

Supplemental data file.

Methods:

Questionnaire

See figure E1.

Diagnosis of venous thromboembolism

Both in the study population and the reference population, all VTE events were objectively verified. In all identified events medical records of the patients were reviewed and adjudicated blindly, using international criteria¹⁻³. A definite DVT was defined as an intraluminal filling defect on venography or a non-compressible venous segment in the popliteal or femoral veins on duplex ultrasound. A probable DVT was defined as no venous filling on ascending contrast venography or no venous flow in the popliteal or femoral veins on duplex ultrasound. Definite PE was defined according to the PIOPED criteria as a high-probability ventilation/perfusion (V/Q) scan, i.e. ≥ 2 segmental perfusion defects (V/Q mismatch), a perfusion scan with ≥ 2 segmental perfusion defects and a normal chest X-ray, or a positive CT scan. Probable PE was defined as an intermediate probability V/Q scan with 1 segmental moderate or large V/Q mismatch.

Results

Comparison between patients who did and did not return the questionnaires is shown in table E2. We conducted a sensitivity analysis by excluding all probable DVT and PE cases. (Table E3) The resulting rate ratio's of the sensitivity analysis are shown in table E4.

References:

1. Gottschalk A, Sostman HD, Coleman RE, et al. Ventilation-perfusion scintigraphy in the PIOPED study. Part II. Evaluation of the scintigraphic criteria and interpretations. *J Nucl Med* 1993; 34(7):1119-1126.
2. Cushman M, Tsai AW, White RH, et al. Deep vein thrombosis and pulmonary embolism in two cohorts: the longitudinal investigation of thromboembolism etiology. *Am J Med* 2004; 117(1):19-25.
3. van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 2006; 295(2):172-179.

Table E2 Baseline characteristics of patients whom did not return the questionnaire

For 2 excluded patients we could not retrieve enough data to place them in 1 of the 2

	Mild-moderate asthma			Severe asthma		
	Excluded (n=78)	Included (n=365)	<i>p-value</i>	Excluded (n=34)	Included (n=283)	<i>p-value</i>
Age (years)	48 (18-86)	50 (18-88)	NS	55 (22-84)	51 (17-77)	NS
Female sex (%)	59.0	58.4	<i>NS</i>	56	61	<i>NS</i>
BMI (kg/m ²)	28.5 (19.3 - 44.7)	27.5 (17.0 - 45.0)	<i><0.05</i>	25.8 (19.4 - 41.9)	27.0 (17.6 - 58.5)	<i>NS</i>
Age of asthma onset (years)	38.5 (4.0 - 84.0)	39 (0.4 - 77.5)	<i>NS</i>	36.0 (3.0 - 81.0)	27.0 (0.4 - 70.0)	<i><0.05</i>
Duration of asthma (years)	6.5 (0.1 - 69.0)	5.0 (0.1 - 78.0)	<i>NS</i>	18.0 (0.2 - 51.0)	20.0 (0.1 - 76.0)	<i>NS</i>
Atopy (%)	60	42	<i><0.05</i>	85	49	<i><0.05</i>
Smoking history						
Never smoker (%)	58	52	<i>NS</i>	65	64	<i>NS</i>
Ex smoker (%)	32	40	<i>NS</i>	26	33	<i>NS</i>
Current smoker (%)	10	8	<i>NS</i>	9	3	<i>NS</i>
Exacerbation frequency*						
<1/year (%)		73			28	
1-2/year (%)		20			31	
>2/year (%)		8			41	
FEV1 post bronchodilator (% pred.)	90.0 (30.0 - 135)	97.0 (22.0 - 146)	<i><0.05</i>	78.0 (37.0 - 116)	85.0 (23.1 - 133)	<i>NS</i>
ICS dose ≥1000 µg/day (%)	0	0	<i>NS</i>	79	85	<i>NS</i>
Chronic oral corticosteroid (%)	0	0	<i>NS</i>	29	38	<i>NS</i>
Omalizumab (%)	0	0	<i>NS</i>	0	7	<i>NS</i>

categories.

* Data could not be retrieved

Table E3. Definite venous thromboembolic events in study population.

	Mild-Moderate asthma (n=365)	Severe asthma (n=283)
Total number of personyears	17914	13975
Before and after asthma onset		
All VTE (n)	13	15
Deep venous thrombosis (n)	9	3
Pulmonary embolism (n)	4	12
Before asthma onset		
All VTE (n)	7	0
Deep venous thrombosis (n)	6	0
Pulmonary embolism (n)	1	0
After onset of asthma		
All VTE (n)	6	15
Deep venous thrombosis (n)	3	3
Pulmonary embolism (n)	3	12

Figure E4 Rate ratio (95% CI) of definite first PE and DVT (asthma population versus general population).

	Mild-moderate asthma (n=365)	Severe asthma (n=283)
Deep-vein thrombosis	1.45 (0.30-4.23)	1.21 (0.25-3.55)
Pulmonary embolism	2.67 (0.55-7.80)	8.93 (4.62-15.63)

Figures

Figure E1 Translation of the provided questionnaire in the study.