

Post-thrombotic syndrome in children: a systematic review of frequency of occurrence, validity of outcome measures, and prognostic factors

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ABSTRACT

Background

Post-thrombotic syndrome is a manifestation of chronic venous insufficiency following deep venous thrombosis. This systematic review was conducted to critically evaluate pediatric evidence on frequency of occurrence, validity of outcome measures, and prognostic indicators of post-thrombotic syndrome.

Design and Methods

A comprehensive literature search of original reports revealed 19 eligible studies, totaling 977 patients with upper/lower extremity deep venous thrombosis. Calculated weighted mean frequency of post-thrombotic syndrome was 26% (95% confidence interval: 23-28%) overall, and differed significantly by prospective/non-prospective analysis and use/non-use of a standardized outcome measure.

Results

Standardized post-thrombotic syndrome outcome measures included an adaptation of the Villalta scale, the Clinical-Etiologic-Anatomic-Pathologic classification, and the Manco-Johnson instrument. Data on validity were reported only for the Manco-Johnson instrument. No publications on post-thrombotic syndrome-related quality of life outcomes were identified. Candidate prognostic factors for post-thrombotic syndrome in prospective studies included use/non-use of thrombolysis and plasma levels of factor VIII activity and D-dimer.

Conclusions

Given that affected children must endure chronic sequelae for many decades, it is imperative that future collaborative pediatric prospective cohort studies and trials assess as key objectives and outcomes the incidence, severity, prognostic indicators, and health impact of post-thrombotic syndrome, using validated measures.

Key words: post-thrombotic syndrome, deep venous thrombosis, children, systematic review.

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Introduction

Post-thrombotic syndrome (PTS) is a syndrome of chronic venous insufficiency following deep venous thrombosis (DVT), affecting both adults and children. Physical findings of PTS can include edema, pain, dilated superficial collateral veins, stasis dermatitis, and ulceration involving the affected limb. As edema and pain are often present acutely in patients with DVT, particularly in the setting of complete veno-occlusion, assessment beyond the acute and subacute periods following DVT onset is important for definitive diagnosis of PTS.

The pathophysiology of PTS is thought to ultimately involve venous hypertension.¹ Venous hypertension, in turn, may result from venous valvular reflux, thrombotic veno-occlusion, and other causes of impaired venous return (e.g. right heart failure). While the correlation of PTS by clinical history or physical examination with valvular reflux by vascular imaging is rather poor, and while venous hypertension without reflux can be sufficient to cause PTS, PTS is nevertheless believed in many instances to be related to valvular reflux. Valvular reflux may be caused by valvular injury following acute thrombotic veno-occlusion (i.e. burst valve) or by vascular inflammation resulting in valvular fibrosis and insufficiency. Whether venous valvular insufficiency may in some cases be reversible remains poorly understood.

While considerable research effort has been devoted to the problem of PTS following DVT in adults in recent years, it has received less attention in pediatrics. However, since affected children will endure sequelae for many decades, there is a critical need to establish high-quality evidence on the burden of PTS in children with DVT. This systematic review was performed to critically evaluate evidence from the pediatric literature on the frequency of occurrence of PTS following DVT in children, the validity of pediatric PTS outcome measures, and prognostic indicators of PTS in children.

Design and Methods

We searched MEDLINE, EMBASE, and The Cochrane Library from 1960 (or earliest date for databases not extending back to

1960) through September 2009 (inclusive). MeSH terms and search strategy employed were as follows: “post-thrombotic syndrome OR post-phlebotic syndrome” AND “children OR pediatrics”. Reference lists of articles identified by the search were also reviewed for inclusion of additional relevant reports. Languages were limited to English, French, German, Italian, and Spanish. Study selection, categorization and data extraction were performed in duplicate by two independent reviewers (NG and MD). Publications were categorized as follows: single case reports; narrative reviews; commentaries; case series, cross-sectional studies; case-control studies; registries and cohort studies; and clinical trials. Single case reports, narrative reviews, commentaries, and conference abstracts were excluded from subsequent review. In case of reports on subsets of larger published series, only the most comprehensive series was included. In the event of conflicting study design classification or decision regarding inclusion/exclusion, consensus was achieved through discussion.

The following data were extracted from each eligible publication, as available: study methodology; age range; selection criteria; catheter-related DVT cases; cancer-associated DVT cases; VTE sites; frequency of PTS occurrence; method(s) employed for PTS outcome measurement; validation of PTS instrument; prognostic factors for PTS development; and quality of life (QOL) outcomes. Mean weighted frequency of PTS was calculated as previously described.²

Results

Overall search results

A flow chart of search results and their distribution by category of publication is provided in Figure 1, showing both included³⁻²¹ and excluded²²⁻⁷² reports. Nineteen original reports met eligibility criteria (Table 1); no systematic reviews were identified. A total of 1,387 VTE patients were reported, including 1,084 with DVT affecting venous outflow from the upper or lower extremities (UE/LE DVT). The percentages of children who had LE DVT, UE DVT, and both were 55%, 44%, and 1%, respectively. Loss to follow up was 8% overall. In total, 997 patients were assessed for PTS.

In evaluating PTS, five studies^{8,13,14,18,20} used a pediatric modification⁸ of the Villalta scoring system for PTS in adults,⁷³ two studies^{11,16} employed the Manco-Johnson

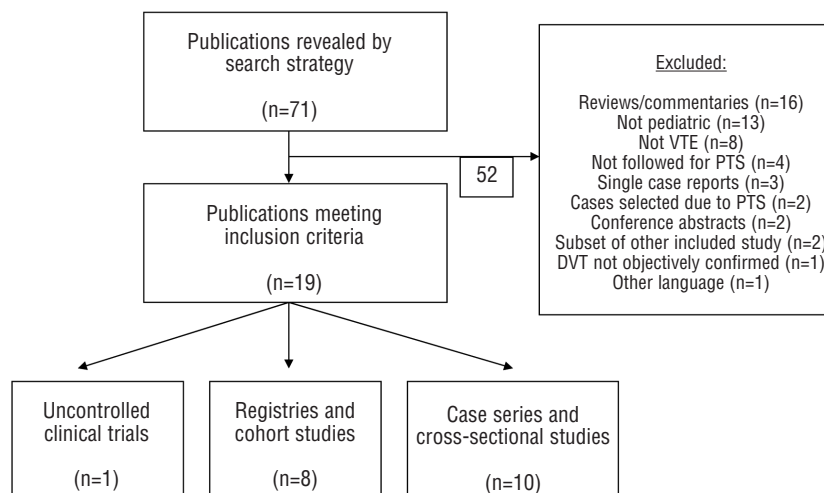


Figure 1. Flow chart of search results and their distribution by category of publication, indicating both included and excluded reports.

instrument,⁵¹ and one study¹⁰ utilized the Clinical-Etiologic-Anatomic-Pathophysiologic (CEAP) classification system.⁷⁴ Components of each of these outcome measures are summarized in Figure 2. The remaining 11 studies^{3-7,9,12,15,17,19,21} did not indicate the use of a standardized outcome measure.

Frequency of post-thrombotic syndrome occurrence

As shown in Table 1, frequency of PTS occurrence varied widely from 0 to 70% across studies. The earliest and largest data on PTS in pediatric DVT were provided by the Canadian Registry of Venous Thromboembolic Complications²² and the Canadian Childhood Thrombophilia Registry,⁵ however, these data preceded the standardization of PTS assessment in children. Findings with the use of a standardized PTS scoring system were first reported in 2003 in a retrospective analysis by the Childhood Thrombophilia Program at the Hospital for Sick Children⁸ in 153 children with a history of UE/LE DVT. This study employed a pediatric adaptation of the

Villalta PTS scoring system,⁷⁵ and defined a striking frequency of 63% for the occurrence of PTS in children with a history of limb DVT, at an average follow-up duration of 16 months post-event. By comparison, a prospective cohort including 52 unselected cases of acute UE/LE DVT found a PTS incidence of 33% at 1-2 years post-event, using the Manco-Johnson instrument.¹¹

Calculated weighted mean frequency of PTS was 26% (95% confidence interval [CI]: 23-28%) overall, and differed significantly for prospective *versus* non-prospective analyses (17% [95% CI: 14-20%] *vs.* 43% [38-48%], respectively; $P < 0.001$) and use/non-use of a standardized outcome measure (41% [36-46%] *vs.* 14% [11-17%]; $P < 0.001$ (Table 2). There was no correlation between follow-up duration and PTS frequency across studies ($r = 0.015$; $P = 0.97$). Subgroup analysis for frequency of PTS in cancer-associated and catheter-associated DVT was not feasible, due to a paucity of studies separately reporting outcomes in these populations. In addition, PTS severity was graded only in studies employing the modified

Table 1. Study characteristics of original reports on post-thrombotic syndrome (PTS) in children that met eligibility criteria for the present systematic review. In total 1,387 children with VTE were reported. Mean weighted frequency of PTS is calculated as the cumulative number of subjects with PTS divided by the cumulative number of subjects with DVT analyzed for PTS, and expressed as percent.

First author	Publication year	Study design	Prospective analysis	Pediatric population	# UE/LE DVT patients assessed for PTS	# UE/LE DVT patients with PTS	Time to PTS assessment *(months post-DVT diagnosis)	Standardized PTS outcome assessment	PTS frequency [†]
Athale ¹⁹	2008	Case series	No	lymphoma	6	3	n/a	No	50%
Kuhle ²⁰	2008	Cross-sectional	No	acute lymphoblastic leukemia	13	7	87.6 [7.2]	Yes	54%
Sharathkumar ¹⁸	2008	Cohort	No	unselected VTE cases	55	11	9.3 (2.8-120)	Yes	20%
Wilkinson ²⁴	2008	Case series	No	ventriculoatrial shunt	2	0	13.5	No	50%
Goldenberg ¹⁶	2007	Cohort	No	proximal LE DVT + high FVIII/D-d	22	12	18-24	Yes	55%
Sirachainan ¹⁷	2007	Case series	No	unselected VTE cases	23	3	36 (0.3-240)	No	13%
Raffini ¹²	2005	Case series	No	May-Thurner syndrome	3	0	16.7	No	0%
Kuhle ⁸	2003	Cross-sectional	No	unselected VTE cases	153	96	16 (1-159)	Yes	63%
Lee ⁹	2003	Case series	No	unselected VTE cases	5	1	50.4 (25.2-96)	No	20%
Norotte ⁴	1989	Case series	No	unselected VTE cases	33	8	n/a	No	25%
Nguyen ³	1986	Case series	No	unselected VTE cases	14	0	n/a	No	0%
Kreuz ¹³	2006	Cohort	Yes	unselected VTE cases	59	5	24	Yes	9%
Newall ¹⁵	2006	Registry	Yes	unselected VTE cases	85	3	0.2-126	No	12%
Schobess ¹⁴	2006	Clinical trial	Yes	unselected VTE cases	40	4	24 (12-60)	Yes	11%
Goldenberg ¹¹	2004	Cohort	Yes	unselected VTE cases	42	14	12 (3-60)	Yes	33%
Van Ommen ¹⁰	2003	Cohort	Yes	unselected VTE cases	33	23	48 (1-144)	Yes	70%
Gurgey ⁷	2001	Cohort	Yes	unselected VTE cases	16	3	27 (12-41)	No	19%
Hausler ⁶	2001	Cohort	Yes**	unselected VTE cases	17	7	123 (3-218)	No	41%
Monagle ⁵	2000	Registry	Yes	unselected VTE cases	356	50	85.8 (0.5-72)	No	12%
Cumulative # subjects					977	250			
Mean weighted PTS frequency (95% confidence interval)									26% (23-28%)

PTS, post-thrombotic syndrome; VTE, venous thromboembolism; freq, frequency; LE DVT, lower extremity deep venous thrombosis; FVIII, factor VIII; D-d, D-dimer * Follow-up periods are given as mean [standard deviation] or median (range), as provided in the original report. † Whenever possible, frequency of PTS is based upon number of subjects with UE/LE DVT rather than all VTE cases.

Villalta instrument,^{8,14,18,20} and functional significance of PTS was reported only in a single study, using the Manco-Johnson instrument.¹⁶

Validity of outcome measures

Published validation data for pediatric PTS outcome assessment are limited to the Manco-Johnson instrument.¹⁶ This instrument (Figure 3) combines the basic CEAP classification system⁷⁴ for physical assessment of signs of chronic venous insufficiency in combination with the Wong-Baker faces scale⁷³ for evaluation of pain symp-

toms. Validity and reliability testing of the Manco-Johnson instrument employed a derivation cohort/validation cohort approach.¹⁶ In a derivation cohort consisting of 78 healthy children without prior DVT or recent leg injury, the upper limit of normal values for contralateral leg circumference difference was determined to be 1.0 cm at both the mid-thigh and mid-calf. No physical stigmata of PTS were found. Additionally, pain that limits aerobic exercise (e.g. sports, recreational activities, age-appropriate play), affects activities of daily living, or that occurs at rest was absent in this population. Subsequently, in an independent validation cohort consisting of 45 children with and without prior DVT, inter-rater reliability for the physical and functional components of the Manco-Johnson instrument (i.e. signs and pain symptoms of PTS) ranged between 91 and 100%. In spite of prior observations of some natural variation in contralateral arm circumference among healthy children,⁶⁸ further validation of the Manco-Johnson instrument for the upper extremities has yielded similar results to those established in the lower limbs.⁷⁶

Additional evidence for validity of a PTS outcome measure is provided by the demonstration of an adverse QOL among affected individuals. However, no pediatric studies to date have reported QOL in relationship to PTS findings, and no venous disease-specific pediatric QOL instrument has yet been developed and validated.

Prognostic factors for development of post-thrombotic syndrome

Over the past several years, knowledge has accumulated regarding prognostic factors for the development of PTS in adults and children. As presented in Table 3, prognostic factors from prospective studies include: patients' characteristics; plasma/serum biomarkers relating to thrombophilia, coagulation activation, or the inflammatory response; and treatment factors. In pediatric thromboembolism, the risk of a composite outcome of recurrent VTE (rare), persistence of thrombosis despite a 3-6 month course of anticoagulation, or the development of PTS (using the Manco-Johnson instrument) is increased when FVIII activity and/or D-dimer concentration are elevated at diagnosis (OR 6.1, 95% CI: 2.1-17.7) or following 3-6 months of anticoagulation (OR 4.7, 95% CI: 1.8-12.6).¹⁰ Specifically, dual marker elevation at presentation increases the risk of adverse outcome from 50% (pre-test probability) to 86% (post-test probability).⁸³ Thrombolysis may decrease PTS risk in pediatric patients with completely

A

<i>Symptoms*</i>	
Pain or abnormal use	1
Swelling	1
<i>Signs</i>	
Increased limb circumference [†]	1
Change in skin color	1
Pitting edema	1
Venous collaterals on skin [‡]	1
Pigmentation of skin	1
Tenderness on palpations of deep veins	1
Varicosities	1 moderate; 2 severe
Head swelling	1 moderate; 2 severe
Ulceration	9
Mild Post-Thrombotic syndrome	1-3
Moderate Post-Thrombotic syndrome	4-8
Severe	≥ 9

* Reported by patient, parent, caregiver or proxy
[†] > 3% compared with contralateral side

B

<i>Signs</i>	
Edema*	1
Dilated superficial collateral veins	1
Venous stasis dermatitis	1
Venous stasis ulcers	1
<i>Symptoms</i>	
Chronic lower-extremity pain	
- limiting aerobic activities	0-5
- limiting activities of daily living	0-5
- at rest	0-5
Post-Thrombotic Syndrome absent	0
Any Post-Thrombotic Syndrome present	≥ 1
Physically and functionally significant PTS	Signs ≥ 1 and Symptoms ≥ 1

* > 1 cm increase in mid-calf or mid-thigh circumference in the affected extremity compared with the contralateral extremity

C

Class 0	No visible or palpable signs of venous disease
Class 1	Telangiectasis, reticular veins, malleolar flare
Class 2	Varicose veins
Class 3	Edema without skin changes
Class 4	Skin changes ascribed to venous disease (eg pigmentation, venous eczema, lipodermatosclerosis)
Class 5	Skin changes as defined above with healed ulceration
Class 6	Skin changes as defined above with active ulceration
Post-Thrombotic Syndrome absent	0
Post-Thrombotic Syndrome present	≥ 1
mild	1-3
moderate	4
severe	5-6

Subjective symptoms are also specified in this scale: lower extremity heaviness, pain and itching or daily impairment.

Figure 2. Components of standardized outcome measures for PTS employed in pediatric studies, including the modified Villalta scoring system, the Manco-Johnson instrument, and Basic CEAP. (A) Modified Villalta Scale.^{8,75} (B) Manco-Johnson instrument.^{16,51} (C) Basic Clinical-Etiologic-Anatomic-Pathophysiologic (CEAP) classification of chronic lower extremity venous disease,⁷⁴ as used in van Ommen et al.⁴⁰

Table 2. Comparison of mean weighted post-thrombotic syndrome frequency by analytic design of studies and standardization of outcome assessment.

Study group characteristic	Mean weighted PTS frequency (95% confidence interval)	P value
Analytic design		
Prospective	17% (14-20%)	<0.0001
Non-prospective	43% (38-48%)	
Outcome assessment		
Standardized	41% (36-46%)	<0.0001
Non-standardized	14% (11-17%)	

Mean weighted frequencies of PTS are calculated as the cumulative number of subjects with PTS divided by the cumulative number of subjects with DVT analyzed for PTS, and expressed as percent.

veno-occlusive proximal leg DVT in whom acute factor VIII and D-dimer levels both exceed prognostic thresholds (OR 0.018, 95% CI: <0.001-0.483);¹⁶ *a priori* PTS risk appears to be high in such children when conventional anticoagulation is employed.

Non-prospective studies have suggested additional potential prognostic factors for PTS in children. In the cross-sectional study of Kuhle *et al.*,⁶ multiple logistic regression analysis revealed that lack of thrombus resolution was associated with a statistically significant 4-fold increase in odds of PTS. With each additional venous segment of involvement by thrombus and each additional year of follow up, odds for PTS increased significantly by 2- and 1.2-fold. In addition, descriptive data from the registry report of Monagle *et al.*⁵ showed a skewed distribution of PTS across the pediatric age range, with infants and children of pre-school age more frequently affected than older children. Lastly, Sharathkumar and Pipe¹⁸ demonstrated in a retrospective series that initiation of anticoagulant treatment greater than 48 h following diagnosis of DVT and a history of recurrent thrombosis were each significantly more frequent among patients affected, *versus* unaffected, by PTS.

Discussion

The present systematic review of the literature revealed that PTS is common following UE/LE DVT in children, with an overall weighted mean frequency of PTS occurrence of 26% (95% CI: 23-28%) among a total of nearly 1,000 UE/LE DVT patients studied. This frequency is in the range of those determined in adult studies, at 20-40%.^{84,85} The review also found considerable variability in the observed frequency of PTS across studies (ranging from less than 10% to approximately 70%), even when analysis of the literature is restricted to prospective analyses of unselected cases. Lastly, it identified a single pediatric PTS outcome measure (the Manco-Johnson instrument) for which validity has been shown.¹⁶ This instrument defined a cumulative incidence of PTS of 33% at 1-2 years following UE/LE DVT in children,¹¹ which was considerably higher than the weighted mean frequency of PTS determined here among prospective analyses (17%

[95% CI: 14-20%]), slightly lower than that for studies similarly employing a standardized outcome measure (41% [36-46%]), and quite consistent with the weighted mean frequency of PTS in the subset of studies that both

**Pediatric Post-Thrombotic Syndrome Outcome Instrument
(Manco-Johnson)**

Patient ID: _____ Date of Birth: _____
 Date of Thrombus Diagnosis: ____-____-____ Date of Assessment: _____
 Affected limb (circle): Arm Leg

PHYSICAL FINDINGS (Signs)
 Please measure to nearest tenth of one centimeter.

Limb Circumference Measurements	Right	Left
Mid-proximal limb	____.____cm	____.____cm
Mid-distal limb	____.____cm	____.____cm

Basic CEAP. Mark an "X" where applicable/present.

Physical Findings	Right	Left
0. No visible or palpable signs of venous disease		
1. Swelling, with or without pitting edema		
2. Dilated collateral circulation of extremity only		
3. Skin changes ascribed to venous disease (i.e., pigmentation, venous eczema)		
4. Skin changes as in 3 with ulceration or superior vena cava syndrome		

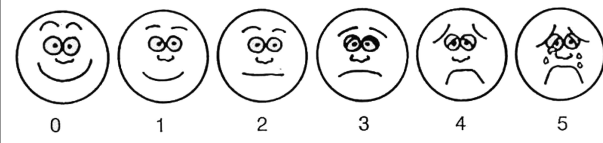
FUNCTIONAL FINDINGS (Pain Symptoms)
 Wong-Baker Faces Pain Rating (Oucher) Scale: Score 0-5 for each.

Pain Outcome: Wong-Baker (Oucher) Scale	Right	Left
With aerobic exercise only		
With activities of daily living		
At rest		

If pain is present (i.e., score 1-5): Does the pain interfere with activities? Yes No

Comments: _____

Wong-Baker Faces Pain Rating Scale



Aerobic exercise only: implies that symptoms are present only when child engages in vigorous age-appropriate sport such as running, lap swimming, soccer, basketball or volleyball.

Activities of daily living: implies that a child is symptomatic when engaging in ordinary age-appropriate activities in the home, school and community short of organized sports and vigorous aerobic activities. These symptoms limit and alter a child's ordinary day-to-day activities such as walking at school, shopping with the family or participation in a birthday party.

At rest: implies a constant presence of symptoms that is independent of activity. The child's daily life is severely limited by symptoms.

Figure 3. Manco-Johnson instrument.

Table 3. Prognostic factors for development of post-thrombotic syndrome following deep venous thrombosis in adults and children, from prospective studies.

Prognostic factor		Evidence in Adults		Evidence in Children	
		Odds Ratio, Risk Ratio, or Hazard Ratio (95% Confidence Interval)	Author and year [Reference #]	Odds Ratio, Risk Ratio, or Hazard Ratio (95% Confidence Interval)	Author and year [Reference #]
Patient characteristics	Obesity	3.5 (1.1-12.1)	Ageno <i>et al.</i> , 2003 ⁷⁷	n/a	n/a
Elevated biomarkers	Positive/elevated	3.79 (1.46-9.85)	Latella <i>et al.</i> , 2008 [Abstract] ⁷⁸	4.7 (1.8-12.6)	Goldenberg <i>et al.</i> , 2004 ^{11*}
3 or more months post-diagnosis	D-dimer				
	Interleukin-6	1.7 (1.1-2.6)	Shbaklo <i>et al.</i> , 2009 ⁷⁹	n/a	n/a
	Graduated compression stockings	0.28 (0.15-0.53)	Brandjes <i>et al.</i> , 1997 ⁸⁰	n/a	n/a
Treatment factors	Thrombolysis	0.34 (0.18-0.64)	Prandoni <i>et al.</i> , 2004 ⁸¹		
		0.55 (0.47-0.94)	Watson <i>et al.</i> , 2004 [Systematic review] ⁸²	0.02 (<0.001-0.48)	Goldenberg <i>et al.</i> , 2007 ^{16*}

*Analysis was performed based upon elevation of either D-dimer or factor VIII activity. *Study population was restricted to patients with completely veno-occlusive LE DVT with elevated D-dimer and factor VIII activity at presentation.

employed prospective analysis and a standardized outcome measure (26% [20-33%]; cumulative n=174 subjects with UE/LE DVT) (*data not shown*).

The above findings are important in establishing key evidence on PTS in children. In 2008, the US Surgeon General's Call-to-Action on Prevention of DVT and pulmonary embolism emphasized chronic venous insufficiency following DVT as an important priority for future investigation.⁸⁶ Recently, the number of pediatric publications reporting on PTS has shown a marked increase, with over 50% of studies included here having been published in the past five years. In addition to prospective/non-prospective analysis and use/non-use of a standardized outcome measure, factors that could contribute to the variability in PTS frequencies reported across these studies include heterogeneity in disease severity among study populations, as well as differences in study population distributions with respect to putative modulators of PTS risk (e.g. patient age, body mass index, and activity level; lag time from symptom onset to antithrombotic therapy; DVT extent, degree of occlusion, and involvement of central vasculature; anticoagulant treatment intensity and duration; graduated compression stocking use and duration thereof). The fact that non-prospective analyses showed a significantly higher weighted mean frequency of PTS than prospective ones serves to emphasize the important potential for disease severity selection bias in retrospective studies. Conversely, our finding that PTS frequency was significantly higher in studies employing a standardized (*vs.* non-standardized) outcome measure suggests that the use of standardized outcome measures is critical for sensitivity in detecting PTS. While considerable differences existed in average follow-up duration across studies, no correlation was found between follow-up duration and PTS frequency.

Limitations of the present work include issues related to the original studies and to the systematic review itself. First, included studies were heterogeneous with respect to design, follow up, and PTS outcome measurement. Not all studies evaluated PTS as a primary objective, potentially limiting study quality. However, formal assessment of study quality was not feasible due to lack of sufficient detail provided by most reports. Nevertheless, categorization according to basic study design and characterization of the study population was

undertaken during systematic review. Second, as noted earlier, time from DVT presentation to PTS assessment was not standardized across studies (nor typically within a study), leading to possible imprecision in composite measurement of PTS occurrence. Standardization of time to PTS assessment and serial assessment in long-term follow up would facilitate comparability of endpoints among future studies, and better define natural history. Thirdly, few studies investigated prognostic factors for PTS development. Consequently, only limited analysis could be performed in this review, and greater emphasis on investigation of prognostic factors for PTS must be underscored. Lastly, perhaps the greatest limitation in synthesizing evidence on PTS in children is the lack of a venous disease-specific pediatric QOL instrument by which to assess the functional significance of PTS. Until such a tool is developed and validated, the understanding of functional significance of PTS is limited to the use of the Manco-Johnson instrument.

In summary, this is the first systematic review of PTS in children. Among a total of 1,387 patients reported (including 997 with UE/LE DVT evaluated for PTS in follow up) across 19 eligible studies, the overall weighted mean frequency of PTS occurrence was 26%. However, validity and reliability in pediatric PTS measurement has been demonstrated only for the Manco-Johnson instrument, employed in two of the studies. Prognostic clinical factors and laboratory markers for development of PTS have recently begun to be prospectively investigated. Given that children must endure disease sequelae that adversely impact QOL for many decades, future collaborative prospective cohort studies and RCTs in the field of pediatric VTE should assess as key study objectives and outcomes the incidence, severity, prognostic indicators, and health impact of PTS, using validated measures.

Authorship and Disclosures

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