Transient synovitis of the hip: Development and validation of a new diagnostic algorithm

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Received: 10 October 2023 | Revised: 24 January 2024 | Accepted: 26 January 2024

DOI: 10.1111/apa.17144

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

ORIGINAL ARTICLE

Transient synovitis of the hip: Development and validation of a new diagnostic algorithm

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Abstract

Aim: To develop and validate an algorithm to rapidly distinguish transient synovitis (TS) of the hip from differential diagnoses without additional tests.

Methods: This retrospective cohort study included all children admitted for non-traumatic limping in the emergency department at Lille University-Hospital between 2016 and 2020. The gold standard was a definitive diagnosis at follow-up visit. All variables associated with acute limping in children were analysed in univariate and multivariable analyses. An algorithm was then developed using recursive partitioning and validated internally on a subset of patients.

Results: There were 995 patients included (mean age 5.3 years; males 63%); 337 had a TS including 210 confirmed at follow-up visit and 354 another diagnosis. After multivariable analysis, the relevant variables for distinguishing between TS and differential diagnoses were: age 3–10 years, absence of fever, absence of local inflammation, sudden onset of limping on awakening. An algorithm combining these variables was developed ($n=297$) and validated internally ($n=175$) for children >12 months with limping for ≤10 days, with a specificity of 98.2% and a positive likelihood ratio of 19.6. No serious differential diagnoses were missed.

Conclusion: Use of this algorithm enables the diagnosis of TS without additional tests and without missing serious differential diagnoses.

KEYWORDS
clinical algorithm, hip pain, limping child, non-traumatic limp, transient synovitis

1 | INTRODUCTION

Non-traumatic limping is a frequent reason for attending a paediatric emergency department (PED). Benign transient synovitis (TS) of the hip is the most common cause of this condition. However, non-traumatic limping may have a more serious cause, such as septic arthritis.[1] The broad range of aetiologies, the difficulty of differential diagnosis, and the fear of serious conditions like septic arthritis prompts clinicians to prescribe laboratory tests and/or imaging in around 80% of children admitted for limping.[2] However, most of these tests do not provide a definitive diagnosis[3–6] and increase the time spent in the PED and the cost of patient management. Several researchers have evaluated the diagnostic performance of combinations of anamnestic, clinical and laboratory criteria.[7,8] These combinations have proven diagnostic value but are also subject to the above-mentioned limitations. It

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; PED, paediatric emergency department; TS, transient synovitis.

has been reported that certain clinical and demographic variables such as fever, weight-bearing status, and age may be relevant in differentiating between TS and other causes of non-traumatic limping.[1,2,4,5,9] However, most of these studies only compare TS with septic arthritis, and the analyses included at least one laboratory variable, that is, invasive blood sampling and a longer waiting time in the PED. We reasoned that a decision rule based on anamnestic and clinical data only might reduce the time spent in the PED and the number of additional tests performed. To the best of our knowledge, the purely anamnestic and clinical differences between TS and its differential diagnoses have not previously been evaluated.

Hence, the objective of the present study was to develop and validate a diagnostic algorithm for TS on the basis of clinical data alone, with a view to limiting the false-positive rate.

Key Notes

- Transient synovitis (TS) is the most frequent cause of limping in children. No algorithm based on anamnestic and clinical criteria alone exists to limit additional tests and prolonged time spent in the emergency department to distinguish TS from serious diagnoses.
- This new algorithm has a high specificity and positive likelihood ratio for the diagnosis of TS, without serious diagnoses missed.
- This algorithm could be helpful to avoid additional tests for children with TS.

2 | METHODS

2.1 | Study design and inclusion criteria

We conducted a descriptive, retrospective, cross-sectional, single-centre study in the PED at Lille University Medical Centre, Lille, France between 01 January 2016 and 31 August 2020. The study report complied with the Standards for Reporting Diagnostic Accuracy Studies guidelines. We screened the PED consultation reports for the term limping. The main inclusion criteria were age under 16, limping as the reason for admission, ability to walk prior to the onset of the limp, management in the PED, and the absence of refusal from the patient or his/her parents to participate. Non-inclusion criteria were clearly traumatic limping, a mention of no limping in the consultation reports, a second admission for the same episode of limping, haemarthrosis in a patient with haemophilia, a vaso-occlusive crisis in a patient with sickle cell disease, and an inflammatory flare-up in a patient with juvenile idiopathic arthritis. Exclusion criteria were a trivial reason for consultation, an obvious diagnosis on admission, self-discharge from the PED before being attended to, and patients diagnosed at another hospital and then transferred to Lille University Medical Centre for treatment.

2.2 | Definitions

Acute, non-traumatic limping was defined as a shortening of the stance phase, a compensatory mechanism adopted to avoid pain in the affected limb, in the absence of an obvious traumatic injury.[10] Confirmed TS was defined as acute, non-traumatic limping in patients with spontaneous resolution in patients with a primary diagnosis of TS according to the clinicians' judgement and the results of any additional examinations. The study's gold standard for a definitive diagnosis was a confirmation of the diagnosis of TS at a follow-up visit with a specialist. Probable TS was defined as limping in patients for whom TS was the diagnosis on discharge from the PED, who did not have any follow-up visits, and did not attend the PED again for the same condition. An indeterminate diagnosis was defined as limping in children who were not given a definitive diagnosis during their management. A serious condition was defined as disease with a major functional impact or that would be life-threatening in the absence of immediate treatment. It included for example all bone and joint infections, primary or metastatic lesions, slipped capital femoral epiphysis.

2.3 | Collected data

Demographic variables recorded were sex and age. Anamnestic variables collected were the date of limping onset, the time since onset, the affected limb, refusal to walk, the site of pain, the onset of pain on awakening, sudden onset of limping, fever at home and any recent viral infections. Clinical variables collected were fever, refusal to walk or put weight on the affected limb, signs of local inflammation and limited rotations of the hip. Additional tests collected were hip and/or lower limb x-rays, ultrasound examinations of lower limb joints, and blood tests. Variables related to management and follow-up were also collected. In line with the French legislation, patients were informed through the consultation report or hospital discharge letter. They were free to oppose the use of their personal data. The study database was registered with the French National Data Protection Commission (registration number DEC 20-281).

2.4 | Statistical analyses

Although all the included patients were analysed, only those aged over 12 months and who had been limping for 10 days or less were considered in our development and validation of the diagnostic algorithm. The investigators who performed the statistical analyses were blinded to the outcome. To create the algorithm, only patients with

a definitive diagnosis were considered. The algorithm was derived from a randomly selected subset of two-thirds of these patients. The remaining third was used as the validation set.

When describing the characteristics of the whole population as a function of the final diagnosis, we expressed categorical variables as the frequency (percentage). For the only continuous variable without an identified threshold, a receiver operating characteristic curve analysis was performed, in order to determine a threshold. In univariate analyses of the ability to predict TS, we calculated the odds ratio (OR) and the 95% confidence interval (CI) for each variable. The variables considered were those identified in the literature as potentially relevant. The univariate analyses were based on a chi-squared test or Fisher's exact test. Multivariable analysis was performed using backward stepwise logistic regression with variables whose p value was below 0.20 in the univariate analysis. Adjusted ORs were calculated with their 95% CIs. The threshold for statistical significance was set to $p < 0.05$.

To create the diagnostic algorithm, we applied recursive partitioning of the variables identified in our study with different combinations tested. To increase the performance of the algorithm we have chosen to add consensus variables in the literature. Patients with an indeterminate diagnosis or probable TS were not included in the set used to develop or validate the diagnostic algorithm. The algorithm's diagnostic performance was assessed in terms of the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio, together with the respective 95% CIs. The algorithm was applied to the validation set of patients. Statistical analyses were done using Excel (Microsoft) and SPSS Statistics (version 22, IBM, France) software.

3 | RESULTS

3.1 | The study population

The initial screening identified 4052 eligible patients. After the application of our non-inclusion and exclusion criteria, 995 patients (63% boys) with a mean age of 5.3 years (range 9 months to 15.1 years) were included in the study. Next, 472 patients with a definitive diagnosis were assessed for the development of the new diagnostic tool (Figure 1).

In all, 337 children (33.9%) had a final diagnosis of TS: there were 210 cases of confirmed TS and 127 cases of probable TS (Table 1). Of the remaining children, 304 (30.6%) had an indeterminate diagnosis and 354 (35.6%) had another diagnosis (Table S1). The main

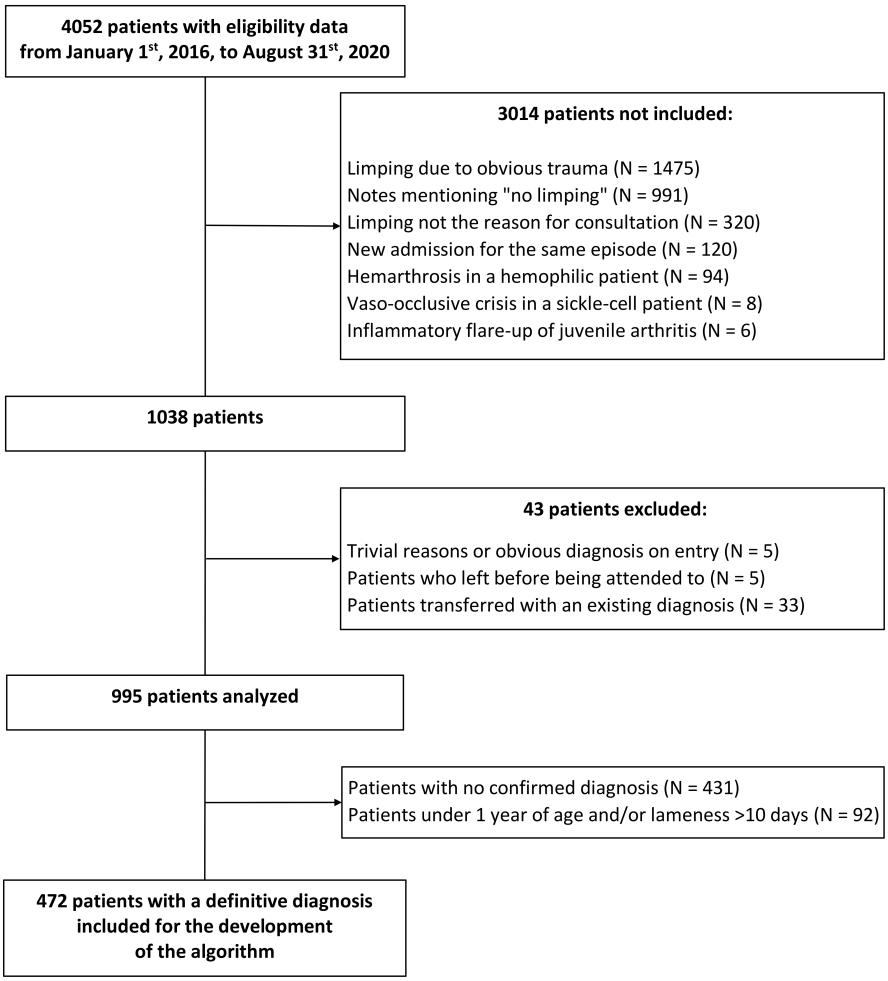

FIGURE 1 Study flow chart.

TABLE 1 Characteristics of the study population, by diagnostic subgroup.

	Total population ($N=995$)		Confirmed TS ($N=210$)		Probable TS ($N=127$)			Other diagnoses ($N=354$)	
Variables	***N***	**(%)**	***N***	**(%)**	***N***	**(%)**	***p***	***N***	**(%)**
Age									
<3 years	336/995	(34)	49/210	(23)	34/127	(27)	0.48	126/354	(36)
3–8 years	430/995	(43)	121/210	(58)	81/127	(64)	0.26	124/354	(35)
8–10 years	94/995	(9)	29/210	(14)	8/127	(6)	0.03	30/354	(8)
>10 years	135/995	(14)	11/210	(5)	4/127	(3)	0.37	74/354	(21)
Male sex	622/995	(62)	149/210	(71)	93/127	(73)	0.65	198/354	(56)
Time since onset of limping[a]									
<3 days	680/988	(69)	172/209	(82)	109/127	(86)	0.52	181/350	(52)
3–10 days	184/988	(19)	30/209	(14)	14/127	(11)	0.38	90/350	(26)
>10 days	124/988	(13)	7/209	(3)	4/127	(3)	0.92	79/350	(23)
Limb									
Right	450/992	(45)	96/209	(46)	58/127	(46)	0.96	146/352	(41)
Left	459/992	(46)	107/209	(51)	66/127	(52)	0.89	156/352	(44)
Both	83/992	(8)	6/209	(2)	3/127	(2)	0.78	50/352	(14)
Fever at home	201/995	(20)	28/210	(13)	27/127	(21)	0.06	98/354	(28)
Fever duration[a]									
<3 days	154/183	(84)	23/26	(88)	22/26	(85)	0.68	67/87	(77)
3–5 days	23/183	(13)	3/26	(11)	4/26	(15)	0.68	16/87	(18)
>5 days	6/183	(3)	0/26	(0)	0/26	(0)	–	4/87	(5)
Recent viral infection									
No	609/995	(61)	103/210	(49)	67/127	(53)	0.51	238/354	(67)
ENT/respiratory	324/995	(33)	95/210	(45)	51/127	(40)	0.36	90/354	(25)
Other viral infection	62/995	(6)	12/210	(6)	9/127	(7)	0.25	26/354	(7)
Refusal to walk or to put weight on the affected leg	150/995	(15)	31/210	(15)	19/127	(15)	0.96	60/354	(17)
Localised hip pain	344/992	(35)	125/210	(59)	69/127	(54)	0.87	76/352	(22)
Sudden onset of pain on awakening	293/844	(35)	80/176	(45)	57/112	(51)	0.81	63/303	(21)
Sudden onset of limping	780/980	(80)	175/209	(84)	117/126	(93)	0.01	229/343	(67)

[a]Rounded up to the nearest full day.

other diagnoses were joint or bone infections ($n=56$), juvenile idiopathic arthritis ($n=35$), post-traumatic concussion ($n=33$), fractures ($n=30$), myalgia/myositis ($n=28$), reactive arthritis ($n=25$), Legg-Calvé-Perthes disease ($n=18$).

3.2 | Development of the diagnostic algorithm of TS

The derivation subgroup contained 297 patients aged over 1 year and who had been limping for 10 days or less: 126 had a diagnosis of TS, and 171 had another diagnosis. In the receiver–operating characteristic curve analysis of the duration of limping, the best sensitivity–specificity ratio was found for a threshold of 2.5 days, with a specificity of 73% and a sensitivity of 51%. Limping for less than 72 h was therefore used as the threshold for further analyses.

The univariate and multivariable analysis identified four variables that appeared to be significantly and independently associated with a diagnosis of TS: the absence of fever, the absence of signs of local inflammation, sudden onset of limping on awakening, and age 3–10 years (Table 2). Since the combination of these four variables did not provide a relevant diagnostic algorithm, we combined them with other variables identified as relevant in the literature: hip limitation regardless of the pain site, localised hip pain, limping for less than 72 h, and a reported recent viral infection. We used recursive partitioning to create a new diagnostic algorithm (Figure 2; Figure S2). The algorithm's diagnostic performance has been calculated and showed very good specificity with few false

TABLE 2 Univariate and multivariable analyses of categorical variables.

	TS									
	Yes ($N=126$)		No ($N=171$)							
Variables	N	(%)	N	(%)	OR	95% CI	p	aOR	95% CI	p
Male sex	82/126	(65)	101/171	(59)	1.29	[0.80–2.08]	0.29	*	–	–
Fever	16/125	(13)	67/171	(39)	0.23	[0.12–0.42]	$<10^{-6}$	0.17	[0.08–0.37]	$<10^{-4}$
Brutal onset	106/126	(84)	133/163	(82)	1.20	[0.64–2.22]	0.57	*	–	–
Sudden onset on awakening	48/107	(45)	33/148	(22)	2.84	[1.65–4.88]	$<10^{-3}$	3.19	[1.56–6.54]	0.002
Refusal to walk or put weight on the limb	18/126	(14)	37/171	(22)	0.61	[0.33–1.12]	0.11	0.91	[0.40–2.08]	0.82
Recent viral infection										
All viral infections	64/126	(51)	62/171	(36)	1.81	[1.13–2.89]	0.01	1.81	[0.96–3.41]	0.07
ENT or respiratory tract infection	55/126	(44)	47/171	(28)	2.04	[1.26–3.32]	0.004	*	–	–
Signs of local inflammation	1/126	(1)	34/168	(20)	0.03	[0.01–0.23]	$<10^{-6}$	0.03	[0.01–0.22]	$<10^{-3}$
Hip limitation										
All movements limited	65/126	(52)	27/169	(16)	5.60	[3.27–9.62]	$<10^{-6}$	1.52	[1.00–2.32]	0.05
Internal rotation limited	52/65	(80)	21/24	(88)	0.57	[0.14–2.21]	0.41	*	–	–
Age <3 years	31/126	(25)	69/171	(40)	0.48	[0.29–0.80]	0.005	*	–	–
Age between 3 and 8 years	73/126	(58)	62/171	(36)	2.42	[1.51–3.88]	$<10^{-3}$	*	–	–
Age between 3 and 10 years	90/126	(71)	75/171	(44)	3.20	[1.96–5.23]	$<10^{-5}$	3.82	[1.94–7.50]	$<10^{-4}$
Age >10 years	5/126	(4)	27/171	(16)	0.22	[0.08–0.59]	0.001	*	–	–
Time since onset of limping <6 days	113/126	(90)	141/171	(83)	1.85	[0.92–3.71]	0.08	*	–	–
Time since onset of limping <72 h	106/126	(84)	112/171	(66)	2.79	[1.58–4.95]	$<10^{-3}$	2.02	[0.96–4.27]	0.06

Abbreviation: aOR, adjusted odds ratio.

*Variables not included in the multivariable analysis either because of $p>0.20$ in the univariate analysis or because of a strong correlation with another introduced variable.

positives (Table 3). It included two cases with bruising, and one case of recurrent limping in the context of confirmed Legg-Calvé-Perthes disease.

3.3 | Validation of this TS diagnostic algorithm

The validation subgroup comprised 175 patients with acute limping: 76 with TS and 99 with another diagnosis (Table 3). The three patients with a false positive diagnosis of TS had a final diagnosis of tendinopathy, mesenteric lymphadenitis, and Legg-Calvé-Perthes disease.

4 | DISCUSSION

By retrospectively assessing a large number of children with acute limping seen in the PED, we developed a new diagnostic algorithm based on clinical data alone. We found that four variables had added value in the diagnosis of TS: the absence of fever, the absence of inflammatory signs, sudden onset of limping on awakening, and age 3–10 years. When combined with four other variables highlighted in the literature, these variables were used to develop and validate the new diagnostic algorithm. The new algorithm was highly specific for the diagnosis of TS and did not miss any serious causes, such as septic arthritis. The algorithm was useful for avoiding additional tests and prolonged management in the PED for most of the children with TS.

A study of 146 children admitted to the PED for non-traumatic limping found similar results by analysing the various symptoms and additional tests. The study investigators suggested that a clinical diagnosis of TS could be made by limiting further investigations to children aged 3–10 years who had been limping for less than 7 days, were not feverish, and lacked signs of systemic disease.[2] We considered this 3–10 year age range because several studies have highlighted the occurrence of TS in patients up to the age of 10 years,[11–13] even

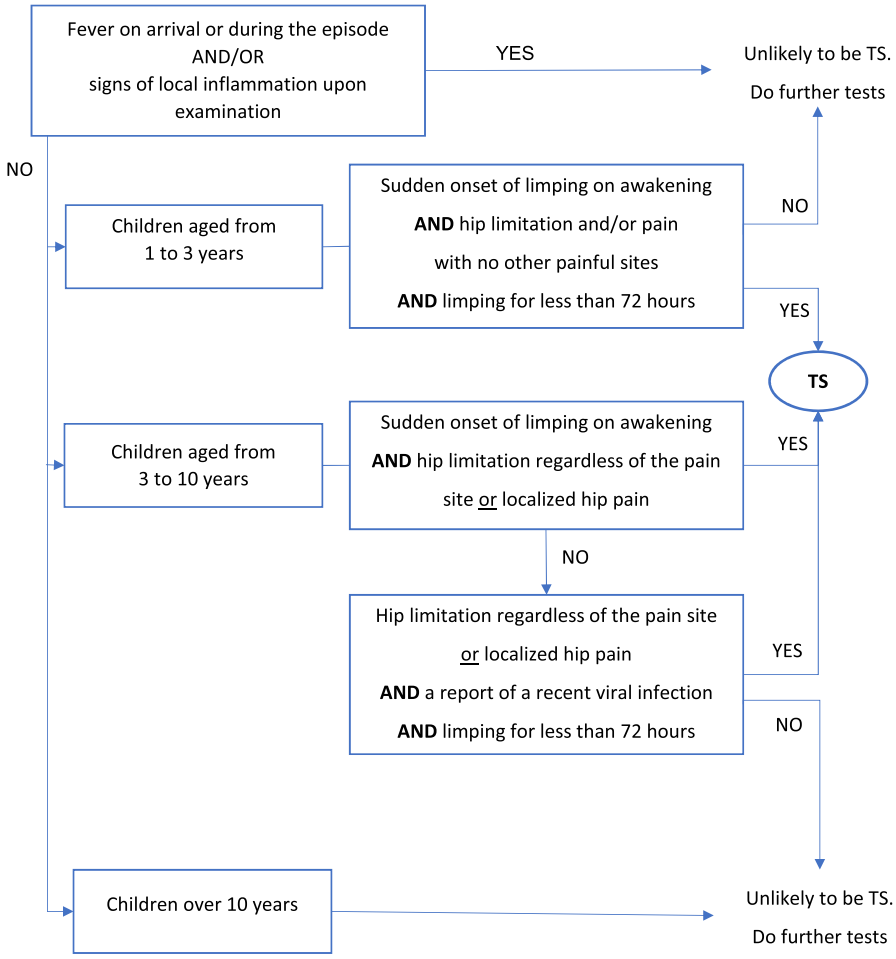

FIGURE 2 A new algorithm for the diagnosis of TS in the context of limping for ≤10 days in children over 1 year of age and who lack clinical signs that are incompatible with TS. Prevalence of TS on which the algorithm was derived: 42% (126/297). TS, transient synovitis.

TABLE 3 Diagnostic performance of the new algorithm.

	Derivation set ($N = 297$)		Validation set ($N = 175$)	
Details	**% or ratio**	**[95% CI]**	**% or ratio**	**[95% CI]**
Sp	98.2	[96.3–100]	97.0	[93.6–100]
Se	34.4	[26.1–42.7]	34.2	[23.5–44.9]
PPV	93.5	[86.3–100]	89.7	[78.6–100]
NPV	67.2	[61.4–73.0]	65.8	[58.1–73.4]
LR+	19.6	[6.2–61.8]	11.3	[3.5–35.9]
LR−	0.67	[0.59–0.76]	0.68	[0.57–0.80]

Abbreviations: CI, confidence interval; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity.

though most patients with TS are between 3 and 8.[14,15] Our new algorithm was tested for limping ≤10 days, in view of the usual duration of TS and studies that recommend additional examinations if the TS was still present after this period of time.[6,16]

Our data showed that 13% of the children with TS had fever at home before attending the PED; in two published studies, this proportion was 14% and 21%.[1,4] However, fever was present in all cases of septic arthritis in the two cited studies. Thus, the presence of fever does not rule out a diagnosis of TS but should prompt further investigations because it is the most specific variable in the diagnosis of septic arthritis.[8,17,18] Although the sudden onset of limping on awakening is a typical presentation of TS, its frequency and diagnostic relevance had not been studied previously. Our analyses showed that this variable can help to distinguish between TS and differential diagnoses. Although several studies have shown that weight-bearing status can help to distinguish between TS and septic arthritis,[1,7] this variable did not appear to be relevant for the diagnosis of TS in our study. The low observed proportion of patients with TS and localised hip pain and/or hip limitation only might be due to referred pain. The latter is frequent in children and is difficult to document as localised hip pain. Our results were in line with those of a Dutch study in which only 57% of patients with TS localised hip pain.[18] This is why we added to the algorithm the notion of localised pain or hip limitation regardless of the pain site. In our derivation subset, a limitation of internal rotation of the hip was not significantly more frequent in children with TS (80%) than in those with other diseases (88%).

The duration of symptoms prior to consultation appears to differentiate significantly between TS and other diagnoses. A duration of less than 72 h was significant in a univariate analysis but not in the subsequent multivariable analysis. However, in Dubois-Ferrière et al.'s study of 383 cases of TS, 192 (51%) had been symptomatic for less than 24 h at the time of the PED visit.[12] When the patients had been symptomatic for longer, the mean duration was 2.1 days.

This was in line with our results and explained why we included this variable in our algorithm.

In order to avoid missing a diagnosis of Legg-Calvé-Perthes disease, an orthopaedic consultation and an x-ray 6 weeks after the PED visit were recommended; this may provide a definitive diagnosis in a patient whose symptoms have resolved at the time of the control. A study of 242 patients published in 2021 investigated the value of systematic radiographic checks for the detection of Legg-Calvé-Perthes disease following TS: none of the asymptomatic patients was diagnosed with Legg-Calvé-Perthes disease during the follow-up period.[19] The study's investigators recommended performing a follow-up x-ray only when the patient remained symptomatic. This approach had already been mentioned in the report on a study of 198 patients with a diagnosis of TS and a follow-up x-ray 3 months after the initial consultation.[20] A diagnosis of Legg-Calvé-Perthes disease is very infrequent in asymptomatic patients. Lastly, other researchers also chose a gold standard that primarily considered the spontaneous resolution of symptoms during follow-up and the absence of sequelae.[5,12]

5 | STRENGTHS AND LIMITATIONS

The study's main strength was the large number of participants. To the best of our knowledge, the present study is the largest yet evaluation of non-traumatic limping in children attending a PED. Moreover, this study was carried out over a period of more than 4 years. It is the first study to have focused on purely clinical and anamnestic criteria, with several dozen variables recorded per patient. Lastly, and contrary to most studies of this topic, we compared TS with all the differential diagnoses and not just with septic arthritis.[7,8,21]

Our study's main limitation was the absence of systematic follow-up after the PED visit. Indeed, some children may have gone on to attend another hospital, where the final diagnosis might have changed. However, our hospital is the region's main paediatric orthopaedic centre, and a serious condition associated with limping would typically have been managed here. Secondly, the numbers of patients with probable but not confirmed TS ($n = 127$) or an indeterminate diagnosis ($n = 304$) were relatively high, due to the retrospective design of the study. However, and given the large number of diagnoses other than TS (Table 2), our choice to consider as the gold standard only patients with a definitive diagnosis, limited classification bias for derivation and validation of the algorithm. The proportion of missing data was low. A maximum value of 14% missing data was recorded for the sudden onset on awakening variable. This value was below 1% for all other variables, which limited biases. Although the data were collected by two different investigators, data entry was homogenised through the use of a standardised form, standard definitions, and close collaboration between the investigators. Despite this, the retrospective design of the study may have had an impact on data quality for some variables, for example sudden onset on awakening, or type of hip limitation. Thirdly, the study's single centre makes it difficult to extrapolate our results to other settings. This limitation might be mitigated by multicentre validation. Lastly, our study concerned only children consulting for limping. Hence, children presenting at the PED for hip pain in the absence of limping might have been missed. However, our screening process was probably broad enough to encompass most such patients.

6 | CONCLUSION

Additional tests, including laboratory tests of biological samples, do not appear to be essential when the clinician is faced with a typical presentation of TS. The algorithm developed here might be of great help to the clinician and might help him/her to avoid failing to diagnose a serious congruent condition. A multicentre study would help to confirm the performance of the new algorithm. It would also help to generalise its use, with a view to shortening stays in the PED and avoiding unnecessary examinations of children with typical presentations of TS.

AUTHOR CONTRIBUTIONS

François Dubos: Conceptualization; writing – original draft; methodology; validation; writing – review and editing; formal analysis; supervision. **Justine Benoit:** Conceptualization; investigation; writing – original draft; methodology; formal analysis; data curation. **Siham El Khalifi:** Conceptualization; writing – original draft; methodology; validation; writing – review and editing; supervision. **Colin Saoudi:** Investigation; writing – review and editing; validation. **Claire de Jorna:** Conceptualization; methodology; validation; writing – review and editing; supervision.

FUNDING INFORMATION

This study did not receive any specific funding.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The full data can be available on request.

ETHICS STATEMENT

In line with the French legislation, the validation by an ethic committee was not necessary for this type of non-interventional research.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Benoit J, El Khalifi S, Saoudi C, De Jorna C, Dubos F. Transient synovitis of the hip: Development and validation of a new diagnostic algorithm. Acta Paediatr. 2024;113:1396–1403. https://doi.org/10.1111/apa.17144