Trombose arterial em Síndrome nefrótica

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Objetivos

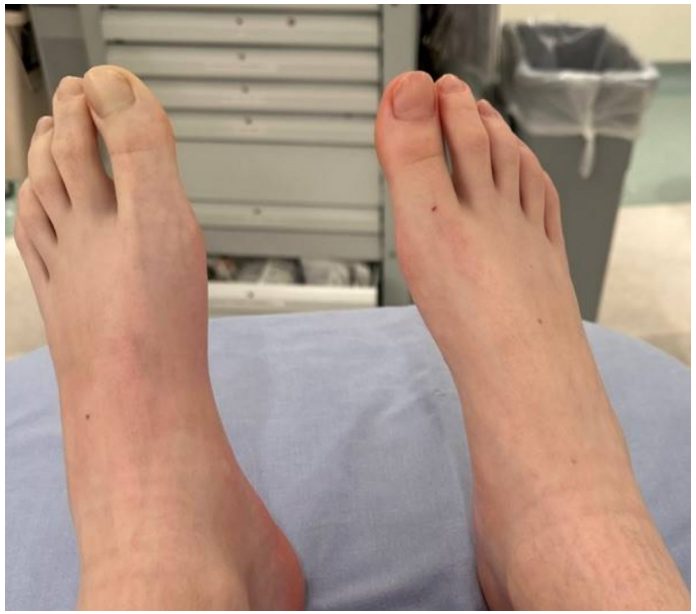
- Apresentação de caso clínico
- Revisão das principais complicações tromboembólicas relacionadas à Síndrome nefrótica
- Abordar as principais recomendações de terapia pertinentes ao tema

Caso

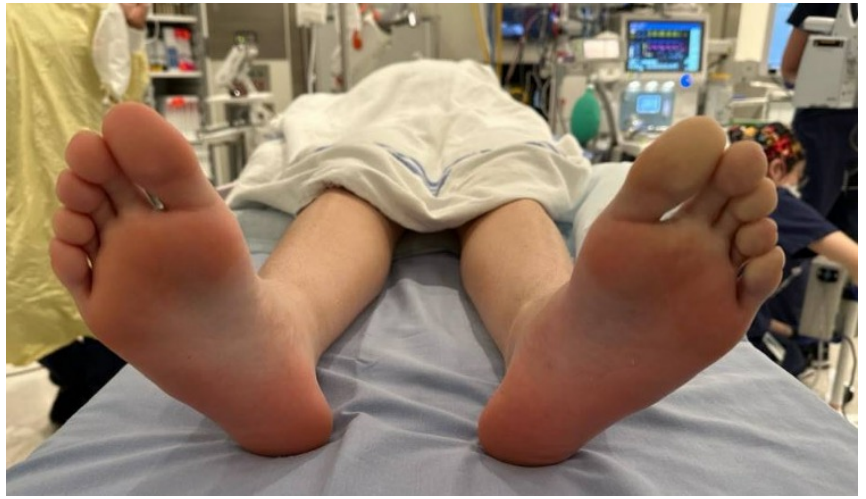
- 14 anos, sexo masculino
- Diagnóstico de síndrome nefrótica em 2012
- Última recaída em Jan 2024
- Em monoterapia com Myfortic, em desmame
- 02/03/24: câimbra em panturrilha esquerda ao andar. US doppler descartou trombose renal, aórtica, e TVP.
- 08/03/24: clinica de nefrologia com dor em panturrilha esquerda e parestesia há 5 dias, com piora há 48 horas

Caso

- Sem história de trauma associado
- Sem histórico familiar ou pessoal de trombose
- AP: ganglioneuroblastoma adrenal esquerda aos 7a → exérese

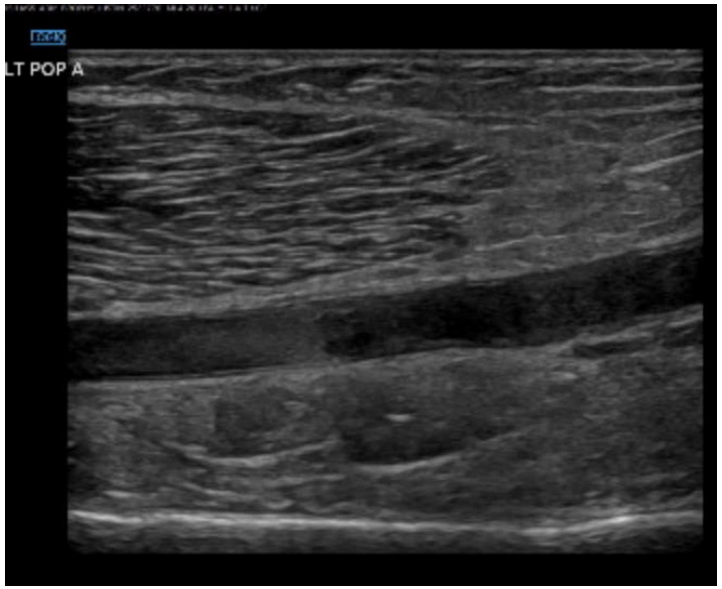


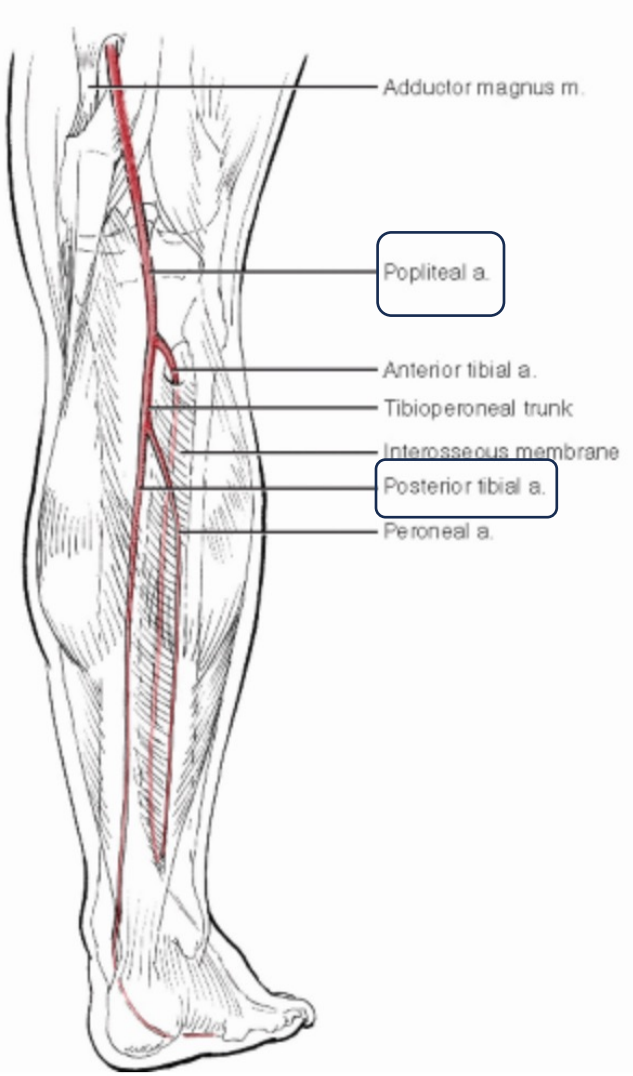
- EF: BEG, corado, hidratado, estável hemodinamicamente, extremidade fria, claudicação, pulsos fracos em EIE, enchimento capilar <3 segs, 73 bpm, PA 115 x 72 mmHg, afebril, 18 FR



Imagem

- Trombose arterial oclusiva da metade da artéria poplítea esquerda, extendendo inferiormente até a artéria tibial posterior





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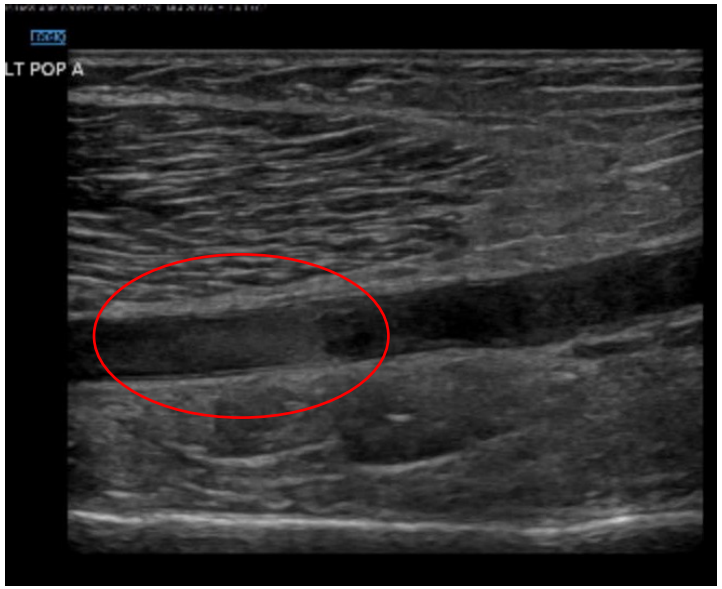

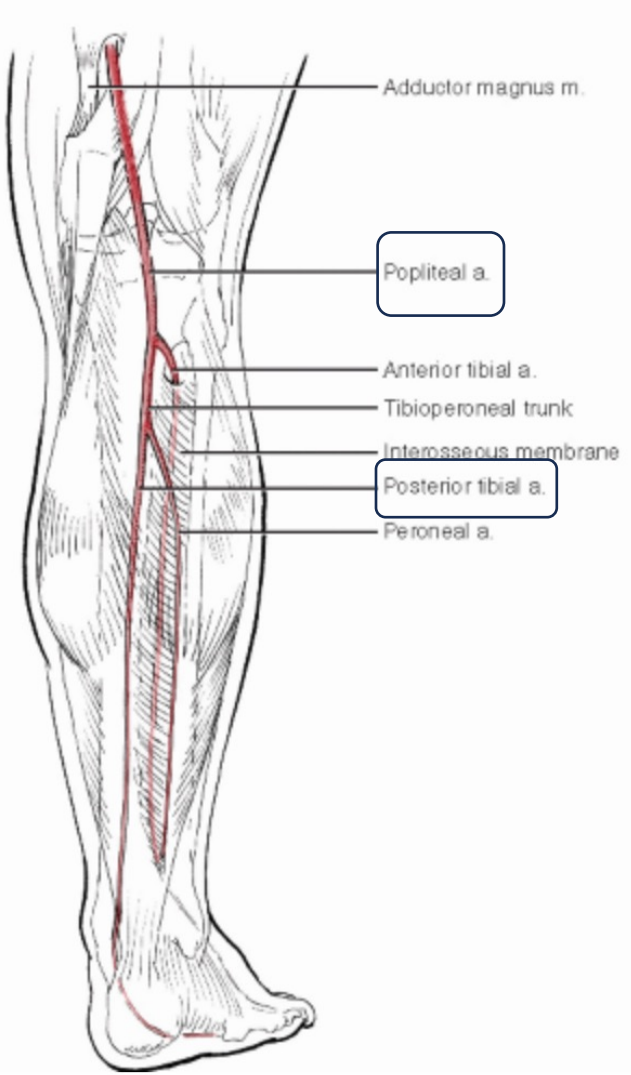

Laboratório/Internação

	08/03/2024
Hgb (129 - 167 g/L)	17
Leuco (4.23 - 9.99 x10^9/L)	14.70
Plaquetas	339.000
INR (0.9 - 1.2) / TTPA	0.9 / 38.4
Fibrinogênio (1.9 - 4.3 g/L)	5.8
D-dímero (<0.50 ug/mL FEU)	0.94
Creatinina (37 - 67 umol/L)	51
Albumina (37 - 50 g/L)	19
Urina 1 (Negativa g/L)	>=5.0
Colesterol total (<4.40 mmol/L)	13.53
Antitrombina 0.80 - 1.20 IU/mL	0.37

- Admitido para furosemida e diurético
- Pesquisa de SAAF
- Iniciada anticoagulação imediata com heparina não fracionada

ASH 2018 – AT ?

Recommendation 8b. The ASH guideline panel *suggests* using AT replacement therapy in addition to standard anticoagulation rather than standard anticoagulation alone in pediatric patients with DVT/CSVT/PE who have failed to respond clinically to standard anticoagulation treatment and in whom subsequent measurement of AT concentrations reveals low AT levels based on age-appropriate reference ranges (conditional recommendation based on very low certainty in the evidence of effects ⊕◯◯◯). **Remarks:** Despite the overall recommendation against AT use, the panel considered several subgroups and specific situations in which they agreed that AT use might be justified. The first is in children with documented inherited AT deficiency, in whom anticoagulation of VTE was not achieving clinical benefit. Other situations included children with low levels of AT compared with age-appropriate levels (as distinct from adult levels), acute lymphoblastic leukemia (ALL) on induction using asparaginase, children with nephrotic syndrome, neonates, postliver transplant patients, and children with disseminated intravascular coagulation and VTE. Usually, AT use would be commenced if there were continuous thrombus growth and/or failure of clinical response, despite adequate anticoagulation. However, there was no evidence to suggest improved outcomes in these patients.

Children with VTE often have both transient and persistent risk factors (eg, inflammatory bowel disease and a CVAD). The thrombotic risk in some diseases, including cancer, nephrotic syndrome, and rheumatic/inflammatory disorders, changes over time with disease control. The duration of anticoagulation therapy in a patient with persistent acquired prothrombotic risk factors is generally made on an individual basis. Less than 10% of pediatric

Conclusions and research needs for these recommendations. The guideline panel determined that there is very low certainty in the evidence for a net health benefit from using AT replacement. The evidence considered was inherently indirect. The panel agreed that, for any child with any VTE, the first line of treatment is anti-coagulation, independent of the AT level (hence, no plasma AT measurements would be required). However, the panel considered the following subgroups: children with age-appropriate low level of AT, children with ALL on induction, children with nephrotic syndrome, neonates, liver transplant patients, and patients with disseminated intravascular coagulation and VTE.

Blood Adv 2018

2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary

Acute limb ischemia (ALI)	Acute (<2 wk), severe hypoperfusion of the limb characterized by these features: pain, pallor, pulselessness, poikilothermia (cold), paresthesias, and paralysis. One of these categories of ALI is assigned (Section 10): I. Viable—Limb is not immediately threatened; no sensory loss; no muscle weakness; audible arterial and venous Doppler. II. Threatened—Mild-to-moderate sensory or motor loss; inaudible arterial Doppler; audible venous Doppler; may be further divided into IIa (marginally threatened) or IIb (immediately threatened). III. Irreversible—Major tissue loss or permanent nerve damage inevitable; profound sensory loss, anesthetic; profound muscle weakness or paralysis (rigor); inaudible arterial and venous Doppler.[21,22]

Anticoagulação (anti-Xa)

Modificado para HBPM

Infusão de tPa (HNF em dose profilática)

Iniciada anticoagulação com HNF

Internação

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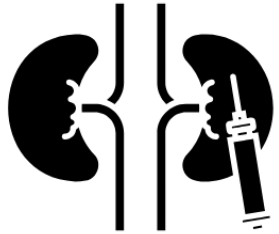
Pesquisa de SAAF	Triplo negativo

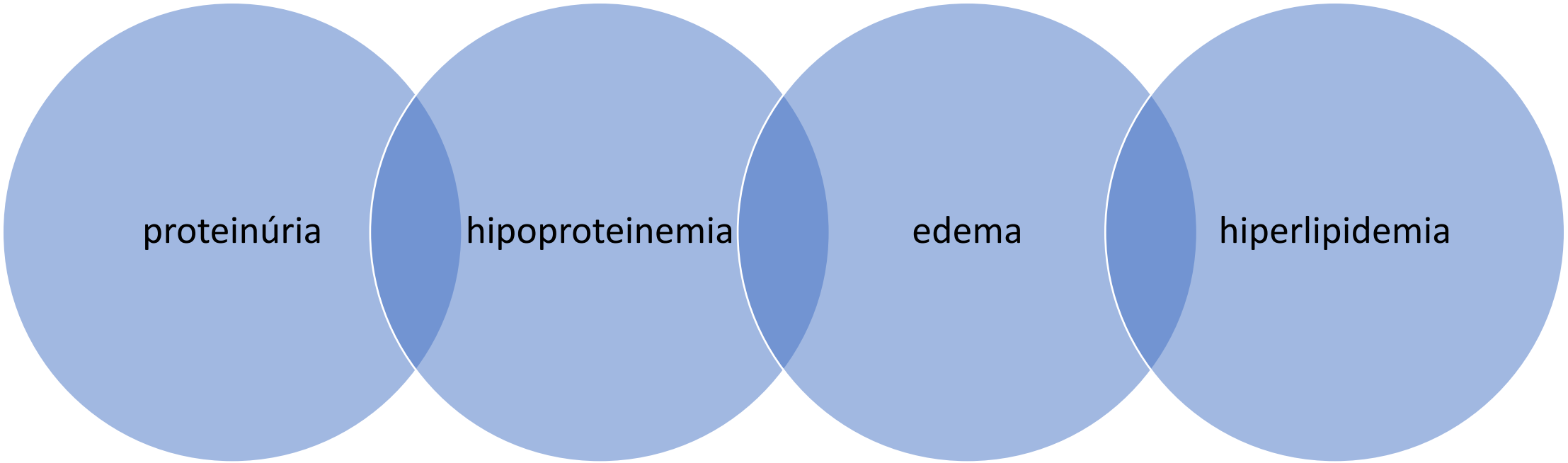
ECO normal



3 biópsias renais

GESF

Síndrome nefrótica



Subtipos
(diferentes formas de classificação)

Subtipos

Primary 95%. It is idiopathic and most common.

1. Pure MCD/Minimal Change Nephrotic Syndrome (MCNS) – 76.4%
2. MCD with mesangial proliferation 2.3%
3. Focal segmental glomerulosclerosis 6.9%
4. Membranoproliferative GN 7.5%
5. Membranous nephropathy 1.5%
6. Others 5.4%

Secondary 3-5%

1. Infections: HBV, HCV, Malaria, HIV, Syphilis
2. Drugs: NSAID, Penicillamine
3. Systemic disease: SLE
4. Malignancy: Leukaemia, Lymphoma

Subtipos

TABLE 12-1 Etiologies of Congenital Nephrotic Syndrome (0-3 Months of Age)

Genetic	Congenital nephrotic syndrome of the Finnish type (CNF) due to mutation in nephrin *(NPHS1)* gene Autosomal recessive FSGS due to mutation in podocin *(NPHS2)* gene Autosomal dominant diffuse mesangial Sclerosis (DMS) due to mutation in *WT1* gene Congenital nephrotic syndrome due to mutation in laminin β_2 gene
Syndromes	Denys-Drash syndrome due to *WT1* mutation with DMS Pierson syndrome Galloway Mowat syndrome Nail-patella syndrome due to mutation in LIM-homeodomain protein *(LMX1B)* Schimke immunoosseous dysplasia with FSGS due to mutation in *SMARCAL1* Cockayne syndrome Jeune's syndrome
Idiopathic	Minimal change nephrotic syndrome FSGS Nonsyndromic DMS
Infections	Congenital syphilis Congenital cytomegalovirus (CMV) infection Congenital toxoplasmosis

TABLE 12-2 Etiologies of Nephrotic Syndrome (Beyond 3 Months of Age)

Idiopathic	Minimal change nephrotic syndrome (MCNS) Focal segmental glomerulosclerosis (FSGS) Mesangial proliferative glomerulonephritis Membranoproliferative glomerulonephritis (MPGN) Membranous nephropathy (MN) IgM nephropathy C1q nephropathy
Genetic	Autosomal recessive FSGS due to mutation in gene encoding podocin *(NPHS2)* Autosomal dominant diffuse mesangial sclerosis (DMS) due to mutation in gene encoding *WT1* Autosomal dominant FSGS due to mutation in gene encoding *α-actinin 4* Autosomal dominant FSGS due to mutation in gene encoding CD2-associated protein *(CD2AP)* Autosomal dominant FSGS due to mutation in gene encoding transient receptor potential cation channel 6 *(TRPC6)*
Infections	Hepatitis B and C HIV Malaria Schistosomiasis Filariasis
Systemic diseases	Henoch-Schönlein purpura Systemic lupus erythematosus Diabetes mellitus Sarcoidosis
Metabolic diseases	Fabry's disease Glutaric acidemia Glycogen storage disease Mitochondrial cytopathies
Hematologic and oncologic diseases	Leukemia Lymphoma (Hodgkin's most likely can lead to minimal change) Sickle cell disease
Drugs	Nonsteroidal antiinflammatory drugs (NSAIDs) Gold Penicillamine Angiotensin converting enzyme inhibitors (ACEIs) Pamidronate Interferon Mercury Heroin Lithium
Others	Bee stings (MCNS) Food allergies Obesity (usually with FSGS) Oligomeganephronia Pregnancy

Subtipos

Primary nephrotic syndrome

Four types of kidney disease can cause primary nephrotic syndrome in children and adolescents.[2]

- Minimal change disease NIH (MCD). MCD is the most common cause of nephrotic syndrome in young children. The disease causes very little change to the glomeruli or nearby kidney tissue. The changes in the kidney can only be seen using an electron microscope, which shows tiny details. Although the cause of MCD is unknown, some health care professionals think the immune system may be involved.
- Focal segmental glomerulosclerosis NIH (FSGS). This disease can cause some of the kidney's glomeruli to become scarred. FSGS may be caused by genetic variants NIH, or changes in genes present at birth.
- Membranous nephropathy NIH (MN). MN is an autoimmune disease that causes immune proteins to build up in the kidney's glomerular basement membrane. As a result, the membrane becomes thick and does not work properly, allowing too much protein to pass into the urine.

Secondary nephrotic syndrome

Causes of secondary nephrotic syndrome in children include[3]

- diseases that involve many organs or the whole body, called systemic diseases. Examples include IgA vasculitis (also known as Henoch-Schönlein purpura) and lupus.
- infections, including hepatitis B and C, HIV NIH, and malaria NIH.
- diseases of the blood, such as leukemia NIH, lymphoma NIH, and sickle cell disease NIH.
- some medicines and drugs, such as nonsteroidal anti-inflammatory drugs, and some medicines used to treat mood disorders, bone loss, or cancer.

Congenital nephrotic syndrome

Among newborns and infants younger than 12 months old, the two most common causes of nephrotic syndrome are[4]

- genetic variants, which account for most cases of congenital nephrotic syndrome
- infections present at or before birth, such as syphilis NIH and toxoplasmosis NIH

Subtipos

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Associação com trombose

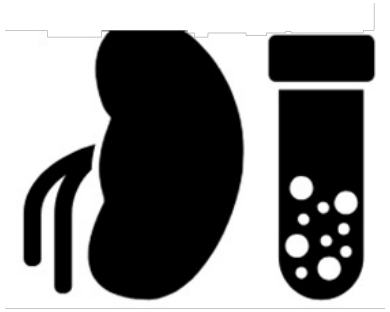
- 1954 → Fisberg et al descreveu eventos tromboembólicos em pacientes com SN
- 1974 → Egli et al estudaram 3377 crianças com SN → 1.8% trombose

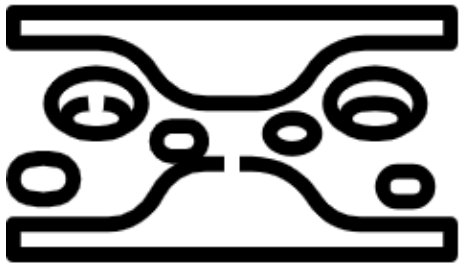
- TVP e trombose de veia renal são complicações bem conhecidas
- Trombose arterial → rara e apresenta manejo controverso

Egli F. Pediatr Res 1974

Fishberg AM. Philadelphia, Lea & Febiger. 1954

Síndrome nefrótica e TVP





Mecanismos para trombose

Llach F. Kidney Int 1985; Zwaginga J.J. J Clin Invest. 1994; Sirolli V, et al. Nephron 2002*

Perda de proteínas envolvidas na inibição da hemostasia sistêmica

Hiperagregação plaquetária

Ativação local do sistema de hemostasia glomerular

Estase venosa associada à imobilidade

Lesão vascular associada às punções

Trombocitose e aumento dos fatores de VW

Mecanismos para trombos

Predisposição genética

Llach F. Kidney Int 1985; Zwaginga J.J. J Clin Invest. 1994; Sirolli V, et al. Nephron 200

Perda de proteínas envolvidas na inibição da hemostasia sistêmica

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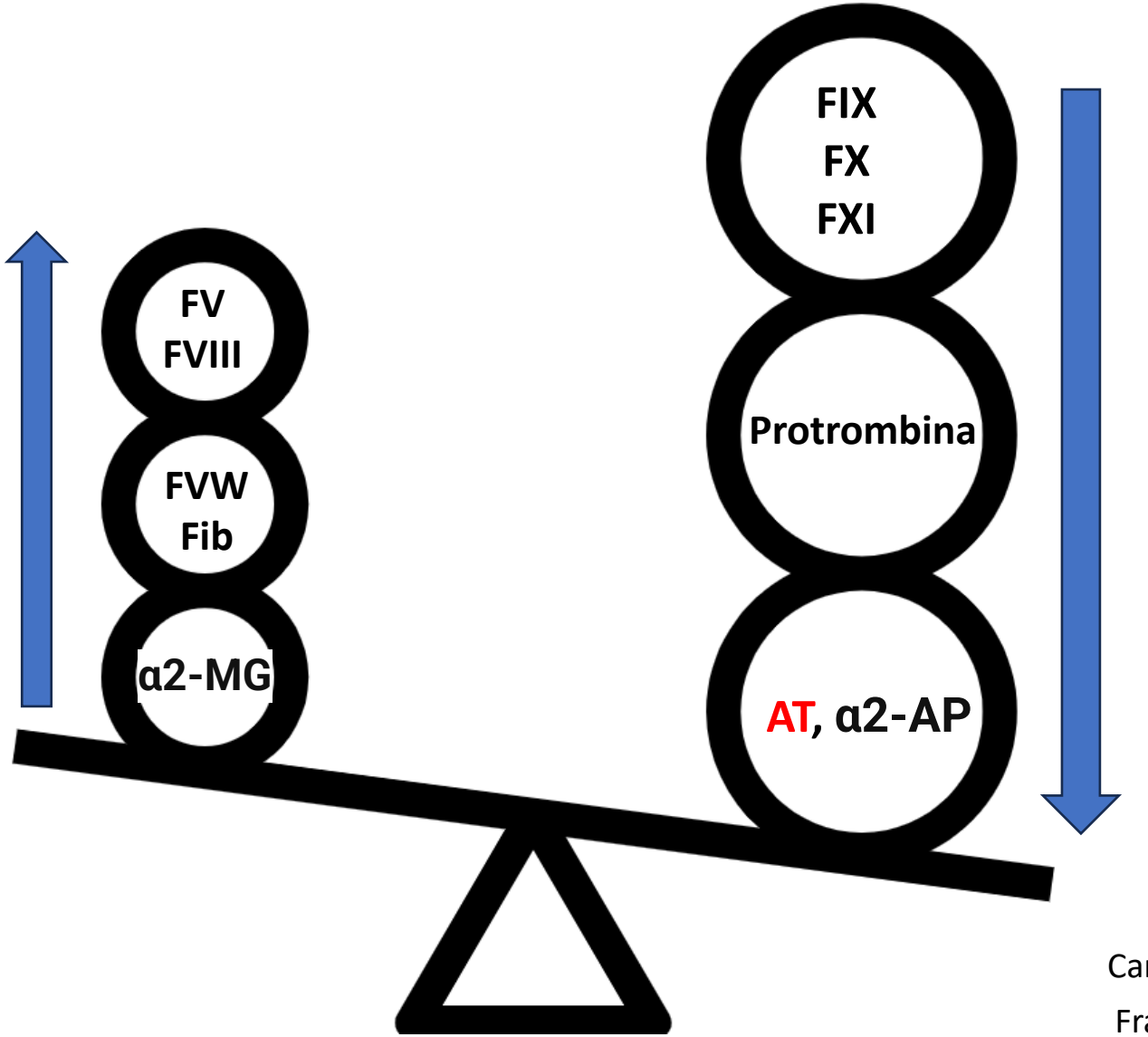
AUMENTO DA PRODUÇÃO



PERDA URINÁRIA

Kanfer A. Am J Nephrol 1990

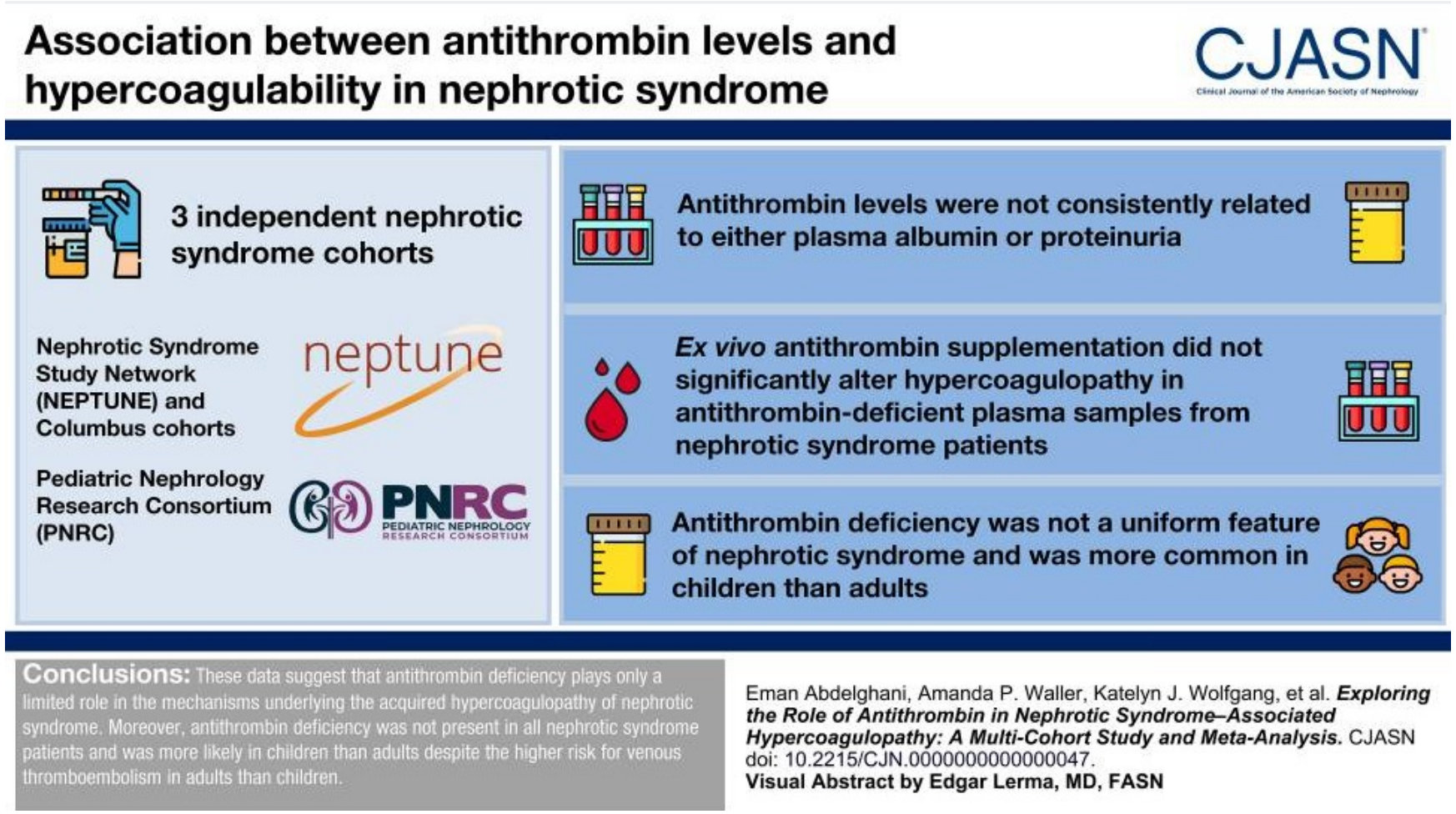
Cameron JS. Am J Kidney Dis 1987

Francis Jr RB, et al. Nephron 1985

No entanto….

- Metanálise
- 208 amostras

- NEPTUNE (147)
- Columbus (23)
- PNRC (38)

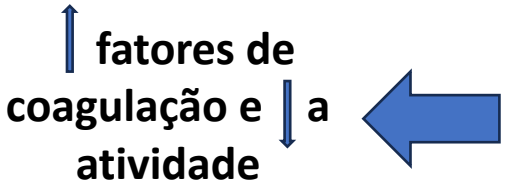


Abdelghani E, et al. *Clin J Am Soc Nephrol.* 2023

Fatores adicionais

- Corticóide
- Diuréticos
- Fibrinogênio
- Antitrombina

Fatores adicionais



Corticóide

Diuréticos

Fibrinogênio

Antitrombina

Fatores adicionais

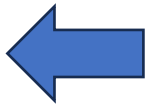
Corticóide

Diuréticos

Fibrinogênio

Antitrombina

Altera a viscosidade plasmática



Fatores adicionais

Corticóide

Diuréticos → **Hemoconcen-tração**

Fibrinogênio

Antitrombina

Fatores adicionais

Corticóide

Diuréticos

Fibrinogênio

Antitrombina → **Inativa os fatores pró-coagulantes**

Conclusão (1)


Diminuição dos anticoagulantes
Aumento dos prócoagulantes
Hipercoagulabilidade

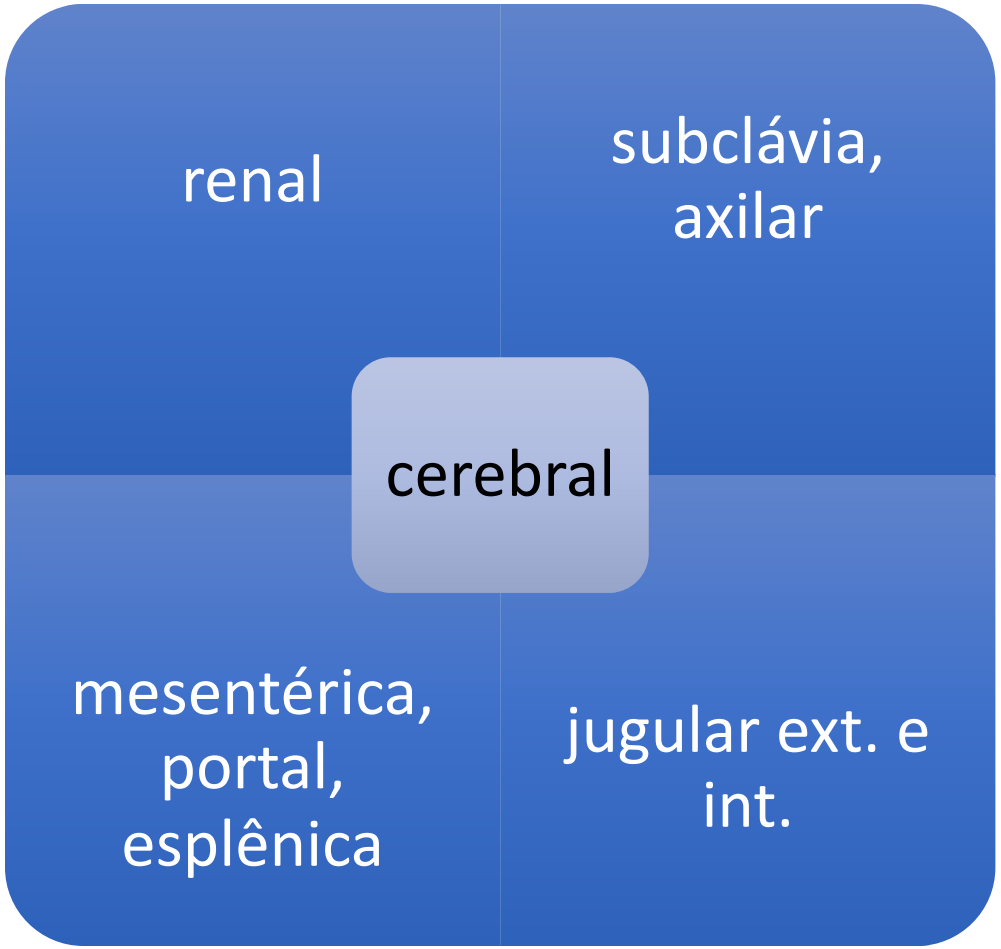
Incidência

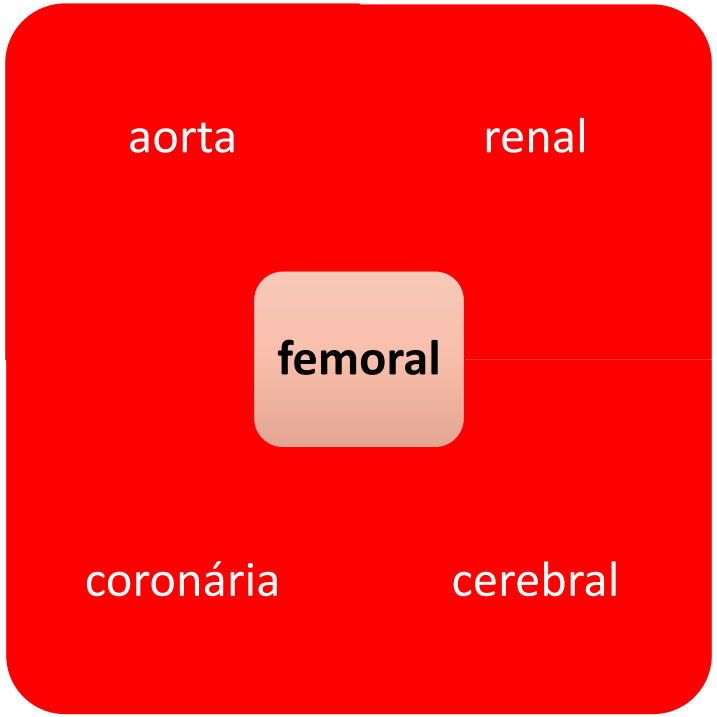
- Variável
- Adultos (25%) > crianças (3%)*

Local	Incidência
Trombose venosa profunda	15%
Embolia pulmonar	10-30%
Trombose de veia renal	25-37%

Greenberg KI, et al. Clin J Am Soc Nephrol. 2023

Locais





Al-Azzawi HF, et al. Int J Crit Illn Inj Sci. 2016
Vijay P. et al. *Nephron.* 1995

Thromboembolic complications in childhood nephrotic syndrome: a clinical profile

Deepti Suri · Jasmina Ahluwalia · Akshay K. Saxena · Kushaljit S. Sodhi · Paramjeet Singh · Bhagwant R. Mittal · Reena Das · Amit Rawat · Surjit Singh

Table 2 Frequency of various thromboembolic complications, clinical profile and outcome

Type of TEC	No. of TECs	Mean age years (range)	Sex female: male	First episode (%)	Infrequent relapse (%)	SDNS/ FRNS (%)	SRNS (%)	No. (%) of patients with proteinuria (>40 mg/m^2/h)	Focus of infection (%)	No. of patients with associated genetic thrombophilia (patient positive/patient tested)	Recovery (%)
CVT	11 (29.4)	7.5 ± 2.6 (3–12)	1:1.2	4 (36)	3 (27.2)	2 (18.1)	2 (18.1)	6 (54.5)	1 (9)	2/7	11 (100)
PTE	9 (25)	7.8 ± 2.3 (3.5–11)	0:9	–	2 (22.2)	4 (44.4)	3 (33.3)	9 (100)	5 (55.5)	1/4	7 (77.7)
DVT and SVC	6 (16.6)	7.3 ± 2.9 (4–12)	1:2	–	1 (16.6)	1 (16.6)	4 (66.6)	6 (100)	4 (66.6)	0/1	6 (100)
ICAT	7 (19.4)	8.1 ±3.6 (2.5–12)	1.3:1	1 (14.2)	1 (14.2)	4 (57.1)	1 (14.2)	6 (85.6)	1 (14.2)	4/5	7 (100)
LA	2 (5.5)	7.5 (3–12)	1:1			1 (50)	1 (50)	2 (100)	–	0/1	1 (50)

TEC thromboembolic complications, *CVT* cortical venous thrombosis, *PTE* pulmonary thromboembolism, *DVT* deep venous thrombosis, *SVC* superior vena cava thrombosis, *ICAT* intracranial arterial thrombosis, *LA* limb artery, *NS* nephrotic syndrome, *SDNS* steroid-dependent nephrotic syndrome, *SRNS* steroid-resistant nephrotic syndrome

35 eventos trombóticos em 34 pacientes

Fatores de risco

a) Albumina baixa (<2.0g/dL)*
b) Trombocitose (>450 x10^9 plaquetas/L)
c) Hipercolesterolemia
d) Fatores locais (ex: causas anatômicas)
e) Desidratação
f) Terapia com corticóide
g) Trauma vascular iatrogênico
h) Fibrinogênio aumentado
i) Antitrombina diminuída (<75%)
j) Idade

Fatores de risco

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h) Fibrinogênio aumentado
i) Antitrombina diminuída (<75%)
j) Idade

* ⬇1g/dL → 2.13⬆risco TEV
(Lionaki ey al. *Clin J Am Soc Nephrol.* 2012)

Spontaneous Arterial Thrombosis Associated with Nephrotic Syndrome: Case Report and Review of the Literature

- 29a, sexo masculino
- GNLM há 4a
- Trombose artéria femoral esq. durante recaída
- Trombectomia → Warfarina

been reported extensively. Arterial thrombosis, however, is a rare complication and is mainly seen in children.

Table 1. Previous reported cases of femoral artery thrombosis in adult nephrotic patients

	Mukherjee et al. [3]	Patel and Mandal [4]	Nitatori et al. [5]		Parag et al. [6]
			case 1	case 2	
Age, years	24	34	40	25	23
Sex	male	male	male	male	male
Renal histology	PGN	FPGN	PGN	PGN	MCGN
Serum albumin, g/dl	0.65	not done	1.5	0.92	0.7
Steroids	+	–	+	+	–
Diuretics	–	+	+	–	+
Anticoagulants	no	yes	yes	yes	yes
Surgical therapy	RAKA	thrombectomy/ bilateral BKA	thrombectomy/ RAKA	thrombectomy	thrombectomy
Recurrence	yes	yes	yes	no	no
Outcome	alive	alive	alive	alive	died

PGN = Proliferative glomerulonephritis; FPGN = focal proliferative glomerulonephritis; MCGN = minimal-change glomerulonephritis; RAKA = righ above-knee amputation; BKA = below-knee amputation.

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Spontaneous Arterial Thrombosis Associated with Nephrotic Syndrome: Case Report and Review of the Literature

PROGNÓSTICO RUIM

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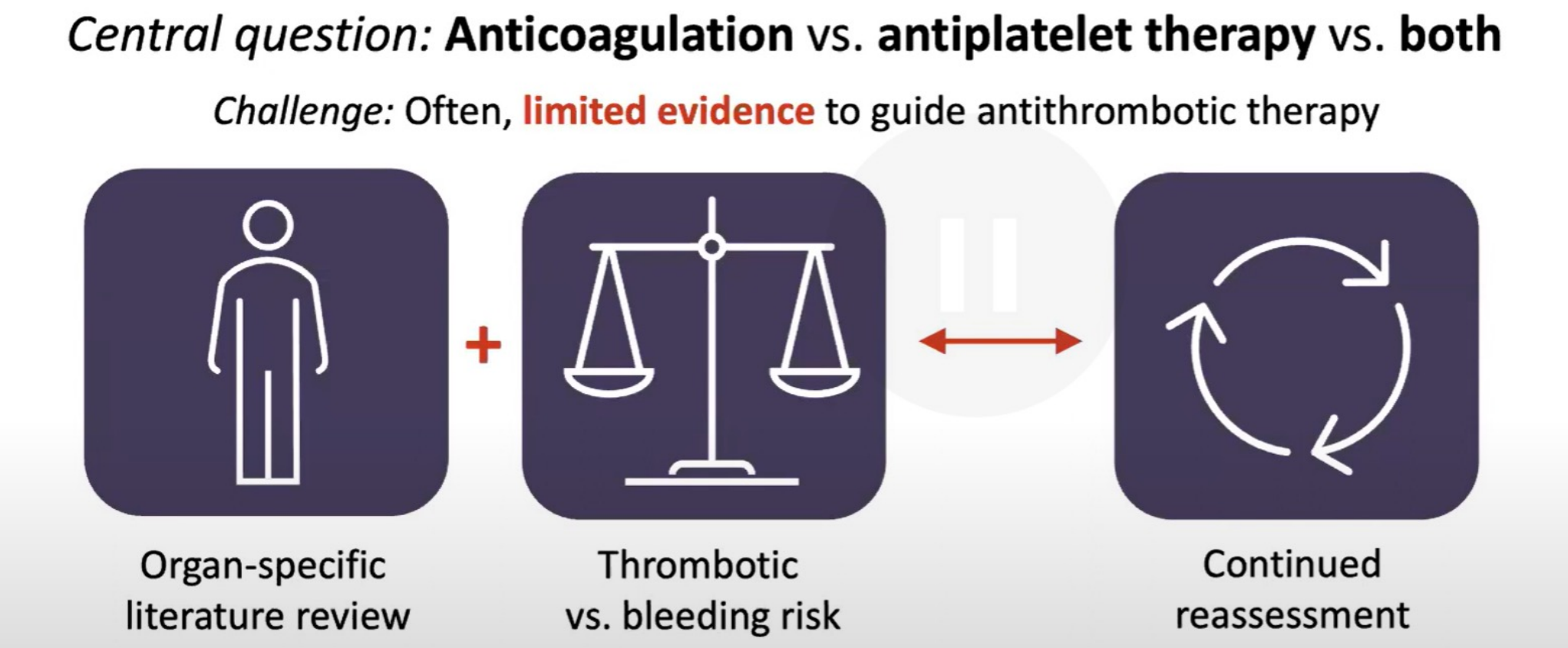
Interconsulta para o hematologista….



De volta ao caso...

- Heparina não fracionada
- Revascularização (com tpa por 1 dia)
- HBPM 2 dias após procedimento + aspirina 81 mg/dia
- Alta após 4 dias
- Medicaçoes:
  - ✓ **Rituximabe**
  - ✓ **Enoxaparina**
  - ✓ **Prednisona**
  - ✓ **Aspirina**
  - ✓ **Vitamina D**

Laboratório	Alta
Hgb (129 - 167 g/L)	13.4
Leuco (4.23 - 9.99 x10^9/L)	9.61
Plaquetas	240.000
INR (0.9 - 1.2) / TTPA	0.9 / 45.2
Fibrinogênio (1.9 - 4.3 g/L)	4.2
D-dímero (<0.50 ug/mL FEU)	0.88
Creatinina (37 - 67 umol/L)	42
Albumina (37 - 50 g/L)	16
Urina 1 (Negativa g/L)	>=3.0
Colesterol total (<4.40 mmol/L)	14.69 (10 dias após)
SAAF	Triplo negativo

Duração do tratamento

a) 5-7 dias
b) 1 mês
c) 3 meses
d) 6 meses
e) Depende

Guidelines

Duração

Duration of therapy: Currently, duration of therapy for venous thrombosis in neonates and children is extrapolated from adult practice, despite considerable evidence that this may not be relevant. Current clinical convention around duration of therapy for many types of arterial thrombosis seems entirely empirical. Multicenter clinical outcome studies are required to address these questions.

2.9. For neonates and children with acute femoral artery thrombosis, we recommend therapeutic doses of IV UFH as initial therapy compared with aspirin or no therapy (Grade 1B) **or LMWH** (Grade 2C). **We suggest subsequent conversion to LMWH, or else continuation of UFH, to complete 5 to 7 days of therapeutic anticoagulation as compared with a shorter or longer duration** (Grade 2C).

Antithrombotic Therapy in Neonates and Children. CHEST, 2012

Aspirina

7.1. For patients undergoing peripheral artery PTA with or without stenting, we recommend long-term aspirin (75-100 mg/d) or clopidogrel (75 mg/d) (Grade 1A). **For patients undergoing peripheral artery PTA with stenting, we suggest single rather than dual antiplatelet therapy** (Grade 2C).

6.1-6.3. In patients with acute limb ischemia due to arterial emboli or thrombosis, we suggest immediate systemic anticoagulation with unfractionated heparin over no anticoagulation (Grade 2C); **we suggest reperfusion therapy (surgery or intraarterial thrombolysis) over no reperfusion therapy** (Grade 2C); **and we recommend surgery over intraarterial thrombolysis** (Grade 1B). **In patients undergoing intraarterial thrombolysis, we suggest rt-PA or urokinase over streptokinase** (Grade 2C).

Patients presenting with **acute limb ischemia** should be treated with heparin in an emergent manner; thereafter, there is clinical uncertainty as to the optimal acute term antiplatelet +/- anticoagulant regimen to use. A recent survey of Canadian vascular surgeons demonstrated that ASA combined with full-dose anticoagulation is the most commonly chosen post-operative antithrombotic regimen when concerned for high risk of postoperative graft/stent re-thrombosis. Most acknowledged that clinical

Table 1. Professional society recommendations for antithrombotic therapy for atherosclerotic occlusive arterial disease, atrial fibrillation, valvular heart disease, and patent foramen ovale

Disorder	Date of last update
Peripheral arterial disease	2017,[1] 2013[2]
Coronary artery disease, myocardial infarction	2014,[3,4] 2016[5,6]
Atrial fibrillation	2018,[7] 2019[8]
Valvular heart disease	2017[9]
Transient ischemic attack, stroke	2014[10]
Patent foramen ovale	2019[11]

PAD CHEST, 2012; Blood, 2020, Thrombosis Canada

Retorno

- 2 semanas após
- US mostrou recanalização, com artérias patentes e ausência de trombo residual
- Assintomático

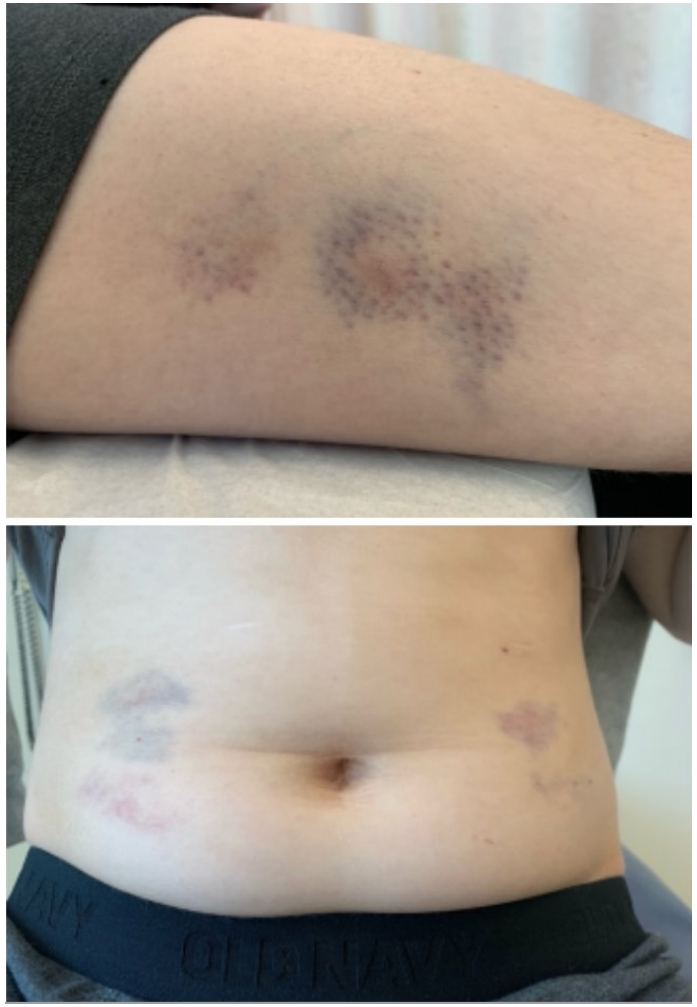
- Descontinuar tratamento - ?
- Quais questões devem ser avaliadas - ?

Retorno

- 2 semanas após
- US mostrou recanalização, com artérias patentes e ausência de trombo residual

- Descontinuar tratamento - ?
- Quais questões devem ser avaliadas - ?

- Enoxaparina → Tinzaparina



Retorno

- 2 semanas após
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- Quais questões devem ser avaliadas - ?

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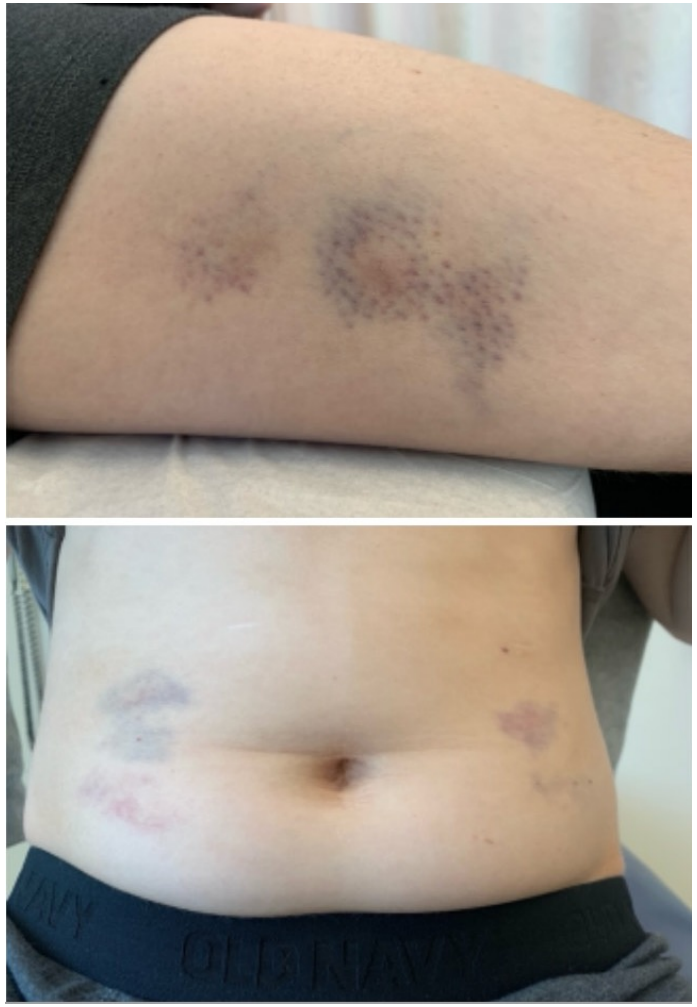
ASPIRINA



Childhood Nephrotic Syndrome Complicated by Catastrophic Multiple Arterial Thrombosis Requiring Bilateral Above-Knee Amputation

Togashi H. Front Pediatr. 2020

TABLE 1 | Published cases of arterial thrombosis of the extremities in pediatric idiopathic nephrotic syndrome.

References	Cameron et al. (11)	Harrison and Wood (12)	Parrish et al. (8)	Maffei et al. (13)	Tarry et al. (9)	Farkas et al. (10)	Büyükçelik et al. (14)	Koh et al. (15)	Han et al. (16)	Chinnadurai et al. (17)	Our case
Age/sex	1/F	3/M	8/M	1/M	15/M	15/M	14/F	15/N/A	2/F	8/M	10/F
Thromboembolic site	Popliteal artery	Femoral artery	Common iliac, external iliac, and femoral arteries	Femoral artery	Brachial, ulnar, and radial arteries	Popliteal artery	Femoral and posterior tibial arteries	Femoral and popliteal arteries	Common iliac, external iliac, and popliteral arteries	Posterior tibial and peroneal arteries	Common iliac and femoral arteries
Episode	N/A	N/A	Relapse	First	First	Relapse	First	Relapse	First	First	First
Steroid administration	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	No
Steroid sensitivity	N/A	Resistant	Sensitive	Sensitive	N/A	Resistant	Resistant	Sensitive	Resistant	Sensitive	–
Type of nephrotic syndrome	N/A	MPGN	MC	MC	N/A	MC	MN	MC	FSGS	FSGS	–
Albumin (g/dL)	N/A	N/A	0.8	N/A	0.4	1.8	2.2	3.8	2.5	1.4	1.0
Fibrinogen (μg/dL)	N/A	N/A	N/A	N/A	N/A	630	381	N/A	362	N/A	949
Antithrombin III (%)	N/A	N/A	N/A	N/A	N/A	65	83	N/A	91	46	66
Thrombectomy	Yes	N/A	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Thrombolysis	Yes	N/A	No	No	Yes	No	No	No	No	Yes	No
Fasciotomy	No	N/A	No	No	Yes	No	No	Yes	No	Yes	Yes
Amputation	Femur	N/A	Femur	No	Digits of the hand	Lower leg	No	No	No	Digits of the foot	Bilateral femurs

N/A, not available; MPGN, membranoproliferative glomerulonephritis; MC, minimal change; MN, membranous nephropathy; FSGS, focal segmental glomerulosclerosis.

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Episode	N/A	N/A	Relapse	First	First	Relapse	First	Relapse	First	First	First
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Type of nephrotic syndrome	N/A	MPGN	MC	MC	N/A	MC	MN	MC	FSGS	FSGS	–
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Thrombectomy	Yes	N/A	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Thrombolysis	Yes	N/A	No	No	Yes	No	No	No	No	Yes	No
Fasciotomy	No	N/A	No	No	Yes	No	No	Yes	No	Yes	Yes
Amputation	Femur	N/A	Femur	No	Digits of the hand	Lower leg	No	No	No	Digits of the foot	Bilateral femurs

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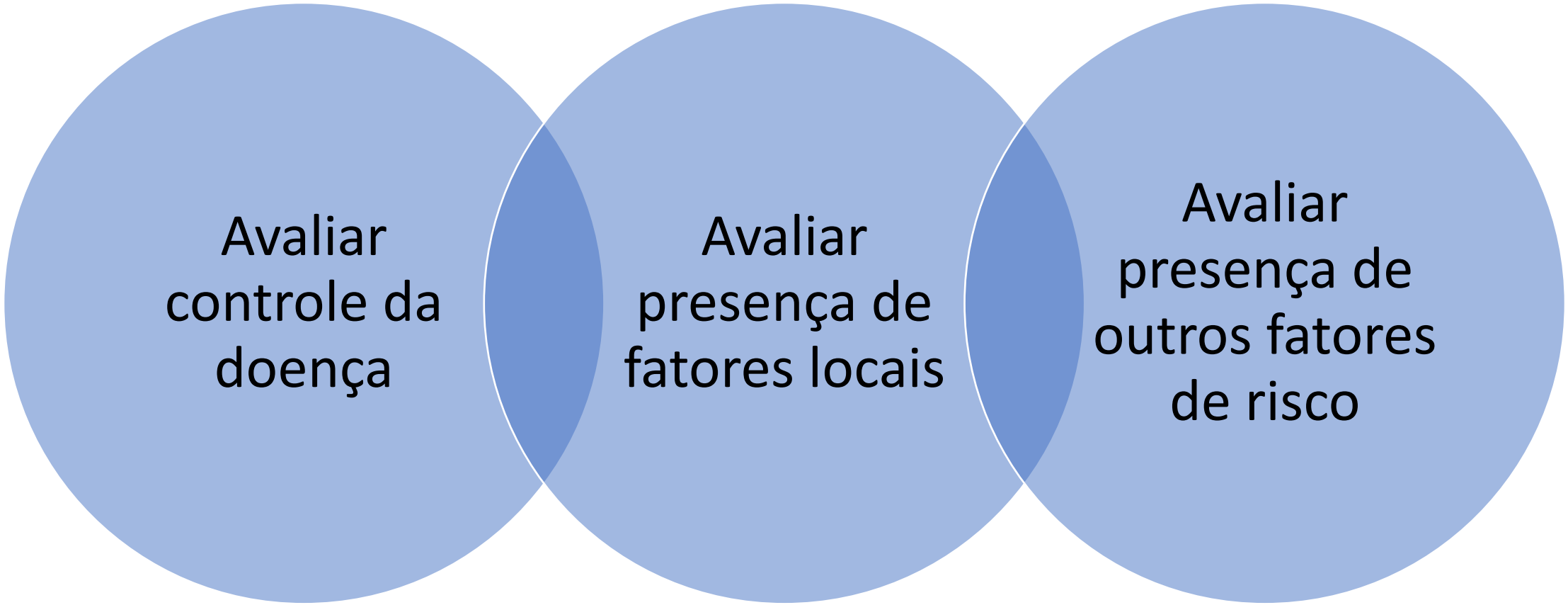
Antes de descontinuar tratamento



Fatores locais

How I treat unexplained arterial thrombosis

Jori E. May[1] and Stephan Moll[2]

[1]Department of Medicine, Division of Hematology/Oncology, University of Alabama at Birmingham, Birmingham, AL; and [2]Department of Medicine, Division of Hematology, University of North Carolina School of Medicine, Chapel Hill, NC

- 3 passos para avaliação e manejo:

1-) definindo o trombo

2-) realizar avaliação diagnóstica

3-) determinar o manejo

How I treat unexplained arterial thrombosis

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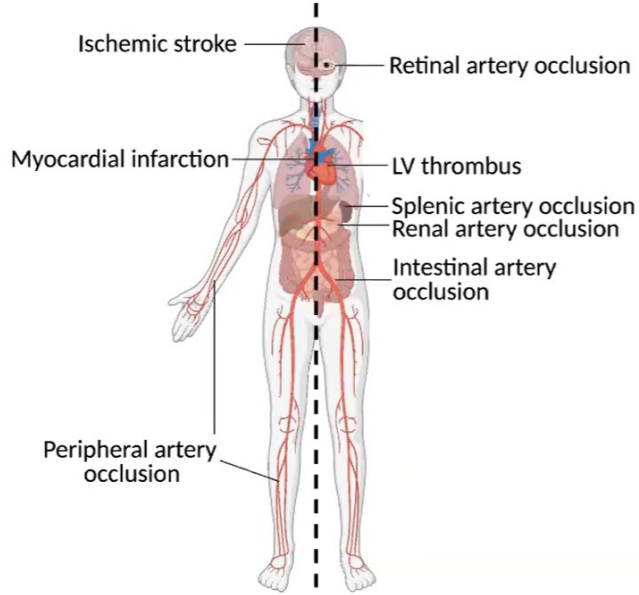
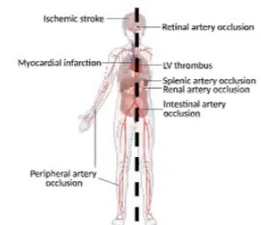
"Usual" arterial thrombosis | ***Unexplained*** **arterial thrombosis**



Anticoagulation FORUM

"Usual" arterial thrombosis | ***Unexplained*** **arterial thrombosis**

1. Location



2. Age

Older | **Younger**

3. Atherosclerotic/cardioembolic risk factors?

Yes | **No**

Anticoagulation FORUM

Fatores locais

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- 3 passos para avaliação e manejo da trombose arterial espontânea*:

1-) definindo o trombo

2-) realizar avaliação diagnóstica →

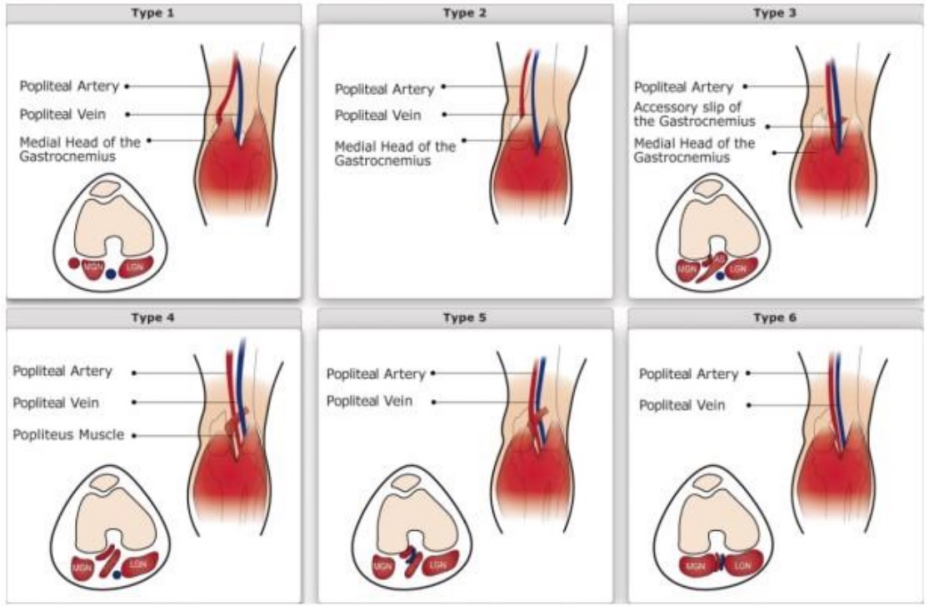
3-) determinar o manejo

- ✓ **Revisar imagem com radiologista**
- ✓ **A qualidade do estudo é suficiente p/ avaliação da vasculatura?**
- ✓ **O paciente tem variação anatômica?**

Fatores locais - SAAP

Anatomy-based Classification of Popliteal Artery Entrapment Syndromes

Syndrome Type	Underlying Anatomic Abnormality
1	Aberrant medial course of the popliteal artery around the normal medial head of the gastrocnemius muscle
2	Aberrant lateral insertion of the medial head of the gastrocnemius muscle on the distal femur, with resultant medial displacement of the popliteal artery
3	Abnormal accessory slip of gastrocnemius muscle
4	Fibrous band or popliteus muscle
5	Any abnormality causing entrapment of the popliteal vein as well as the artery
6	Hypertrophy of the gastrocnemius muscle



Miller et al. Journal of the American Academy of Orthopaedic Surgeons 2021

Fatores locais - RM

“Ausência de trombose arterial ou venosa, ou variante anatômica identificada nas extremidades inferiores abaixo dos níveis do joelho”

Retorno

- Após 2 meses → warfarina (aspirina)
- Aos 3 meses retorno na clínica com RNM
- Duração do tratamento:

a) 3 meses
b) 6 meses
c) Depende

Retorno

- Após 2 meses → warfarina (aspirina)
- Aos 3 meses retorno na clínica com RNM
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Retorno

- Após 2 meses → warfarina (aspirina)
- Aos 3 meses retorno na clínica com RNM
- Duração do tratamento:

a) 3 meses

b) 6 meses

c) Depende

INR = 1.3
Paciente parou as duas medicações por contra própria, pois "cansou de tomá-las"

Remissão da doença

Acute lower extremity arterial thrombosis associated with nephrotic syndrome in adults: case series and literature review

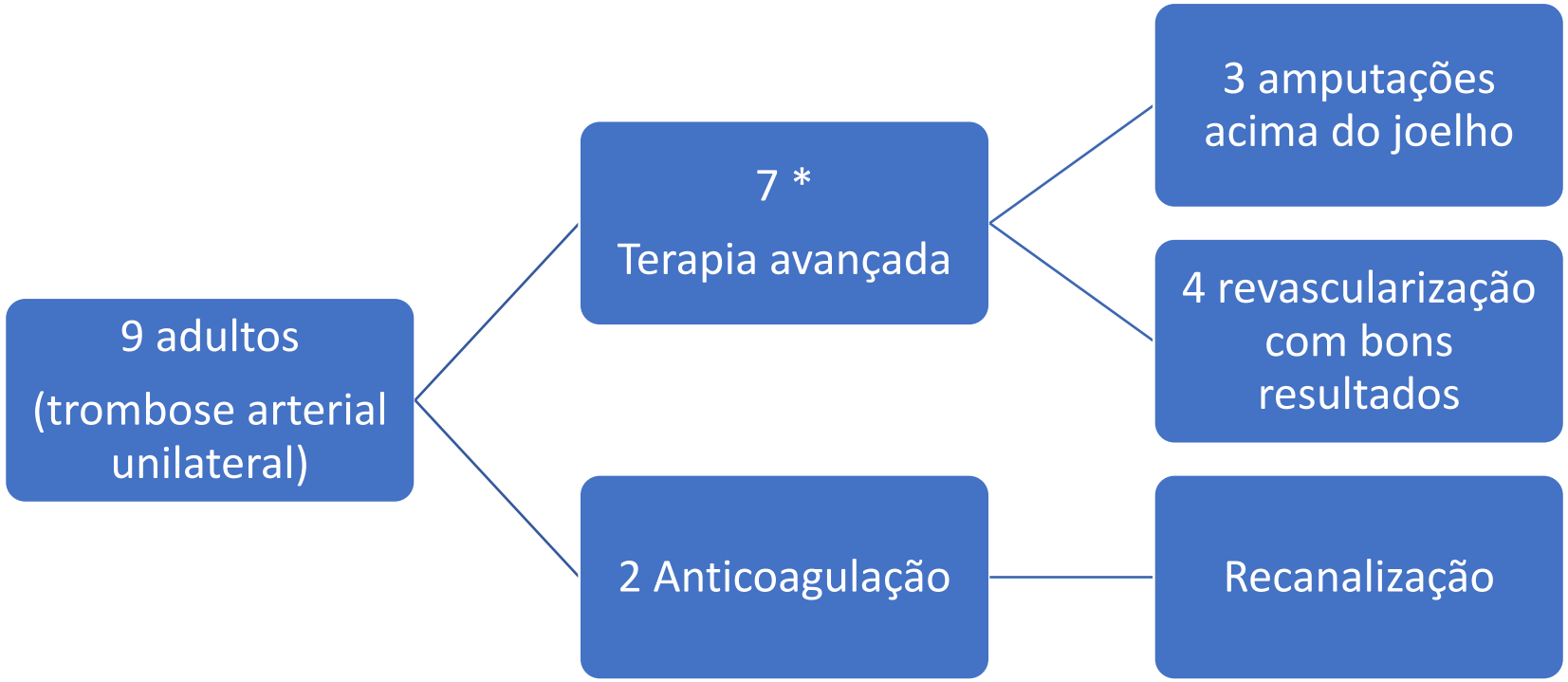
Xinqiang Han,[#1] Peng Zhao,[#2] Zhu Wang,[1] Xingang Ji,[1] and Mengpeng Zhao[✉1]

- Estudo retrospectivo
- Jan 2011 – Out 2022
- 9 adultos (8 H / 1 M)
- Idade média 43.1 anos (23-67)

Nephrotic syndrome (NS) is a condition associated with hypercoagulability. Thromboembolic events are a well-recognized complication of NS. Venous thrombosis is well known, while arterial thrombosis, which is more severe, occurs less frequently and is mainly reported in children in the literature.

Acute lower extremity arterial thrombosis associated with nephrotic syndrome in adults: case series and literature review

Xinqiang Han,[#1] Peng Zhao,[#2] Zhu Wang,[1] Xingang Ji,[1] and Mengpeng Zhao[✉1]



*1 paciente com SN há 14ª
6 pacientes com trombose precedendo o diagnóstico de SN

Acute lower extremity arterial thrombosis associated with nephrotic syndrome in adults: case series and literature review

Xinqiang Han,[#1] Peng Zhao,[#2] Zhu Wang,[1] Xingang Ji,[1] and Mengpeng Zhao[✉1]

Case series	Gender	Gender	*Time (months)	Serum albumin (g/L)	Urinary protein (g/24 h)	D-dimer (mg/L)	Fibrinogen (g/L)	Arterial thrombus localization	Amputation	Diabetes mellitus	Hypertension	Dyslipidemia	Smoke
No.1	Male	26	5	15.2	26.5	7.86	7.99	Iliac	Yes	No	No	Yes	Yes
No.2	Female	33	4	24.2	7.84	12.5	6.97	Iliac-femoral-popliteal	Yes	No	No	Yes	No
No.3	Male	52	5	15.6	10.65	13.69	5.39	Femoral-popliteal	No	No	Yes	Yes	Yes
No.4	Male	50	7	20.5	8.21	3.59	5.59	Popliteal	Yes	No	No	Yes	Yes
No.5	Male	23	6	14.8	5.55	12.13	6.20	Popliteal	No	No	Yes	Yes	No
No.6	Male	42	9	18.3	22.53	17.17	6.86	Popliteal	No	No	Yes	Yes	Yes
No.7	Male	39	13	22.9	6.3	2.56	4.25	Femoral	No	No	Yes	Yes	No
No.8	Male	67	8	21.0	11.08	5.07	6.10	Iliac	No	No	Yes	Yes	Yes
No.9	Male	56	7	19.95	17.35	4.38	5.72	Femoral-popliteal	No	No	Yes	Yes	Yes

* Time from clinical onset to clinical remission of nephrotic syndrome

Thrombose artérielle d'un membre inférieur au cours d'une rechute de syndrome néphrotique

Lower-limb arterial thrombosis in a relapse of nephrotic syndrome

S. Haddad*, L. Ghédira-Besbes, K. Lajmi, S. Hammami, S. Chouchene, C. Ben Meriem, M.N. Guediche

Service de pédiatrie, CHU Fattouma Bourguiba, 5000 Monastir, Tunisie

Introduction. Venous thromboembolic complications are well-known in patients with nephrotic syndrome. Arterial thrombosis has rarely been reported and is mainly observed in adults.

- 9a, sexo masculino
- SN córtico-dependente (DLM)
- Dor no pé direito após trauma
- Trombose arterial de tibial anterior e posterior
- ↓ alb (13g/L), Urina +, AT 95%
- Heparina + vasodilatador
- Amputação de 2 dedos
- Warfarina → 6 meses

Thrombose artérielle du membre inférieur sur un syndrome néphrotique

Raja Arrab, Aicha Bourrahouate, Mohamed Sbihi, Imane Ait Sab

June 2017, 13(4), p.248 - 250 - Néphrologie & Thérapeutique

- 9a, sexo masculino
- SN córtico-dependente
- Sem história de trauma
- Dor pé direito há 2 dias
- ⇓ alb (13.9g/L), Urina +, AT n/a
- Trombose arterial de poplítea
- Embolectomia
- HBPM → warfarina → 3 meses

Thrombose artérielle du membre inférieur sur un syndrome néphrotique

Raja Arrab, Aicha Bourrahouate, Mohamed Sbihi, Imane Ait Sab

June 2017, 13(4), p.248 - 250 - Néphrologie & Thérapeutique

- Sugestão de profilaxia:

✓Histórico pessoal de trombose

✓Albuminemia <20g/L

✓Fibrinogenemia > 6g/L

✓D-dímero plasmático>1000ng/mL

✓AT <70% do valor normal

Trombofilia

- Papel pouco definido na trombose arterial
- Lembrar das ressalvas (SAAF)!

Jori E. May. How I treat unexplained arterial thrombosis. *Blood* 2020

Table 5. Summary of evidence for thrombophilia testing practices and considerations for anticoagulation vs antiplatelet therapy

Thrombophilia		Summary of evidence	Testing	Anticoagulation vs antiplatelet
FVL	Heterozygous	Evidence against association with MI, CAD, PVD in all-comers. Small association with stroke in all-comers and MI in patients <45-55 y; clinical significance unclear	Consider testing to identify homozygous FVL or double heterozygous FVL/PT	No influence
	Homozygous	Insufficient data to clearly identify association with arterial thrombosis		Anticoagulation and/or antiplatelet therapy could be considered
PT20210	Heterozygous	Small association with MI, CAD, stroke; clinical significance unclear. Evidence against association with PVD.	Consider testing to identify homozygous PT or double heterozygous FVL/PT	No influence
	Homozygous	Insufficient data to clearly identify association with arterial thrombosis		Anticoagulation and/or antiplatelet therapy could be considered
PC PS		Moderate association with MI, stroke, TIA, PVD in younger patients (<55 y)	Consider testing in patients <55 y	Anticoagulation and/or antiplatelet therapy could be considered
AT		Insufficient data to identify association with arterial thrombosis	Consider testing in patients <55 y. Testing based on expert guidelines[66]	Anticoagulation and/or antiplatelet therapy could be considered
APS		Proven association with arterial thrombosis	Recommended in patients with no etiology identified. Testing based on expert guidelines[67]	Some experts favor anticoagulation; antiplatelet and/or anticoagulation could be considered; initial data suggest DOACs inferior to warfarin
FVIII		Inconsistent correlation with arterial thrombosis	Not recommended	No influence
Homocysteine		Slight association with CAD, stroke; however, no benefit of therapy to lower levels	Consider testing only in patients <30 y if concern for homocystinuria	No influence
MTHFR*		No consistent association with arterial thrombosis	Not recommended	No influence

CAD, coronary artery disease; DOAC, direct oral anticoagulant; MI, myocardial infarction; PVD, peripheral vascular disease; TIA, transient ischemic attack.
*MTHFR polymorphisms are not considered to be a thrombophilia.

Papel dos DOACs (adultos)

Emergent Revascularization		
Acute Limb Ischemia or Critical Limb Ischemia	Optimal antithrombotic management is unclear, and more studies are needed. Options include: full-dose anticoagulation in combination with single antiplatelet therapy; ASA in addition to rivaroxaban 2.5 mg BID, with or without short-term use of clopidogrel; or DAPT.	In those with high risk of subsequent adverse limb events, with low bleeding risk, full dose anticoagulation in addition to ASA is the most commonly chosen regimen.

ASA, acetylsalicylic acid; CAD, coronary artery disease; DAPT, dual antiplatelet therapy; DOACs, direct oral anticoagulants; PAD, peripheral artery disease

- Terapia Compass – rivaroxabana 2.5 mg + ASA 81 mg - ?
- Pediatria - ?

Conclusão (2)

- Síndrome nefrótica está associada a um estado de hipercoagulabilidade
- Tromboses são complicações possíveis, sendo venosas > arteriais
- Parece haver uma predileção gênero-especifica (H>M) -?
- Não há consenso sobre a melhor abordagem (anticoagulação + antiagregante plaquetário) - ?
- Diagnóstico precoce e tratamento rápido da trombose arterial são essenciais para um bom desfecho
- Papel dos DOACs - ?

Dúvidas

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