

# Underuse of risk assessment and overuse of CTPA in patients with suspected pulmonary thromboembolism

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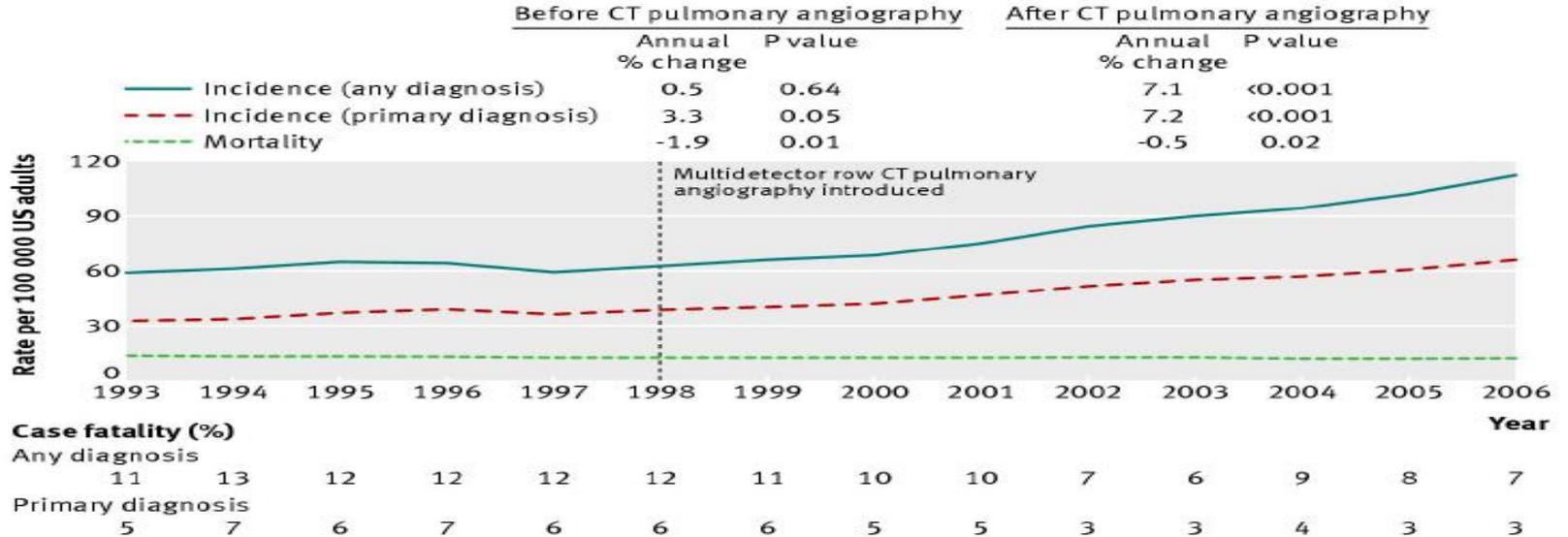
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# Background

- PTE potentially fatal but treatable disease which can present atypically with non-specific symptoms and signs
- CTPA highly sensitive and specific in diagnosing PTE
  - but too sensitive in detecting small sub-segmental thrombi of no clinical significance



# Background

- Emerging over overuse of CTPA
  - up to a third of CTPA requests in emergency departments (EDs) unwarranted
    - » *Venkatesh et al. Arch Intern Med 2012*
- Overuse incur avoidable harms of radiation, contrast nephropathy, allergies, and over-treatment of clinically inconsequential PTE with anticoagulation and associated bleeding risk

# Background

- Several prediction rules have been developed and validated for use in patients with suspected PTE in multiple settings
  - » *Wells et al. Ann Intern Med 2001; 135: 98-107*
  - » *Le Gal et al. Ann Intern Med. 2006 ;144(3):165-71.*
  - » *Ceriani et al. J Thromb Haemost. 2010;;8(5):957-70*
  - » *Miniati et al. Am J Med. 2003;114(3):173-9.*
- Studies have demonstrated a reduction in requests for imaging when pre-test use of clinical prediction rules is combined with rapid plasma D-dimer assays of cross-linked fibrin degradation products
  - » *Righini et al. J Thromb Haemost 2008; 6: 1059-1071.*
  - » *Wells et al. Ann Intern Med 2001; 135: 98-107*
- Commonly used algorithm for identifying patients at low risk of PTE is a modified (two-level) Wells score (mWS)  $\leq 4$  and a quantitative D-dimer test result below a pre-defined cut-off value
  - observed incidence of death or recurrent presentation with PTE in such cases  $< 1\%$ .
    - » *Pasha et al Thromb Res 2010; 125: e123-e127*

# Aims

- To determine the rate of use and relative diagnostic utility of clinical prediction rules and the rate of use of D-dimer assays in unselected patients with suspected PTE who underwent CTPA in a tertiary hospital
- To determine the extent of avoidable overuse of CTPA in patients with low pre-test probability of PTE

# Methods

- Retrospective study of all consecutive patients aged  $\geq 18$  years who underwent CTPA at PAH between August 1<sup>st</sup> and December 31<sup>st</sup> 2013
  - in-patients or patients presenting to, and discharged from, the ED
  - ascertained by interrogating electronic radiology database for all CTPA requests
  - CTPAs were performed using a 256 slice helical CT scanner (Siemens Flash CT, Phillips) with 50-75 ml of optiray contrast medium
  - D-dimer assay: Instrumentation Laboratory (IL)-test D-dimer, an automated quantitative latex enhanced immunoassay, for which a normal result was defined as a value up to 0.243.

# Methods

- Data collected from medical records and electronic investigational databases pertaining to demographics (age, sex), clinical signs and symptoms, risk factors for venous thromboembolism (VTE), results of D-dimer assays (when performed) and findings on CTPA.
- Pre-test risk scores for PTE calculated retrospectively for each patient for each of 3 prediction rules by researcher (MP) blinded to the CTPA result, and expressed dichotomously as low (PTE unlikely) or high (PTE likely) risk scores.
  - Modified Wells score (mWS), revised Geneva score, PISA model
- Sensitivity, specificity, LRs, predictive value and AUC calculated for each rule based on dichotomised scores, using CTPA results as the reference standard for PTE

# Methods

- Potentially avoidable overuse of CTPA
  - imaging in a low risk patient without prior D-dimer testing (after adjusting for the false negative rate for PTE in low risk patients) OR
  - imaging in a low risk patient with negative D-dimer
- Low risk was defined as a mWS  $\leq 4$  in keeping with current guidelines
  - » 2014 ESC Guidelines on the Diagnosis and Management of Acute Pulmonary Embolism
- Diagnostic yield of CTPA was measured in each of four categories of imaging: low risk, no D-dimer; low risk + D-dimer (-); low risk + D-dimer (+); and high risk

# Methods

## *Statistical analysis*

- Chi-square Fisher exact test and t-tests were used to compare proportions and normally distributed means involving binary or continuous variables respectively.
- Performance characteristics for each prediction rule applied to individual patients were compared using McNemar's test for paired data.
- Kappa statistics were used to assess level of agreement.
- Statistical analysis was performed using SPSS statistical package 2013 version 22.0

# Results

- 344 patients
- 53 patients (15.4%) diagnosed with PTE
  - all had thrombus involving at least segmental pulmonary artery branches, with 13 (3.8%) showing central artery involvement
- Use of pre-test clinical prediction rule documented in only 5.0% of cases
- Of 269 low risk patients (78.2% of total cohort) with  $mWS \leq 4$ 
  - 30 (11.1%) had PTE on CTPA
  - 63 (23.4%) had a D-Dimer assay performed
    - 0/8 with a negative D-dimer had PTE
    - 6/57 (10.7%) with a positive D-dimer had PTE
- Of 75 high risk patients with a  $mWS > 4$ 
  - 23 (30.7%) had PTE on CTPA ( $p < 0.001$ )

# Results

Variable	Pulmonary Embolism		P-value
	No	Yes	
n (344)	290	54	
age	56.25 (54.32-58.17)	59 (54.29-63.71)	0.2
HR	88.21 (85.69-90.73)	96.61 (89.28-103.94)	0.03
BPSys	128.51 (125.93-131.09)	127.13 (120-134.25)	0.73
BPDiaast	73.12 (71.47-74.76)	73.5 (69.1-77.9)	0.86
RR	19.66 (19.12-20.2)	21.04 (19.63-22.44)	0.02
TEMP	36.56 (36.47-36.66)	36.63 (36.44-36.83)	0.5
Well.score	6.42 (5.91-6.93)	9.15 (7.87-10.42)	0
Male (%)	49	53.7	0.62
Malignancy (%)	27.2	20.4	0.38
Postoperative (%)	19	22.2	0.71
Immobilization (%)	9	13	0.51
Chest.Pain (%)	49.7	50	1
Dyspnoea (%)	56.6	74.1	0.02
Cough (%)	17.9	20.4	0.82
Hemoptosys (%)	4.5	9.3	0.27
Previous.DVT (%)	49	53.7	0.62
Pedal.edema (%)	10.3	22.2	0.03

# Results

Score	Modified Wells score <sup>1</sup>	Revised Geneva score <sup>2</sup>	PISA score <sup>3</sup>
Sensitivity	0.43	0.57	0.22
Specificity	0.82	0.59	0.88
Positive likelihood ratio	2.43	1.41	1.83
Negative likelihood ratio	0.69	0.71	0.89
Positive predictive value <sup>4</sup>	0.31	0.20	0.19
Negative predictive value <sup>4</sup>	0.89	0.88	0.87
Area under the ROC curve (AUC)	0.67 (0.59-0.75)	0.61 (0.56-0.70)	0.58 (0.49-0.66)

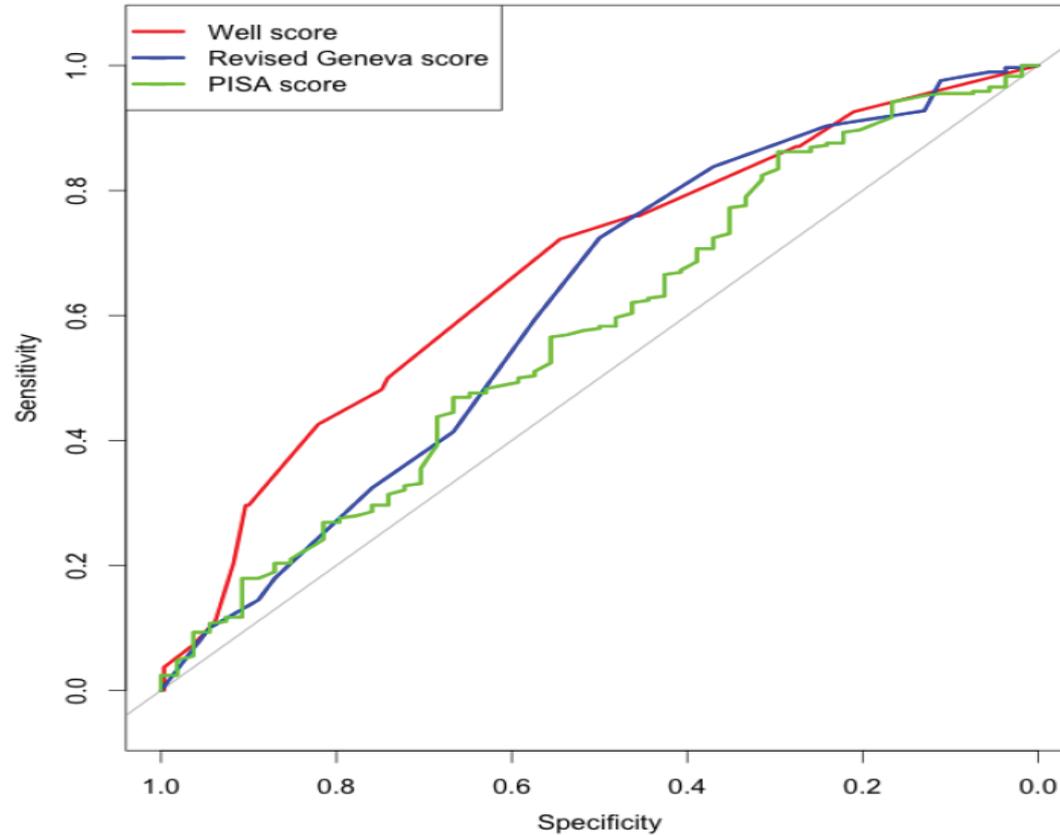
<sup>1</sup>Using a cut-point for Modified Wells score (mWS) of  $\leq 4$  = low risk patients ('negative' mWS),  $> 4$  = high risk patients ('positive' mWS)

<sup>2</sup>Using a cut-point for revised Geneva score of  $< 3$  = low risk patients ('negative'),  $\geq 3$  = high risk patients ('positive')

<sup>3</sup>Using a cut-point for PISA score of  $\leq 10\%$  = low risk patients,  $> 10\%$  = high risk patients

<sup>4</sup> Predictive values calculated on prevalence (pre-test probability) of PTE in study patients of 15.4%

# Results



# Results

- 214 patients low risk (61.6% total cohort)
- Defined as being subjected to potentially avoidable CTPA
  - 206 low risk mWS and no D-dimer testing
  - 8 low risk mWS and negative D-dimer
- 24 (11%) had PTE
  - Of 206 with low risk mWS and no D-Dimer NPV = 89%  
ie 11% false negatives = 24 patients
  - Leaves 182 with no PTE
  - Add 8 patients with low risk mWS and negative D-dimer
  - Total of 190 patients with no PTE
  - 55.2% of total cohort; 70.6% of low risk (mWS  $\leq 4$ ) cohort of 269 patients

# Results

Variable	Avoidable imaging		P-value
	No	Yes	
n (344)	132	212	
age	54.39 (51.25-57.53)	58.11 (55.99-60.22)	0.08
HR	91.5 (87.59-95.41)	88.3 (85.2-91.4)	0.17
BPSys	127.05 (123.41-130.7)	129.07 (125.82-132.31)	0.3
BPDiaast	72.98 (70.49-75.48)	73.3 (71.32-75.27)	0.9
RR	20.19 (19.32-21.06)	19.68 (19.06-20.3)	0.62
TEMP	36.58 (36.46-36.71)	36.57 (36.46-36.68)	0.91
Well.score	9.21 (8.28-10.15)	5.37 (4.95-5.8)	0
Male (%)	40.2	55.7	0.01
Malignancy (%)	22	28.8	0.2
Postoperative (%)	22	17.9	0.43
Immobilization (%)	10.6	9	0.75
Chest.Pain (%)	54.5	46.7	0.19
Dyspnoea (%)	59.1	59.4	1
Cough (%)	15.9	19.8	0.44
Hemoptosys (%)	3.8	6.1	0.48
Previous.DVT (%)	40.2	55.7	0.01
Pedal.edema (%)	9.8	13.7	0.38

# Summary

- Less than 1 in 8 patients with suspected PTE had PTE on CTPA
- Very little use of clinical prediction rules in estimating pre-test probability despite more than three quarters of the cohort being low risk based on mWS
- Of 3 clinical prediction rules applied to unselected 'real-world' patients, all showed modest predictive accuracy of no more than 65%-70% (based on AUCs) with mWS being the most accurate
  - Predictive values indicated all rules were most useful in reducing the risk of PTE to less than 12% in patients with low risk scores
- D-dimer assays requested in only 1 in 4 low risk patients
- CTPA was likely overused in more than half the total cohort and in almost three quarters of patients at low risk
  - Male gender and previous DVT were associated with more avoidable imaging.

# Discussion

- Drivers of overuse
  - Clinician concerns about missing a potentially life threatening PTE
  - Desire to request investigations that exclude other pathologies simultaneously even if clinical circumstances may not warrant it
  - Penalties for failure to diagnose serious abnormalities but not for overuse of testing
  - Little faith in using clinical prediction rules
  - Under-appreciation of deleterious consequences of over-imaging
    - radiation exposure with carcinogenic risk (especially in younger patients)
    - overtreatment of clinically inconsequential isolated subsegmental emboli

# Discussion

- Comparison with other studies
  - Similar prevalence of PTE overall and in risk subgroups

	Wells <i>et al.</i> 2000 <sup>7</sup> <i>n</i> = 1219 (% cohort)	Chagnon <i>et al.</i> 2002 <sup>8</sup> <i>n</i> = 277	Yap <i>et al.</i> 2007 <sup>9</sup> <i>n</i> = 625	Box Hill Hospital study 2007 <sup>†</sup> <i>n</i> = 138	Box Hill Hospital study 2009 (current study) <i>n</i> = 268	Current study
Low probability	3% (40)	12% (58)	4% (66)	0% (63)	8% (21)	11%
Intermediate probability	20% (52)	40% (38)	13% (31)	22% (33)	11% (63)	
High probability	63% (8)	91% (4)	67% (3)	50% (4)	23% (16)	31%
Overall prevalence	16%	26%	9%	9%	14%	15%

# Discussion

- Comparison with other studies
  - Predictive values of clinical prediction rules similar to those reported from other centres
    - » *Penaloza et al. Ann Emerg Med 2013*
    - » *Ouatu et al. Rev Med Chir Soc Med Nat Iasi 2014*
    - » *Di Marca et al. J Am Geriatr Soc 2015*
  - Overuse rates of CTPA in ED
    - 33% to 71.5% of patients depending on criteria used to determine overuse
      - » *Venkatesh et al. Arch Intern Med 2012;172:1028-1032*
      - » *Perelas et al. Am J Med Qual 2015; 30(6):571-7.*

# Discussion

- Implications for practice
  - Consistent application of clinical prediction rules can reduce use of CTPA in low risk patients
    - Reductions of 6 to 27 percentage points
      - » Ong et al Intern Med J 2012
      - » Murthy et al S Afr Med J 2015
      - » Jimenez et al Thorax 2015
      - » Hoo et al Am J Roentgenol 2011
      - » Crichlow et al Acad Emerg Med 2012
    - But negative studies too
      - » Geeting et al Am J Roentgenol 2016