原因不明のCOPD急性増悪における肺塞栓症の有病率

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PGY4

栗栖美由希

Prevalence and Localization of Pulmonary Embolism in Unexplained Acute Exacerbations of COPD

A Systematic Review and Meta-analysis

Floor E. Aleva, MD; Lucas W. L. M. Voets, BSc; Sami O. Simons, MD, PhD; Quirijn de Mast, MD, PhD; André J. A. M. van der Ven, MD, PhD; and Yvonne F. Heijdra, MD, PhD

Chest.2017;151(3):544-554

背景

・COPDは近年、世界の死亡率・罹患率の原因の第3位

N Engl J Med.2013;369(5):448-457

・COPDの急性増悪（AE-COPD）は以下の３点に関わる重要な病態
①呼吸器症状の増悪
②呼吸機能の低下
③予後の悪化

・主要なAE-COPDの原因は感染症に対する反応
→しかし、約30%のAE-COPDは原因不明

Am J Respir Crit Care Med.1996;154(4 Pt 1):959-967

COPDのstage

Table 2.5. Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV_1)

In patients with $FEV_1/FVC < 0.70$:

GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

GOLD guideline updated 2015

COPDのstage別増悪率、入院率、死亡率

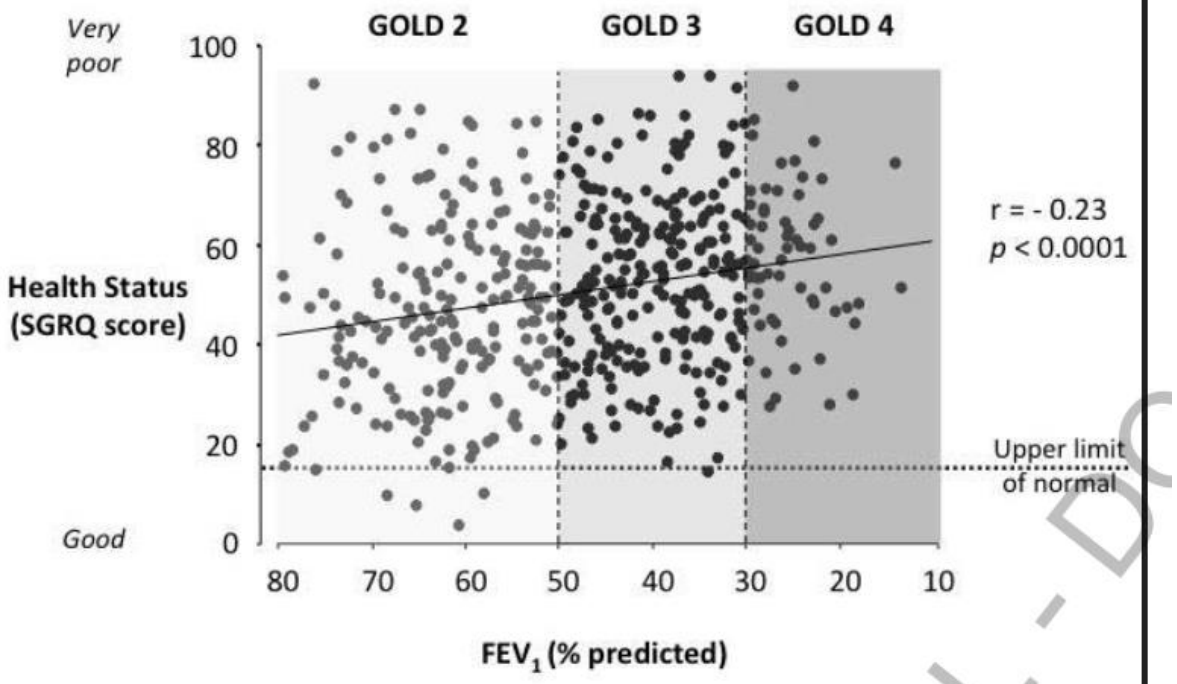
Table 2.6: RISK IN COPD: Placebo-limb data from TORCH[134*], Uplift[133†] and Eclipse[132 ≠]

GOLD spirometric level	Exacerbations (per year)*†≠	Hospitalizations (per year)* ≠	3-year Mortality*†
GOLD 1: Mild	?	?	?
GOLD 2: Moderate	0.7 – 0.9	0.11 – 0.2	11%*†
GOLD 3: Severe	1.1 – 1.3	0.25 – 0.3	15%*
GOLD 4: Very severe	1.2 – 2.0	0.4 – 0.54	24%*

GOLD guideline updated 2015

COPDのstage別Health-related QOL

Figure 2.2. Relationship Between Health-related Quality of Life, Post-bronchodilator FEV_1 and GOLD Spirometric Classification (Adapted from Jones[127])



GOLD guideline updated 2015

背景

COPD and Incident Cardiovascular Disease Hospitalizations and Mortality: Kaiser Permanente Medical Care Program*

Stephen Sidney, MD, MPH; Michael Sorel, MPH; Charles P. Quesenberry, Jr., PhD; Cynthia DeLuise, RPA-C, MPH; Stephan Lanes, PhD; and Mark D. Eisner, MD, MPH, FCCP

Outcomes	Case Patients, No.	Case Patient Rate*	Control Subjects, No.	Control Subject Rate*	Age-Adjusted Rate Ratio†	Model†‡	Model Excluding CVD Prevalent at Baseline†‡
MI	487	385.8	241	213.8	2.27 (1.95–2.65)	1.81 (1.54–2.12)	1.85 (1.55–2.21)
CHF	138	109.3	32	30.5	4.93 (3.36–7.24)	3.53 (2.38–5.25)	3.50 (2.22–5.50)
Stroke	260	206.0	204	171.6	1.46 (1.21–1.75)	1.25 (1.03–1.51)	1.35 (1.09–1.66)
Pulmonary embolism	29	19.8	12	10.2	2.35 (1.18–4.67)	1.89 (0.93–3.85)	1.54 (0.72–3.31)
Other CVD§	1,407	1,114.7	614	542.0	2.59 (2.35–2.84)	1.96 (1.77–2.16)	1.95 (1.74–2.18)
Any study end points‖	918	727.2	498	434.9	2.09 (1.87–2.33)	1.68 (1.50–1.88)	1.71 (1.51–1.94)
All CVD	2,325	1,842.2	1,112	977.2	2.36 (2.20–2.54)	1.84 (1.70–1.98)	1.84 (1.69–2.00)

*Age-adjusted rate per 100,000 person-years.
†Values given as RR (95% CI).
‡Model includes independent variables age, gender, hypertension, hyperlipidemia, and diabetes.
§Includes all CVD diagnostic codes (ICD-9 codes 390x to 459x) not included in the main study end points (*ie*, the first eight end points on the list in this table).
‖Any study end point refers to the first eight end points on the list in this table.

Chest.2005;128(4)2068-2075

AE-COPDでは他疾患を合併していることが優位に予後に関与する

1996年１月-1999年12月
COPDと診断された45966人
前向き研究

Medical error—the third leading cause of death in the US

Medical error is not included on death certificates or in rankings of cause of death. **Martin Makary** and **Michael Daniel** assess its contribution to mortality and call for better reporting

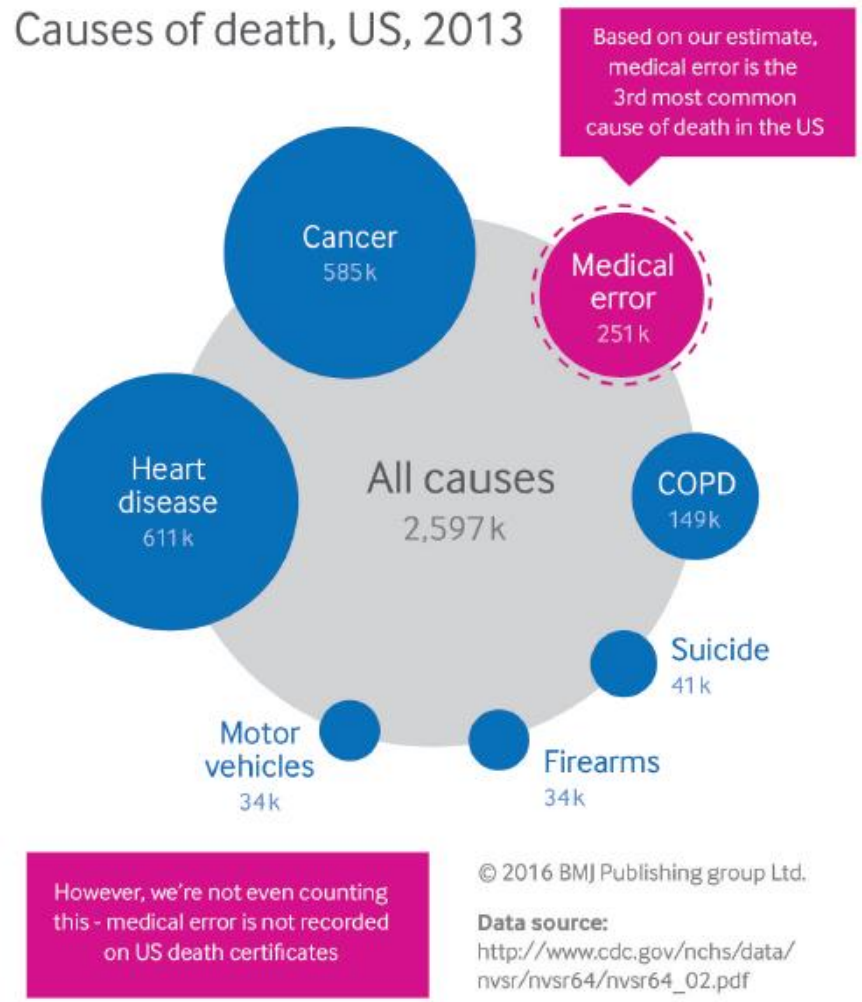


Fig 1 Most common causes of death in the United States, 2013[2]

BMJ 2016;353:i2139 doi: 10.1136/bmj.i2139 (Published 3 May 2016)

背景

- PEは合併症の中でも予後を悪化させる因子

- 過去の研究では合併率は18-25%と報告

Chest.2009 ;135(3):786-793

- 統計学的研究はCOPDにおけるPE合併はオッズ比2.51-5.46とリスク高値
  →一方で関連がないとしている論文も存在

Eur Respir J.2016;47(2):473-481

- 炎症と凝固反応に相互関係が存在
  →AE-COPDの間は特にPEのリスクが高いと考えられる

日本でのVTEの現状（沖縄中部病院）

Prevalence of venous thromboembolism at a teaching hospital in Okinawa, Japan

Table 3: Odds ratios (OR) and 95% confidence intervals (95%CI) of VTE diagnosis in women as compared to men, stratified by age (n=131,060).

Age (years)	OR	95%CI
<30	0.96	0.00 – 2.84
30–49	0.63	0.15 – 1.10
50–69	3.88	1.45 – 6.31
70–79	2.44	0.64 – 4.24
≥ 80	1.73	0.12 – 3.35
All women	1.97	1.26 – 2.68

VTE = venous thromboembolism

女性では、50－69歳台でVTEのリスクが一番高い

Table 4: Multivariable-adjusted odds ratios (OR) and 95% confidence intervals (CI) of characteristics associated with VTE diagnosis in women as compared to men (n=141)*.

Characteristic	OR	95% CI
Age (continuous)	1.02	1.00–1.05
Diagnosed as inpatient – n (%)	1.37	0.41–4.61
Postoperatively – n (%)	1.26	0.37–4.29
Institutionalized within 3 months prior to admission †	1.19	0.41–3.51
Prior VTE	3.01	0.59–15.62
Current cancer	1.66	0.51–5.35
BMI ≥ 25 (kg/m^2)	1.42	0.73–2.76
Lower extremity paralysis	0.54	0.19–1.55
Immobilization > 7 days	1.05	0.36–3.03
Hypercoagulable state	1.55	0.35–6.90
Heart failure	3.42	0.68–17.24
Varicose veins	0.91	0.06–12.99

*Adjusted for all other variables listed. †Hospital or non-acute care facility (ie, psychiatry hospital, rehabilitation hospital, nursing home).

女性では、VTEの既往と心不全がリスクとして高い

Thromb Haemost 2005; 93: 876-9

Padua Prediction Score

Table 1 Risk assessment model (high risk of VTE: ≥4)

Baseline features	Score
Active cancer*	3
Previous VTE (with the exclusion of superficial vein thrombosis)	3
Reduced mobility†	3
Already known thrombophilic condition‡	3
Recent (≤1 month) trauma and/or surgery	2
Elderly age (≥70 years)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI ≥30)	1
Ongoing hormonal treatment	1

*Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 months. †Bedrest with bathroom privileges (either due to patient's limitations or on physicians order) for at least 3 days. ‡Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome.

J Thromb Haemost . 2010 ; 8 (11): 2450 - 2457

背景

Prevalence of Pulmonary Embolism in Acute Exacerbations of COPD*

A Systematic Review and Metaanalysis

Jacques Rizkallah, MD; S. F. Paul Man, MD, FCCP; and Don D. Sin, MD, FCCP

Chest.2009 ;135(3):786-793

2009年に発表された、AE-COPD患者におけるPEの有病率についての
システマティックレビュー/メタ解析

背景

Table 1—*Characteristics of Individual Studies Included in This Review*

Study	Study Date	Country	Patients, No.	Setting	No. of Centers	Diagnostic Modality	PE, %	DVT, %	Important Issues	STROBE* Quality Score (Maximum Score Is 22)[7]
Tillie-Leblond et al[12]	April 1999 to December 2002	France	197	Inpatients	1	Lower-leg ultrasound**; spiral CT angiography**	25	12.69	High rate of malignancy (29%); criteria for PE diagnosis†; only included severe COPD exacerbation‡	22
Rutschmann et al[11]	February 2003 to December 2004	Switzerland	123	Emergency department	2	d-Dimer**; lower-leg ultrasound**; spiral CT angiography**	3.30	1.63	Criteria for PE diagnosis§; included moderate and severe COPD exacerbation‖	21
Mispelaere et al[10]	May 1998 to April 1999	France	31	Inpatients	1	d-Dimer**; lower-leg ultrasound**; spiral CT angiography**; pulmonary angiography**	29	25.81	Excluded patients with negative d-dimer; patients with moderate-to-severe COPD exacerbation¶	20
Lesser et al[9]	January 1985 to September 1986	United States	108	Inpatients and outpatients	6	V̇/Q̇ scan**; pulmonary angiography**; autopsy (in one patient)	19	Not available	Patients with mild-to-severe COPD exacerbation#; pulmonary function tests done only in 39.8% of patients	19
Hartmann et al[8]	May 1997 to March 1998	Netherlands	91	Inpatients and outpatients	6	d-Dimer**; lower-leg ultrasound**; V̇/Q̇ scan††; spiral CT angiography‡‡; pulmonary angiography	29	21.98	Possibility of patients misclassified as COPD; severity of COPD not documented	21

Chest.2009;135(3):786-793.

背景

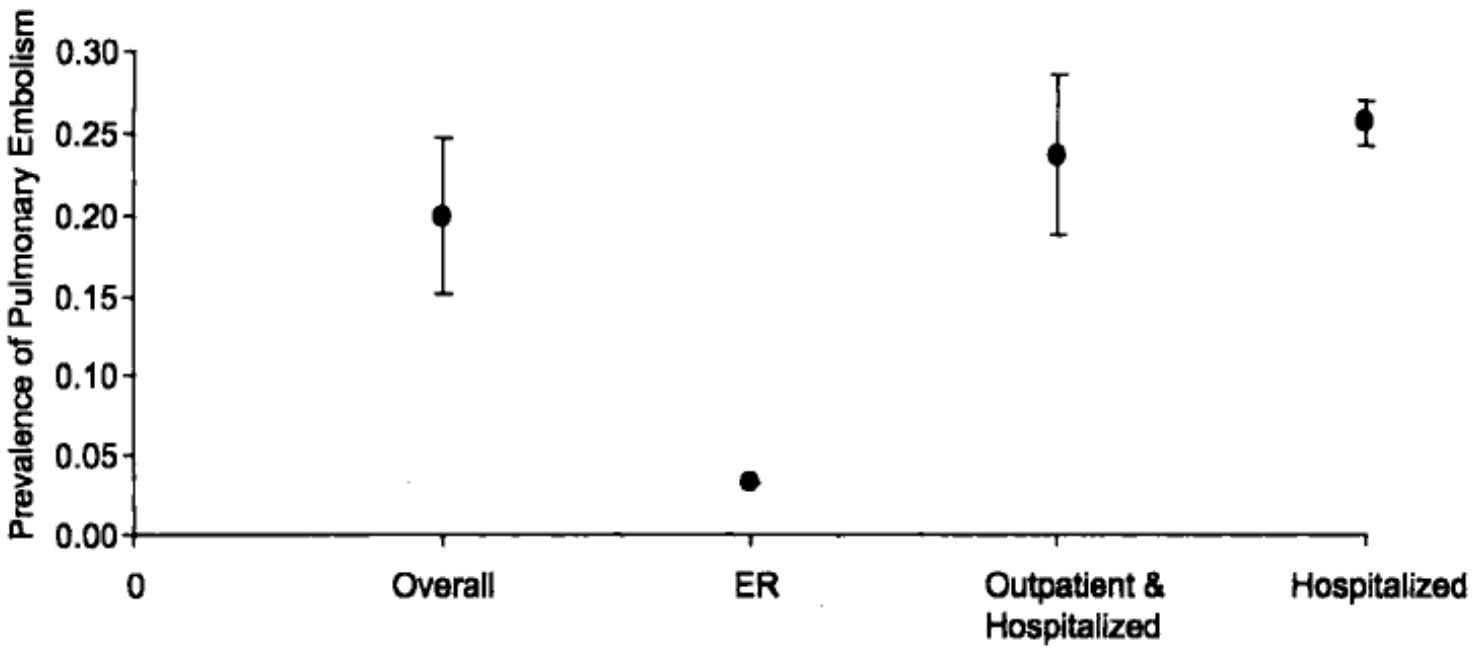


FIGURE 2. The prevalence of PE across different sites. The filled circles represent the mean, and the line bars represent SE; p value for overall = 0.014; p value for emergency department (ER) is not calculable because there was only one study; p value for studies that evaluated inpatients and outpatients = 0.133; p value for studies that evaluated only hospitalized patients = 0.034.

- PEの有病率は19.9%
  (95%CI,6.7%-33.0%)
- 入院患者のみでは24.7%
  (95%CI,17.9%-31.4%)
- 外来のみでは3.3%

背景

- AE-COPDにおけるPEの臨床的評価が困難

  ①マルチスライス肺動脈CT(CTPA)

  直径2-3mmの陰影欠損(孤立性亜区域性)も分かるようになった

  →AE-COPDでどのくらい孤立性亜区域性のPEが合併するか不明

  ②AE-COPDにおけるPEを特定する臨床的なマーカーがない

  →臨床症状がオーバーラップしているため

本日の論文

Prevalence and Localization of Pulmonary Embolism in Unexplained Acute Exacerbations of COPD

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Chest.2017;151(3):544-554

本日の論文では

・目的

①過去の論文から原因不明のAE-COPDでのPEの有病率をupdate

②AE-COPDでのPEの局在とCTPAでの陰影欠損の臨床的関連を評価

③臨床マーカーを特定する

方法-論文の検索-

- MEDLINE(1946年-2015年10月)とEMBASE(1974年-2015年10月)
- 英語論文
- ”pulmonary disease,chronic obstructive”と”pulmonary embolism”
- タイトル、アブストラクト、キーワードに含まれる

方法-論文の選択-

- Inclusion
  AE-COPDの患者におけるPEの有病率を示した論文
  PEの診断をCTPAで行っている

- Exclusion
  COPDの安定している症例、後ろ向き研究、すでにPEが診断

方法-論文の選択-

- Step1:タイトルスクリーニング
  一人の評価者によって行われる

- Step2:アブストラクトスクリーニング
  二人の評価者によって行われる
  意見の相違があった際には第三者にコンサルトする

- Step3:レポートの評価
  二人の評価者によって行われる
  意見の相違があった際には第三者にコンサルトする

Outcome

- Primary Outcome
  原因不明のAE-COPDにおけるPEの有病率

- Secondary Outcome
  DVTの有病率、PEの局在、臨床的予後、臨床マーカーの設定

  ＊患者の特徴、疾患の特徴、臨床症状、身体検査、呼吸機能、血液ガス検査、検査所見、他の診断的検査、臨床予測スコア、治療等

データの抽出

・二人の評価者が独立して行う

・標準化されたプロトコールを使用して行う
タイトル、筆者、発表された日付、研究が行われた場所、研究期間、参加施設数、研究デザイン、inclusion/exclusion criteria、研究目的、診断方法、D-dimmerの情報、患者数、平均年齢と範囲、性別、PEの有病率、DVTの有病率、PEの局在
臨床マーカーの抽出

論文の質評価

- 二人の評価者が独立して評価
- Strengthening the Reporting of Observational Studies in Epidemiology scoreを使用

STROBEのための声明より

TABLE 1. The STROBE statement—Checklist of Items That Should be Addressed in Reports of Observational Studies

	Item Number	Recommendation
TITLE and ABSTRACT	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
INTRODUCTION		
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
METHODS		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants (b) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
RESULTS		
Participants	13*	(a) Report the numbers of individuals at each stage of the study—eg, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study*—Summarize follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time *Case-control study*—Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*—Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg 95% confidence intervals). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorised (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg, analyses of subgroups and interactions, and sensitivity analyses
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalizability	21	Discuss the generalizability (external validity) of the study results
OTHER INFORMATION		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give such information separately for cases and controls in case-control studies, and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Separate versions of the checklist for cohort, case-control and cross-sectional studies are available on the STROBE website at www.strobe-statement.org.

STROBE SCOREとは

・観察研究の質を評価するための項目。タイトルやアブストラクト等全部で22項目。

・多くの医学研究は観察研究であり、観察研究には報告の質が不十分なものが散見される

・観察研究の報告の質を改善する目的

⇒経験上のエビデンスや理論を考慮した上で、STROBE（Strengthen the Reporting of Observational Studies in Epidemiology）を作成

STROBE　SCOREとは

・各項目の有用性については、それぞれの項目ごとに例を用いて記載

タイトル・抄録（TITLE AND ABSTRACT）

1(a)タイトルまたは抄録の中で研究デザインを一般に用いられている用語で明示する。

記載例

製靴業に従事する労働者における白血病の発症：ケース・コントロール研究[18]

解説

読者がタイトル・抄録を見て、容易にその研究デザインについてわかるようにするべきである。通常用いられる語句で明確に記すことによって、電子データベース上の論文のインデックスを正しく作成することにも役立つ[19,20]。

・さらにHPではこれらのチェックリストの改善のための議論も施行

http://www.strobe-statement.org

統計学的解析

- 安定したデータバリアンスのため二重逆正弦変換を施行

- 研究間の異質性(Heterogeneity)について
  P＜0.10を有意と定義して、χ^2二乗検定を施行
  異質性はI^2統計量で評価

- プールされた全症例に対して異質性を観察するためランダムモデルを算出

- 論文の異質性を体系的に予測する因子を確実にするため
  混合効果モデルのメタ回帰分析を以下の項目に対して施行
  ①年齢　②性別　③肺炎の除外

- すべての解析はR statistical software metaphor packageを使用

統計学的解析

- CTPAでの陰影欠損の局在は肺動脈幹・主肺動脈・区域動脈・孤立性亜区域に分類

- PEの存在と局在が死亡率・入院期間に関与するかレビュー

- 臨床マーカーに関してのデータの収集はいくつかの論文で抜粋が不可能であったが可能な範囲で統合

Result

Result

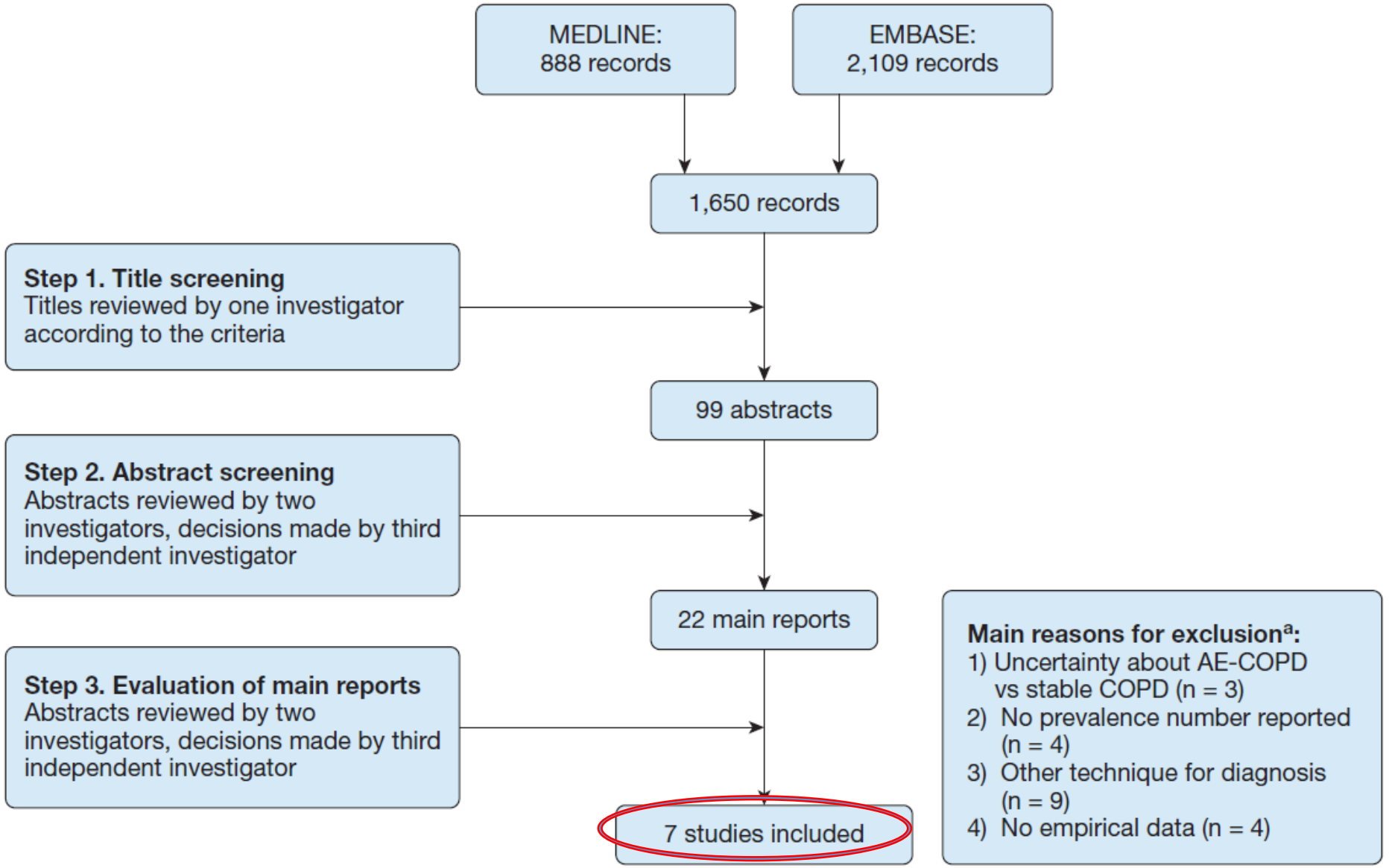


Figure 1 – *Flow diagram of the study selection process and numbers of studies identified. AE-COPD = acute exacerbation of COPD. [a]Studies could have fulfilled more than one criterion.*

Result

TABLE 1 | Characteristics of Studies Included With Descriptive Statistics on Rates of PE and DVT

Study/Year	Country	Patient Selection Criteria	Definition of AE-COPD	Setting	Patients With AE- COPD	Age, Mean (SD)	Sex (% Male)	PE (%)	DVT (%)	Mortality in PE	STROBE score
Shapira-Rootman et al[12]/2015	Israel	All patients with COPD admitted to the hospital for AE-COPD and COPD confirmed by spirometric data	Worsening of dyspnea that required admission to the hospital	Inpatients	49	65.5[a]	71.4	18.4	NA	Not described	19
Akpinar et al[31]/ 2014	Turkey	All patients with COPD hospitalized for AE-COPD and COPD confirmed by medical history and medical records	Worsening in respiratory symptoms beyond normal day to day variations that led to a change in medication	Inpatients	172	71.31 (9.6)	82.6	29.1	29.1	No significant difference	20
Choi et al[38]/2013	South Korea	All patients with COPD hospitalized for AE-COPD and COPD confirmed by spirometric data and medical records	Acute deterioration from a stable condition that required admission to the hospital	Inpatients	103	71 (6.0)	70	5.0	6	No significant difference	19
Kamel et al[40]/ 2013	Egypt	Not described	Not described	Inpatients	105	49.3 (8.4)	100	28.6	10.5	Not described	18
Gunen et al[39]/ 2010	Turkey	All patients with COPD admitted to the hospital for AE-COPD and COPD confirmed by	Acute deterioration from a stable condition that required admission to the hospital	ED	131	67 (10.1)	79.40	13.7	10.6	Increased in-hospital mortality and increased 1-y mortality	19

Result

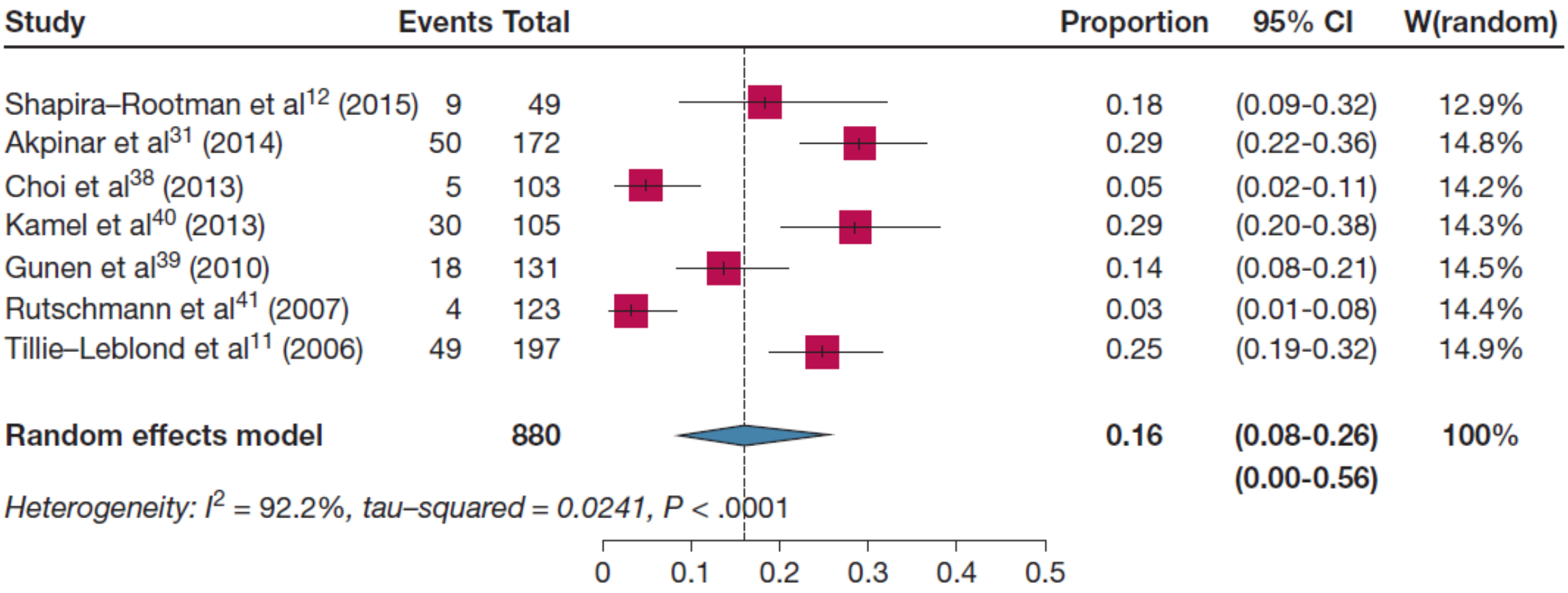
TABLE 1] *(Continued)*

Study/Year	Country	Patient Selection Criteria	Definition of AE-COPD	Setting	Patients With AE- COPD	Age, Mean (SD)	Sex (% Male)	PE (%)	DVT (%)	Mortality in PE	STROBE score
		medical history, medical records, and medications used									
Rutschmann et al[41]/2007	Switzerland	All patients admitted to the ED for a AE-COPD and moderate to severe COPD according to GOLD definition	Worsening of dyspnea that required admission to the ED	Inpatients	123	71 (8.0)	68	3.3	2.2	Not described	20
Tillie-Leblond et al[11]/2006	France	All patients with COPD admitted to the hospital for AE-COPD and COPD diagnosed according to ATS criteria	Acute deterioration from a stable condition that required admission to the hospital	Inpatients	197	60.5 (12.1)	83.6	25.0	12.7	Not described	21

AE-COPD = acute exacerbation COPD; ATS = American Thoracic Society; GOLD = Global Initiative for Obstructive Lung Disease; NA = not available; PE = pulmonary embolism; STROBE = Strengthening the Reporting of Observational Studies in Epidemiology.

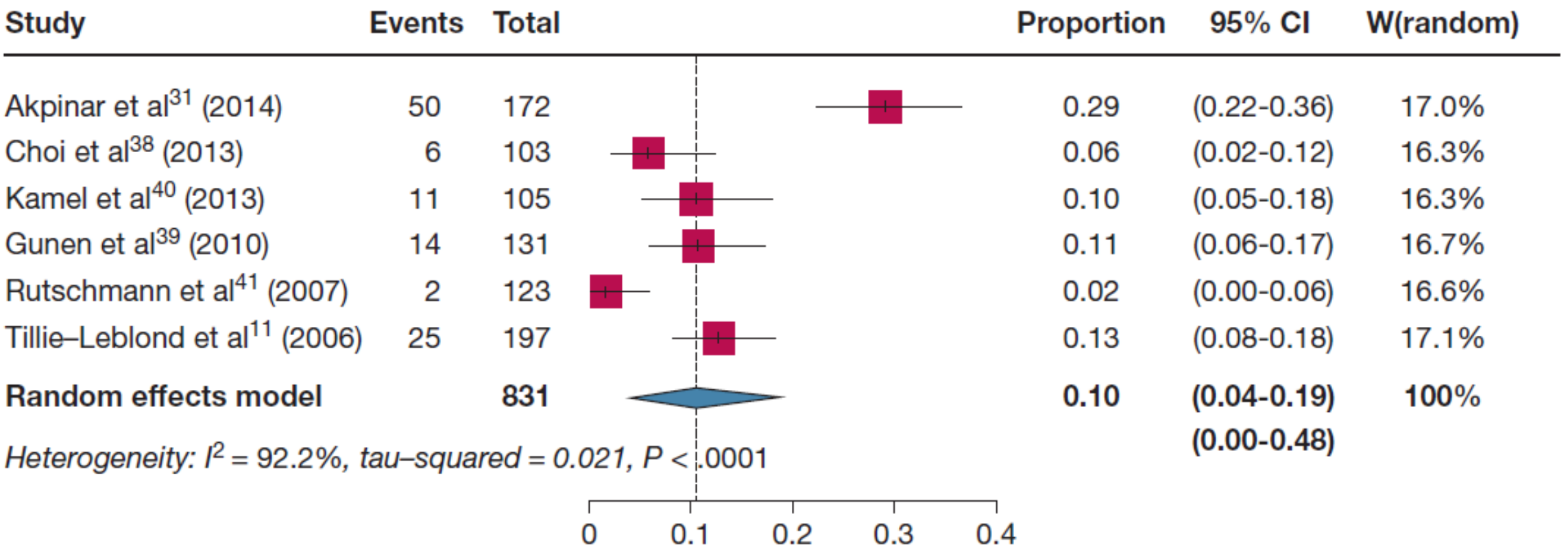
[3]Range = 43-92 years.

Primary Outcome　Prevalence of PE in AE-COPD



16.1%(95%CI,8.3%-25.8%)のAE-COPDの患者にPEを認めた
研究間での差が大きく、有病率は3.3%-29.1%

Primary Outcome -おまけ-
Prevalence of DVT in AE-COPD



10.5%(95%CI,4.3%-19.0%)のAE-COPDの患者にDVTを認めた
Inclusionされた研究のうち6つの研究から解析

Secondary Outcome
Localization and Clinical Relevance of PE in AE-COPD

・5つの研究

・32.5%が孤立性亜区域性
その他はそれより近位に存在

・孤立性亜区域性PEとそれより近位に局在するPEと、臨床予後の関連は報告なし。

TABLE 2] Localization of PE Found in AE-COPD

Anatomical Region	Cases	%
Pulmonary trunk	1	0.8
Main pulmonary arteries	42	35.0
Lobar and interlobar arteries	38	31.7
Isolated subsegmental arteries	39	32.5
Total	120	100

AE-COPD = acute exacerbation of COPD; PE = pulmonary embolism.

Tillie-Leblond et al, Akpinar et al, Choi et al, Gunen et al, Rutschmann et al.

Secondary Outcome
Localization and Clinical Relevance of PE in AE-COPD

- 3つの研究で入院期間について評価
  →2つはPEを有すると入院期間が延長したと報告
  Akpinar et al, Choi et al, Gunen et al.

- 院内死亡率と1年死亡率が増加すると報告しているのは1つのみ (P=0.26)
  Gunen et al.

- Gunen et alはCox回帰解析を行い、VTEの存在のみが1年死亡率を増加させると報告

Secondary Outcome Clinical Markers

・胸膜痛は優位に頻度が高い

・心不全兆候(低血圧、失神、エコーでの右心不全所見)も多い

・呼吸器感染の症状は少ない

・増悪の頻度や、重症度、ステロイド治療などは関与しない

TABLE 3] Markers for Identification of PE in AE-COPD[a]

Markers	Significant Findings	Not Significant Findings
Patient characteristics		
Sex	Gunen et al[39]	Akpinar et al,[31] Choi et al,[38] Tillie-Leblond et al[11]
Obesity	Akpinar et al[31]	Choi et al,[38] Gunen et al,[39] Tillie-Leblond et al[11]
Clinical symptoms		
No symptoms of RTI	Choi et al[38]	
Increased sputum	Choi et al[38]	Akpinar et al[31]
Pleuritic chest pain	Akpinar et al,[31] Gunen et al[39]	Tillie-Leblond et al[11]
Physical examination		
Hypotension	Gunen et al[39]	
Lower leg asymmetry	Akpinar et al[31]	Tillie-Leblond et al[11]
Syncope	Gunen et al[39]	
Respiratory function		
FEV_1	Shapira-Rootman et al[12]	Choi et al[38]
Arterial blood gas		
$Paco_2$ lower in PE	Akpinar et al[31]	Choi et al[38]
pH value higher in PE	Akpinar et al[31]	Gunen et al,[39] Tillie-Leblond et al[11]
Decrease in $Paco_2$	Tillie-Leblond et al[11]	
Laboratory findings		
NT-proBNP	Akpinar et al[31]	Choi et al[38]
Polycythemia	Kamel et al[40]	
Diagnostics		
ECG		
AF	Gunen et al[39]	
Ultrasonography		
Cardiac failure	Gunen et al[39]	Tillie-Leblond et al[11]
Chest radiography		
Atelectasis	Shapira-Rootman et al[12]	
Pulmonary artery enlargement	Shapira-Rootman et al[12]	
Wells score		
Previous VTE	Tillie-Leblond et al[11]	Akpinar et al,[31] Gunen et al[39]
Malignancy	Akpinar et al,[31] Gunen et al[39]	
Immobility	Gunen et al[39]	Tillie-Leblond et al[11]
Outcome measures		
Length of stay	Akpinar et al,[31] Gunen et al[39]	Choi et al[38]
Mortality		Choi et al[38]
Need for ICU treatment	Gunen et al[39,a]	Akpinar et al[31]

AF = atrial fibrillation; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; RTI = respiratory tract infection.
[a]Cox regression analyses revealed that VTE was the only factor that significantly increased mortality.

Result　まとめ

- 原因不明のAE-COPDでPEは16%
- PEの2/3は臨床転帰に重要な主肺動脈、区域動脈などに局在
- AE-COPDに合併しているPEでは胸膜痛や心不全兆候の頻度が高い
- 呼吸器感染症の頻度は低い
- PEの局在は臨床予後に関連しないが、PEを合併している原因不明のAE-COPD患者は死亡率および入院期間が増加する傾向にある

Discussion

- 前回のシステマティックレビューと比較すると、PEの有病率はやや低い
(19.9% vs 16%)
Chest.2009;135(3):786-793.

- 2009年の公表後、新たに5つの関連論文が公表
Shapira-Rootman et al, Akpinar et al, Choi et al, Kamel et al, Gunen et al.

- 前回の論文でincludeされていた5つの論文のうち、3つは除外
→1つはフランス語
2つはAE-COPD以外の疾患・安定期COPDも含む
Lesser et al, Hartmann et al.

- 今回除外した英語論文を追加して解析すると有病率は軽度上昇
(18.5%;95%CI,10.1%-27.5%)

Discussion

- 他疾患の入院患者でのPEの有病率(5.7%-6.0%)と比較すると
  原因不明のAE-COPDの患者でのPEの有病率は増加している。
  →全身感染症と血栓症に密接に関連があるという報告がある

Chest.2005;128(4)2068-2075

- AE-COPD患者はステロイドで治療→ステロイド自体がVTEのリスク

JAMA Intern Med.2013;173(9):743-752

- PEがAE-COPDのtrigger

- 偽性の増悪様の症状を起こす→血管閉塞が気道狭窄を起こすため

Circulation.1963;27:339-345

Discussion　PEの局在

・PEの局在

★2/3→亜区域動脈より近位→抗凝固療法適応(ACCPガイドライン)

Chest.2016;149(2):315-352

★1/3→孤立性亜区域→治療？

→さらなる疫学的調査が必要

・今回のレビューではPEの局在は予後には関与しなかった

Discussion 臨床マーカー

・胸膜痛と心不全兆候はPE合併のAE-COPDに多い臨床マーカー

・逆に、気道感染症症状のあるAE-COPDはPEの可能性が低い

・AE-COPDでのCTPA使用を軽減に向け、今後さらなる検討が必要
→年齢補正D-dimmerによるPEの除外等

Limitation

First

- **PEの有病率が研究ごとに3.3%から29.1%までばらつきが大きいこと**

- 民族性の是非
  アジア人はVTEになるリスクがより低いという研究
  ↕
  その一方、今回有病率が最も低い研究は白人が主な対象となった研究

- D-dimmer陰性症例を除外

- 論文個々の症例数が少ない
  →ばらつきが多く、混合効果モデルのメタ回帰分析できず

Limitation

Second

・Publicarion biasのリスクがある

・MEDLINEとEMBASEにない論文は含んでいない

Third

・含まれる論文の患者のほとんどが男性

Conclusions

- AE-COPD患者の16%にPEを合併
- 2/3は抗凝固療法が適応である部分に局在
- PEを合併しているAE-COPD患者では胸膜痛や心不全兆候が認められ、感染兆候がないことが特徴

私見

☆AE-COPDに関して、Trigerが明確でない場合、PEの関与を鑑別に入れる必要がある

☆原因不明のAE-COPD症例に対して

- 明確な感染兆候が認められない場合
- 喘息・腎機能障害などの造影剤禁忌がない場合

→ PEの可能性を考慮し、造影CT施行を検討する

☆造影剤に対する相対的禁忌がある場合

D-dimmerや炎症反応など、他の臨床所見をふまえて PEの精査を行うべきか 個々に検討する必要がある