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EDITORIAL

End-tidal CO_2 for exclusion of suspected pulmonary embolism: a new partner for Wells?

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Pulmonary embolism (PE) has been labelled as one of the leading causes of cardiovascular death in the Western World [1] and, still today, more than 40,000 patients in Germany and 200,000 in the USA die of acute PE each year. However, hospital mortality rates can fall from as high as 30% to 8% [2] when diagnosis and treatment are properly provided.

The diagnosis of PE remains a challenge because of highly variable clinical symptoms. Consequently, the diagnosis of PE has been finally confirmed in <35% of patients with a clinical suspicion of PE [3]. A simple bedside test with the ability to exclude PE in patients who do not have it, while not overlooking true-positive cases, is desired and will prevent unnecessary exposure to contrast agents and radiation.

The assessment of alveolar dead space ventilation and the expired tracer gas CO_2 as surrogates for pulmonary vascular obstruction have been proposed as valuable tools for excluding PE. The underlying pathophysiological principle is based on the three-compartment model of the lung, [4, 5] consisting of one compartment that is both ventilated and perfused (ideal compartment), one that is perfused but not ventilated (shunt compartment), and a third compartment that is ventilated but not perfused (dead space). Dead space comprises the anatomic dead space as the ventilated airway space, and alveolar dead space as the volume of unperfused alveoli. The size of the alveolar dead space can be approximated by measuring the CO_2 arterial tension to end-tidal CO_2 gradient as a percentage of the ventilated but not perfused lung [6], and ought to increase in thromboembolic obstruction.

KLINE *et al.* [7] were the first to demonstrate the excellent ability to rule out PE by combining alveolar dead space fraction calculations and plasma D-dimer assays. In 170 ambulatory patients, the combination of a normal alveolar dead space fraction with negative D-dimer was 100% sensitive to exclude PE. Specificity was reported to be only 65%.

RODGER *et al.* [8] studied 246 in-patients, outpatients and emergency department patients with suspected PE. A negative D-dimer result excluded PE with a sensitivity of 83% and a specificity of 58%. A low steady-state end-tidal alveolar dead space fraction excluded PE with a sensitivity of 80% and a specificity of 70%. The simple combination of both diagnostic tests improved sensitivity to 98%, thus ruling out PE without further diagnostic testing.

However, despite its non-invasiveness and rapid availability, measurement of the CO_2 gradient for the assessment of alveolar dead space in PE has not been practised. Cumbersome data acquisition, a weak diagnostic performance, technical limitations and artefacts, and the lack of sufficient validation were the main drawbacks.

In the current issue of the *European Respiratory Journal*, HEMNES *et al.* [9] hypothesised that PE exclusion may be based on capnography. Instead of measuring total exhaled CO_2 tension and arterial CO_2 tension, which requires specialised equipment and an arterial puncture, simply end-tidal CO_2 was measured utilising a handheld capnograph (Nellcor NBP 75, Miallinckrodt: Nellcor, St Louis, MO, USA), assuming that end-tidal CO_2 must decrease if dead space increases. The Microstream® (Nellcor) technology with a highly sensitive and CO_2-specific emission source is expected to make a significant difference compared with conventional capnography which requires special algorithms to correct for contaminant gases. To prove their concept, HEMNES *et al.* [9] studied a total of 298 patients with a suspicion of PE seen in the emergency department or in-patient wards of an academic university hospital. All study participants underwent end-tidal CO_2 determination within 24 h of state-of-the-art diagnostic imaging. In the group of patients finally diagnosed with PE (n=39), end-tidal CO_2 was significantly lower than in the group without PE or in healthy volunteers. At a cut-off of ⩾36 mmHg, capnography achieved a negative predictive value of 96.6%. In the same cohort, a Wells score [10] of <4 had a negative predictive value of 93.8%. Combining capnography results with a Wells score of <4 improved the negative predictive value further to 97.6%.

The novel aspect created here is that a simple capnographic assessment of alveolar end-tidal CO_2 tension has a diagnostic accuracy similar to D-dimer [11]. Both bedside tests improve their accuracy when combined with the Wells score [12]. As HEMNES *et al.* [9] state, the disadvantages of D-dimer testing are mostly of a practical nature and include the requirement for venepuncture, as well as time and cost for transportation, storage, measurement and reporting of blood samples. This simple proof-of-concept study is therefore remarkable and is an example of continuous technological advances allowing the revival of an old concept.

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Despite all the shortcomings of capnography, especially its limited applicability in patients with underlying chronic lung disease who are prone to PE [13] and the potential that small PEs may be missed, there is room for new optimism. Capnography will have to be validated prospectively in an appropriately sized multicentre setting against D-dimer testing to decide who will be the future partner of the Wells score in ruling out PE.

STATEMENT OF INTEREST

None declared.

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