CRITICAL ROUNDS

MICRO LABS LIMITED

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring "CRITICAL ROUNDS" containing latest information in the field of Critical care medicine.

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Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Ltd

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Staphylococcus aureus ventilator-associated pneumonia in patients with COVID-19: clinical features and potential inference with lung dysbiosis

Introduction

Many SARS-CoV-2 infected individuals undergo a mild disease, a significant proportion of hospitalized patients require admission to the intensive care unit (ICU). In this setting, mechanical ventilation (MV) is used commonly to provide supportive care, especially in patients with acute respiratory distress syndrome (ARDS), which is a well-established feature of COVID-19 pathophysiology. ICU patients have a greater risk of secondary infection or superinfection by bacterial pathogens compared to patients in mixed ward/ICU settings. It is likely that SARS-CoV-2 infection impairs pulmonary immune responses against bacteria or alters the dynamics of inter-microbial interactions, thereby leading to enhanced growth of pathogenic species. It is also credible that co-infection exacerbates the lung damage triggered by SARS-CoV-2 and, then, facilitate pathogen's systemic dissemination. To date it is unclear whether specific co-infecting pathogens are associated with poor outcomes, as well as they correlate with the microbial community in the lung of patients suffering from SARS-CoV-2 infection. A recent study investigating the lung-tissue microbiota characteristics of 20 deceased patients with COVID-19 reported that Staphylococcus aureus (SA) accounted for~70% of bacteria isolated from early sampled lower respiratory tract of COVID-19 patients, who required mechanical ventilation for ARDS. Thus, any colonizing SA isolate may induce bacterial superinfection, suggesting that an altered balance between commensals and potential pathogens in a virus conditioned lung microbiota may contribute to aggravate SARS-CoV-2-induced pneumonia.

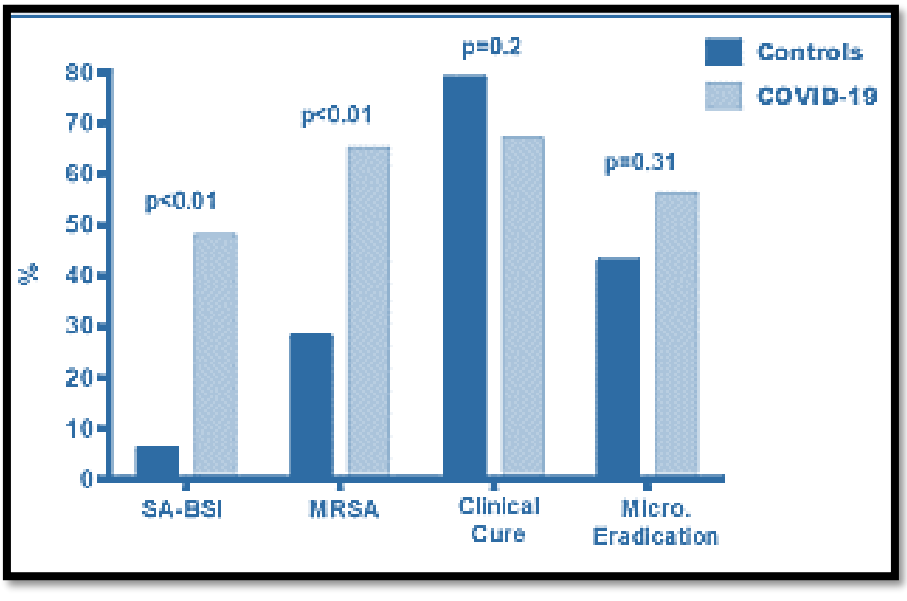
Aim: To investigate clinical features of SA ventilator-associated pneumonia (SA-VAP) in ICU patients with or without COVID-19 and also to investigated the lung microbiota of patients for whom lower respiratory tract samples were available to identify bacterial community features related to COVID-19.

Methods: Prospective inclusion of hospitalized patients with COVID-19 across two medical ICUs, who developed SA-VAP. After 1:2 matching based on the simplifed acute physiology score II (SAPS II) and the sequential organ failure assessment (SOFA) score, cases were compared with SA-VAP patients without COVID-19 (controls). Clinical, microbiological, and lung microbiota data were analysed.

Results: Two groups of patients (40 COVID-19 and 80 non-COVID-19) were studied. COVID-19 patients had a higher rate of late-onset (87.5% versus 63.8%; p=0.01), methicillin-resistant (65.0% vs 27.5%; p were

significantly enriched in the COVID-19 group compared to the non–COVID-19 group of SA-VAP patients.

Microbiological and clinical features of SA VAP in COVID-19 patients and controls



Conclusions: In this study population, COVID-19 seemed to significantly affect microbiological and clinical features of SA-VAP as well as to be associated with a peculiar lung microbiota composition.

Source: De Pascale et al. Staphylococcus aureus ventilator-associated pneumonia in patients with COVID-19: clinical features and potential inference with lung dysbiosis. Crit Care. 2021;25:197

Flow Index: a novel, non-invasive, continuous, quantitative method to evaluate patient inspiratory effort during pressure support ventilation

Introduction

During pressure support ventilation (PSV), assessing patient inspiratory effort could allow the titration of respiratory assistance in order to minimize over- and under assistance. In fact, during under-assistance, a vigorous spontaneous effort may generate excessive diaphragmatic loading and muscle injury, as well as regional lung injury due to stress and strain. Over-assistance, on the other hand, may lead to pulmonary hyperinflation and diaphragmatic atrophy and dysfunction, thus impairing weaning and prolonging the dependency from mechanical ventilation. Independently from the appropriateness of inspiratory assistance, the patient's neuro-ventilatory drive and hence the breathing effort may unpredictably vary over time due to pain, anxiety, delirium, sepsis, sedation or other pathological conditions. Despite its perceived importance, however, the inspiratory effort is seldom monitored. Qualitative clinical surrogates to infer patient effort include respiratory rate (RR), tidal volume (VT), rapid shallow breathing index (RSBI, calculated as respiratory rate over tidal volume) and the use of accessory muscles. Esophageal pressure measurement is the reference technique used to quantify inspiratory effort, but it requires technical proficiency and the insertion of an esophageal catheter. Other methods include monitoring of the diaphragm's electrical activity and ultrasound assessment of inspiratory diaphragmatic displacement and thickness. Both are associated with drawbacks, such as availability, costs, non-continuous monitoring and operator-dependency. During PSV, the inspiratory portion of the flow-time waveform may provide important information regarding patient effort. Deviations of inspiratory flow from the exponential decay pattern that is typical of the passive patient ventilated in pressumetric ventilation, suggest that the patient is active during inspiration. However, to our knowledge, the quantitative relationship between the inspiratory flow-time waveform and the inspiratory effort at the bedside has not been formally evaluated. In this study, we hypothesized that, during PSV, the concavity of the inspiratory flow-time waveform can be quantified by a numeric indicator, named Flow Index, similarly to the Stress Index on airway opening pressure.

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Aim: To assess if Flow Index was associated with patient inspiratory effort during PSV.

Methods: Twenty-four patients in pressure support ventilation were enrolled. A mathematical relationship describing the decay pattern of the inspiratory flow profile was developed. The parameter hypothesized to estimate effort was named Flow Index. Esophageal pressure, airway pressure, airflow, and volume waveforms were recorded at three support levels (maximum, minimum and baseline). The association between Flow Index and reference measures of patient effort (pressure time product and pressure generated by respiratory muscles) was evaluated using linear mixed effects models adjusted for tidal volume, respiratory rate and respiratory rate/tidal volume.

Results: Flow Index was different at the three pressure support levels and all group comparisons were statistically significant. In all tested models, Flow Index was independently associated with patient effort ($p < 0.001$). Flow Index prediction of inspiratory effort agreed with esophageal pressure-based methods.

Flow Index coefficient of unadjusted and adjusted linear mixed effects models

	Flow Index coefficient (95% CI)	*P* value	*Flow Index* coefficient (95% CI) adjusted for RR and V_T	*P* value
$PTP_{ratio, breath}$	0.03 (0.03, 0.04)	< 0.0001	0.03 (0.03,0.04)	< 0.0001
$PTP_{pt,breath}$	0.19 (0.13, 0.25)	< 0.0001	0.23 (0.17, 0.29)	< 0.0001
P_{musc}	0.34 (0.24, 0.43)	< 0.0001	0.33 (0.23 0.42)	< 0.0001

Conclusions: Flow Index is associated with patient inspiratory effort during pressure support ventilation, and may provide potentially useful information for setting inspiratory support and monitoring patient-ventilator interactions.

Source: Albani et al. Flow Index: a novel, non-invasive, continuous, quantitative method to evaluate patient inspiratory effort during pressure support ventilation. Crit Care (2021) 25:196

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Derivation and Validation of a 4-Level Clinical Pretest Probability Score for Suspected Pulmonary Embolism to Safely Decrease Imaging Testing

Introduction:

Despite **many** progress in the last decades, diagnosing pulmonary **embolism** (PE) remains a clinical challenge. The standard diagnostic strategy, **supported** clinical probability assessment, D-dimer testing, and **computerized tomography** pulmonary angiography (CTPA), is proven **to possess** low rate of diagnostic failure. However, there has been **an outsized** increase in CTPA for suspected PE. The exact reasons are likely multifactorial. The signs and symptoms of PE are **quite common** and unspecific. As such, clinicians fear **they could** be missing a life-threatening condition and are **susceptible to** initiate a diagnostic process. Due to the lack of specificity of D-dimer testing, a large proportion of patients have a false-positive result and require imaging to rule out PE. Finally, CTPA **is quickly** available, fast, minimally invasive, and more sensitive than ventilation/perfusion (V/Q) scans. A slight increase in PE diagnosis has been observed as a result but with no clear benefits in terms of outcome, especially PE-related mortality. CTPA exposes patients to risks of allergies, **renal failure** , and cumulative radiation-induced cancer. Several strategies have therefore been proposed to reduce PE over testing and over diagnosis These have proved satisfactory in terms of safety and efficacy, but they are based on different methods of assessing clinical pretest probability thus making it difficult to combine them and increasing the risk of misuse in clinical practice.

Aim:

To develop and validate a pretest probability score **to securely** reduce imaging testing by integrating all the previously proposed strategies: the 4-Level **embolism** Clinical Probability Score (4PEPS).

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To retrospectively assess **the security** of a diagnostic strategy **supported** this new score and its efficacy in reducing imaging testing.

Objective:

To derive and validate a 4-level pretest probability rule (4-Level Pulmonary Embolism Clinical Probability Score [4PEPS]) that makes it possible to rule out PE solely on clinical criteria and optimized D-dimer measurement to safely decrease imaging testing for suspected PE.

Methods:

Study included consecutive outpatients suspected of having PE emergency departments. Individual data from three merged management studies (n = 11 114; overall prevalence of PE, 11%) were used for the derivation cohort and internal validation cohort. The external validation cohorts were taken from two independent studies, the first with a high PE prevalence (n = 1548; prevalence, 21.5%) and the second with a moderate PE prevalence (n = 1669; prevalence, 11.7%). A prior definition of pretest probability target values to achieve a posttest probability less than 2% was used on the basis of the negative likelihood ratios of D-dimer.

Outcome: The rate of PE diagnosed during the initial workup or during follow-up and the rate of imaging testing.

Results:

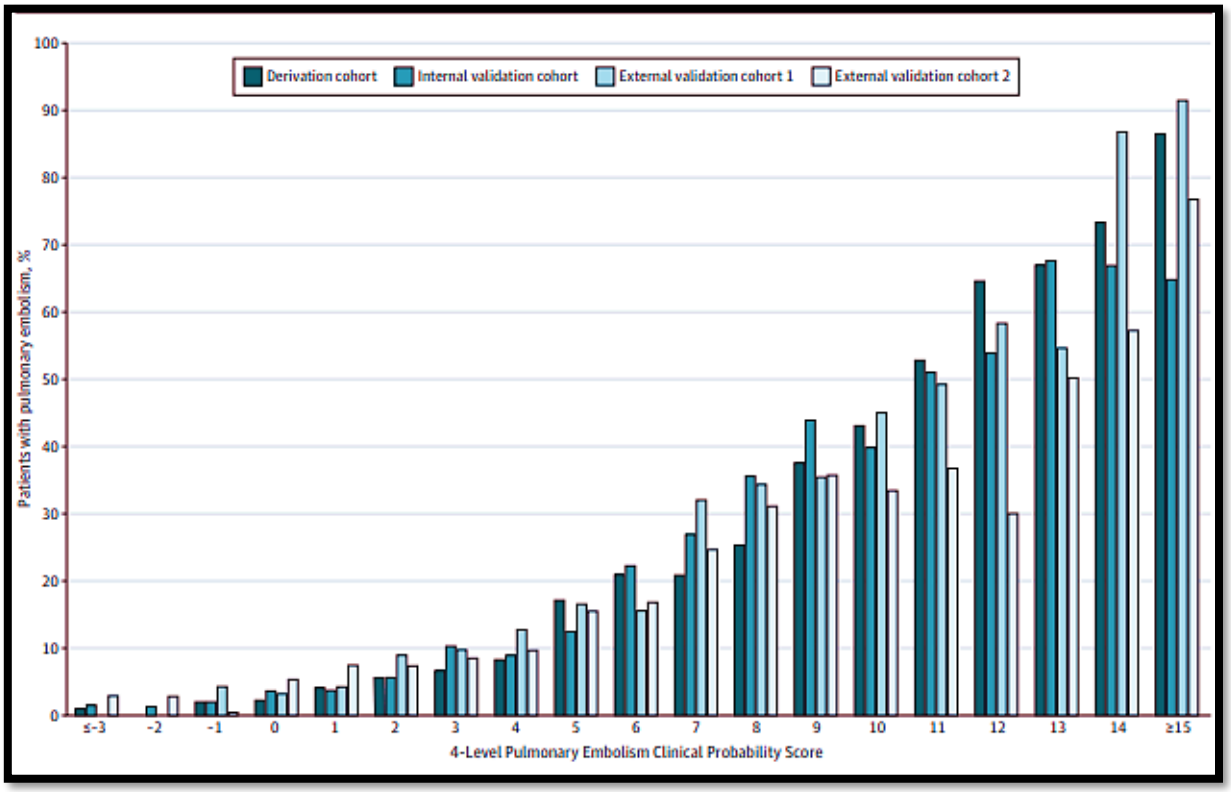
Of the 5588 patients, 3441 (61.8%) were female, and the mean (SD) age was 52 (18.5) years. The 4PEPS comprises 13 clinical variables scored from −2 to 5. It results in the following strategy:

- Very low probability of PE if 4PEPS is less than 0: PE ruled out without testing;
- Low probability of PE if 4PEPS is 0 to 5: PE ruled out if D-dimer level is less than 1.0 μg/mL;
- Moderate probability of PE if 4PEPS is 6 to 12: PE ruled out if D-dimer level is less than the age-adjusted cutoff value;

- High probability of PE if 4PEPS is greater than 12: PE ruled out by imaging without preceding D-dimer test.

In the first and the second external validation cohorts, the area under the receiver operator characteristic curves were 0.79 (95% CI, 0.76 to 0.82) and 0.78 (95% CI, 0.74 to 0.81), respectively. The false-negative testing rates if the 4PEPS strategy had been applied were 0.71% (95% CI, 0.37 to 1.23) and 0.89% (95% CI, 0.53 to 1.49), respectively. The absolute reductions in imaging testing were −22% (95% CI, −26 to −19) and −19% (95% CI, −22 to −16) in the first and second external validation cohorts, respectively. The 4PEPS strategy compared favorably with all recent strategies in terms of imaging testing.

Pulmonary Embolism Prevalence by 4-Level Pulmonary Embolism Clinical Probability Score (4PEPS) in the Derivation and Validation Cohorts



Conclusion: The 4PEPS strategy may lead to a substantial and safe reduction in imaging testing for patients with suspected PE. It should now be tested in a formal outcome study.

Key Points:

Question: *Can a pretest probability score make it possible to rule out pulmonary embolism solely on clinical criteria and optimized D-dimer measurement to safely decrease imaging testing?*

Source: Roy PM, Et al. Derivation and Validation of a 4-Level Clinical Pretest Probability Score for Suspected Pulmonary Embolism to Safely Decrease Imaging TestingJAMA Cardiol. 2021;6(6):669-677

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