CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Monitoring for Pulmonary Hypertension Following Pulmonary Embolism: The INFORM Study

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ABSTRACT

BACKGROUND: Pulmonary hypertension and chronic thromboembolic pulmonary hypertension may develop after a pulmonary embolism event. A ventilation-perfusion scan is recommended as a first-line modality for suspected chronic thromboembolic pulmonary hypertension. In this study, we determined the prevalence of pulmonary hypertension following incident pulmonary embolism and the disease-monitoring patterns in this population.

METHODS: We conducted a retrospective claims database analysis of incident pulmonary embolism cases (July 1, 2010 to September 30, 2011) and extracted data for 1 year prior to and 2 years after the incident pulmonary embolism event. Data were analyzed for diagnoses and symptoms related to pulmonary hypertension, claims consistent with other heart or lung diseases, diagnostic imaging tests, and time to first diagnostic imaging test post pulmonary embolism.

RESULTS: Of the 7068 incident pulmonary embolism patients that met eligibility criteria, 87% had a claim for a pulmonary hypertension-related symptom and 7.6% had a claim for pulmonary hypertension during follow-up. Only 55% of all pulmonary embolism patients had diagnostic procedural claim(s) post pulmonary embolism: echocardiogram, 47%; computed tomographic angiography, 20%; ventilation-perfusion scan, 6%; and right heart catheterization or pulmonary angiography, <1%. The mean time from pulmonary embolism diagnosis to first screening test was 131 days.

CONCLUSIONS: Despite exhibiting pulmonary hypertension-related symptoms, many pulmonary embolism patients did not undergo imaging tests that could diagnose pulmonary hypertension or chronic thromboembolic pulmonary hypertension. This study suggests that physician education about the risk of pulmonary hypertension and chronic thromboembolic pulmonary hypertension after pulmonary embolism may need to be improved.

 • The American Journal of Medicine (2016) 129, 978-985

KEYWORDS: Chronic thromboembolic pulmonary hypertension; CTEPH; Pulmonary embolism; Pulmonary hypertension; VQ scan

Funding: Bayer HealthCare Pharmaceuticals (Berlin, Germany).

Conflict of Interest: VFT has consulted for Actelion, Bayer, Gilead, Inari, Janssen, and United Therapeutics; has had research support from Actelion, Bayer, Gilead, Inari, Janssen, United Therapeutics, EKOS, and BiO2; and has Honoraria from Actelion, Bayer, and Janssen. RNC has been a consultant to Bayer, Actelion, and United Therapeutics. The remaining authors report no conflict of interest.

Authorship: All authors had access to the data and had a role in writing the manuscript. Authors DP, SAT, CHD, MO, CAS, and VNJ were involved in planning and conduct of the study. FX was the lead data analyst. VFT and RNC assisted with the interpretation and presentation of the data.

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0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2016.03.006

Pulmonary embolism affects 300,000 to 600,000 people each year in the US and is a major public health concern.[1] Chronic thromboembolic pulmonary hypertension, a form of pulmonary hypertension, is commonly seen as a long-term sequela of acute pulmonary embolism.[2] Studies suggest that chronic thromboembolic pulmonary hypertension occurs in 1% to 3.8% of patients surviving acute pulmonary embolism.[3,4] The natural history of pulmonary embolism typically includes restoration of normal hemodynamics and gas exchange and total resolution of thromboemboli or resolution with minimal residua within 30 days.[5] However, up to 50% of patients will experience residual defects for at least 11 months[6] and may be at risk for developing chronic thromboembolic pulmonary hypertension.

Chronic thromboembolic pulmonary hypertension is a rare and serious disease characterized by progressive dyspnea, and if unrecognized and untreated, right heart failure and death.[7,8] In many patients with chronic thromboembolic pulmonary hypertension, dyspnea is attributed to other conditions, leading to a delayed diagnosis. The mean duration from onset of symptoms to chronic thromboembolic pulmonary hypertension diagnosis was estimated to be 2.7 years.[7-14] Effective diagnosis is crucial, as chronic thromboembolic pulmonary hypertension is a treatable condition. The treatment of choice is pulmonary endarterectomy, in which the chronic thromboembolic material is dissected from the vessel wall, usually resulting in marked improvement or resolution of pulmonary hypertension. However, 20% to 40% of patients are deemed inoperable, while another 10% to 40% of patients experience recurrent or persistent pulmonary hypertension post pulmonary endarterectomy.[15-18]

Historically, medications indicated for use in pulmonary arterial hypertension have been prescribed off-label to select subgroups of chronic thromboembolic pulmonary hypertension patients.[10,15,19] Recently, a pharmacotherapy has been approved to treat chronic thromboembolic pulmonary hypertension patients. Riociguat is a soluble guanylate cyclase stimulator indicated for the treatment of adults with inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (World Health Organization Group 4) after surgical treatment to improve exercise capacity and World Health Organization functional class.[20-22] However, the impact of pharmacotherapy on long-term survival in these patients requires further study.

The 2014 guidelines on managing pulmonary embolism from the European Society of Cardiology and from the Fifth World Symposium on Pulmonary Hypertension state that a ventilation-perfusion scan should be the first-line imaging modality for diagnosing chronic thromboembolic pulmonary hypertension following pulmonary embolism. A ventilation-perfusion scan suggestive of chronic thromboembolic pulmonary hypertension should be followed by right heart catheterization to confirm pulmonary hypertension and computed tomographic angiography or pulmonary angiography to confirm pulmonary embolism as the cause. Chronic thromboembolic pulmonary hypertension is thus diagnosed, and suitability for surgery can be determined (**Figure 1**).[23,24] However, a recent report indicates the underutilization of ventilation-perfusion scans as part of the diagnostic work-up of pulmonary arterial hypertension, which may lead to missing cases or misclassification of pulmonary hypertension.[25] The report also disclosed that in roughly one-third of the cases without a ventilation-perfusion scan, the provider reported that the scan was not relevant. Therefore, physicians appear to be undereducated with regard to the appropriate evaluation of pulmonary hypertension in general.

CLINICAL SIGNIFICANCE

- A majority (87%) of incident pulmonary embolism (PE) patients experienced persistent symptoms suggestive of pulmonary hypertension, but only 61% of these patients underwent follow-up diagnostic testing.
- We observed underutilization of the ventilation-perfusion scan, which is recommended to screen for chronic thromboembolic pulmonary hypertension in patients with persistent respiratory symptoms following a PE.
- The 2-year cumulative incidence of pulmonary hypertension was 7.6%, suggesting the need to closely monitor this patient population.

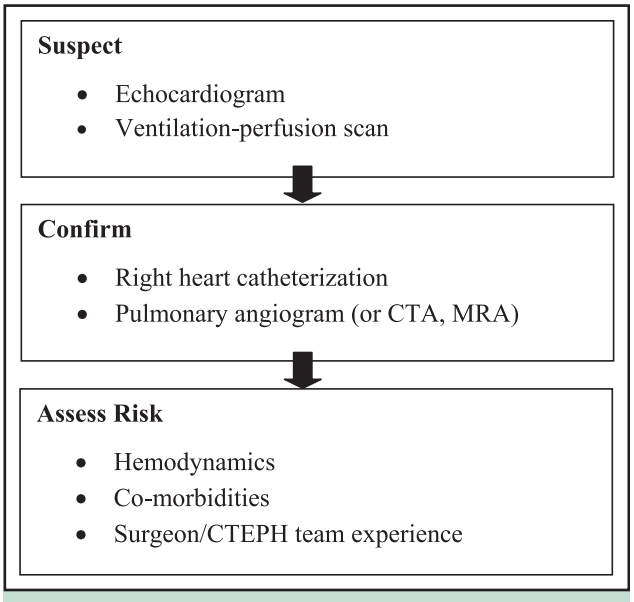

Figure 1 Stepwise process for the diagnosis of chronic thromboembolic pulmonary hypertension. CTA = computed tomographic angiography; CTEPH = chronic thromboembolic pulmonary embolism; MRA = magnetic resonance angiogram. Reproduced with permission; Kim et al.[24]