Cohort Study
Potential PURL Review Form
PURL Jam Version
PURLs Surveillance System
Family Physicians Inquiries Network

SECTION 1: Identifying Information for Nominated Potential PURL
[to be completed by PURLs Project Manager]


C. First date published study available to readers: 5/23/2017

D. PubMed ID: 28549662

E. Nominated By: Jim Stevermer

F. Institutional Affiliation of Nominator: University of Missouri

G. Date Nominated: 8/9/2017

H. Identified Through: POEMs

I. PURLs Editor Reviewing Nominated Potential PURL: Dean Seehusen

J. Nomination Decision Date: 8/16/2017

K. Potential PURL Review Form (PPRF) Type: Cohort Study

L. Assigned Potential PURL Reviewer: Robert Oh

M. Reviewer Affiliation: Madigan Army Medical Center

A. Abstract: BACKGROUND:
Validated diagnostic algorithms in patients with suspected pulmonary embolism are often not used correctly or only benefit subgroups of patients, leading to overuse of computed tomography pulmonary angiography (CTPA). The YEARS clinical decision rule that incorporates differential D-dimer cutoff values at presentation, has been developed to be fast, to be compatible with clinical practice, and to reduce the number of CTPA investigations in all age groups. We aimed to prospectively evaluate this novel and simplified diagnostic algorithm for suspected acute pulmonary embolism.

METHODS:
We did a prospective, multicentre, cohort study in 12 hospitals in the Netherlands, including consecutive patients with suspected pulmonary embolism between Oct 5, 2013, to July 9, 2015. Patients were managed by simultaneous assessment of the YEARS clinical decision rule, consisting of three items (clinical signs of deep vein thrombosis, haemoptysis, and whether pulmonary embolism is the most likely diagnosis), and D-dimer concentrations. In patients without YEARS items and D-dimer less than 1000 ng/mL, or in patients with one or more YEARS items and D-dimer less than 500 ng/mL, pulmonary embolism was considered excluded. All other patients had CTPA. The primary outcome was the number of independently adjudicated events of venous thromboembolism during 3 months of follow-up after pulmonary embolism.

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embolism was excluded, and the secondary outcome was the number of required CTPA compared with the Wells' diagnostic algorithm. For the primary outcome regarding the safety of the diagnostic strategy, we used a per-protocol approach. For the secondary outcome regarding the efficiency of the diagnostic strategy, we used an intention-to-diagnose approach. This trial is registered with the Netherlands Trial Registry, number NTR4193.

FINDINGS:
3616 consecutive patients with clinically suspected pulmonary embolism were screened, of whom 151 (4%) were excluded. The remaining 3465 patients were assessed of whom 456 (13%) were diagnosed with pulmonary embolism at baseline. Of the 2946 patients (85%) in whom pulmonary embolism was ruled out at baseline and remained untreated, 18 patients were diagnosed with symptomatic venous thromboembolism during 3-month follow-up (0.61%, 95% CI 0.36-0.96) of whom six had fatal pulmonary embolism (0.20%, 0.07-0.44). CTPA was not indicated in 1651 (48%) patients with the YEARS algorithm compared with 1174 (34%) patients, if Wells' rule and fixed D-dimer threshold of less than 500 ng/mL would have been applied, a difference of 14% (95% CI 12-16).

INTERPRETATION:
In our study pulmonary embolism was safely excluded by the YEARS diagnostic algorithm in patients with suspected pulmonary embolism. The main advantage of the YEARS algorithm in our patients is the absolute 14% decrease of CTPA examinations in all ages and across several relevant subgroups.

FUNDING:
This study was supported by unrestricted grants from the participating hospitals.

SECTION 2: Critical Appraisal of Validity
[to be completed by the Potential PURL Reviewer]

A. The study address an appropriate and clearly focused question.  Well covered
   Comments: Question: Is there a simplified accurate algorithm for evaluation of PE that may also reduce need for CT?

B. The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.  Not applicable
   Comments:

C. The study indicates how many of the people asked to take part in it in each of the groups being studied.  Well covered
   Comments: Figure 2

D. The likelihood that some eligible subjects might have the outcome at the time of enrollment is assessed and taken into account in the analysis.  Adequately addressed
   Comments:

E. What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?
   151 excluded (4.1%), 5 lost to follow-up (<1%)
F. Comparison is made between full participants and those lost to follow up, by exposure status.
   Not applicable
   Comments:

G. The outcomes are clearly defined. Well covered
   Comments: Primary outcome of PE diagnosis with secondary outcome # of CTs.

H. The assessment of outcome is made blind to exposure status. Adequately addressed
   Comments: No blinding performed but this is stated.

I. Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome. Not applicable
   Comments:

J. What are the key findings of the study? PE is safely excluded by the YEARS algorithm and following this algorithm would theoretically lessen the number of CT scans by 14% compared to traditional means

K. How was the study funded? Any conflicts of interest? Any reason to believe that the results may be influenced by other interests? Unrestricted grants from participating hospitals. No conflicts or influences suspected.

SECTION 3: Review of Secondary Literature
[to be completed by the Potential PURL Reviewer]
[to be revised by the Pending PURL Reviewer as needed]

Citation Instructions: For up-to-date citations, use style modified from http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite & AMA style. Always use Basow DS on editor & current year as publication year.

Example: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: http://www.upToDate.com. {Insert date modified if given.} Accesses February 12, 2009. [whatever date PPRF reviewer did their search.]

For DynaMed, use the following style:

A. DynaMed excerpts

- Clinical prediction rules: for patients with or without risk factors for PE and for patients with high-suspicion of PE, use clinical assessment of likelihood of pulmonary embolism using validated
prediction rules and clinical judgement to distinguish between low-, intermediate-, and high-risk PE
   – clinical decision rules may be comparable to clinical gestalt of experienced clinician in diagnosing PE
     - when combined with D-dimer testing, both diagnostic approaches associated with about 85% sensitivity and 99% negative predictive value (level 2 [mid-level] evidence)
     - they appear to have similar ability to classify patients as having low, medium, or high risk for PE (level 3 [lacking direct] evidence)
     - clinical decision rules can avoid unnecessary and potentially harmful tests without risk of underdiagnosis


C. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)
   Clinical decision rules combining D-dimer are effective in diagnosing PE

D. UpToDate excerpts
   - Computed tomography pulmonary angiography — For most patients with suspected PE, CTPA, also called chest CT angiogram with contrast, is the first-choice diagnostic imaging modality because it is sensitive and specific for the diagnosis of PE, especially when incorporated into diagnostic algorithms, and alternate diagnoses may be discovered using this modality [94]. The imaging technology is widely available and, in most settings, the exam can be performed on an urgent or emergent basis
   - Results interpretation — Support for our preference for CTPA-based algorithms is derived from a prospective, multicenter cohort study (Christopher study) of 3306 patients with clinically suspected PE [51]. Patients were from an inpatient or outpatient setting and categorized according to the modified Wells score as PE "likely" (score >4) or PE "unlikely" (score ≤4) (table 2) (calculator 1). Patients classified as PE unlikely underwent sensitive D-dimer testing; PE was considered excluded when the D-dimer level was <500 ng/mL (fibrinogen equivalent units). PE unlikely patients who had a D-dimer level ≥500 ng/mL (fibrinogen equivalent units) and PE likely patients underwent CTPA.


F. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)
   CTPA-based algorithms utilizing D-dimer are effective in diagnosing PE.

G. Other excerpts (USPSTF; other guidelines; etc.)
H. Citations for other excerpts

I. Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences)

SECTION 4: Conclusions
[to be completed by the Potential PURL Reviewer]
[to be revised by the Pending PURL Reviewer as needed]

A. **Validity**: Are the findings scientifically valid? Yes

B. If A was coded “Other, explain or No”, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results?

C. **Relevance**: Is the topic relevant to the practice of family medicine and primary care practice, including outpatient, inpatient, obstetrics, emergency and long-term care? Are the patients being studied sufficiently similar to patients cared for in family medicine and primary care in the US such that results can be generalized? Yes

D. If C was coded “Other, explain or No”, please provide an explanation.

E. **Practice changing potential**: If the findings of the study are both valid and relevant, are they not a currently widely accepted recommendation among family physicians and primary care clinicians for whom the recommendation is relevant to their patient care? Or are the findings likely to be a meaningful variation regarding awareness and acceptance of the recommendation? Yes

F. If E was coded as “Yes”, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

G. **Applicability to a Family Medical Care Setting**:
   Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc.), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, education or counseling a patient; or creating a system for implementing an intervention? Yes

H. Please explain your answer to G.

I. **Immediacy of Implementation**:
   Are there major barriers to immediate implementation? Would the cost or the potential for
reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug, or other essentials available on the market?  Yes

J. If I was coded “Other, explain or No”, please explain why.

K. **Clinically meaningful outcomes or patient oriented outcomes:**
   Do the expected benefits outweigh the expected harms? Are the outcomes patient oriented (as opposed to disease oriented)? Are the measured outcomes, if true, clinically meaningful from a patient perspective?  Yes

L. If K was coded “Other, explain or No”, please explain why.

M. In your opinion, is this a pending PUf?  Yes
   1. Valid: Strong internal scientific validity; the findings appear to be true.
   2. Relevant: Relevant to the practice of family medicine.
   3. Practice Changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
   4. Applicability in medical setting.
   5. Immediacy of implementation

N. Comments on your response for question M.