CHEST IMAGING

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Evaluation of the Correlation of Pulmonary Arterial Hypertension (PAH) with the Pulmonary Artery Trunk Diameter and Serum Level of N-Terminal Pro B-Type Natriuretic Peptide (NT-proBNP) in Patients with PAH

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Abstract

Background: Due to its non-specific symptoms, pulmonary arterial hypertension (PAH) is difficult to diagnose via non-invasive methods. Various diagnostic tests are required to evaluate PAH patients. The increased diameter of the main pulmonary artery in computed tomography (CT) imaging represents a high probability of PAH. Moreover, N-terminal pro B-type natriuretic peptide (NT-proBNP) and pro B-type natriuretic peptide (proBNP) can be considered as prognostic predictors in patients with PAH.
Objectives: This study aimed to evaluate the correlation of CT-based main pulmonary artery diameter (MPAD) and the serum level of NT-proBNP (as a strong pro-inflammatory factor) with the severity of PAH in echocardiography among patients with PAH.
Patients and Methods: In this cross-sectional study, a total of 63 hospitalized patients with PAH due to chronic obstructive pulmonary disease were recruited from 2019 to 2020 after initial evaluations and collection of serum NT-proBNP measurements and echocardiographic findings. On the chest CT scans, the largest diameter of the pulmonary artery trunk was determined, and then, correlation of CT-based MPAD with both PAH severity on echocardiography and NT-proBNP level in patients with PAH were evaluated.
Results: The results of the present study on 63 patients (70% male; mean age, 67.02 years) showed a significant positive correlation between the MPAD and NT-proBNP level ($r = 0.444$, $P < 0.001$). Moreover, a significant positive relationship was observed between the pulmonary artery pressure (PAP) and NT-proBNP ($r = 0.353$, $P = 0.005$) and also between MPAD and PAP ($r = 0.306$, $P = 0.015$). In PAH patients, the mean values of MPAD, PAP, and NT-proBNP were 32.58 mm, 47.9 mmHg, and 6563 pg/mL, respectively.
Conclusion: Considering the significant positive correlation between PAP, MPAD, and NT-proBNP level in subgroup comparisons based on MPAD and PAP, if the MPAD is abnormal on CT scan, additional echocardiographic assessments and serum NT-proBNP measurements can be helpful.

Keywords: Pulmonary Arterial Hypertension, Pulmonary Artery Diameter, N-Terminal Pro B-Type Natriuretic Peptide, Pulmonary Arterial Pressure

1. Background

Pulmonary arterial hypertension (PAH) is a devastating and progressive pulmonary vascular disease, leading to right-sided heart failure and death (1, 2). Diagnostic delay in PAH leads to irreversible changes in patients (3). Many factors are associated with PAH, which has different manifestations (4, 5). Commonly, it is defined as a resting mean pulmonary arterial pressure (mPAP) > 25 mmHg or mPAP > 30 mmHg during exercise (5). Echocardiography is considered a non-invasive tool for evaluating the extent, cause, and prognosis of PAH and management approaches (6). However, the diagnostic sensitivity of echocardiography is lower than that of right heart catheterization (RHC) (7).

Although RHC remains the gold standard diagnostic tool for PAH, it is an invasive strategy (8, 9). Computed tomography (CT) scan is also used to assess the lung parenchyma and pulmonary vasculature. CT findings, such as the main pulmonary artery diameter (MPAD) and MPAD/ascending aorta diameter (AAD) ratio, are the predictors of PAH (10, 11). It should be noted that the absence of CT findings does not exclude the diagnosis of PAH (12). Evidence suggests that a combination of CT and echocardiographic markers of PAH has a significantly higher diagnostic accuracy than either test used in isolation and may identify other potential causes of respiratory discomfort (13, 14). Overall, the presence of MPAD > 28 mm and MPAD/ADD ratio > 1 on CT scan represent a very high probability of PAH (11, 12). Additionally, N-terminal pro B-type natriuretic peptide (NT-proBNP) and prohormone B-type natriuretic peptide (proBNP) can be regarded as prognostic predictors in patients with PAH (15).

2. Objectives

The current study aimed to assess the correlation of CT-based MPAD with both PAH severity on echocardiography and NT-proBNP level in patients with PAH due to chronic obstructive pulmonary disease (COPD).

3. Patients and Methods

3.1. Study Description

This cross-sectional study was performed on patients with a diagnosis of COPD exacerbation, who were admitted to Imam Khomeini Hospital Complex (IKHC), a general university-affiliated center in Tehran, Iran, from March 2019 to March 2020. Patients with MPAD > 29 mm on CT scan were considered eligible for the study. The patients underwent additional paraclinical evaluations, such as echocardiography and laboratory tests. Their demographic and clinical characteristics, laboratory findings, echocardiographic parameters, and CT findings were retrieved from the hospital/medical records.

All the patients underwent imaging in the supine position, with inspiration breath holding. In this study, CT scanning, including pulmonary CT angiography and spiral chest CT scan with or without contrast with 3D reconstruction, was performed using a single multi-detector CT scanner (a 16-slice CT scanner, SOMATOM Sensation 16, Siemens, Forchheim, Germany) and reported by an experienced radiologist. The MPAD on CT scan was measured using true axial and 3D reconstruction models.

Echocardiography was performed using an echocardiographic device (Vivid S60, GE Healthcare, Chicago, IL, USA) by an experienced cardiologist. Multiple views were used for the optimal Doppler estimation of tricuspid regurgitation velocity (TRV). The tricuspid regurgitation gradient (TRG) was then calculated based on the modified Bernoulli equation ($TRG = 4V^2$). Moreover, blood samples were drawn from the peripheral vein for NT-proBNP measurements. The plasma levels of NT-proBNP were analyzed using the enzyme-linked immunosorbent assay (ELISA).

The exclusion criteria were as follows: (1) artifacts on CT scans; (2) lack of NT-proBNP measurements and/or accurate mPAP measurements via echocardiography; and (3) conditions leading to either elevated NT-proBNP levels or increased MPAD, including heart failure with preserved or reduced ejection fraction, myocarditis, takotsubo cardiomyopathy, acute myocardial infarction/coronary artery disease, cerebrovascular accidents, subarachnoid hemorrhage, septic shock, acute respiratory distress syndrome, hepatic cirrhosis, hyperthyroidism, atrial fibrillation, history of congenital heart disease, acute and chronic thromboembolic pulmonary hypertension, chronic kidney disease, connective tissue disorders, and vasculitis. Finally, 63 patients who met the inclusion criteria were enrolled in the final analysis.

3.2. Definitions of Variables

In this study, COPD was defined as a chronic condition, associated with abnormal pulmonary function (post-bronchodilator forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] ratio < 0.70 and FEV1 < 80% with frequent exacerbation, necessitating recurrent hospitalization and long-term use of bronchodilators) (16). Also, PAH was defined as resting mPAP > 25 mmHg or mPAP with exercise > 30 mmHg on echocardiography (5).

3.3. Ethical Statement

All the participants provided written informed consent before inclusion in the study. The investigations conformed to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the institutional ethics committee of IKHC (ethical code: IR.TUMS.IKHC.REC.1398.284).

3.4. Statistical Analysis

Continuous data were described by measuring mean and standard deviation (SD) or median with 25th and 75th percentiles for variables with normal and skewed distributions, respectively. The normal distribution of variables was examined using histogram charts, as well as descriptive indices. Number and frequency (%) were measured for describing categorical variables. Chi-square test was also used to compare discrete variables, and student's *t*-test was employed to compare the mean values of two quantitative variables. Additionally, bivariate correlations between two normally distributed variables were measured by Pearson's correlation coefficient test. Also, to compare categorical groups, one-way analysis of variance (ANOVA) test was performed. Differences were considered significant at a P-value < 0.05. All statistical analyses were conducted in IBM SPSS Statistics for Windows Version 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

4. Results

In this study, 63 patients were examined, including 44 male and 19 female patients. The mean age of the patients was 66.16 ± 11.20 years (Table 1).

Table 1. The Mean Age, Main Pulmonary Artery Diameter, Pulmonary Arterial Pressure, and N-Terminal Pro B-Type Natriuretic Peptide Level of the Participants

Variables	Mean ± SD
Age (y)	66.16 ± 11.20
MPAD (mm)	32.58 ± 5.57
PAP (mmHg)	47.90 ± 16.97
NT-proBNP (pg/mL)	6569.62 ± 17415.01

Abbreviations: MPAD, mean pulmonary artery diameter; PAP, pulmonary artery pressure; NT-proBNP, N-terminal pro B-type natriuretic peptide.

The mean, minimum, and maximum values of MPAD were 32.58, 21, and 55 mm, respectively. The mean PAP was 47.90 mmHg, ranging from 21 to 97 mmHg. The NT-proBNP level ranged from 2 pg/mL to 122,971 pg/mL, with an average value of 6569.62 pg/mL. Overall, 86% of the patients had serum NT-proBNP levels < 10,000 pg/mL, and only two patients had a serum NT-proBNP level of about 120,000 pg/mL. The MPAD mainly ranged from 30 mm to 40 mm, and only two patients showed MPAD > 50 mm.

Based on the results, PAP was in the range of 20 - 70 mmHg in the majority of the patients. PAP < 20 mmHg was not detected in any of the patients. Age was not significantly correlated with MPAD, PAP, or NT-proBNP level. On the other hand, MPAD showed a significant positive correlation with the level of NT-proBNP (r = 0.444, P < 0.001). Overall, PAP had a significant positive correlation with MPAD (r = 0.306, P = 0.015). A similar relationship was also observed between PAP and NT-proBNP level (r = 0.353, P = 0.005) (Table 2).

In the majority of the patients (74.7%), MPAD was > 30 mm. Based on the results, half of the patients (50.7%) had a PAP of 40 - 60 mmHg, 17 (27%) patients had a PAP < 40 mmHg, and 14 (22.3%) patients had a PAP > 60 mmHg. The mean PAP was 41.06 mmHg in patients with MPAD < 30 mm and 54.45 mmHg in patients with MPAD > 30 mm; however, the difference was not significant (P = 0.221). Regarding the NT-proBNP level, the difference was greater, with significantly higher NT-proBNP levels detected in patients with MPAD > 30 mm (P = 0.009). Only the NT-proBNP level was significantly different between three levels of PAP (20 - 40, 41 - 60 and > 60 mmHg) (P = 0.042), and regarding MPAD, the difference was not significant (P = 0.221) (Table 3).

5. Discussion

In this study, relationships between CT-based MPAD, PAH severity based on echocardiography, and NT-proBNP level were evaluated in patients with PAH. Expectedly, PAP was positively correlated with the NT-proBNP level, and MPAD had significant positive correlations with the NT-proBNP level and PAP. In this regard, according to a study by Corson et al., the sensitivity and specificity of MPAD > 29 mm for PAH identification were 0.89 and 0.83, respectively (17). According to the present results, the sensitivity of vascular criteria for PAH identification was high; however, specificity did not appear to be acceptable for routine clinical use in a patient population (17).

In another similar study by Sabri et al. in 2013, patients with MPAD > 29 mm were divided into three groups: < 35 mm, 35 - 40 mm, and > 40 mm. In this study, a significant strong relationship was found between MPAD and PAP (18). Moreover, Caravita et al. (19) concluded that in patients with connective tissue disorders and PAH, PAP is positively correlated with the NT-proBNP level. Additionally, Mohammedi et al. reported a significant association between the MPAD and PAP (11). The sensitivity of MPAD > 29.5 mm and > 31.5 mm for PAH detection was estimated at 70.8% and 52.0%, respectively, and the specificity of MPAD > 29.5 mm and MPAD > 31.5 mm was 79.4 % and 90.2%, respectively (11). Also, according to a study by Fakharian et al. (20), CT-based MPAD > 29 mm was of diagnostic value for PAH, with 63% sensitivity and 41.5% specificity. Overall, the results of these studies are consistent with the present research.

Additionally, Greig et al. (21) detected a positive relationship between the BNP level and pulmonary vascular resistance, whereas no significant relationship was found between PAP and the BNP level. Meanwhile, another study by Bernus et al. (22) on 78 pediatric patients showed no significant correlation between a single BNP

Table 2. Correlations of N-Terminal Pro B-Type Natriuretic Peptide Level with Age, Main Pulmonary Artery Diameter, and Pulmonary Arterial Pressure (Section A) and Correlation of Pulmonary Arterial Pressure with Main Pulmonary Artery Diameter (Section B)

Variables	NT-proBNP		PAP	
	Pearson's correlation coefficient (r)	P-value	Pearson's correlation coefficient (r)	P-value
Section A				
Age	0.008	0.937	-	-
MPAD	0.444	< 0.001	-	-
PAP	0.353	0.005	-	-
Section B				
MPAD	-	-	0.306	0.015

Abbreviations: MPAD, mean pulmonary artery diameter; PAP, Pulmonary artery pressure; NT-proBNP, N-terminal pro B-type natriuretic peptide.

Table 3. Relationship of Pulmonary Arterial Pressure, Main Pulmonary Artery Diameter, and N-Terminal Pro B-Type Natriuretic Peptide Level in Patients with Pulmonary Arterial Hypertension [a]

Variables	MPAD (mm)			PAP (mmHg)		
	No. (%)	Mean ± SD	P-value	No. (%)	Mean ± SD	P-value
Section A						
PAP (mmHg)			0.221			-
< 30	16 (25.3)	41.06 ± 12.40		-	-	
≥ 30	47 (74.7)	54.45 ± 16.59		-	-	
NT-proBNP (pg/mL)			0.009			-
< 30	16 (25.3)	1533.75 ± 2024.12		-	-	
≥ 30	47 (74.7)	4150.81 ± 2762.91		-	-	
Section B						
MPAD (mm)			-			0.126
20 - 40	-	-		17 (27)	30.94 ± 6.86	
41 - 60	-	-		32 (50.7)	33.31 ± 4.70	
> 60	-	-		14 (22.3)	34.79 ± 4.26	
NT-proBNP (pg/mL)			-			0.042
20 - 40	-	-		17 (27)	2294.71 ± 2352.38	
41 - 60	-	-		32 (50.7)	3528.91 ± 2838.03	
> 60				14 (22.3)	4835.21 ± 2860.13	

Abbreviations: MPAD, mean pulmonary artery diameter; PAP, pulmonary artery pressure; NT-proBNP, N-terminal pro B-type natriuretic peptide; PAH, Pulmonary arterial hypertension.
[a] Section A: Comparison of pulmonary arterial pressure and N-terminal pro B-type natriuretic peptide in different subgroups based on main pulmonary artery diameter; Section B: Comparison of main pulmonary artery diameter and N-terminal pro B-type natriuretic peptide in different subgroups based on pulmonary arterial pressure.

measurement and echocardiographic or hemodynamic parameters. However, changes in the BNP level over time were strongly related to echocardiographic and hemodynamic data; the results of this study highlighted the importance of BNP monitoring.

To the best of our knowledge, no study has yet found a significant correlation between MPAD and NT-proBNP. The present study showed a significant positive correlation between the serum NT-proBNP level and the pulmonary artery diameter. However, since a small sample size may indicate a non-significant relationship between variables in some subgroups, further prospective research with a larger sample size may be more helpful. Also, this study only included patients with MPAD > 29 mm; therefore, specificity and sensitivity could not be assessed, which is another limitation of this study. Finally, since this study had a retrospective design and only evaluated patients undergoing CT scan without contrast, measurement biases due to non-contrast imaging studies and CT angiography with different slice thicknesses may be its other limitations.

In conclusion, the results of the present study showed that PAP was positively correlated with the MPAD. The serum NT-proBNP level also had a significant positive correlation with both MPAD and PAH. In the subgroup comparisons (two subgroups of PAP and three subgroups of MPAD), the patients' NT-proBNP levels also differed. Therefore, if the MPAD is abnormal on CT scan, additional echocardiographic assessments and measurement of serum NT-proBNP level can be helpful. However, future prospective studies with a larger sample size are needed to evaluate the accuracy of CT-based MPAD as a prognostic factor for PAH.

Footnotes

Authors' Contributions: Study conception and design: Fahimeh Zeinalkhani; acquisition of data: Sara Gharibi; analysis and interpretation of data: Soheila Dabiran and Mojgan Ghavami; drafting of the manuscript: Mojgan Ghavami, Hamid Khederlou, and Seyyed Mojtaba Ghorashi; critical revision of the manuscript for important intellectual content: Fahimeh Zeinalkhani; statistical analysis: Soheila Dabiran; administrative, technical, and material support: Mojgan Ghavami and Sara Gharibi; and study supervision: Fahimeh Zeinalkhani.

Conflict of Interests: Fahimeh Zeinalkhani and Soheila Dabiran are the faculty members of Tehran University of Medical Sciences.

Ethical Approval: The study protocol was approved by the institutional ethics committee of IKHC (ethical code: IR.TUMS.IKHC.REC.1398.284).

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References

1. Voelkel NF, Quaife RA, Leinwand LA, Barst RJ, McGoon MD, Meldrum DR, et al. Right ventricular function and failure: report of a National Heart, Lung, and Blood Institute working group on cellular and molecular mechanisms of right heart failure. *Circulation*. 2006;**114**(17):1883–91. [PubMed ID: 17060398]. https://doi.org/10.1161/CIRCULATIONAHA.106.632208.
2. Farber HW, Loscalzo J. Pulmonary arterial hypertension. *N Engl J Med*. 2004;**351**(16):1655–65. [PubMed ID: 15483284]. https://doi.org/10.1056/NEJMra035488.
3. Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, et al. Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med*. 2006;**173**(9):1023–30. [PubMed ID: 16456139]. https://doi.org/10.1164/rccm.200510-1668OC.
4. Simonneau G, Robbins IM, Beghetti M, Channick RN, Delcroix M, Denton CP, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2009;**54**(1 Suppl):S43–54. [PubMed ID: 19555858]. https://doi.org/10.1016/j.jacc.2009.04.012.
5. Barst RJ, McGoon M, Torbicki A, Sitbon O, Krowka MJ, Olschewski H, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. *J Am Coll Cardiol*. 2004;**43**(12 Suppl S):40S–7S. [PubMed ID: 15194177]. https://doi.org/10.1016/j.jacc.2004.02.032.
6. Bossone E, Bodini BD, Mazza A, Allegra L. Pulmonary arterial hypertension: the key role of echocardiography. *Chest*. 2005;**127**(5):1836–43. [PubMed ID: 15888866]. https://doi.org/10.1378/chest.127.5.1836.
7. Hsu VM, Moreyra AE, Wilson AC, Shinnar M, Shindler DM, Wilson JE, et al. Assessment of pulmonary arterial hypertension in patients with systemic sclerosis: comparison of noninvasive tests with results of right-heart catheterization. *J Rheumatol*. 2008;**35**(3):458–65. [PubMed ID: 18203320].
8. McGoon M, Gutterman D, Steen V, Barst R, McCrory DC, Fortin TA, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;**126**(1 Suppl):14S–34S. [PubMed ID: 15249493]. https://doi.org/10.1378/chest.126.1_suppl.14S.
9. Simonneau G, Galie N, Rubin LJ, Langleben D, Seeger W, Domenighetti G, et al. Clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2004;**43**(12 Suppl S):5S–12S. [PubMed ID: 15194173]. https://doi.org/10.1016/j.jacc.2004.02.037.
10. Sanal S, Aronow WS, Ravipati G, Maguire GP, Belkin RN, Lehrman SG. Prediction of moderate or severe pulmonary hypertension by main pulmonary artery diameter and main pulmonary artery diameter/ascending aorta diameter in pulmonary embolism. *Cardiol Rev*. 2006;**14**(5):213–4. [PubMed ID: 16924160]. https://doi.org/10.1097/01.crd.0000181619.87084.8b.
11. Mahammedi A, Oshmyansky A, Hassoun PM, Thiemann DR, Siegelman SS. Pulmonary artery measurements in pulmonary hypertension: the role of computed tomography. *J Thorac Imaging*. 2013;**28**(2):96–103. [PubMed ID: 23096163]. https://doi.org/10.1097/RTI.0b013e318271c2eb.
12. Perez-Enguix D, Morales P, Tomas JM, Vera F, Lloret RM. Computed tomographic screening of pulmonary arterial hypertension in candidates for lung transplantation. *Transplant Proc*. 2007;**39**(7):2405–8. [PubMed ID: 17889203]. https://doi.org/10.1016/j.transproceed.2007.07.055.
13. Devaraj A, Wells AU, Meister MG, Corte TJ, Wort SJ, Hansell DM. Detection of pulmonary hypertension with multidetector CT and echocardiography alone and in combination. *Radiology*. 2010;**254**(2):609–16. [PubMed ID: 20093532]. https://doi.org/10.1148/radiol.09090548.
14. Condliffe R, Radon M, Hurdman J, Davies C, Hill C, Akil M, et al. CT pulmonary angiography combined with echocardiography in suspected systemic sclerosis-associated pulmonary arterial hypertension. *Rheumatology (Oxford)*. 2011;**50**(8):1480–6. [PubMed ID: 21447566]. https://doi.org/10.1093/rheumatology/ker114.
15. Leuchte HH, El Nounou M, Tuerpe JC, Hartmann B, Baumgartner RA, Vogeser M, et al. N-terminal pro-brain natriuretic peptide and renal insufficiency as predictors of mortality in pulmonary hypertension. *Chest*. 2007;**131**(2):402–9. [PubMed ID: 17296640]. https://doi.org/10.1378/chest.06-1758.
16. Iheanacho I, Zhang S, King D, Rizzo M, Ismaila AS. Economic Burden of Chronic Obstructive Pulmonary Disease (COPD): A Systematic Literature Review. *Int J Chron Obstruct Pulmon Dis*. 2020;**15**:439–60. [PubMed ID: 32161455]. [PubMed Central ID: PMC7049777]. https://doi.org/10.2147/COPD.S234942.

17. Corson N, Armato S3, Labby ZE, Straus C, Starkey A, Gomberg-Maitland M. CT-based pulmonary artery measurements for the assessment of pulmonary hypertension. *Acad Radiol*. 2014;**21**(4):523–30. [PubMed ID: 24594422]. [PubMed Central ID: PMC3985437]. https://doi.org/10.1016/j.acra.2013.12.015.
18. Sabri YY, Hamdy IM, Sabry IM, Saif Al-Hadi AA. Studying the signs of pulmonary hypertension shown by CT scans and correlating data obtained with echocardiography in suspected patients of pulmonary hypertension. *Egypt J Bronchol*. 2013;**7**(2):60–6. https://doi.org/10.4103/1687-8426.123998.
19. Caravita S, Wu SC, Secchi MB, Dadone V, Bencini C, Pierini S. Long-term effects of intermittent Iloprost infusion on pulmonary arterial pressure in connective tissue disease. *Eur J Intern Med*. 2011;**22**(5):518–21. [PubMed ID: 21925064]. https://doi.org/10.1016/j.ejim.2011.02.005.
20. Fakharian A, Hamidi N, Hosseinloo BH, Rezaei S, Afshar EE, Sharif-Kashani B, et al. Correlation between the Pulmonary Artery Pressure Measured in Echocardiography and Pulmonary Artery Diameter in the CT-Scan of Patients Suffering from Interstitial Lung Disease. *Tanaffos*. 2011;**10**(3):37–41. [PubMed ID: 25191374]. [PubMed Central ID: PMC4153157].
21. Greig D, Castro P, Ferrada M, Lim J, Lopez C, Braun S, et al. [Brain natriuretic peptide in primary pulmonary hypertension]. *Rev Med Chil*. 2006;**134**(3):299–304. [PubMed ID: 16676101]. https://doi.org/10.4067/s0034-98872006000300005.
22. Bernus A, Wagner BD, Accurso F, Doran A, Kaess H, Ivy DD. Brain natriuretic peptide levels in managing pediatric patients with pulmonary arterial hypertension. *Chest*. 2009;**135**(3):745–51. [PubMed ID: 18849405]. [PubMed Central ID: PMC2715554]. https://doi.org/10.1378/chest.08-0187.