

# Enlarged pulmonary artery on computed tomography and respiratory failure in sickle cell disease acute chest syndrome

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## Abstract

Predicting the severity of acute chest syndrome is an important research priority in sickle cell disease. In this retrospective study of patients with acute chest syndrome, an enlarged pulmonary artery on computed tomography was associated with severe respiratory failure defined by the need for either noninvasive or mechanical ventilation.

## Keywords

sickle cell disease, pulmonary hypertension, pulmonary artery diameter

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## Introduction

Acute chest syndrome is a pulmonary complication of sickle cell disease defined by a new infiltrate on chest imaging along with chest pain, cough, wheezing, tachypnea, or fever in a patient with sickle cell disease.<sup>1</sup> It is a clinical diagnosis with several etiologies, including bacterial or viral respiratory infection, fat embolism, and pulmonary infarction from aggregates of sickled red blood cells or thrombosis.<sup>1</sup> Because episodes vary from mild disease to critical illness with rapidly progressive respiratory and multiorgan failure, predicting the severity of acute chest syndrome episodes is an important research priority.

Pulmonary hypertension is common in adults with sickle cell disease and is an important risk factor for mortality.<sup>2–4</sup> Right heart catheterization remains the gold standard in diagnosing pulmonary hypertension, but Doppler echocardiography is the preferred screening test for pulmonary hypertension<sup>5</sup> due to its noninvasiveness. Elevated pulmonary pressures estimated with Doppler echocardiography are associated with death in patients with sickle cell disease in several studies,<sup>6–8</sup> but pulmonary hypertension in this population at times remains undiagnosed. Pulmonary pressures often increase transiently during acute chest syndrome, and pulmonary hypertension is also associated with mortality in acute chest syndrome.<sup>9</sup> Estimation of pulmonary artery (PA) pressures using Doppler

echocardiography may be logistically unavailable in the acute setting or technically limited due to poor ultrasound windows. Alternatively, computed tomography (CT) of the chest is frequently obtained in the emergency department for patients presenting with pulmonary symptoms and measurement of the PA diameter is often already available to the clinician.

PA enlargement on CT scan is an underutilized diagnostic resource for screening for pulmonary hypertension and has been described by Troung et al.<sup>10</sup> as a main PA diameter exceeding 29 mm in men and 27 mm in women. PA enlargement on CT is comparable in sensitivity and specificity to Doppler echocardiography in predicting pulmonary hypertension, based on recent meta-analyses.<sup>11,12</sup> A retrospective study in patients with sickle cell disease showed that PA size on CT angiogram differed between patients with and without pulmonary hypertension, demonstrating potential as an indicator of pulmonary hypertension in this population.<sup>13</sup> An enlarged PA on CT is marker of poor outcomes in

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multiple respiratory diseases including chronic obstructive pulmonary disease,<sup>14,15</sup> obstructive sleep apnea,<sup>16</sup> and chronic thromboembolic disease.<sup>17</sup>

Since pulmonary hypertension is a risk factor for mortality in patients with sickle cell disease, we sought to determine whether the presence of an enlarged PA on CT would be useful for risk stratification in acute chest syndrome. Although the extent to which the PA may dilate due to acute and transient elevations in pulmonary pressure associated with acute chest syndrome<sup>9</sup> is unclear, an enlarged PA on CT may raise suspicion for underlying pulmonary hypertension.<sup>18</sup> In this study, we tested the hypothesis that an enlarged PA on CT would be associated with a high-risk phenotype in acute chest syndrome characterized by severe respiratory failure requiring either noninvasive or mechanical ventilation.

## Methods

We retrospectively reviewed all cases of acute chest syndrome treated in the medical intensive care unit (ICU) at two tertiary care hospitals from January 2011 to August 2016 and included all adult patients with a CT of the chest before or during their admission ( $n=63$ ). Patients with sickle cell disease treated in the ICU were identified using billing codes and were screened to ensure they met criteria during their admission for acute chest syndrome, defined as presence of a new infiltrate on chest imaging along with chest pain, cough, wheezing, tachypnea, or fever in a patient with sickle cell disease.<sup>1</sup> High-resolution noncontrast and contrast-enhanced chest CTs for included patients were analyzed in mediastinal windows using axial thin sections with width of 1.25 mm. Standard viewing Carestream Vue PACS software was used to analyze the images. As in Mahammedi et al.,<sup>19</sup> the axial diameter of the main PA was measured at the level of the PA bifurcation along the line originating from the center of the adjacent ascending aorta and passing perpendicular to the long axis of the main PA.

We compared clinical characteristics in our subject cohort using Student's T-test for continuous variables and Fisher's Exact Test for categorical variables. We then used Fisher's Exact Test to test whether an enlarged PA diameter on CT (defined as  $>29$  mm in men and  $>27$  mm in women based on Troung et al.<sup>10</sup>) would be associated with the primary outcome of severe respiratory failure requiring noninvasive ventilation or mechanical ventilation in patients with acute chest syndrome. Secondary outcomes of noninvasive ventilation, mechanical ventilation, ICU length of stay, hospital length of stay, and mortality were also compared using Student's T-test for continuous variables and Fisher's Exact Test for categorical variables. Approval for the study was obtained from our Institutional Review Board and research was conducted in accordance with the Declaration of Helsinki.

## Results

In our cohort of adult patients treated in the medical ICU for acute chest syndrome, the PA diameter was enlarged on CT in 37 of 63 patients (58.7%) and normal in 26 of 63 patients (41.3%) (Table 1). On average, the PA was  $34 \pm 4$  mm in the enlarged PA group and  $26 \pm 2$  mm in the normal PA group ( $P < 0.01$ ). Patients in the enlarged PA group were older than patients in the normal PA group, with an average age of  $35 \pm 12$  years versus  $28 \pm 8$  years ( $P = 0.02$ ). Treatment with-exchange transfusion, simple transfusion, antibiotics, intravenous fluids, and analgesia did not differ between groups. All CT scans were performed within five years of admission. The average time distance was six months and 46% occurred at the time of admission for acute chest syndrome.

Among patients with an enlarged PA diameter on CT, 12 of the 37 (32.4%) patients developed the primary outcome of severe respiratory failure requiring mechanical or noninvasive ventilation compared to 1 of the 26 (3.8%) patients with a normal PA diameter ( $P < 0.01$ ) (Table 1); 7 of the 37 patients in the enlarged PA group required noninvasive ventilation (18.9%) compared to 0 of the 26 patients (0%) in the normal PA group ( $P = 0.04$ ). There was no difference between the groups in requirement for mechanical ventilation, ICU length of stay, and hospital length of stay. There were no deaths.

## Discussion

In this retrospective study of adult patients with sickle cell disease acute chest syndrome, we found that patients with enlarged PA diameter on CT were more likely to develop severe respiratory failure requiring mechanical or noninvasive ventilation, demonstrating that an enlarged PA diameter on CT may be a useful resource for risk stratification of patients with acute chest syndrome. Pulmonary hypertension is a known risk factor for morbidity and mortality in patients with sickle cell disease.<sup>2-4</sup> It is likely the most common cause of PA enlargement on CT;<sup>18</sup> and the PA diameter in patients with sickle cell disease has been shown to be larger in patients with pulmonary hypertension compared to those without.<sup>13</sup> While further research is needed to establish the specificity of an enlarged PA diameter for pulmonary hypertension in patients with sickle cell disease, it is possible that the increased morbidity of severe respiratory failure observed in subjects with an enlarged PA diameter could be associated with underlying pulmonary hypertension.

Recognition of pulmonary hypertension is critical in managing acute chest syndrome because standard of care treatment for acute chest syndrome, in addition to empiric antibiotics, includes intravenous fluids and blood transfusion. Pulmonary hypertension in sickle cell disease is classified as World Health Organization Group V given its multifactorial etiology, with patients having hemodynamics that are either precapillary, postcapillary, or having features

**Table 1.** Clinical characteristics and outcomes for patients with enlarged and normal pulmonary artery diameter.<sup>a</sup>

	Enlarged pulmonary artery diameter N = 37	Normal pulmonary artery diameter N = 26	P <sup>b</sup> (T-test or Fisher's Exact Test)
<b>Clinical characteristics</b>			
Age, years	35 (12)	28 (8)	<b>0.02</b>
Female	22 (59%)	10 (38%)	0.41
African American race	34 (92%)	25 (96%)	0.90
Hemoglobin SS disease	30 (81%)	22 (85%)	0.99
History of acute chest syndrome	12 (32%)	12 (46%)	0.40
Main pulmonary artery diameter, mm	34 (4)	26 (2)	<b>&lt;0.01</b>
Estimated PA systolic pressure on TTE, mmHg	50 (17)	43 (14)	0.29
Baseline hemoglobin, mg/dl	8.1 (1.4)	8.5 (1.8)	0.38
Hemoglobin, mg/dl	7.0 (1.4)	7.6 (1.7)	0.17
White blood cell count, 10 <sup>9</sup> /L	21.7 (9.0)	24.3 (8.8)	0.22
Platelets, 10 <sup>9</sup> /L	280 (137)	301 (123)	0.54
Reticulocytes, 10 <sup>9</sup> /L	292 (169)	338 (159)	0.32
<b>Treatments</b>			
Analgesia	36 (97%)	26 (100%)	>0.99
Intravenous fluids	31 (84%)	23 (88%)	0.89
Antibiotics	37 (100%)	26 (100%)	>0.99
Simple transfusion	18 (49%)	13 (50%)	>0.99
Exchange transfusion	23 (62%)	18 (69%)	0.76
<b>Outcomes</b>			
Severe respiratory failure	12 (32.4%)	1 (3.8%)	<b>&lt;0.01</b>
Non-invasive ventilation	7 (18.9%)	0 (0%)	<b>0.04</b>
Mechanical ventilation	5 (13.5%)	1 (3.8%)	0.4
ICU length of stay, days	3 (2.6)	2.1 (1.5)	0.12
Hospital length of stay, days	13.9 (10.9)	12.8 (11.7)	0.7
Mortality	0 (0%)	0 (0%)	>0.99

Note: PA: pulmonary artery; TTE: transthoracic echocardiogram; ICU: intensive care unit.

<sup>a</sup>Data are summarized as mean (standard deviation) for continuous variables and n (%) for categorical variables.

<sup>b</sup>P are from Student's T-tests for continuous variables and Fisher's Exact Tests for categorical variables.

<sup>c</sup>P-values less than 0.05 were considered statistically significant.

of both.<sup>5,20</sup> In the presence of suspected pulmonary hypertension, avoidance of excess intravenous fluid administration is important to prevent decreased oxygen delivery and hemodynamic compromise from right heart failure. Suspicion for pulmonary hypertension may also affect transfusion strategy to minimize the risk of transfusion associated circulatory overload. Given its comparable sensitivity to Doppler echocardiogram<sup>11,12</sup> and availability in the acute setting, PA enlargement on CT should be more widely recognized as a useful screening tool for pulmonary hypertension in patients with acute chest syndrome.

Our study is limited by its retrospective design and small sample size of 63 patients. Small sample size may have precluded identification of a relationship between PA enlargement on CT and the outcomes of need for mechanical ventilation and mortality. In addition, due to small sample size, we were unable to limit subjects to patients with a CT chest at the time of admission for acute chest syndrome, and therefore the PA diameter may not reflect the hemodynamics at the time of each patient's presentation. However, the inclusion of all subjects with a prior or concurrent CT chest may be more realistic, as clinicians

screening for pulmonary hypertension in the acute setting often must rely on prior imaging to guide management.

Enlarged PA diameter on CT is a valuable tool to screen for pulmonary hypertension; and this investigation demonstrates that it is associated with severe respiratory failure in patients with acute chest syndrome. Enlarged PA diameter on CT is a promising resource for risk stratification of patients with acute chest syndrome, and future prospective studies are needed to further validate its use for this purpose.

#### Author Contributions

J. L. S. designed the research, performed data acquisition, analysis, and interpretation, and wrote the manuscript; D. P. contributed to data acquisition, analysis, and interpretation; J. K. contributed to data acquisition and analysis; A. T. contributed to research design, data interpretation, and manuscript revision; and G. Z. contributed to research design, data interpretation, and manuscript revision.

#### Authors' Note

This study was presented in abstract form at the Chest 2020 Virtual Annual Meeting, 20 October 2020.

**Conflict of interest**

The author(s) declare that there is no conflict of interest.


**Ethical Approval**

Approval for the study was obtained from Northwell Health's Institutional Review Board and research was conducted in accordance with the Declaration of Helsinki.

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**References**

- Vinchinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. *N Engl J Med* 2000; 342: 1855–1865.
- Parent F, Bachir D, Inamo J, et al. A hemodynamic study of pulmonary hypertension in sickle cell disease. *N Engl J Med* 2011; 365: 44–53.
- Fonseca GH, Souza R, Salemia VM, et al. Pulmonary hypertension diagnosed by right heart catheterization in sickle cell disease. *Eur Respir J* 2012; 39: 112–118.
- Mehari A, Gladwin MT, Tian X, et al. Mortality in adults with sickle cell disease and pulmonary hypertension. *J Am Med Assoc* 2012; 307: 1254–1256.
- Klings ES, Machado RF, Barst RJ, et al. An official American Thoracic Society clinical practice guideline: diagnosis, risk stratification, and management of pulmonary hypertension of sickle cell disease. *Am J Respir Crit Care Med* 2014; 189: 727–740.
- Ataga KI, Moore CG, Jones S, et al. Pulmonary hypertension in patients with sickle cell disease: a longitudinal study. *Br J Haematol* 2006; 134: 109–115.
- DeCastro LM, Jonassaint JC, Graham FL, et al. Pulmonary hypertension associated with sickle cell disease: clinical and laboratory end-points and disease outcomes. *Am J Hematol* 2008; 83: 19–25.
- Gladwin MT, Sachdev V, Jison ML, et al. Pulmonary hypertension as a risk factor for death in patients with sickle cell disease. *N Engl J Med* 2004; 350: 886–895.
- Dessap AM, Leon R, Habibi A, et al. Pulmonary hypertension and cor pulmonale during severe acute chest syndrome in sickle cell disease. *Am J Respir Crit Care Med* 2008; 177: 646–653.
- Truong QA, Massaro JM, Rogers IS, et al. Reference values for normal pulmonary artery dimensions by noncontrast cardiac computed tomography: the Framingham heart study. *Circ Cardiovasc Imaging* 2012; 5: 147–154.
- Shen Y, Wan C, Tian P, et al. CT-base pulmonary artery measurements in the detection of pulmonary hypertension: a meta-analysis and systematic review. *Medicine* 2014; 93: e256.
- Ni J, Yan P, Liu S, et al. Diagnostic accuracy of transthoracic echocardiography for pulmonary hypertension: a systematic review and meta-analysis. *BMJ Open* 2019; 9: e033084.
- Linguraru MG, Pura JA, Gladwin MT, et al. Computed tomography correlates with cardiopulmonary hemodynamics in pulmonary hypertension in adults with sickle cell disease. *Pulm Circ* 2014; 4: 319–329.
- Wells JM, Washko GR, Han MK, et al. Pulmonary arterial enlargement and acute exacerbations of COPD. *N Engl J Med* 2012; 367: 913–921.
- Shin S, King CS, Brown AW, et al. Pulmonary artery size as a predictor of pulmonary hypertension and outcomes in patients with chronic obstructive pulmonary disease. *Respir Med* 2014; 108: 1626–1632.
- Dobrowolski P, Florczak E, Klisiewicz A, et al. Pulmonary artery dilation indicates severe obstructive sleep apnea in patients with resistant hypertension: the resist-POL study. *Pol Arch Med Wewn* 2016; 126: 222–229.
- Scholzel BE, Post MC, Dymarkowski S, et al. Prediction of outcome after PEA in chronic thromboembolic pulmonary hypertension using indexed PA diameter. *Eur Respir J* 2014; 43: 909–912.
- Raymond TE, Khabbaza JE, Yadav R, et al. Significance of main pulmonary artery dilation on imaging studies. *Ann Am Thorac Soc* 2014; 11: 1623–1632.
- Mahammedi A, Oshmyansky A, Hassoun PM, et al. Pulmonary artery measurement in pulmonary hypertension. *J Thorac Imaging* 2013; 28: 96–103.
- Niss O, Quinn CT, Lane A, et al. Cardiomyopathy with restrictive physiology in sickle cell disease. *JACC Cardiovasc Imaging* 2016; 9: 243–252.