25)	1 (20)	0.749
Peripheral blood	3 (23)	2 (25)	1 (20)	
Central line blood	2 (15)	2 (25)	0 (0)	
Tracheal secretion	4 (31)	2 (25)	2 (40)	
Soft tissue	1(8)	0 (0)	1 (20)	
Positive culture considered colonisation during hospital stay	5 (4)	3 (3)	2 (8)	0.302
(n-%)				
Anal/inguinal/axilla swab	3 (60)	2 (67)	1 (50)	1.000
Peripheral blood	1 (20)	1 (33)	0 (0)	
Urine	1 (20)	0 (0)	1 (50)	

Table 4: Infectious agents isolated in cultures at admission according to infectious/colonisation site for the 89 patients admitted with an infectious diagnosis.

	Infectious diagnosis at admission (n=89)
Positive culture considered infection at	25 (28)
admission (<i>n</i> -%)	
Urine	13 (52)
Escherichia coli	7
Pseudomonas aeruginosa	2
Enterococcus faecium	2
Klebsiella pneumoniae	1
Citrobacter freundii	1
Peripheral Blood	8 (32)
Staphylococcus aureus	2
Staphylococcus coagulase (-)	1
Proteus mirabilis	1
Klebsiella pneumoniae	1
Haemophilus influenzae	1
Enterococcus faecium	1
Enterobacter gergoviae	1
Lung abscess	1 (4)
Acinetobacter baumannii	1
Soft tissue	1 (4)
Proteus mirabilis	1
Gallbladder empyema	1 (4)
Enterococcus faecalis	1
Tracheal secretion	1 (4)
Escherichia coli	1
Positive culture considered colonisation	14 (16)
at admission (<i>n</i> -%)	
Anal/inguinal/axilla swab	10 (71)
Klebsiella spp. ESBL+	5
Escherichia coli ESBL+	4
Pseudomonas aeruginosa	1
Peripheral blood	3 (21)
Staphylococcus coagulase (-)	3
Urine	1 (8)
Candida albicans	1
ESBL: Extended-spectrum beta-lactamase	

palliation and, most importantly, MDRO colonisation prevalence, antibiotic use and their impact on mortality.

In addition to the expected findings that palliative care patients are usually old (even older if infection was the reason for admission) and have serious terminal illnesses, this study highlights the high prevalence of patients with suspected or confirmed infectious diagnosis at hospital admission. Furthermore, our study is in line with the findings of a previous investigation,[1] indicating that infection is the main reason for hospital admission in this population. Most of our patients were admitted to the ICU at least once during hospital stay, and this suggests a severe stage of their acute illnesses, frequently infectious in origin, which then demands a large amount of resources for the appropriate care. However, we observed that

Table 5: Infectious agents isolated in cultures during hospital stay according to infectious/colonisation site for the 89 patients admitted with an infectious diagnosis.

	Infectious diagnosis at admission (n=89)
Positive culture considered infection during hospital stay (<i>n</i> -%)	8 (9)
Catheter-associated Urine	2 (25)
Escherichia coli	1
Klebsiella pneumoniae	1
Peripheral blood	2 (25)
Staphylococcus aureus	1
Acinetobacter baumannii	1
Central line blood	2 (25)
Escherichia coli	1
Aeromonas hydrophila	1
Tracheal secretion	2 (25)
Acinetobacter baumannii	1
Pseudomonas aeruginosa	1
Positive culture considered colonisation	3 (3)
during hospital stay (<i>n</i> -%)	
Anal/inguinal/axilla swab	2 (67)
Klebsiella spp. ESBL+	1
Klebsiella pneumoniae carbapenemase	1
Peripheral blood	1 (33)
Aerococcus viridans	1
ESBL: Extended-spectrum beta-lactamase	

antibiotic use in this population is widespread and not restricted to patients with a well-documented infection. Most patients, even those with no clear evidence of infection, received two or more large spectrum antibiotics during their hospitalisation. Unfortunately, our study was not powered to evaluate a causal relationship between this practice and the emergence of MDRO colonisation or infection. Interestingly, mortality was similar between patients admitted with an infectious or a non-infectious diagnosis and the presence of previous MDRO colonisation was also similar between these two groups and did not have an impact on mortality. A previous study^[9] has also found a MDRO prevalence at hospital admission of around 20% and no difference in overall mortality during follow-up comparing carriers and non-carriers.

Most of the antibiotic use during hospital stay was empirical and not culture guided. Even in patients admitted with an infectious diagnosis, most of them were empirically treated for respiratory tract infection [Table 2] for which no cultures are routinely obtained, except in tracheostomised patients. In addition, these patients usually live in hospice care or other health-care facilities and are repeatedly admitted to the hospital over a short period of time. This may be the cause of the recurring use of large spectrum antibiotics as those infections are considered healthcare-associated infections from the outset. The considerable number of patients

Table 6: Predictors of death in palliative patients admitted to the hospital.

Coefficient	Estimate	Standard error	Odds ratio (OR)	CI 95%		P-value
Age (years)	0.00	0.02	1.00	0.97	1.03	0.837
Gender (female)	0.10	0.41	1.10	0.50	2.44	0.812
Infectious diagnosis at admission	0.42	0.49	1.52	0.58	3.96	0.394
Main reason for palliation – Advanced non-hematologic Cancer *	1.58	0.75	4.85	1.11	21.22	0.036
Main reason for palliation – Frailty *	1.05	0.48	2.87	1.12	7.34	0.028
Main reason for palliation – Others *	0.72	0.65	2.05	0.58	7.30	0.268
Previous MDRO colonisation	0.20	0.46	1.23	0.50	2.99	0.654

^{*}This odds ratio used dementia as the main reason for palliation as a reference because it was, in the univariate analysis, the variable less associated with the outcome (death). MDRO: Multidrug-resistant organisms

admitted with a non-infectious diagnosis who used first- and second-generation cephalosporins was explained by their use as surgical prophylaxis. Macrolides and clindamycin were not used in the group of patients with a non-infectious diagnosis at admission because these antibiotics are commonly used for community-acquired infections in our service. In this group of patients, the majority of antibiotics was prescribed for lately, hospital-acquired infections.

Our study has some limitations. First, the retrospective nature could lead to potential bias regarding the availability of relevant data or misinformation in the electronic medical records. Fortunately, at least the presence of significant missing data did not seem to be the case in the present analysis. Second, the fact that it was a single-centre study precludes an extrapolation of our results to other hospitals with distinct characteristics which include different palliative care management as well as different microbiological profile and antibiotic therapy choices. We cannot affirm that all antibiotics were correctly prescribed or indicated and if adequate preventive measures were followed which certainly could be of help in reduce hospital-acquired infections. Finally, the limited sample might be a cause of type II error, which means unrevealed statistical differences when they actually exist.

CONCLUSION

Our data confirm the previous finding that infectious complications are very common in palliative care patients leading to disseminated use of antibiotics as well as other expensive medical care resources for their treatment. However, the lack of well-documented presence of infection or isolated agent in most cases has possibly led to an excessive use of antibiotics and also an overestimation of infection occurrence in our population. Although the presence of previous MDRO colonisation did not seem to have an impact in terms of increased mortality in our study, it emphasises the harm of widespread empirical large spectrum antibiotic use. Since mortality was similar in patients admitted with an infectious diagnosis or not, it is hard to define the real impact of antibiotic treatment in improving survival. Therefore, the fact that mortality was significantly high regardless of the presence of

infection or large spectrum antibiotic use confirms that further studies are needed to determine in which cases antibiotics and ICU admission are meaningful rather than expensive, stressful and futile interventions for end-of-life patients.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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