

## Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study

Righini M, Van es J, Den exter PL, et al. JAMA. 2014;311(11):1117-24.

## 背景

- 臨床懷疑急性肺栓塞 ( pulmonary embolism · PE ) 時，診斷決策的重要步驟為量測 D-dimer 。
- 對老年患者實用價值有限。

## 研究目的

- 前瞻性評估
- 依年齡校正之 D-dimer 邊界值是否能提高疑肺栓塞之老年患者的診斷率？
- $\geq 50y/o$ ，邊界值定為「年齡 \*10」

## 方法

• 研究設計及設定 (2010-01-01 ~ 2013-02-28)  
 跨醫學中心、跨國之前瞻性研究 (計有比利時、法國、荷蘭、瑞士共 19 家醫學中心)

- 介入方式  
 臨床懷疑肺栓塞之急診患者  
 ( 1 ) simplified-revised Geneva score 或 2-level Wells score → clinical probability  
 ( 2 ) 高敏感量測 D-dimer  
 ( 3 ) 電腦斷層肺動脈血管攝影 ( CTPA )  
 傳統邊界值 ( 500mcg/L )  $\leq$  D-dimer 量測值 < 年齡校正邊界值  
 → 不做 CTPA、不治療、追蹤三個月。

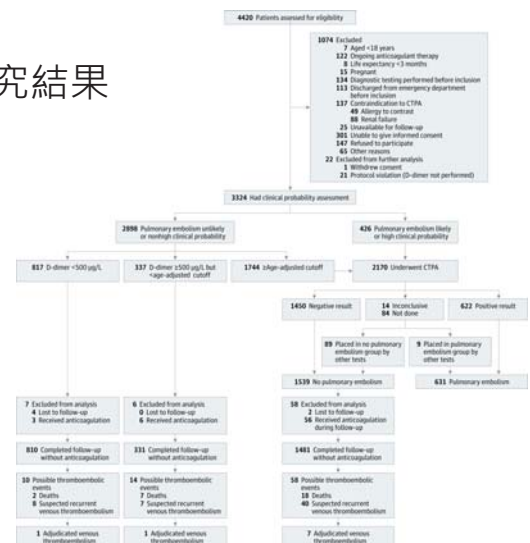
• 主要研究結果：此診斷流程之失敗率  
 患者在三個月追蹤期內確認為 thromboembolic event  
 ( 均因 D-dimer 量測值低於年齡校正邊界值而沒有使用抗凝血劑 )

Table 1. The Simplified, Revised Geneva Score and the 2-Level Wells Score

Score	Points
Simplified, revised Geneva score <sup>11</sup>	
Age >65 y	1.0
Previous history of PE or DVT	1.0
Surgery or fracture within 1 mo	1.0
Active malignancy	1.0
Unilateral leg pain	1.0
Hemoptysis	1.0
Heart rate, beats/min	
75-94	1.0
$\geq 95$	2.0
Pain on lower-limb deep venous palpation and unilateral edema	1.0
Clinical probability	
Low	0-1
Intermediate	2-4
High	$\geq 5$
2-Level Wells score <sup>12</sup>	
Clinical signs and symptoms of DVT	3.0
Immobilization or surgery in the previous 4 wk	1.5
Heart rate greater than 100 beats/min	1.5
Previous history of PE or DVT	1.5
Hemoptysis	1.0
Malignancy	1.0
Alternative diagnosis is less likely than PE	3.0
Clinical probability	
Unlikely	$\leq 4$
Likely	$> 4$

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism.

## 研究結果



**Table 2. Characteristics of Included Patients**

Characteristics	No. (%) (n = 3324)
Women	1887 (56.8)
Age, median (IQR), y	63 (53-74)
Personal history of VTE	466 (14.0)
Active malignancy	429 (12.9)
Surgery within 1 month	392 (11.8)
Estrogen use	183 (5.5)
Chest pain	1608 (48.3)
Dyspnea	2092 (62.9)
Syncope	263 (7.9)
Hemoptysis	134 (4.1)
Heart rate, mean (SD), beats/min	87.1 (19.6)
Respiratory rate, mean (SD), beats/min	19.2 (6.2)

Abbreviations: IQR, interquartile range; VTE, venous thromboembolism.

## 研究結果

- 此研究共納入 3346 位疑肺栓塞患者
  - 肺栓塞盛行率為 19%
- clinical probability 為 nonhigh 或 unlikely 的患者有 2898 位
- 75 歲以上患者有 766 位
  - 其中 673 位 (87.9%) 為 nonhigh clinical probability
  - 以年齡校正邊界值 (而非傳統邊界值 500mcg/L) 可將依
  - D-dimer < 500mcg/L: 43/673 ( 6.4% [95% CI : 4.8%-8.5%] )
  - age-adjusted D-dimer: 200/673 ( 29.7% [95% CI : 26.4%-33.3%] )
    - 無人在追蹤期間確診為 venous thromboembolism (0/195 patients (0.0% [95% CI, 0.0%-1.9%]))

**Table 3. Study Results According to D-Dimer Assays**

D-Dimer Assay	Low/Intermediate or Unlikely Clinical Probability, No. of Patients	D-Dimer < 500 µg/L	3-mo Thromboembolism Risk		D-Dimer ≥ 500 µg/L and < Age-Adjusted Cutoff	3-mo Thromboembolism Risk	
			No. of Events/ Total Patients	% (95% CI)		No. of Events/ Total Patients	% (95% CI)
VIDAS D-Dimer Exclusion	1345	423	0/417	0.0 (0.0-0.9)	130	0/127	0.0 (0.0-2.9)
Innovance D-Dimer	838	202	1/202	0.5 (0.1-2.8)	103	1/103	1.0 (0.2-5.3)
STA-Liatest D-Dimer	389	132	0/132	0.0 (0.0-2.8)	49	0/47	0.0 (0.0-7.6)
D-Dimer HS 500	185	32	0/31	0.0 (0.0-11.0)	23	0/23	0.0 (0.0-14.3)
Second-generation Tina-quant	128	26	0/26	0.0 (0.0-12.9)	32	0/31	0.0 (0.0-11.0)
Cobas h 232	13	2	0/2	0.0 (0.0-65.8)	0		
Total	2898	817	1/8	0.1 (0.0-0.7)	337	1/331	0.3 (0.1-1.7)

## 結論

- 併用 pretest clinical probability 評估工具及 Age-adjusted D-dimer cutoff
  - 可排除較多疑肺栓塞患者
  - 繼發靜脈血栓栓塞之可能性低
- 成本效益及是否能提高照護品質尚待評估

## 討論

- age-adjusted cutoff 的好處
  - 很好記 (年齡 \*10 )
  - 減少 radiation 、 contrast 及 anticoagulant therapy
    - 老人常見 renal impairment 甚或 contrast-induced nephropathy
    - 75 歲以上，選擇 age-adjusted cutoff 可排除的疑似患者較 500mcg/L 多五倍
  - 不影響病患安全

- 研究缺陷
  - 非單一介入方式
    - 2 種 pretest probability assessment tools
    - 6 種 D-dimer assays
  - 非 randomised clinical study
    - 沒有對照組 ( 500mcg/L )
  - D-dimer = 500mcg/L ~ age-adjusted cutoff
    - 七名死亡患者僅一位有解剖
  - 肺栓塞盛行率比其它北美研究高