Table II. Pertinent medical data from cases

Variable	Cases (N = 18), No. (%)
Indication	
Nail biopsy	1
Malignancy	1
Onychocryptosis	1
Acid burn	1
Carpal tunnel syndrome	1
Subclavian vein thrombosis	1
Hallux flexus	2
Hallux valgus	2
Severed tendon	4
Fracture	4
Error cited by plaintiff	
Improper tourniquet use	13 (72)
Bandage/dressing applied too tight	2 (11)
Local anesthesia injection	1 (6)
Local calcium gluconate injection	1 (6)
Subclavian vein ligation	1 (6)
Type of improper tourniquet use	
Excess duration of use	8 (62)
Excess pressure (>300 mm Hg)	5 (38)
Anatomic site	
Fingers/hand	5 (28)
Digits affected	
Right 1, 2	1
Left 2	1
Right 2, 3	1
Right 4, 5	1
All	1
Toes/foot/leg	13 (72)
Digits affected	
Right 1	1
Right 1, 2	1
Right 2,3,4	1
Left 2, 3, 4	1
Left 3, 4, 5	1
Right 4	1
All	7
Relevant patient history	
Raynaud phenomenon	3 (18)
Diabetes mellitus	1 (6)

No., Number.

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Aberrant venous anatomy as a risk factor for thromboembolic events in patients with Klippel-Trénaunay syndrome: Case-control study within a cohort study

To the Editor: Klippel-Trénaunay syndrome (KTS) is a rare congenital vascular malformation disorder (1 of 20,000-40,000 live births).[1] The cause is a somatic mosaicism of the affected tissues.[2] KTS affects 1 or more limb(s) with a capillary malformation and lymphatic and venous malformations, including an aberrant venous anatomy, combined with hypertrophy (Supplemental Fig 1, available via Mendeley https://doi.org/10.17632/s6gvr59g3x.1).[3]

Patients with KTS are prone to develop thromboembolic events (TEE): superficial vein thrombosis (SVT), deep vein thrombosis (DVT), or pulmonary embolism (PE).[4,5] The mechanism behind the increased risk for TEE in KTS is unclear.[4] Our objective was to investigate the prevalence of TEE in patients with KTS and subsequently to determine whether, and to what extent, aberrant venous anatomy represents a risk factor for TEE.

A retrospective cohort study was performed with data from medical records, recorded between 2000 and June 2019, of a large cohort with KTS (n = 173) from a large tertiary referral center. A case-control study was performed of 97 patients with KTS with affected lower limb(s), within the cohort, who had been examined with color duplex ultrasonography (CDU). The 97 patients were divided

Table I. Baseline characteristics of the total cohort, cases, and controls

Variables	Total cohort (N = 173)	Cases with CDU (n = 37)	Controls with CDU (n = 60)	*P* value*
Characteristic				
Age, median (IQR), y	26.0 (13.0-44.0)	33.0 (21.5-44.0)	28.5 (15.3-43.5)	.329
Female sex, No. (%)	104 (60.1)	19 (51.4)	39 (65.0)	.183
Location, No. (%)				.414
1 lower limb†	118 (68.2)	32 (86.5)	48 (80.0)	…
Both lower limbs†	12 (6.9)	5 (13.5)	12 (20.0)	…
1 upper limb	16 (9.2)	…	…	…
Both upper limbs	3 (1.7)	…	…	…
1 upper and 1 lower limb	10 (5.8)	…	…	…
1 upper and both lower limbs	7 (4.0)	…	…	…
All limbs	7 (4.0)	…	…	…
Risk factors, No. (%)				
Previous TEE	35 (20.2)	24 (64.9)	…	…
Immobilization‡§	6 (3.5)	3 (8.3)	1 (1.7)	.147
Recent surgery (<90 days)§	3 (1.7)	1 (2.8)	1 (1.7)	>.99
Contraceptives (women only)§‖	13 (12.7)	3 (16.7)	5 (13.2)	.703
Pregnancy (women only)¶	1 (1.0)	0 (0.0)	0 (0.0)	NA
Known cancer§	1 (0.6)	0 (0.0)	1 (1.7)	>.99
Protective measures, No. (%)				
Oral anticoagulant medication§#	9 (5.3)	6 (16.7)	0 (0.0)	**.002**
Vitamin K antagonists	4 (2.3)	3 (8.3)	0 (0.0)	
Direct oral anticoagulants	1 (0.6)	0 (0.0)	0 (0.0)	
Heparin(-derivatives)	3 (1.7)	2 (5.6)	0 (0.0)	
Antiplatelet drug	1 (0.6)	1 (2.8)	0 (0.0)	
Use of therapeutic elastic stockings§	78 (47.3)	23 (62.2)	41 (68.3)	.533
Varicose vein treatment§	47 (28.1)	19 (54.3)	21 (36.2)	.088

CDU, Color duplex ultrasonography; *IQR*, interquartile range. *NA*, not applicable; *No.*, number; *TEE*, thromboembolic events.
**P* values are calculated by Mann-Whitney *U* test (numerical variables), Fisher exact test, or the χ^2 (categorical variables) to compare the case and control groups. The bold *P* value indicates statistical significance ($P < .05$).
†Pooled data in the case and control group, the "1 lower limb" category consists of the original category in addition to the "1 upper limb and 1 lower limb" category. All other categories (expect for "1 or both upper limbs") are merged into the "both lower limbs" category.
‡Defined as bed rest ≥3 days, paralysis of the leg(s), prolonged sitting (eg, travel, wheelchair), or the use of walking aids.
§Missing values in <5% of the cases, valid percentage reported.
‖Defined as current use of contraceptives at the index date.
¶Defined as current pregnancy confirmed by pregnancy test or ultrasonography, including 3 months after delivery.
#Most patients started using oral anticoagulant medication after the CDU investigation or first TEE, or both.

Table II. Presence of a specific venous aberrations and the risk for thromboembolic events

Presence of venous aberrations		Total (N = 97), No. (%)	Cases (n = 37), No. (%)	Controls (n = 60), No. (%)	Crude odds ratio (95% CI)	*P* value*
Discontinuity DVS	Yes	23 (23.7)	7 (18.9)	16 (26.7)	0.642 (0.236-1.748)	.386
	No	74 (76.3)	30 (81.1)	44 (73.3)		
Reflux in DVS	Yes	42 (43.3)	19 (51.4)	23 (38.3)	1.698 (0.742-3.888)	.210
	No	55 (56.7)	18 (48.6)	37 (61.7)		
Reflux in SVS	Yes	62 (63.9)	27 (73.0)	35 (58.3)	1.929 (0.793-4.690)	.147
	No	35 (36.1)	10 (27.0)	25 (41.7)		
Vena marginalis lateralis	Yes	23 (23.7)	13 (35.1)	10 (16.7)	2.708 (1.040-7.055)	**.041**
	No	74 (76.3)	24 (64.9)	50 (83.3)		
Insufficient vena perforans						
In upper leg†	Yes	52 (54.7)	27 (75.0)	25 (42.4)	4.080 (1.635-10.179)	**.003**
	No	43 (45.3)	9 (25.0)	34 (57.6)		
In lower leg†	Yes	59 (63.4)	24 (70.6)	35 (59.3)	1.646 (0.668-4.057)	.279
	No	34 (36.6)	10 (29.4)	24 (40.7)		
Intramuscular convolutes†	Yes	27 (28.1)	15 (40.5)	12 (20.3)	2.670 (1.072-6.651)	**.035**
	No	69 (71.9)	22 (59.5)	47 (79.7)		

CI, Confidence interval; *DVS*, deep venous system; *SVS*, superficial venous system.
**P* value is calculated by Wald statistic. Bold values are statistically significant ($P < .05$).
†Missing values in <5% of the cases, valid percentage reported.

into 2 groups: those with a history of TEE (cases, n = 37) and without a history of TEE (controls, n = 60). The Radboud University Medical Center Research Ethics Committee approved the study.

Patient demographics, risk factors, protective measures, presence of TEE, and results from the CDU investigation (Supplemental Fig 2, available via Mendeley at https://doi.org/10.17632/yxjbp28tjz.1) were recorded in a good clinical practice-approved database system (Castor EDC, Ciwit BV, Amsterdam, the Netherlands) (Table I).

At least 1 TEE occurred in 56 of 173 patients (32.4%): 16 (9.2%) experienced DVT and 10 (5.8%) a PE. The mean age for a first severe event (DVT or PE) was 33.75 years (SD, 16.93; range, 0-71 years). In the case-control univariate analysis, patients with a vena marginalis lateralis, insufficient vena perforans in the upper leg, or intramuscular convolutes had an increased risk of TEE, with an odds ratio (OR) of 2.71 ($P = .041$), 4.01 ($P = .003$), and 2.67 ($P = .035$), respectively (Table II).

Our retrospective cohort study with nested case-control analysis confirms the high prevalence of TEE among patients with KTS: 1 in 3 experienced a TEE. We also determined that the 3 specific venous aberrations of vena marginalis lateralis, insufficient vena perforans in the upper leg, and intramuscular convolutes each represent an independent risk factor for TEE. Knowing this, patients prone for TEE can be better identified. Subsequently, they can be counseled with regard to prophylactic surgical or medical treatment. Further research will certainly also need to focus on possible hematologic and genetic coagulation problems in patients with KTS patients. More insight into risk factors might lead to tailor-made thrombosis prophylaxis for each patient.

Limitations include the retrospective single center design, lack of genetic analysis, possibility of selection bias, and that only crude odds ratios were reported. The strengths of our study include the large sample size, especially for a rare disease, and the high-quality CDU reports, with CDU investigation being the gold standard for assessment of venous anatomy and flow characteristics.

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Characteristics of nonmelanoma skin cancer in children without identifiable risk factors

To the Editor: Pediatric nonmelanoma skin cancer (NMSC) is rare and often associated with genetic conditions or iatrogenic risk factors.[1,2] Children who develop NMSC without identifiable risk factors have not been well described. The objective of this study was to describe the demographic and clinical features of children with NMSC without identifiable risk factors and compare them with those who have genetic or iatrogenic risk factors.

We conducted a retrospective study at 11 tertiary care institutions. Eligibility criteria included a diagnosis of NMSC, age <20 years old upon initial histopathologic diagnosis of NMSC, and diagnosed between January 1, 1995, and June 30, 2016. Risk factors before NMSC diagnosis were used to