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Full Length Article

Risk factors and clinical features of acute pulmonary embolism in children from the community

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ABSTRACT

Background and aims: Current clinical decision rules for pulmonary embolism are based on adult populations and have not been validated in children. The objective was to identify and evaluate clinical features for a first lifetime episode of pulmonary embolism in children presenting to the emergency department.
Materials and methods: We present a case–control study of children (≤18 years) presenting to the emergency department of the Royal Children's Hospital, Melbourne between November 2007 and February 2015. Children with radiologically proven pulmonary embolism formed the case group, whilst children in whom there was a clinical suspicion of pulmonary embolism but negative diagnostic imaging formed the control group. Charts, electronic medical and imaging records of both cases and controls were reviewed and analysed.
Results: There were a total of 50 patients in this study (11 cases and 39 controls). Current or recent (within three months) use of the oral contraceptive pill was the most significant risk factor in our study (odds ratio 14.667, 95% confidence interval 3.001–71.678, $P < 0.001$). Most other features failed to discriminate between cases and controls, although there was a trend towards increased heart rate in cases.
Conclusions: Pulmonary embolism is perhaps the most common presenting spontaneous venous thromboembolism in the community and teenage girls on the oral contraceptive pill are most at-risk amongst children. The clinical signs and symptoms are often non-specific. Additional larger studies are required to determine the significance and magnitude of potential clinical predictors identified in this study. This may lead to derivation of a paediatric-specific pre-test probability tool.

1. Introduction

Acute pulmonary embolism (PE) is uncommon in childhood. Nevertheless, PE is a potentially fatal condition requiring prompt diagnosis and management. Currently, most studies in childhood venous thromboembolism (VTE) and PE indicate that "sick" hospitalised children are at highest risk, especially those with central venous lines and severe medical illnesses [1,2,3,4]. Children in the community can also develop PE and often present to emergency departments with non-specific cardiopulmonary symptoms such as chest pain and dyspnoea. Arguably, community-based children have different clinical characteristics than inpatient children. To date, only a single case series has analysed the clinical features of PE in children in the setting of an emergency department [5].

The diagnosis of PE in children can be challenging. Typical symptoms of PE are very common presenting complaints in emergency departments and can be confused with illnesses such as respiratory tract infections and asthma, potentially leading to delayed or even missed diagnosis. In adults, clinical decision rules for the diagnosis of PE have

Abbreviations: PE, Pulmonary embolism; VTE, Venous thromboembolism; OCP, Oral contraceptive pill; CTPA, Computed tomographic pulmonary angiography; VQ, Ventilation-perfusion; CDC, Centers for Disease Control and Prevention; BP, Blood pressure; HR, Heart rate; DVT, Deep vein thrombosis.

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been formulated to help clinicians objectively identify at-risk patients who require further diagnostic testing or low-risk patients who can be safely excluded without further testing. Retrospective studies indicate that tools such as the Well's score for PE and the Pulmonary Embolism Rule-out criteria are of limited utility in children [5,6]. Paediatric-specific clinical decision rules would be especially useful in emergency departments to stratify risk and avoid unnecessary radiation exposure from diagnostic imaging.

The objective of this study was to evaluate potential risk factors and clinical features for a first lifetime episode of pulmonary embolism in children presenting to the paediatric emergency department.

2. Materials and methods

Ethics approval for low-risk human research was obtained from The Royal Children's Hospital, Melbourne (project no. DA001-2013-13) and Monash University Human Research Ethics Committee (project no. CF15/1640 — 2015000824) in accordance with the Declaration of Helsinki. Informed consent was not required, however all data was de-identified for analysis.

2.1. Search strategy

We sought to identify all patients in whom there was a clinical suspicion of PE that had diagnostic imaging. We deemed that there was clinical suspicion for PE if the reason supplied on the radiology order form by the treating clinician was to query, exclude, diagnose or confirm PE. We then performed a search of the radiology database for computed tomographic pulmonary angiography (CTPA) and ventilation-perfusion (VQ) scans from November 2007 to February 2015 at The Royal Children's Hospital, Melbourne. We applied two search strategies for the identification of study subjects. Firstly, a keyword search was performed with the terms “pulmonary embolism”, “pulmonary emboli”, “pulmonary embolus”, “pulmonary thromboembolism”, “pulmonary thromboemboli”, “pulmonary thromboembolus” and “PE”. We then manually accessed every VQ scan and CTPA in the radiology database for the study period to verify the results from the keyword search. Results from both search strategies were compiled together.

2.2. Selection of cases and controls

Electronic and paper medical records were accessed to determine eligibility for the study. We applied the following exclusion criteria: 1) age > 18 years, 2) inpatients or patients not admitted through emergency, 3) asymptomatic patients and 4) previous PE.

As The Royal Children's Hospital, Melbourne is the major tertiary paediatric hospital for the state of Victoria, we also included patients who were diagnosed at an external institution but referred for treatment at this hospital. These patients were only included if copies of the diagnostic imaging and details of the initial admission were forwarded to the hospital.

Cases consisted of children ≤18 years admitted with the diagnosis of PE supported by confirmatory imaging. Children in whom there was a clinical suspicion of PE but negative diagnostic imaging formed the control group.

2.3. Data collection

A case-report form using the REDCap™ web application was created to extract data from cases and controls. Information collected included patient demographics, clinical presentation, risk factors, investigations and clinical outcome.

Demographic data collected included age, gender and physical measurements. Height and weight at admission was collected wherever possible. If unavailable, physical measurements closest to and within six months of the admission date were accepted. Children were classified as obese if the calculated BMI was >95th centile according to the Centers for Disease Control and Prevention (CDC) age- and sex-adjusted BMI charts. If weight was only available, obesity was defined as >95th percentile in the CDC age- and sex-adjusted weight-for-age growth chart.

Information on the clinical presentation was recorded from the emergency department and ward admission notes. Recorded symptoms included chest pain, pleuritic nature of chest pain, dyspnoea, cough, haemoptysis and syncope. We assumed that a subject did not have a particular symptom if it was not indicated in the admission notes.

Physical examination results prior to diagnostic imaging were also noted, including the presence of increased respiratory effort, findings on auscultation, signs and symptoms suggestive of DVT (limb pain, tenderness, swelling or redness), and vital signs on admission. Heart rate and respiratory rate were analysed to paediatric-specific ranges [7]. Tachycardia and tachypnoea was defined as recordings above the 99th percentile for age. We also defined hypotension if the systolic blood pressure was <90 mm Hg, fever if the temperature was ≥38.0 °C, and hypoxia if the oxygen saturation was <95%.

A list of risk factors for venous thromboembolism was established on based on the paediatric literature [3,8]. Risk factors included personal history of VTE, family history of VTE in a first-degree relative, obesity (according to CDC age-and sex-adjusted BMI and weight-for-age charts), oral contraceptive pill use/exogenous oestrogen therapy (current or recent use within 3 months), recent surgery (within 1 month), trauma or fracture requiring hospitalisation or surgery (within 1 month), immobility, central venous line present at admission, acute infection requiring hospitalisation (either concurrent or within the last month), malignancy, proven thrombophilia/hypercoagulability and prothrombotic diseases. We defined the following conditions as prothrombotic; chronic heart disease (coronary artery disease, heart failure, symptomatic congenital heart disease), systemic lupus erythematosus, nephrotic syndrome, inflammatory bowel disease, venous malformation, varicose veins, pregnancy or post-partum or post-abortion, chronic kidney disease, chronic liver disease and diabetes. Other active medical illnesses were also noted.

If a particular risk factor was not recorded in the hospital notes during the admission, we assumed that risk factor was absent. The number of risk factors identifiable on clinical assessment (i.e. excluding detection of occult malignancies or thrombophilia after the diagnosis of PE) and the total number of risk factors were tallied for every patient.

All available original or scanned electrocardiograms performed at admission prior to confirmatory imaging were collected and analysed by a blinded paediatric cardiologist for signs associated with PE. The results of other investigations including blood tests, chest radiographs and diagnostic imaging were also recorded.

2.4. Statistics

All analyses were performed using a statistical software package (SPSS Statistics Version 23.0. IBM Corp. Armonk, New York). Variables used for the case–control analysis were dichotomised into binary categorical variables. In univariate analysis, odds ratios were derived through standard protocols and strength of association was determined using the two-sided Fisher's exact test. In view of the high number of variables analysed, the critical P-value for significance was $P < 0.0014$ based on a Bonferroni correction. Multivariable regression analysis was not performed due to insufficient sample size. Continuous variables were not analysed in this study.

3. Results

From November 2007 to February 2015, the radiology database search yielded 24 children with PE and 129 potential controls. After accessing electronic and paper records, we excluded 13 cases (nine were inpatients, two had a history of PE, one had insufficient clinical