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Letter to the Editor

Early administered antibiotics do not impact mortality in critically ill patients with COVID-19.

Dear Editor,

The recently published article by Lansbury L et al. showed that a low proportion of COVID-19 patients have a bacterial co-infection.[1] However, Huttner B *et al.* recommended antibiotics for most severe COVID-19 presentations.[2] Rawson TM *et al.* described a widespread use of broad-spectrum antibacterials in 72% (1450 out of 2010) COVID-19 patients, despite a paucity of evidence for bacterial co-infection.[3] COVID-19 may mimic bacterial pneumonia[2,4] and, therefore, antibiotics for possible bacterial coinfection are frequently administered. We conducted a retrospective analysis aimed at describing the impact of early antibiotic therapy (*i.e.*, before intensive care unit [ICU] admission) on mortality and delayed severe healthcare-associated infections in the ICU.

From 9th April to 20th May 2020 we retrospectively reviewed all medical charts of intubated ICU patients admitted to a community hospital dedicated to the care of COVID-19 patients in the Southern part of Switzerland. This hospital served as a reference center for a population of 350'000 inhabitants (seven public hospitals).

We described patients who received antibiotics (*versus* no antibiotics) before ICU stay and we analyzed differences in mortality, ventilator-associated pneumonia (VAP), catheter-related bloodstream infections (CRBSIs), urinary tract infections (UTIs) and candidemias (*i.e.*, outcomes) between both groups. Importantly, antibiotics before ICU admission were administered at the discretion of the attending physician and this variable was routinely collected. Characteristics of patients were described as count (percent) or median (interquartile range) for qualitative and quantitative variables, respectively, and were compared between groups using Chi-square, Fisher or Mann–Whitney tests, as appropriate. The study was approved by the regional Ethics Committee (number: 2020-01216 CE 36641).

We included 48 ICU patients with COVID-19. The median age was 66.5 (interquartile range [IQR] 60 -71) and 33% (n=11) were female. Antibiotics before ICU admission were administered in 40% (n=19) of cases, in all cases the clinical indication was a suspected bacterial co-infection. The most frequently used antibiotic was amoxicillin/clavulanate (68%, n=13). Characteristics of patients with or without antibiotics are reported in the Table 1. In general, patients' characteristics in both group swere similar. In patients without antibiotics cardiovascular disease was more frequently observed (38% *versus* 16% in patients with antibiotics, p=0.12); whereas women (32% *versus* 17% in patients without antibiotics, p=0.25) and antivirals (68% versus 48%, p=0.17) were more frequently observed in the group with antibiotics. Mortality was similar between the two groups (24% without antibiotics *versus* 26% with antibiotics, p=0.86). Interestingly, no difference in the number of delayed healthcare-associated infections during ICU stay was observed between groups. UTI tended to be more frequent in the group without antibiotic, whereas candidemias appeared to be more frequent in the antibiotic group. The low number of patients included in our analysis did not allow a firm conclusion. However, our preliminary results illustrate that early administered antibiotics do not appear to significantly impact mortality or delayed hospital-acquired infections in critically ill patients and call into question the utility of early treatment of a presumptive bacterial superinfection in COVID-19 patients. Large multi-centric studies are urgently needed[5] to investigate the impact of early antibiotics therapy on[1] mortality,[2] subsequent healthcare associated infections and[3] ICU complications (*i.e.*, duration of mechanical ventilation).

Declaration of Competing Interest

None.

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Table 1
Patients characteristics with and without antibiotics before ICU stay

	Without antibiotics (n=29)	With antibiotics (n=19)	p-value
Age, median (IQR)	66 [60; 71]	67 [60; 72]	0.74
Sex, female	5 (17.2)	6 (31.6)	0.25
≥1 comorbidity	22 (75.9)	16 (84.2)	0.49
Cardiovascular disease	11 (37.9)	3 (15.8)	0.12
Diabetes mellitus	7 (24.1)	6 (31.6)	0.57
Hypertension	16 (55.2)	8 (42.1)	0.38
Lymphopenia at admission, median (IQR)	0.7 [0.6; 0.9]	0.7 [0.4; 0.9]	0.33
CRP at admission, median (IQR)	128 [57; 206]	83 [47; 132]	0.29
Creatinin at admission, median (IQR)	95 [84; 118]	98 [81; 128]	0.92
Lymphopenia duration, median (IQR)	23 [16; 31]	25 [23; 35]	0.11
SAPS at ICU admission, median (IQR)	45 [40; 65]	47 [37; 55]	0.79
Corticosteroids during ICU stay	15 (51.7)	10 (52.6)	0.95
Antivirals*	14 (48.3)	13 (68.4)	0.17
Tocilizumab	3 (10.3)	2 (10.5)	0.99
Healthcare-associated infections during ICU stay			
Infection number per patient, median (IQR)	1 [1; 2]	1 [1; 2]	0.98
VAP	19 (65.5)	14 (73.7)	0.55
UTI	8 (27.6)	2 (10.5)	0.28
CRBSI	7 (24.1)	5 (26.3)	0.86
Colitis	0 (0)	1 (5.3)	0.39
Candidemia	2 (6.9)	3 (15.8)	0.37
Mortality	7 (24.1)	5 (26.3)	0.86

Legends. *Antivirals commonly administered at our institution were: hydroxychloroquin, lopinavir/ritonavir and remdesivir. IQR: interquartile range. CRP: C-reactive protein. SAPS: Simplified Acute Physiology Score. ICU: Intensive care unit. VAP: Ventilator-associated pneumonia. UTI: Urinary tract infection. CRBSI: Catheter-related bloodstream infection.

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