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LETTER

Dichotomy between ventilator-associated pneumonia/-tracheobronchitis: did you ask the lung its opinion?

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Dear Editor,

We found the recent article about ventilator-associated tracheobronchitis (VAT) and pneumonia (VAP) by Martin-Loeches et al. of great interest [1]. The authors highlighted that the discrimination between both entities is challenging and cannot rely on microbiology nor usual biological parameters or chest X-ray findings. Finally, they recommend using the ventilator-associated lower respiratory tract infection (VA-LTRI) term to simplify the pathophysiology puzzle and suggest a shorter antibiotic duration for the treatment of VAT than for VAP.

If we agree that identification of lung parenchyma infection cannot be definitely confirmed with usual paraclinical exams, we regret that no attention was paid to the lung parenchyma function. Herein, the alteration of gas exchange might constitute a good reflection of parenchyma involvement in the VA-LRTI physiopathology, allowing us to distinguish between a situation requiring either no or shorter antibiotic duration and those requiring full treatment.

In order to evaluate the impact of hypoxemia during VA-LRTI, we conducted a retrospective, monocentric observational study, from April 2019 to April 2021, with inclusion of mechanically ventilated patients for 48 hours or more in whom a VA-LRTI was diagnosed. Primary objective was to assess association between decrease oxygenation and death during the 28 days following VA-LRTI diagnosis.

Cox proportional hazard model was used for survival analysis, and variables associated with the death with a p-value < 0.2 in univariate analysis were included in multivariable model. All tests were two-sided, and a p-value less than 0.05 was considered statistically significant. Due to the observational nature of this study, written consent was waived. The French Society of Anaesthesia and Intensive Care Medicine (SFAR) Committee approved the study protocol on 24th of April 2021, IRB 00010254-2021-090.

Among 601 patients intubated for 48 hours or more, 137 (23%) developed VA-LRTI of whom 43 died during follow up (31%). At the time of VA-LRTI diagnosis, the majority of patients had purulent sputum (80%), hyperthermia (38.6°C [38.2–39]), half had auscultatory signs (49%), and a new radiological opacity was reported in only 40% of them (Table 1). PaO_2/FiO_2 ratio was calculated at 157 mmHg [120–220], and sequential organ failure assessment (SOFA) on the day of VA-LRTI diagnosis was 7 [5–9]. White blood cells increased to 1.6 G/L in between 48 hours before VA-LRITI and the day of diagnosis, conversely PaO_2/FiO_2 decreased to 50 mmHg [0–86] during the same period.

Variables independently associated with 28-day mortality were increased leukocyte count (hazard ratio (HR) = 1 per 1 G/L increase [1–1.01] p = 0. 39), admission during 2021 (hazard ratio (HR) = 3.63 [1.40–9.42] p = 0.008), and decrease in PaO_2/FiO_2 ratio as compared with 48 hours before VA-LRTI (HR = 1.05, per 10 mmHg decrease [1.01–1.09] p = 0.016).

Beyond VAP and VAT classification, we presently observed that alteration of lung function, through

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NM and EP contributed equally to the realisation of this study and share first authorship.

Table 1 Baseline characteristics at admission and VA-LRTI onset

	All patients with VA-LRTI *n*=137	Dead *n*=43	Alive *n*=94	*p-value*
Age, years,	66 [55–72]	70 [60–73]	65 [53–71]	0.048
SAPS II	52 [39–68]	52 [44–74]	52 [38–67]	0.23
Male – no. (%)	97 (71)	32 (74)	65 (69)	0.67
Immunodepression – no. (%)	1 (1)	0	1 (2)	1
Localization before admission				0.42
Acute care ward – no. (%)	41 (30)	12 (30)	29 (31)	
Home – no. (%)	89 (65)	27 (63)	62 (66)	
Long-term care facility– no. (%)	7 (5)	4 (9)	3 (3)	
Reason for admission				
Trauma – no. (%)	7 (5)	2 (5)	5 (5)	1
Medical (vs surgical) – no. (%)	123 (90)	39 (90)	84 (89)	0.57
SARS-CoV-2 infection – no. (%)	29 (21)	11 (26)	18 (19)	0.53
Antibiotic before admission – no. (%)	99 (72)	32 (74)	67 (71)	0.86
Years of admission				0.002
2019 – no. (%)	50 (36)	15 (35)	35 (37)	
2020 – no. (%)	71 (52)	17 (40)	54 (57)	
2021 – no. (%)	16 (12)	11 (26)	5 (5)	
Length of intubation before VA-LRTI – no. (%)	6 [4–10]	5 [4–8]	7 [4–11]	0.15
Clinical findings on the day of VA-LRTI				
Purulent sputum – no. (%)	113 (82)	35 (81)	78 (83)	1
New auscultatory abnormality – no. (%)	67 (49)	20 (46)	47 (50)	0.84
Fever – no. (%)	102 (74)	31 (72)	71 (76)	0.83
Body temperature, °C	38.6 [38.2–39]	38.6 [37.9–39]	38.6 [38.2–39]	0.60
Shock – no. (%)	23 (17)	8 (19)	15 (16)	0.89
Biological and radiological findings on the day of VA-LRTI				
Leucocytes, G/L	12 [9.4–17.2]	13 [9.6–18.7]	12.8 [9.2–17.1]	0.65
Change in leukocytes[a], G/L	1.6 [-0.6–4.8]	1.8 [-1.1–6.8]	1.5 [0.3–4.5]	0.74
PaO_2/FiO_2, mmHg	157 [120–220]	136 [115–186]	163 [129–225]	0.054
Change in PaO_2/FiO_2[a], mmHg	– 50 [0–(– 86)]	– 64 [– 23–(– 111)]	– 33 [0–(– 68)]	0.009
New opacity on Chest X-ray – no. (%)	54 (39)	16 (37)	38 (40)	0.87
SOFA on the day of VA-LRTI	7 [5–9]	8 [6–10]	6 [4–8]	0.001
Microbiological culture				
Negative	8 (6)	4 (9)	4 (4)	0.26
NF-GNB	16 (12)	4 (9)	12 (13)	0.76
Enterobacteriaceae	41 (30)	13 (30)	28 (30)	1
Staphylococcus Aureus	31 (23)	7 (16)	24 (26)	0.33
Other GPC	9 (7)	3 (7)	6 (6)	1
Flora	69 (50)	22 (51)	47 (50)	1
Number of CFU	6 [5–7]	6 [5–7]	5 [5–7]	0.74

ICU: intensive care unit, *VA-LRTI*: Ventilator-associated lower respiratory tract infection, *VAP*: ventilator-associated pneumonia, *SOFA*: sequential organ failure assessment

[a] *As compared with variable* 48h *before VA-LRTI*

decrease in oxygenation parameters, is independently associated with death in VA-LRTI patients. Through a review of major articles available in the literature, we noticed that hypoxemia is rarely reported in studies regarding VAP or VA-LRTI [1–5]. In the future, it seems crucial to clearly report oxygenation parameters in all studies involving patients with VA-LRTI to better define the study population.

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Author contributions
All authors contributed to the acquisition of data. EP, PF, and NM conducted the statistical analysis, contributed to the study conception and design as well as the analysis and interpretation of the data. EP and NM drafted the manuscript, and all authors critically revised the manuscript and approved the final version.

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Declarations

Conflicts of interest
None.

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