Can the alveolar dead space fraction be used in the diagnosis of pulmonary embolism? A literature review

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Introduction

Alveolar dead space fraction (AVDSf) is calculated as the difference between end-tidal and arterial carbon dioxide and can be potentially used to represent the degree of dead space present in the lungs. Pulmonary embolism (PE) increases dead space; measurement of AVDSf could therefore potentially aid in acute diagnosis.

Aim

Our aim was to undertake a literature review to evaluate the diagnostic accuracy of an abnormal alveolar dead space fraction (AVDSf) measurement for diagnosis of acute pulmonary embolism (PE), across a spectrum of clinical severity.

Methods and Materials

Using the Healthcare Databases Advanced Search, Medline and Embase were searched from 1946 to 16/06/2021 using the following terms ((Pulmonary embol* OR pulmonary thromboembol*) AND (end-tidal OR capnogra* OR alveolar dead space OR dead space fraction)).ti,ab. The search was limited to human studies. An additional search of the Cochrane library was conducted using the terms 'pulmonary embol*' and 'carbon dioxide'. Two reviewers ran concurrent searches and sifted titles and abstracts for results independently. A third senior review adjudicated cases of disagreement. Studies that looked at ETCO2 without PaCO2 were not included. 358 results were identified, 186 from Embase and 172 from Medline. No relevant Cochrane reviews were identified.

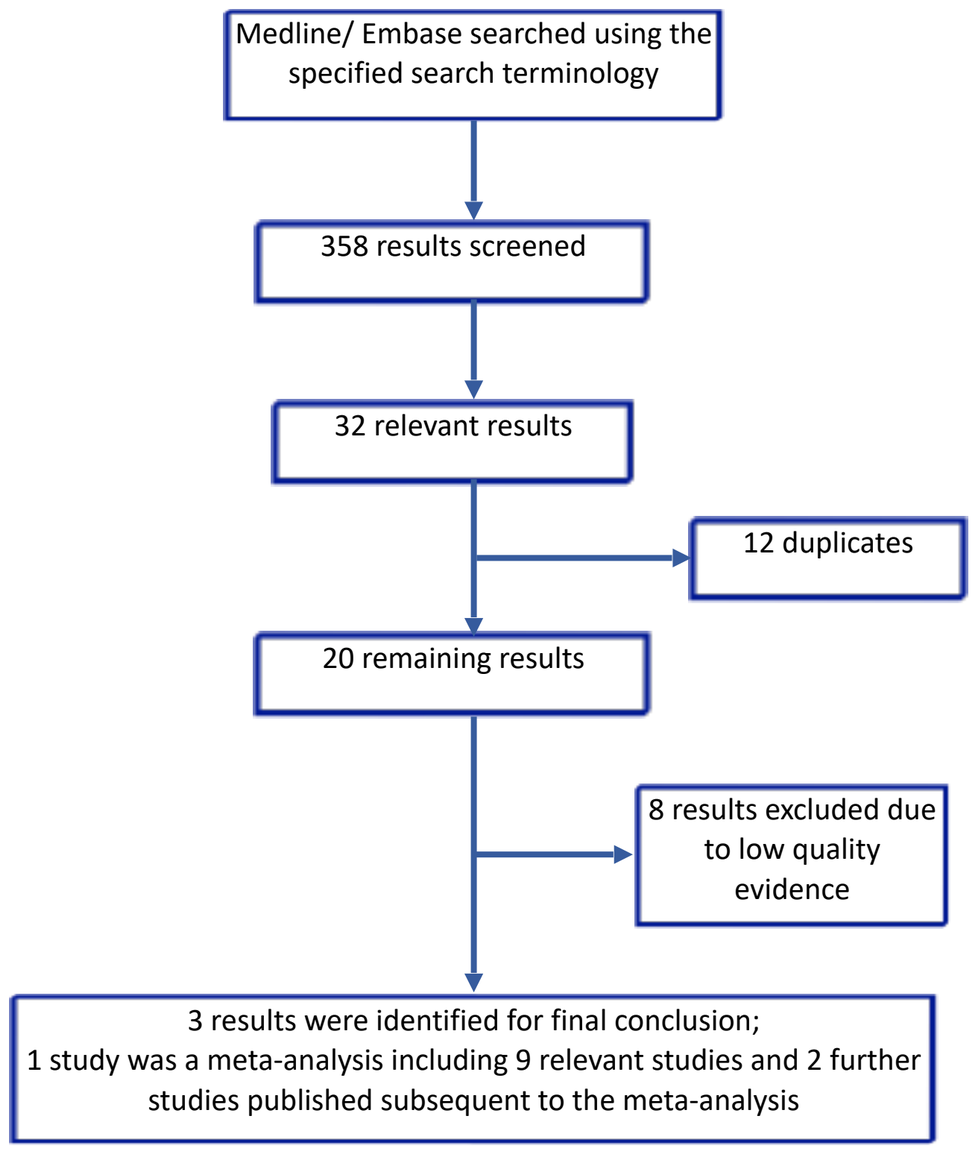

Figure 1:Literature search

Results

Author, Date, Country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Manara *et* al, 2013, Belgium (1).	Systematic review and pooled meta-analysis of 14 observational studies between 1997 and 2010 looking at AVDSf. 2991 patients with suspected PE were included. 1781 had AVDSf calculated and compared to a reference standard diagnosis.	Level 1b. Pooled analysis of cross-sectional studies with risk of bias assessment.	Pooled sensitivity	0.73 (95% CI 0.69-0.78).	Significant heterogeneity between included studies (I^2 = 31.3%) and half the included studies within the systematic review were found to be at high risk of bias. Many studies used ETCO2 readings in awake and spontaneously ventilating patients thus limiting generalisability to those patients requiring mechanical ventilation. In addition, $ETCO_2$ was measured using different types of equipment and different methods.
			Pooled specificity	0.61 (95% CI 0.58-0.64).	
			Pooled positive likelihood ratio	2.76 (95% CI 1.62-4.7).	
			Pooled negative likelihood ratio	0.38 (95% CI 0.31-0.48).	
Yüksel *et al*, 2016, Turkey (2).	159 patients presenting to the Emergency Department (ED) with symptoms suggestive of PE. All patients had AVDSf calculated and compared to a reference standard diagnosis.	Level 3b. Single-centre observational study.	Sensitivity	0.68 (95% CI 0.50 to 0.82).	Single-centre, observational study with subjective inclusion and exclusion criteria. Patients lost to follow up were excluded from the results. A high proportion (a third) of included patients had an underlying pulmonary malignancy. Minimal numbers of patients required mechanical ventilation.
			Specificity	0.74% (95% CI 0.65 to 0.81).	
			AVDSf by diagnosis	AVDSf was significantly higher in patients with PE than those without (0.48 vs 0.35, p<0.001).	
			AUC	0.74 (95% CI 0.65 to 0.82).	
Yücel *et al*, 2020, Turkey (3).	100 ED patients presenting with symptoms of PE who had a positive d-dimer or a high clinical risk prediction score. All patients had AVDSf calculated and compared to a reference standard diagnosis.	Level 3b. Single-centre observational study.	Sensitivity	0.81 (95% CI NR)	Single-centre, observational study. Only patients at high risk for PE were included Main analysis and discussion focused on AVDSf in combination with risk-stratification tools although patients with a negative d-dimer were excluded. 50% of patients were excluded, implying potential convenience sample or selection bias.
			Specificity	0.63 (95% CI NR)	
			AVDSf by diagnosis	AVDSf was significantly higher in patients with PE than those without (0.217 vs 0.098).	
			AUC	0.734 (95% CI NR)	

Table 1: Summary of relevant papers

Conclusions

Overall, the studies found that AVDSf was significantly higher in patients with PE than without. However there is significant heterogeneity in the studies to date and there is no clear cut-off value for the AVDSf that would be used in a 'rule-out' protocol. Diagnostic accuracy was improved when AVDSf was applied to stable patients with a low pretest probability, through Wells scoring or d-dimer measurement. Our review found that there is insufficient evidence to support using AVDSf to diagnose acute PE given the low sensitivity and specificity. In particular, we found no evidence to support using AVDSf to exclude or confirm the diagnosis of PE in critically ill patients with a high pretest probability.

References

(1) Manara A, D'hoore W, Thys F. Capnography as a diagnostic tool for pulmonary embolism: a meta-analysis. *Ann Emerg Med* 2013; 62: 584-91.

(2) Yüksel M, Pekdemir M, Yilmaz S, *et al.* Diagnostic accuracy of noninvasive end-tidal carbon dioxide measurement in emergency department patients with suspected pulmonary embolism84-90. *Turk J med Sci* 2016; 46:84-90.

(3) Songur Yücel Z, Metin Aksu N, Akkas M. The combined use of end-tidal carbon dioxide and alveolar dead space fraction values in the diagnosis of pulmonary embolism. *Pulmonology* 2020; 26: 192-7