Best Evidence Topic Report

Title	The role of saturation measurements in the diagnosis and prognosis of viral pneumonia
Report by	Leen Verhelst, Linde Vanhessche
Search checked by	Professor Jean-Marie Degryse
Clinical scenario	In December 2019 a new type of coronavirus, named Covid-19, was identified as the origin of a pneumonia of unknown cause in Wuhan, China. Since then, infection with Covid-19 has been declared a pandemic, given its spread worldwide. Low saturations have been observed, even in young patients, which led to a suspicion of a serious condition. Therefore, can saturation measurement play a role in the diagnosis of viral pneumonia (or ARDS)? What is the correlation with clinical signs and symptoms and prognosis?
Answerable question	Is saturation measurement an added value in the diagnosis and prediction of the prognosis of patients with viral pneumonia?
Search terms	PUBMED: (("Pneumonia/diagnosis"[Mesh]) AND "Prognosis"[Mesh]) AND "Severity of Illness Index"[Mesh] AND ("blood gas monitoring, transcutaneous"[MeSH Terms] OR cutaneous oximetry[Text Word] OR pulse oximetry[Text Word] OR SpO2[Text Word] OR oxygen saturation[Text Word])) COCHRANE: "pneumonia pulse oximetry" International guidelines (European Respiratory Society, American Thoracic Society, British Thoracic Society, German Respiratory Society and Brazilian Thoracic Association) were consulted from which appropriate references were filtered
Search date	19/03/2020
Search outcome (number of hits)	PUBMED: 13 results COCHRANE: 2 Cochrane reviews and 82 trials
Relevant papers (number of final inclusions)	PUBMED: 2 relevant papers. Afterwards, a backwards search was performed on the relevant papers, but this didn't result in new relevant papers COCHRANE: 1 relevant paper International Guidelines: 2 relevant papers
Flow chart	Patient with clinical suspicion of community-acquired pneumonia $\rightarrow$ SpO$_2$ $\leq$ 90% and a higher level of severity of pneumonia as assessed by another clinical tool (e.g. CRB65) $\rightarrow$ increased risk of mortality within 30 days $\rightarrow$ strong advice to refer to the emergency department or hospital

Evidence tables

DATA-BASE	Author, date, country	Study type (evidence level)	Main risks of bias	Patient characteristics	Intervention	Compari-son	Outcome	Key results: RR, AR, NNT, Sens/Spec, LR+/LR-, OR, etc
COCHRANE	Bewick T et al, 2010, UK[1]	Prospective cohort study	Exclusively hospitalised cohort of patients and therefore the applicability to primary care population is questionable (possible selection bias). The study allows no comment to be made concerning the value of pulse oximetry in discriminating pneumonic from non-pneumonic lower respiratory tract infection.	>16 years old, at least 1 acute symptom of lower respiratory tract infection, new infiltrates on RX thorax and receiving treatment for CAP in the hospital. Exclusion criteria: hospital admission in the preceding 10 days, tuberculosis, post-obstructive pneumonia due to lung cancer.	SpO_2 measurement on room air (FiO_2 = 0,21)	CRB-65	Inpatient mortality within 30 days of admission or admission to a critical care area	There was a statistically significant association between decreasing thresholds of SpO_2 and incidence of adverse outcome (for each decrease in threshold, OR 1.42, 95% CI 1.22-1.66, p<0.001). Further analysed showed that the value of $SpO_2 \leq 90\%$ has a good specificity (76%), but low sensitivity (46,4%) in predicting 30-day mortality or critical care admission. $SpO_2 \leq 90\%$ complements rather than replaces clinical severity scoring tools.

| PUBMED | Ochoa-Gondar O et al, 2013, Spain[2] | Comparative, retrospective, population-based study | This is a retrospective study (lower level of evidence) with only use of data available from a registered clinical assessment. There was a relatively small number of outpatient CAP cases. Significance levels are not clearly mentioned. There are no results on oxygen saturation and age separately. | 65 years or older patients with a radiographically confirmed symptomatic CAP diagnosed between 2008 and 2011 in Tarragona, Spain. Excluded: aspiration pneumonia, healthcare-related and nosocomial pneumonias, readmissions, or other diagnosis | CORB75 score (confusion, $SpO_2 \le$ 90%, respiratory rate $\ge$ 30/min, systolic blood pressure <90 mmHg or diastolic blood pressure $\le$60 mmHg, and age $\ge$ 75 years | CRB65 severity score at diagnosis (one point each for confusion, respiratory rate $\ge$30/min, systolic blood pressure <90 mmHg or diastolic blood pressure $\le$60 mmHg, and age $\ge$65 years | 30-day mortality (in- and out-of-hospital) | Sensitivity and specificity of CORB75 $\ge$2 was 78,3% and 65,5% in the derivation cohort and 82,4% and 71,7% in the validation cohort. For comparison: the sensitivity and specificity of CRB65 $\ge$ 2 was 58,7% and 75% in the derivation cohort and 64,7 and 78,3% in the validation cohort. PPV for CORB75 $\ge$ 2 was 30,4%, for CORB75 $\ge$ 3 45,2% compared with a PPV of 31% and 42,9% for CRB65 $\ge$ 2 and CRB65 $\ge$ 3. NPV for CORB75 $\ge$ 2 was 96,4%, for CORB75 $\ge$ 3 91,3% compared with a NPV of 93,7% and 88,6% for CRB65 $\ge$ 2 and CRB65 $\ge$ 3. For CORB75 $\ge$ 2 and for CORB75 $\ge$ 3 the proportion of correctly classified patients was 73,08% and 85,77%. For CRB65 $\ge$ 2 and for CRB65 $\ge$ 3 the proportion of correctly classified patients was 76,54% and 86,15%. |

								In short: CORB75 has a higher sensitivity in predicting 30-day mortality but a lower specificity and it has higher negative predictive values, however, there is an overlap between all confidence intervals in this study.

| PUBMED | Kolditz M et al, 2015, Germany[3] | Retrospective study of prospectively enrolled patients with CAP | Some patients already received supplemental oxygen at the moment of measurement. Only 15% were treated as outpatients. Retrospective analysis: a prospective interventional trial would provide a better level of evidence. | Recruited from multicentre CAPNETZ study with inclusion criteria age ≥18 years, pulmonary infiltrate diagnosed by chest X-ray and at least one of the following: history of fever (temperature ≥ 38.3 °C), cough, production of purulent sputum or focal chest signs on auscultation. Excluded: acquired or therapeutically induced immune deficiency, active tuberculosis or possibility of nosocomial infection. | CRB65 + oxygen saturation <90% or partial pressure of oxygen <8 kPa at admission + extra-pulmonary comorbidities | CRB65 only | 28-day mortality, requirement for mechanical ventilation or vasopressors and requirement for or intensive care unit admission. | Both comorbidity and oxygen saturation added independently to the CRB65 score for reduction of mortality (OR 3,18 and 1,91 with p <0,001). The addition of oxygen saturation improved the CRB65 criteria for prediction of need for ventilation and need for ICU admission (OR 2,05 with p<0,007 and OR 2,21 with p<0,001). There were no significant changes if the saturation threshold was defined by oxygen saturation of <92% instead of <90%. |

PUBMED	Majumdar S et al, 2010, Canada[4]	Retrospective population-based cohort study	This study is a retrospective study (lower level of evidence). The causes of the 30-day mortality or hospitalisation are unknown.	Patients assessed at an emergency department with pneumonia and then discharged. Pneumonia defined as 2 or more symptoms or signs (cough, pleurisy, shortness of breath, temperature >38°C, crackles or bronchial breathing on auscultation) AND radiographic evidence of pneumonia. Excluded: tuberculosis, cystic fibrosis, immunocompromised status or pregnancy.	Oxygen saturation measured by pulse oximetry of <90%	Oxygen saturation measured by pulse oximetry of <88%; 88-89,9%; 90-91,9%; 92-93,9%; ≥ 94%	30-day all-cause mortality or all-cause hospitalisation	Saturation <90%: 6% 30-day mortality, 18% hospitalization and 21% for composite outcome (mortality+ hospitalisation) vs respectively 1%, 7% and 8%with saturation ≥ 90% (p<0,001 for all of them). With a threshold of 92% saturation, there was no longer an independent association with the composite outcome of 30-day mortality and hospitalization and with this threshold, the number-needed-to-admit preventing 1 major adverse event (not specified) would be 14.

PUBMED	Dwyer R et al, 2014, Sweden[5]	Retrospective study	Retrospective study, all patients recruited from one hospital. In 144 patients chest radiography or chest CT was not performed, and two of these patients died (yet this had no statistically significant impact on the study results). Eighth patients who suffered from HIV where included (yet this had no statistically significant impact on study results)	Patients with CAP (as registered by ICD-10 in the hospital records) admitted or treated as outpatients from December 2008 until March 2010. The patients had a principal diagnosis of pneumonia or of sepsis due to *Streptococcus Pneumoniae* plus a secondary diagnosis of pneumonia. Exclusion criteria: hospitalization during the preceding 2 weeks before enrolment, not able to be followed for 30 days after admission or visit to the emergency department, radiographic findings due to congestive heart failure, pulmonary embolus, carcinoma or other abnormalities with no signs consistent with pneumonia.	DS CRB65 = CRB65 + Peripheral oxygen saturation <90% + underlying disease	CRB65 only	Death within 30 days of admission	DS CRB65 improves the accuracy in predicting 30-day mortality when compared to CRB65 alone. DS CRB-65 ≥ 3 was found as an accurate cut-off score (sensitivity 82%, specificity 75%) (measured by the Youden Index). DS CRB-65 score ≥ 2 predicted 98% and score ≥ 3 82% of all deaths. CRB-65 scores 1-4 predicted 99% of the deaths.

Conclusions of overall body of evidence

- Main results

  It is useful to add the measurement of oxygen saturation (SpO2) to the diagnosis of pneumonia and it can be a valuable addition to the CRB65 tool. The oxygen saturation is a predictor of prognosis where a level under 90% saturation is associated with a higher 28- to 30-day mortality and a higher need for ventilation and stay in an Intensive Care Unit (ICU). There is no clear evidence that a threshold of 92% is a better predictor of outcome.

  The measurement of oxygen saturation has a good specificity but a rather low sensitivity in one study, while in another study these results are opposite. In short, the measurement of SpO2 should complement rather than replace other clinical severity scores and diagnostic tests. It should be noted that there are no studies on the role of saturation measurements in viral pneumonia.

- Risks of bias

  There were no studies with a high evidence level on this topic. Most studies are retrospective and therefore are less reliable, for example due to the risk of selection bias. Also, the applicability to the primary care population is rather questionable in an exclusively hospitalised cohort of patients, like the study of Bewick T et al.

- Heterogeneity (statistical or clinical)

  Both clinical and statistical heterogeneity could be observed.

  The clinical heterogeneity concerns the patient population. One study included only patients of 65 years or older while the other studies adopted a minimum age limit of 16 years or 18 years old or did not define an age limit. Furthermore, there was a difference in population between the studies as some studies included hospitalized patients while other studies only included outpatients.

  Statistical heterogeneity could be observed between the study of Bewick et al and Majumdar et al. The first described SpO_2 as having a good specificity and a low sensitivity, while the latter described the opposite.

Clinical bottom line (response to clinical scenario)

Measurement of oxygen saturation can be an added value for the diagnosis and prognosis of patients with pneumonia, in this case caused by Covid-19. An important remark is that there were no specific studies on viral pneumonia in combination with oxygen saturation, so there is no clear evidence in these specific cases.

References

1. Bewick T, Greenwood S, Lim WS. What is the role of pulse oximetry in the assessment of patients with community-acquired pneumonia in primary care? *Prim Care Respir J*. 2010;19(4):378-382. doi:10.4104/pcrj.2010.00049

2. Ochoa-Gondar O, Vila-Corcoles A, Rodriguez-Blanco T, et al. Validation of the CORB75 (confusion, oxygen saturation, respiratory rate, blood pressure, and age ≥75 years) as a simpler pneumonia severity rule. *Infection*. 2014;42(2):371-378. doi:10.1007/s15010-013-0565-1

3. Kolditz M, Ewig S, Schütte H, Suttorp N, Welte T, Rohde G. Assessment of oxygenation and comorbidities improves outcome prediction in patients with community-acquired pneumonia with a low CRB-65 score. *J Intern Med*. 2015;278(2):193-202. doi:10.1111/joim.12349

4. Majumdar SR, Eurich DT, Gamble JM, Senthilselvan A, Marrie TJ. Oxygen saturations less than 92% are associated with major adverse events in outpatients with pneumonia: A population-based cohort study. *Clin Infect Dis*. 2011;52(3):325-331. doi:10.1093/cid/ciq076

5. Dwyer R, Hedlund J, Henriques-Normark B, Kalin M. Improvement of CRB-65 as a prognostic tool in adult patients with community-acquired pneumonia. *BMJ Open Respir Res*. 2014;1(1):1-6. doi:10.1136/bmjresp-2014-000038