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Silent Pulmonary Embolism in Patients with Deep Venous Thrombosis: A Systematic Review

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ABSTRACT

PURPOSE: To determine, by systematic review of the literature, the prevalence of silent pulmonary embolism in patients with deep venous thrombosis.

METHODS: Twenty-eight included published investigations were identified through PubMed. Studies were selected if methods of diagnosis of pulmonary embolism were described; if pulmonary embolism was stated to be asymptomatic; and if raw data were presented. Studies were stratified according to whether silent pulmonary embolism was diagnosed by a high-probability ventilation-perfusion lung scan using criteria from the Prospective Investigation of Pulmonary Embolism Diagnosis, computed tomography pulmonary angiography, or conventional pulmonary angiography (Tier 1), or by lung scans based on non-Prospective Investigation of Pulmonary Embolism Diagnosis criteria (Tier 2).

RESULTS: Silent pulmonary embolism was diagnosed in 1665 of 5233 patients (32%) with deep venous thrombosis. This is a conservative estimate because many of the investigations used stringent criteria for the diagnosis of pulmonary embolism. The incidence of silent pulmonary embolism was higher with proximal deep venous thrombosis than with distal deep venous thrombosis. Silent pulmonary embolism seemed to increase the risk of recurrent pulmonary embolism: 25 of 488 (5.1%) with silent pulmonary embolism versus 7 of 1093 (0.6%) without silent pulmonary embolism.

CONCLUSION: Silent pulmonary embolism sometimes involved central pulmonary arteries. Because approximately one third of patients with deep venous thrombosis have silent pulmonary embolism, routine screening for pulmonary embolism may be advantageous.

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KEYWORDS: Deep venous thrombosis; Pulmonary embolism; Venous thromboembolic disease

Pulmonary embolism was unsuspected or undiagnosed antemortem in 3268 of 3876 patients in general hospitals or communities who had pulmonary embolism at autopsy (84%; range 80%-93%).[1] Even in patients with large or fatal pulmonary embolism at autopsy, the majority (1902/2448 [78%]) of embolisms were unsuspected or undiagnosed antemortem.[1] Many patients with unsuspected large or fatal pulmonary embolism had advanced associated disease.[1] It has been tacitly assumed that diligence and increased awareness might diminish the proportion of unsuspected cases of pulmonary embolism. Patients who have sudden and unexplained catastrophic events in the hospital are a group in whom the diagnosis might be suspected more frequently if physicians maintain a high index of suspicion.[1] However, the extent to which silent pulmonary embolism explains some of the unsuspected pulmonary embolism at autopsy is uncertain. Silent pulmonary embolism has been diagnosed in living patients with deep venous thrombosis since the early 1970s.[2,3] Silent pulmonary embolism may lead to pulmonary hypertension.[4] Data indicate that incidentally detected pulmonary embolism may lead to death.[5]

These reports of silent pulmonary embolism identify an important problem. For patients with deep venous thrombosis, is it sufficient to have a high level of suspicion of

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pulmonary embolism? Should patients with deep venous thrombosis undergo pulmonary imaging even if they have no respiratory symptoms? Should routine screening be performed to prevent a misdiagnosis of pulmonary embolism resulting from treatment failure? Might unnecessary insertion of an inferior vena cava filter be avoided if it were known that silent pulmonary embolism had been present and there was no failure of treatment of deep venous thrombosis[6]? To approach these issues, an assessment of the prevalence of silent pulmonary embolism in patients with deep venous thrombosis is needed. Whether routine imaging of pulmonary embolism would be appropriate depends in part on the prevalence of silent pulmonary embolism in patients with deep venous thrombosis. Therefore, this systematic review was undertaken.

CLINICAL SIGNIFICANCE

- Silent pulmonary embolism occurs in approximately one third of patients with deep venous thrombosis.
- Silent pulmonary embolism is more frequent in patients with proximal deep venous thrombosis than in those with distal deep venous thrombosis.
- Recurrent pulmonary embolism during treatment for deep venous thrombosis is more frequent in those with silent pulmonary embolism than a first pulmonary embolism in those with no silent pulmonary embolism.
- Silent pulmonary embolism may occur in the central pulmonary arteries.

MATERIALS AND METHODS

We attempted to identify all published trials in all languages that reported the prevalence of silent pulmonary embolism in patients with deep venous thrombosis. Studies were identified by searching PubMed through July 2009. Key words were "silent," "asymptomatic," "incidental," "symptomless," and "occult pulmonary embolism." We augmented our searches by manually reviewing the reference lists of all original articles. This was done by 2 of the authors, who worked separately and then reviewed their findings together. Authors were not blinded to journal, author, or institution.

Studies were included if they met the following criteria: the methods of diagnosis of pulmonary embolism were described; the pulmonary embolism was stated to be asymptomatic; raw data on the occurrence of silent pulmonary embolism were presented in sufficient detail to permit calculations of the prevalence.

The literature search identified 958 citations. Complete versions of the articles were obtained if, from review of the title or abstract, they satisfied the inclusion criteria. Among these, 720 were unrelated to silent pulmonary embolism, 48 were case reports or case series without data on the prevalence, 151 were reviews or editorials, 22 were related to silent pulmonary embolism in circumstances other than patients with deep venous thrombosis, and 4 had data that were included in a previous investigation. The literature search identified 13 investigations that met the inclusion criteria. An additional 15 investigations were identified from the references in these investigations and from a review article of antithrombotic therapy. Although retrospective investigations were not excluded, none were found.

Investigations were stratified into 2 tiers: Tier 1 included those in which silent pulmonary embolism was diagnosed on the basis of a high-probability interpretation of the ventilation-perfusion lung scan using criteria from the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED), computed tomography (CT) pulmonary angiography, or conventional pulmonary angiography[5,7-17] (Table 1). Tier 2 included those in which silent pulmonary embolism was diagnosed by ventilation-perfusion lung scan based on unstated criteria or criteria other than PIOPED[2,3,18-31] (Table 2). Criteria for ventilation-perfusion lung scan other than the PIOPED criteria were those of McNeil et al[32] and Biello et al.[33] All included investigations (both Tier 1 and Tier 2) were prospective. In several investigations, the authors indicated that consecutive patients were studied.[2,5,11-13,15-17,20-22,24-26,28-30]

RESULTS

Twelve Tier 1 studies and 16 Tier 2 studies met the inclusion criteria. Among Tier 1 studies, silent pulmonary embolism, based on pooled data, was detected in 703 of 2656 patients (27%) with deep venous thrombosis[5,7-17] (Table 1). Among Tier 2 studies, silent pulmonary embolism, based on pooled data, was detected in 962 of 2577 patients (37%) with deep venous thrombosis[2,3,18-31] (Table 2). Altogether, by recognizing that there was heterogeneity in the methods of diagnosis, silent pulmonary embolism was diagnosed in 1665 of 5233 patients (32%) with deep venous thrombosis.[2,3,5,7-31]

By considering only those with proximal deep venous thrombosis, the prevalence of silent pulmonary embolism was 600 of 2269 (26%) in Tier 1 patients[5,7,11-14,16,17] (Table 1) and 291 of 538 (54%) in Tier 2 patients[19,22,24,27-29,31] (Table 2). The overall prevalence of silent pulmonary embolism in patients with proximal deep venous thrombosis was 891 of 2807 (32%).[5,7,11-14,16,17,19,22,24,27-29,31] In 5 investigations, comparisons were made of the prevalence of silent pulmonary embolism with proximal and distal deep venous thrombosis.[10,15,20,25,26] In those with proximal deep venous thrombosis, silent pulmonary embolism occurred in 196 of 546 patients (36%) compared with 15 of 113 patients (13%) with distal deep venous thrombosis ($P < .0001$) (Tables 1 and 2). In an investigation of prox-