The Initial Approach to Paediatric Thrombosis

An Van Damme

Department of Paediatric Haematology and Oncology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

an.vandamme@saintluc.uclouvain.be

Keywords

Thrombosis ; Central Venous Catheters ; Neoplasms ; Heart Defects, Congenital ; Venous Thromboembolism ; Anticoagulants ; Child

Abstract

Venous thromboembolism (VTE) in children presents unique challenges distinct from adult thrombosis, primarily due to developmental differences in the haemostatic system and the rarity of traditional adult risk factors. Paediatric VTE is increasingly recognized, especially in neonates and adolescents, and is predominantly associated with underlying comorbidities such as central venous catheters (CVCs), cancer, or congenital heart disease. The concept of "developmental haemostasis" underscores the age-dependent evolution of coagulation, influencing both risk and management strategies.

Diagnosis relies on clinical signs and is confirmed via Doppler ultrasonography, MRI, or CT, depending on the site. Pulmonary embolism, though rare, requires prompt evaluation in cases of respiratory distress or collapse. Laboratory tests, including D-dimer, are less specific in children due to overlapping inflammatory conditions.

Anticoagulation therapy, typically initiated with heparinoids, must account for age-related pharmacokinetic differences and the risk of bleeding. Low-molecular-weight heparin (LMWH) and direct oral anticoagulants (DOACs) are increasingly used, though evidence-based guidelines remain limited. Treatment duration and intensity are tailored to clinical context, with special considerations for asymptomatic CVC-related thrombosis and high-risk scenarios like neonatal renal vein thrombosis or purpura fulminans.

Thrombophilia testing is reserved for recurrent or unprovoked VTE, with genetic confirmation advised for severe deficiencies. While paediatric VTE management has advanced, ongoing research is essential to address unresolved questions and optimize evidence-based care, ensuring therapies align with the unique physiology of children.

Introduction

The risk and context of thrombo-embolism (TE) in children are substantially different compared to adults. Diseases that damage the vascular endothelium and that are typically associated with thrombosis risk in adults, occur less frequently in children and they are less frequently exposed to acquired prothrombotic risk factors such as smoking, the use of hormonal therapies, etc. Moreover, the haemostatic system of children differs substantially from adults. The systematic description of the evolution and development of the haemostatic system of children of all ages by Maureen Andrew has led to the concept of 'developmental haemostasis' (1-3). This concept provides the framework and background for the approach to paediatric bleeding and thrombosis and describes the evolution of the haemostatic system from foetal life through adulthood. Paediatric TE has historically been considered of little significance, but is being increasingly recognized, especially in infancy and adolescence.

Contrary to the typical risk factors considered in adults, TE is a problem most frequently occurring in "the sick child", paralleling the risk factors for venous thrombosis from Virchow's triad: endothelial injury, impaired blood flow (stasis) and hypercoagulability. Over 90% of paediatric thromboses are related to underlying medical or surgical risk factors and/or, most commonly, the presence of central venous catheters (CVC) (4). Other risk factors include inherited hypercoagulable states, cardiovascular diseases, infection, trauma, malignancy, immobility and chronic inflammation. Idiopathic primary TE is exceedingly rare in children. It is important to note, however, that adult risk factors, such as obesity and the use of oral contraceptives, are on the rise in the adolescent age group (5). Inherited thrombophilia is a coagulation disorder associated with an increased genetic predisposition to develop thrombosis. Most other acquired risk factors mentioned above are associated with the development of acquired hypercoagulable states.

This review concerns exclusively venous thrombo-embolism (VTE) of various types. Arterial thrombosis is not discussed here.

Diagnostic approach to venous thrombosis

Clinical manifestations of VTE depend on the affected blood vessel and the degree of occlusion caused by the thrombosis. Initial assessment of paediatric TE should start with careful personal and family history in order to identify potential underlying conditions associated with increased risk for thrombosis.

Venous thrombosis in the upper or lower limbs causes acute onset of pain and swelling of the limb and represents the most frequent clinical manifestation of VTE in children. Measurement of limb circumference and clinical pictures are helpful in the diagnosis of limb VTE in children. Several clinical investigations may provide additional clues in the clinical suspicion of thrombosis, such as Homan's sign (calf pain upon dorsiflexion of the foot), May's sign (calf pain upon compression) or Payr's sign (sole pain upon sole compression).

VTE of vessels of internal organs causes specific symptoms, usually related to organ swelling and subsequent loss of function. For example, renal vein thrombosis (RVT) causes abdominal pain, palpable mass, haematuria and renal failure, while cerebral sinus thrombosis (CSVT) is related to signs and symptoms of intracranial hypertension. Portal vein thrombosis usually remains asymptomatic until symptoms of chronic portal hypertension occur, or may present acutely with symptoms of acute abdomen (6).

Pulmonary embolism (PE) is rare in children, but has to be considered in cases of chest pain, acute respiratory distress or sudden collapse in case of massive PE. Clinical signs of deep vein thrombosis may be present, but this is not always the case. Later onset clinical manifestations may include prominent collateral circulation, stroke and chylothorax.

Clinical suspicion of TE is most commonly confirmed by Doppler ultrasonography (US), echocardiography, computed tomography (CT) or magnetic resonance (MRI), depending on the location. Compression Doppler US is most frequently used for diagnosing limb TE in children. Vessels with thrombosis are identified by absent Doppler signals and non-compressibility of the affected vein, with or without visible intraluminal thrombotic material. As with all US-based imaging, diagnostic yield depends on the experience of the operator and patient compliance. Specific anatomic regions such as the upper intrathoracic venous system, are more difficult to access, influencing the sensitivity of Doppler US. MRI (MR venography) or CT scan (CT venography) should be considered in cases of high suspicion when Doppler US fails to reveal thrombosis.

Conventional venography is still considered the gold standard for diagnosing VTE, although in practice, this technique is rarely used in children. However, injection of contrast through the line followed by X-ray is commonly used for diagnosis of CVC-related thrombosis or dysfunction.

CT pulmonary angiography (spiral CT) is the diagnostic modality of choice for suspected PE in children, in cases without contra-indications to contrast injection (6, 7). Ventilation perfusion scans are associated with lower irradiation but they can only be used in cooperative children with normal chest X-ray and no concurrent cardiopulmonary disease. They are more time-consuming and often require sedation, making them less widely applicable. In case of suspected PE, echocardiography is indicated to rule out signs of right ventricular dysfunction. Echocardiography may also be preferred for diagnosing PE in neonates.

There are no specific laboratory tests that can accurately confirm the diagnosis of thrombosis in children. In neonates, thrombosis is often associated with sudden onset unexplained thrombocytopenia, which should raise suspicion for CVC thrombosis. For example, thrombocytopenia associated with haematuria in a newborn is suggestive of RVT. Routine coagulation analyses such as aPTT and PT/INR, as well as fibrinogen levels, may indicate low or high coagulation factor levels. D-dimer testing has limited usefulness because it lacks specificity as high D-Dimer levels can also occur in pro-inflammatory states such as sepsis or malignancy.

Anticoagulation therapy

Anticoagulation therapy in children is usually initiated with heparinoids, either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH), for at least 5 days. Treatment can then continue with either ongoing LMWH therapy, vitamin K antagonists (VKAs) or a direct oral anticoagulant (DOAC). There are relatively few clinical trials evaluating the use of these treatments in children across all age groups and various underlying pathologies, which limits evidence-based care. Additionally, there is a lack of general and global consensus regarding the best therapeutic and monitoring recommendations for the different treatment options. It is important to keep in mind that the use of antithrombotic drugs in children differs from adults, due to age-dependent differences in the haemostatic system and drug metabolism (8).

Children generally require higher doses of UFH and LMWH, with weight-specific doses varying depending on age (8). Heparin anticoagulant activity is related to its binding to antithrombin (AT), thereby activating AT. The response to heparinoids may be impaired by low AT levels, which can be related to AT deficiency, young age or iatrogenic factors such as asparaginase use. Treatment with UFH or LMWH in children therefore needs to be monitored through regular anti-Xa activity measurements, which assess the degree of inhibition of activated factor X by heparinoids, and according dose adaptations (Table 1). AT replacement therapy should be reserved for children who fail to respond clinically to heparinoid treatment and have low AT levels, as well as for children with inherited or iatrogenic AT deficiency, nephrotic syndrome, liver failure or disseminated intravascular coagulation (9).

VKAs are generally used for children who require long-term anticoagulant treatment, especially in indications where the safety and efficacy of DOACs are so far not well established or insufficient, such as thromboprophylaxis for mechanical valves or antiphospholipid syndrome. VKA treatment requires regular INR measurements that can be performed by home point-of-care systems, and regular dose adaptations. Control of adequate

TABLE 1: Proposed dose adaptations of LMWH in children, based on anti-Xa level measurements.

anti-Xa level (U/ml)	delay next injection	dose change
<0.35	no	increase by 25%
0.35-0.49	no	increase by 10%
0.5-1.0	no	no change
1.1-1.5	no	decrease by 20%
1.6-2.0	after 3 hours	decrease by 30%
>2.0	discontinue until anti-Xa ≤ 0.5	decrease by 40%

if dose is changed, recheck next day

INR ranges is challenging due to the myriad of factors influencing VKA induced anticoagulation, such as dietary factors, many medications and intercurrent viral infections.

In recent years, DOACs have more frequently been used in children, thanks to the paediatric development programs that have been performed. Their use is discussed in more detail elsewhere in this issue.

Thrombosis in specific situations and age groups

CVC-related thrombosis

CVC-related thrombosis represents the most frequent cause of secondary thrombosis in neonates, infants and children and is caused by endothelial damage, disruption of blood flow and infusion of potentially prothrombotic agents. Factors influencing catheter-related thrombosis risk extend beyond host-related elements such as congenital heart disease and low birth weight, which is associated with increased catheter-to-vessel size ratio. They also include catheter-related risk factors like the type of CVC (e.g., PICC lines), insertion technique and the nature of infused therapy (e.g., total parenteral nutrition) (10).

CVC-related thrombosis should be suspected whenever regular symptoms of limb thrombosis occur in the presence of a CVC, but equally in cases of repeated loss of CVC patency, CVC sepsis or the appearance of collateral circulation in the skin.

CVC-related thrombosis can be asymptomatic. The true incidence, clinical significance and complication risk of asymptomatic CVC-related thrombosis are unknown. Jones et al. reviewed the literature to determine the incidence of asymptomatic VTE after screening in different clinical settings, and found widely variable incidences, ranging from 5-15.2% in neonates to 5.9-65% in paediatric cancer patients, with critically ill children, children with congenital heart disease or other cohorts, displaying intermediate incidences ranging from 7.1 up to 46% (11).

Decisions about treatment of these asymptomatic VTEs depend on recurrence risk, residual thrombosis risk, post thrombotic syndrome occurrence and risk of embolism or mortality. Decisions about anticoagulation in unwell children should be informed by the risk of not treating balanced by the risk of acute or long-term morbidity.

Symptomatic CVC-related thrombosis, however, requires anticoagulant treatment, especially if extension of the thrombus occurs after initial observation in patients who were deemed too unwell to receive anticoagulant treatment. Given the risk of development of paradoxical emboli after CVC removal, it has been suggested that the CVC be removed after 3-5 days of treatment, especially in neonates (8). However, based on two multicentre observational studies that addressed this question and could not corroborate this finding, the most recent guidelines do not advise against immediate removal of a non-functioning catheter (12-14). Duration of treatment is generally shorter than in non-CVC related thrombosis, and can be limited to 6 weeks, especially after CVC removal and complete thrombus resolution. Prophylactic anticoagulation should be considered, however, if the CVC is still in place at the end of the therapeutic treatment period.

Neonates

Neonates represent the paediatric age group associated with the highest thrombosis risk, which is associated with gestational diabetes, the use of intravascular catheters in small vessels, sepsis, inflammation and hypoxia.

Treatment decisions for neonatal thrombosis should be based on careful consideration of the haemorrhagic risk versus anticoagulation benefit. In cases with increased haemorrhagic risk, such as low gestational age and/or weight, necrotizing enterocolitis, intraventricular haemorrhage or other co-morbidities, initial observation may be preferred before initiation of anticoagulation therapy. If thrombosis extension is identified after initial radiologic observation of the thrombus, anticoagulation is recommended.

Renal vein thrombosis

RVT is the most prevalent form of thrombosis in neonates, apart from CVC-related thrombosis, and should be suspected in cases of abdominal pain, abdominal mass, haematuria and/or thrombocytopenia.

Anticoagulation therapy is recommended because of the potential benefit for reducing hypertension and kidney function damage, although 75% of affected kidneys become atrophic regardless of whether anticoagulation treatment is initiated. In cases of bilateral RVT, thrombolytic treatment followed by anticoagulation is suggested (14).

Anticoagulation therapy in the setting of neonatal RVT requires strict therapeutic monitoring (anti-Xa), especially if LMWH are used, because of potential drug accumulation in the presence of renal failure. Continuous infusion of UFH may be the preferred treatment option. Evidence regarding the use of DOACs in this setting is limited (15).

Purpura fulminans

Purpura fulminans is a rare, life-threatening condition caused by congenital severe (homozygous or compound heterozygous) protein C and/or protein S deficiency and presents in the first days of life with progressive haemorrhagic skin necrosis. It may be associated with concurrent large vessel thrombosis (16).

Later-onset purpura fulminans may be due to consumption or decreased synthesis of protein C and S due to sepsis or hepatic failure or acquired antibodies to protein S in the setting of chickenpox.

Treatment should consist of the prompt initiation of anticoagulation therapy and urgent analysis of protein C and S levels. Fresh frozen plasma infusions and/or administration of protein C concentrate should be added after confirmation of the deficiency. Genetic confirmation of *PROC* and *PROS1* genes and genetic consultation should be offered.

Cancer

Paediatric cancer patients are particularly prone to the development of VTE and its aetiology is multifactorial. Prevalence is variable, from 16% of symptomatic to 40% of asymptomatic TE in children with cancer (17). Occurrence of TE in children with cancer is related to the interaction of cancer with prothrombotic factors in the patient, and factors related to cancer treatment.

For example, children with acute lymphoblastic leukaemia (ALL) are shown to have activated coagulation at diagnosis (18). Cancer in general can lead to pro-inflammatory states. Chemotherapeutic agents such as Asparaginase influence the production of anticoagulant and procoagulant factors and cause endothelial activation. The presence of a CVC and surgical procedures further lead to endothelial damage and activation.

The decision to treat VTE in cancer patients is particularly challenging because of the delicate risk/benefit equilibrium and the haemorrhagic risk in these patients, and should be made on an individual basis. Most experts recommend maintaining a platelet count of greater than 50 x 10^9/L for anticoagulated patients. Special attention is required for anticoagulated patients undergoing invasive procedures.

For patients who develop thrombo-embolic complications after asparaginase therapy, it is generally recommended to restart asparaginase treatment provided the thrombosis is stabilized after treatment, and to continue thromboprophylaxis until at least 4 weeks after the last dose of PEGylated asparaginase.

Thrombosis in paediatric cancer patients can be treated by either LMWH or DOACs such as rivaroxaban (19).

Congenital heart disease

Paediatric cardiac disease represents an important risk factor for the development of thrombo-embolic complications. VTE in the setting of paediatric cardiac surgery occurs in 19-40% of children. Prevalence is influenced by the type of surgery, the severity of the heart defect and the degree of cardiac insufficiency. This patient group is also particularly at risk for arterial ischemic stroke. Management of these thrombotic complications does not differ substantially from TE in other children. Long-term thromboprophylaxis is required for patients with mechanical valves or other risk factors that predispose to a high risk of thrombosis, such as coronary dilatation after Kawasaki disease, or uncorrected states of cardiac insufficiency (16).

Cerebral sinovenous thrombosis

Thrombosis occurring in the venous sinuses of the brain results in venous outflow obstruction, causing a specific set of symptoms and complications. Subsequent increase in capillary hydrostatic pressure may lead to infarction, which is often haemorrhagic.

The occurrence of CSVT is multifactorial, and a comorbid condition can usually be identified (20). Around 40% of cases occur in the neonatal period. Symptoms can be non-specific, especially in neonates, and consist of progressive headache, altered consciousness, seizures and focal neurological deficits. Diagnosis is confirmed by contrast-enhanced venous imaging by MRI or CT. Mortality may be as high as 10% in neonates and older children, whereas up to 40-50% of patients suffer long-term neurological sequelae (21).

Anticoagulant treatment with LMWH or DOACs for a minimum of 3 months is recommended, and may be prolonged if imaging studies reveal persistent thrombosis, especially in the presence of ongoing symptoms (8, 14). Specific consideration is required for neonates, patients with associated haemorrhage or infection. However, haemorrhagic transformation of an infarction is not a contraindication for anticoagulation in the setting of CSVT. Treatment duration may be safely reduced to 6 weeks for patients with low-risk CSVT such as partially occlusive thrombosis and the absence of ongoing risk factors (22).

Thrombophilia

Thrombophilia refers to the propensity to form blood clots and may be inherited or acquired. Thrombophilia contributes to the risk of VTE, but given the fact that TE most commonly occurs in the setting of certain clinical conditions as described above, it constitutes rather a risk factor than an isolated cause of most occurrences of TE in children. The inherited thrombophilias for which a pathogenic link is most clearly established include the Factor V Leiden mutation, the prothrombin G20210A mutation, antithrombin deficiency, protein C deficiency and protein S deficiency (5, 23). Acquired risk factors include the presence of antiphospholipid antibodies (lupus anticoagulant, anti-cardiolipid antibodies, anti-b2-glycoprotein antibodies). Other factors, with less clear association to thrombotic risk include elevated factor VIII, elevated lipoprotein(a) and hyperhomocystinaemia. Some children may present a combination of thrombophilic factors, further increasing their thrombotic risk.

Indications for thrombophilia testing remain based on expert opinion, given the small patient numbers and heterogeneity of patient groups, as well as the multifactorial origin of paediatric thrombosis. Most importantly, the usefulness of diagnostic testing should be discussed on an individual basis. These discussions should include detailed information on the pros and cons of testing, as well as on adequate information regarding consequences of positive or negative results.

Thrombophilia testing is indicated, however, in cases of unprovoked or recurrent VTE. It is generally not indicated for patients with CVC-related VTE.

For patients with other provoked VTE, the utility for testing should be discussed with patients and parents.

Thrombophilia test results rarely influence acute treatment decisions in children with VTE, with the exception of neonates presenting with purpura fulminans, for whom AT, protein C and S analysis is recommended. For all other cases, test results do currently not provide a risk-based therapeutic approach.

Testing of asymptomatic children based on positive family history of VTE or thrombophilia remains controversial. It may be considered in situations where the child will be exposed to other thrombotic risk factors such as oral contraceptives, or cases of severe thrombo-embolic family history.

In all other cases, it is reasonable to postpone testing in asymptomatic children until they reach an age at which they can decide for themselves whether or not they want to know that they may be at increased risk for thrombosis.

In the case that the patient and the family decide against thrombophilia testing for a first VTE or positive family history, strict thromboprophylactic measures are indicated in situations of increased risk, such as prolonged immobilisation, complex surgery, CVC, etc.

Thrombophilia testing in the acute thrombotic phase may be difficult and should in most cases be deferred for 3-6 months and until after stopping the anticoagulant treatment. As for most haemostasis laboratory analysis, abnormal test results should be confirmed on a separate blood sample. Inherited thrombophilia should additionally be confirmed by testing of both parents whenever possible.

Conclusion

Paediatric thrombosis, while historically considered of little significance, is increasingly recognized, especially in neonates and adolescents, and is most frequently associated with underlying co-morbidities such as cancer, the presence of a CVC or heart disease. The diagnostic and therapeutic approach must take into consideration the unique developmental aspects of the haemostatic system in children, which means that adult guidelines must not be extrapolated. Continued research and dedicated clinical trials are essential to addressing the many remaining unresolved questions, to establish evidence-based guidelines and improve the management of paediatric thrombosis.

References

1. Andrew M, Paes B, Milner R, Johnston M, Mitchell L, Tollefsen DM, et al. Development of the human coagulation system in the full-term infant. Blood. 1987;70(1):165-72.
2. Andrew M, Paes B, Milner R, Johnston M, Mitchell L, Tollefsen DM, et al. Development of the human coagulation system in the healthy premature infant. Blood. 1988;72(5):1651-7.
3. Andrew M, Paes B, Johnston M. Development of the hemostatic system in the neonate and young infant. Am J Pediatr Hematol Oncol. 1990;12(1):95-104.

4. van Ommen CH, Peters M. Venous thromboembolic disease in childhood. Semin Thromb Hemost. 2003;29(4):391-404.
5. Young G, Albisetti M, Bonduel M, Brandao L, Chan A, Friedrichs F, et al. Impact of inherited thrombophilia on venous thromboembolism in children: a systematic review and meta-analysis of observational studies. Circulation. 2008;118(13):1373-82.
6. Lassandro G, Palmieri VV, Palladino V, Amoruso A, Faienza MF, Giordano P. Venous Thromboembolism in Children: From Diagnosis to Management. Int J Environ Res Public Health. 2020;17(14).
7. Chalmers E, Ganesen V, Liesner R, Maroo S, Nokes T, Saunders D, et al. Guideline on the investigation, management and prevention of venous thrombosis in children. Br J Haematol. 2011;154(2):196-207.
8. Monagle P, Chan AKC, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Gottl U, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e737S-e801S.
9. Monagle P, Cuello CA, Augustine C, Bonduel M, Brandao LR, Capman T, et al. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. Blood Adv. 2018;2(22):3292-316.
10. Pelland-Marcotte MC, Avila L, Temple M, Williams S. Venous Thrombosis. In: Blanchette V, Brandao L, Carcao M, Kumar R, Rand M, Revel-Vilk S, editors. SickKids Handbook of Pediatric Thrombosis and Hemostasis. 3rd. rev. an ext. ed. Basel, Switzerland: Karger AG; 2024. p. 256-74.
11. Jones S, Monagle P, Newall F. Do asymptomatic clots in children matter? Thromb Res. 2020;189:24-34.
12. van Ommen CH, Bergman KA, Boerma M, Bouma HA, Donker AE, Gouvernante M, et al. NEOnatal Central-venous Line Observational study on Thrombosis (NEOCLOT): evaluation of a national guideline on management of neonatal catheter-related venous thrombosis. J Thromb Haemost. 2023;21(4):963-74.
13. Jaffray J, Baumann Kreuziger L, Branchford B, Wee CP, Faustino EVS, Zakai NA, et al. Symptomatic pulmonary embolus after catheter removal in children with catheter related thrombosis: A report from the CHAT Consortium. J Thromb Haemost. 2022;20(1):133-7.
14. Monagle P, Azzam M, Bercovitz R, Betensky M, Bhat R, Biss T, et al. American Society of Hematology/International Society on Thrombosis and Haemostasis 2024 updated guidelines for treatment of venous thromboembolism in pediatric patients. Blood Adv. 2025;9(10):2587-636.
15. Labarque V, Mandel-Shorer N, Robertson J, Williams S. Thromboembolic Events at Specific Organ Sites. In: Blanchette V, Brandao L, Carcao M, Kumar R, Rand M, Revel-Vilk S, editors. SickKids Handbook of Pediatric Thrombosis. 3rd. rev. and ext. ed. Basel Switzerland: Karger AG; 2024. p. 288-306.
16. Sabapathy C, Amid A, Kumar R, Avila L, van Ommen CH. Diagnostic Approach to Thrombosis and Thrombophilia. In: Blanchette V, Brandao L, Carcao M, Kumar R, Rand M, Revel-Vilk S, editors. SickKids Handbook of Pediatric Thrombosis. 3rd. rev. and ext. ed. Basel Switzerland: Karger AG; 2024. p. 233-55.
17. Athale U. Thrombosis in pediatric cancer: identifying the risk factors to improve care. Expert Rev Hematol. 2013;6(5):599-609.
18. Athale UH, Chan AK. Thromboembolic complications in pediatric hematologic malignancies. Semin Thromb Hemost. 2007;33(4):416-26.
19. Palumbo JS, Lensing AWA, Brandao LR, Hooimeijer HL, Kenet G, van Ommen H, et al. Anticoagulation in pediatric cancer-associated venous thromboembolism: a subgroup analysis of EINSTEIN-Jr. Blood Adv. 2022;6(22):5821-8.
20. Pulcine E, Andrade A, Vargas Nino AC, Williams S, Ichord RN, Dlamini N. Stroke. In: Blanchette V, Brandao L, Carcao M, Kumar R, Rand M, Revel-Vilk S, editors. SickKids Handbook of Pediatric Thrombosis. 3rd. rev. and ext. ed. Basel Switzerland: Karger AG; 2024. p. 307-35.
21. Moharir MD, Shroff M, Pontigon AM, Askalan R, Yau I, Macgregor D, et al. A prospective outcome study of neonatal cerebral sinovenous thrombosis. J Child Neurol. 2011;26(9):1137-44.
22. Goldenberg NA, Kittelson JM, Abshire TC, Bonaca M, Casella JF, Dale RA, et al. Effect of Anticoagulant Therapy for 6 Weeks vs 3 Months on Recurrence and Bleeding Events in Patients Younger Than 21 Years of Age With Provoked Venous Thromboembolism: The Kids-DOTT Randomized Clinical Trial. JAMA. 2022;327(2):129-37.
23. van Ommen CH, Nowak-Gottl U. Inherited Thrombophilia in Pediatric Venous Thromboembolic Disease: Why and Who to Test. Front Pediatr. 2017;5:50.