Appendix A: Summary of evidence from surveillance

2022 exceptional surveillance: NICE response to HSIB report on diagnosis and treatment of pulmonary embolism in emergency departments

(NICE guidelines NG158 and NG191)

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Topic 4: D-dimer result thresholds and the Wells score for patients with COVID-19

Tables 1 and 2 below include details of the 9 identified studies relevant to Wells score and D-dimer tests for patients with COVID-19 and suspected PE.

Table 1: studies assessing D-dimer tests in patients with suspected PE

Text citation	Objective	Study design	Population	% of patients with PE	D-dimer with PE	D-dimer without PE	Optimal D-dimer threshold	Sens.	Spec.	Conclusion
Mikhjian G et al	To examine the utility of the quantitative D-dimer lab marker	Retrospective study	426 patients with COVID-19	18.50%	9.15 mug./mL	2.95 mug./mL	< 0.89 mug./mL	100%	27.95%	Results support the utilisation of alternative D-dimer thresholds to exclude PE in COVID-19 patients. Based on these findings, providers may be able to observe increased D-dimer cut-off values to reduce unnecessary pulmonary CT angiography scans.
Riyahi S et al	To determine the incidence of PE in COVID-19 and its associations with clinical and laboratory parameters	Retrospective study across 4 hospitals	413 patients with COVID-19	25%	NR	NR	>1600 ng/mL	100%	62%	D-dimer>1600ng/mL was sensitive for identifying which patients need CTPA.

Text citation	Objective	Study design	Population	% of patients with PE	D-dimer with PE	D-dimer without PE	Optimal D-dimer threshold	Sens.	Spec.	Conclusion
Planquette B et al	To derive a new algorithm with specific D-dimer threshold in COVID-19 patients	Multicenter retrospective observational cohort study across five urban and suburban EDs in the same health care system	773 patients with COVID-19	NR	NR	NR	900 ng/mL threshold when lung damage <50%	98.2%	28.4%	The Co-LEAD algorithm safely excludes PE, and allows reducing the use of CTPA among COVID-19 patients. Further prospective studies are necessary to validate this strategy.
As above							1700 ng/mL when lung damage extent was >=50%	96.7%	39.2%	
Elberts S et al	To evaluate the test characteristics of D-dimer for pulmonary embolism (PE)	Multicenter, retrospective cohort study	1158 patients who underwent CTPA had D-dimer and	N/A	NR	NR	662 D-dimer units	100%	59%	Results did not find a significant difference in sensitivity of D-dimer for PE due to concomitant COVID-19 infection. Further

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	in patients with a concurrent diagnosis of COVID-19		COVID-19 testing							study is required to determine if PE can safely be excluded based on D-dimer results alone in patients with suspected or proven COVID-19 or if adjusted D-dimer levels could have a role in management.
Estrada VH et al	To determine the operational characteristics of D-dimer as a diagnostic method for PE in patients with COVID-19 treated at a university hospital	Diagnostic test study	209 patients with COVID-19 with suspected PE	14.4%	2888 ng/mL	1114 ng/mL	2.281 ng/mL	60%	76%	D-dimer does not have appropriate characteristics to be used alone for the diagnosis PE in patients with severe COVID-19. It can be used as part of a rational diagnostic process, being just as specific as the patient's signs and symptoms.

Text citation	Objective	Study design	Population	% of patients with PE	D-dimer with PE	D-dimer without PE	Optimal D-dimer threshold	Sens.	Spec.	Conclusion
Brem LF et al	To establish an optimal D-dimer cut-off to predict the occurrence of PE	Retrospective study	84 patients with COVID-19 with suspected PE who underwent a CTPA	36.90%	14 680 ng/mL	2980 ng/mL	2600 ng/mL	90.30%	Not reported	A D-dimer cut-off value of 2600 ng/mL is a significant predictor of PE in COVID-19-patients.
Revel MP et al	To identify which level of D-dimer would allow the safe exclusion of PE in COVID-19 patients presenting to ED	Retrospective study	781 COVID-19 patients who had CTPA following D-dimer dosage within 48h of presentation	7.70%	4013 ng/mL	1198 ng/mL	500 ng.mL	90%	Not reported	The same D-Dimer thresholds as those validated in non-COVID outpatients should be used to safely rule out PE. Using higher D-dimer cut-offs could have avoided more CTPAs, but would have lowered the sensitivity and increased the failure rate.
Ventura-Diaz S et al	To establish a new cut-off	Retrospective study	242 COVID-19 patients	30%	22,494 ng/mL	15,705 ng/mL	2903 ng/mL	81%	Not reported	A higher threshold (2903 ng/mL) for D-

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	value which accurately determines when a CTPA is needed in patients with suspected PE		who underwent a CTPA due to suspected PE							dimer could predict the risk of PE in COVID-19 patients with a sensitivity of 81%.

Abbreviations: PE – pulmonary embolism; sens. – sensitivity; spec. –specificity

Table 2: studies assessing Wells score combined with a D-dimer test in patients with suspected PE

Text citation	Objective	Study design	Population	% of patients with PE	Wells score >2	Optimal D-dimer threshold	Sens.	Spec.	Conclusion
Polo Friz et al	To investigate the association of clinical and biochemical variables with a confirmed diagnosis of PE	Retrospective cohort study	41 patients hospitalised for non-critical COVID-19 who presented	20%	Did not associate with confirmed PE	2454 ng/mL	63%	73%	Traditional diagnostic tools to identify high PE pre-test probability patients do not seem to be clinically useful. These results support the use of a high index of suspicion for

Text citation	Objective	Study design	Population	% of patients with PE	Wells score >2	Optimal D-dimer threshold	Sens.	Spec.	Conclusion
	in these subjects		with clinical deterioration						performing CTPA to exclude or confirm PE as the most appropriate diagnostic approach in this clinical setting.

Abbreviations: PE – pulmonary embolism; sens. – sensitivity; spec. –specificity

References

Table 1

Brem LF,. et al (2021) Diagnostic Accuracy of D-Dimers for Predicting Pulmonary Embolism in COVID-19-Patients. Clin Appl Thromb Hemost.; 27: doi: 10.1177/10760296211057901

Elberts S,. et al (2021) The impact of COVID-19 on the sensitivity of D-dimer for pulmonary embolism. Acad Emerg Med. 28:1142–1149. doi: 10.1111/acem.14348

Estrada VH,. et al (2022) Rethinking D-dimer's role in the diagnosis of pulmonary thromboembolism in patients with COVID-19: analysis of a diagnostic test study. J Thrombo Cir. 8:191. doi: 10.35248/2572-9462.22.8.191.

Mikhjian G,. et al (2021) Using Quantitative D-Dimer to Determine the Need for Pulmonary CT Angiography in COVID-19 Patients. *SMRJ*. 6(1). doi: 10.51894/001c.18652

Planquette B,. et al. (2022) Adjusting D-dimer to lung disease extent to exclude Pulmonary Embolism in COVID-19 patients (Co-LEAD). Thrombosis and Haemostasis. doi: 10.1055/a-1768-4371.

Revel MP,. et al (2022) What level of D-dimers can safely exclude pulmonary embolism in COVID-19 patients presenting to the emergency department? Eur Radiol;32(4):2704-2712. doi: 10.1007/s00330-021-08377-9

Riyahi S,. et al (2021). Pulmonary Embolism in Hospitalized Patients with COVID-19: A Multicenter Study. Radiology; 301: E426–E433. doi: 10.1148/radiol.2021210777

Ventura-Diaz S,. et al (2020) A higher D-dimer threshold for predicting pulmonary embolism in patients with COVID-19: a retrospective study. Emerg Radiol. 27(6):679-689. doi: 10.1007/s10140-020-01859-1

Table 2

Polo Friz,. et al (2021) Acute pulmonary embolism in patients presenting pulmonary deterioration after hospitalization for non-critical COVID-19. Internal Medicine Journal 51. 1236–1242. doi: 10.1111/imj.15307