Paediatric pulmonary thromboembolism

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Background
Pulmonary thromboembolism is a rare but life-threatening event that may be encountered by general paediatricians and paediatric subspecialists, as well as physicians in other disciplines. Thrombotic occlusion of the blood vessels leaving the right side of the heart and entering the lungs results in significant strain on the right side of the heart, and a reduction in the amount of oxygen rich blood returning to the left side of the heart for delivery to the tissues of the body (1). The most common signs and symptoms of pulmonary thromboembolism, including tachycardia and respiratory distress, are very similar to those of much more common childhood illnesses (1-5). Due to the rarity and non-specific clinical presentation of paediatric pulmonary thromboembolism, many cases are not diagnosed and treated in time, resulting in fatal outcomes (2-4, 6).

Adequate epidemiological data regarding paediatric pulmonary thromboembolism are lacking. A systematic review in 2017 that specifically focused on paediatric pulmonary embolism and in situ pulmonary artery thrombosis identified only a few case reports, case series, and cohort studies, describing children with non-specific presentation, delayed
diagnosis, variable treatment regimens, and frequent post-mortem diagnosis (7). Best estimates regarding the incidence, age distribution, associated conditions, diagnostic modalities, location of thrombus, treatment patterns, and clinical outcomes of pulmonary thromboembolism in Canadian children were published two decades ago, using information obtained from a national registry of paediatric thromboembolic disease (8,9). The aforementioned registry included only patients older than one month of age who were referred to the paediatric haematology service for deep vein thrombosis, cross-referenced with hospital medical records that had relevant institution-specific codes for thrombotic complications, at one of 15 tertiary care paediatric hospitals in Canada. Primarily designed to study the broader condition of venous thromboembolism, pulmonary embolism was only examined as a related complication. Patients with thrombotic occlusion of the central nervous system, portal system, renal veins, or other non-extremity venous systems were excluded. It is likely that rates of pulmonary thromboembolism in Canadian children have increased in recent years (6,10).

A large, population-based surveillance study is required to establish more valid estimates of incidence, clinical features, and outcomes of paediatric pulmonary thromboembolism in Canada. In 2012, the Paediatric and Neonatal Thrombosis and Hemostasis Subcommittee of the International Society on Thrombosis and Haemostasis formed a paediatric pulmonary embolism working group that has since recommended that “an important first step is to collect high quality, standardized, prospective data on the presenting features and outcomes of paediatric pulmonary embolism” (11). Establishing the true incidence rate, age-specific clinical presentation, risk factors, and short-term outcomes of pulmonary thromboembolism in Canadian children will allow clinical researchers to establish the basis for future studies regarding optimal diagnosis and treatment, as well as support knowledge mobilization activities to improve recognition and management of this rare paediatric condition among frontline health care providers, thereby improving the health of Canadian children.

**Methods**

Through the established methodology of the CPSP, approximately 2,800 paediatricians and paediatric subspecialists who are actively practising in Canada will receive a monthly reporting form, either electronically or by mail, based on their indicated preference. Participants will be asked to voluntarily record the number of new cases of suspected or confirmed pulmonary thromboembolism seen in the prior month. Clinicians who report a case on the initial reporting form will receive a secondary detailed questionnaire to complete.

**Case definition**

Report any patient less than 16 years of age (up to their 16th birthday) with a new diagnosis of pulmonary thromboembolism. Pulmonary thromboembolism is defined as in situ thrombus or embolism, including fragments and fat embolism, situated anywhere in the pulmonary arterial circulation from the right ventricle (RV), through the outflow tract, to the peripheral and subsegmental regions of the pulmonary arteries. Report patients including, but not limited to, asymptomatic patients, postoperative patients, pregnant or recently pregnant patients, and deceased patients.

**Confirmed pulmonary thromboembolism**  patient fulfills one of four criteria:

1. Pulmonary thromboembolism diagnosed on computerized tomography (CT) pulmonary
Suspected pulmonary embolism patient fulfills one of two criteria:
1. Clinical suspicion of pulmonary thromboembolism AND V/Q scan reporting intermediate probability of pulmonary thromboembolism
2. Clinical suspicion of pulmonary thromboembolism AND echocardiogram demonstrating RV dysfunction with no other explanation

Objectives
Primary objective
Document the minimum national incidence of pulmonary thromboembolism in children (age < 16 years), by age, gender, and province/territory of residence.

Secondary objectives
1) Describe the clinical presentation of pulmonary thromboembolism in children.
2) Identify risk factors associated with pulmonary thromboembolism in children.
3) Describe the diagnostic modalities used to identify pulmonary thromboembolism in children and the therapeutic regimens used for treatment.

Duration
January 2020 to December 2021

Expected number of cases
This study aims to establish the minimum national incidence of paediatric pulmonary thromboembolism. The sample size will be determined by the number of cases identified using surveillance methodology. A national registry of venous thromboembolism in Canadian children identified 69 cases of pulmonary embolism between May 1990 and November 1996 (8), for an estimated annual incidence rate of 2 cases per million Canadian children, calculated using 1996 census data (12). A retrospective study conducted over an 8-year period at one Canadian paediatric hospital identified a cohort of 56 paediatric patients with radiologically proven pulmonary thromboembolism (4). Based on these studies, a minimum of 12 cases per annum are expected to be reported from across the country.
Study limitations
As with any voluntary reporting surveillance system, the Canadian Paediatric Surveillance Program (CPSP) recognizes that reporting on minimum incidence rates can have limitations, including under-representation of the disease in the population. It is possible that some groups of children will be missed, for example, those who live in rural or remote areas as they may be less likely to receive timely specialist care. Additionally, case-level surveillance data is extracted from patient charts following the clinical encounter. Data elements, including details of history, physical examination, and relevant components of the diagnostic assessment not collected as part of routine care, will be absent from the surveillance totals.

Despite its limitations, surveillance serves a very important purpose and provides rich clinical data that will allow a better understanding of pulmonary thromboembolism in Canadian children and youth.

Ethical approval
Health Canada and the Public Health Agency of Canada’s Research Ethics Board
IWK Health Centre Research Ethics Board

Analysis and publications
Descriptive analyses will be performed to quantitatively summarize demographic variables. Event rates will be calculated using population denominators, based on Canadian Census data (13).

Findings of this study will be summarized and published in the annual CPSP Results, presented at the Canadian Paediatric Society annual conference, and prepared as a manuscript for publication in a high-impact, peer-reviewed journal to allow for the dissemination of findings through national and international communities of practice. A presentation will be prepared and shared with site champions for knowledge dissemination at the local level.

References


