Conclusions: Although a direct comparison can not be made to reported pediatric thrombosis in hospitalized patients (0.58%) due to inclusion of patients 18-20 years in our study, our prevalence rate of 4.71% suggests COVID-19/MIS-C should be considered an additional risk factor for pediatric thrombosis.

OC 40.4 | Novel, Point-of-care Coagulation Test Detects Anticoagulation Resistance Predictive of Thrombotic Events in Pediatric ECMO Patients

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Background: Bivalirudin, an injectable direct thrombin (factor IIa) inhibitor, and unfractionated heparin (UFH) are both frequently used for anticoagulation therapy in the pediatric critical care setting. A functional test for the quantification and detection of resistance to these anticoagulants is not currently available.

Aims: Evaluate the ability of a point-of-care (POC) microliter volume coagulation test to detect the effect of bivalirudin and UFH and quantify the level of anticoagulation using a functional, clot time end point in pediatric critical care patients.

Methods: Under IRB approval, a retrospective analysis of 41 citrated, frozen, bio-banked plasma specimens from 15 anticoagulated pediatric patients was performed. Thirteen patients were on extracorporeal membrane oxygenation, one patient had a submassive pulmonary embolus and one patient was on a left ventricular assist device, providing 21 bivalirudin and 20 UFH samples. Each sample was tested and a Clotting Time Score (CTS) was derived. Reference CTS curves for each drug were made using spiked healthy adult samples. CTS results were compared to clinician-ordered coagulation tests.

Results: Using the CTS, the patients that had developed a pathological clotting event were detected with 100% sensitivity/ 72% specificity, as compared to 25% sensitivity/76% specificity and 0% sensitivity/0% specificity (per the reference ranges) for prothrombin time and activated partial thromboplastin time, respectively (Figure 1A). The CTS was able to detect sub-therapeutic anticoagulation levels in patients that were determined to be clinically-resistant and required to switch from UFH to bivalirudin (Figure 1B).

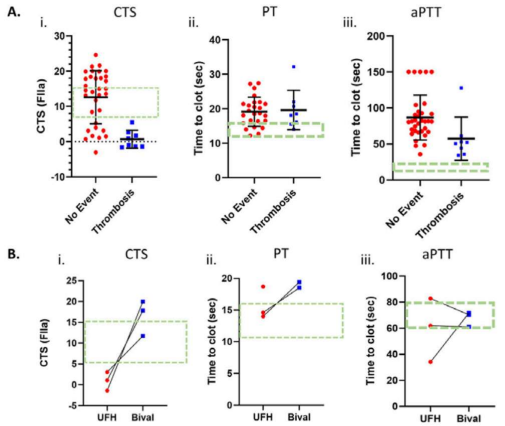

FIGURE 1 Comparison between CTS, PT and aPTT in pediatric ECMO patients

Conclusions: The CTS appears to be a good indicator of the level of anticoagulation for both UFH and bivalirudin and may be predictive of pathological clot formation, potentially due to anticoagulation resistance. The small sample volume required allows for more frequent testing without causing iatrogenic anemia, reducing the risk of anticoagulation-related complications and enabling the rapid identification of patients at high-risk for pathologic thrombotic events.

OC 69.1 | Management Practices of Catheter-related Arterial Thrombosis in Children and Neonates: Results of a Multinational Survey

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Background: Catheter-related arterial thrombosis (CAT) is increasingly recognized in children. No evidence-based guidelines on the diagnosis, treatment and follow-up of pediatric CAT are available.

Aims: To evaluate current practice patterns and gaps in the management of CAT in children.

Methods: REDcap based survey questions were sent to members of the Pediatric/Neonatal Thrombosis and Hemostasis Subcommittee of the International Society on Thrombosis and Haemostasis (ISTH) and the International Pediatric Thrombosis Network (IPTN).

Results: Of the 54 responders completing the survey 49 (91%) are care providers of pediatric hematology/oncology facilities. Of these, 56% treats 1-10, 35% 11-40, and 9% more than 40 CAT cases per year. Doppler ultrasound is the preferred diagnostic modality in 94% and 96% of CAT related to umbilical arterial catheter (UAC) and to extremity indwelling arterial catheter (EIC) or cardiac catheter (CC), respectively. Antithrombotic treatment is usually considered for symptomatic and/or occlusive CAT and consists of unfractionated heparin (UFH) and/or low molecular weight heparin (LMWH) in 98% and 94% of UAC- and EIC/CC-related CAT, respectively. For UAC-related CAT, 15%, 4% and 4% of responders consider switch of initial heparin to acetylsalicylic acid (ASA), vitamin K antagonists (VKAs) and direct oral anticoagulants (DOACs), respectively. For EIC/CC-related CAT, a similar switch is considered in 13%, 10%, and 2%, respectively. Treatment duration varies between 3 months in 50%, 6 weeks in 29% and less than 2 weeks in 13% of UAC-related CAT and 3 months in 44%, 6 weeks in 41% and less than 2 weeks in 11% of EIC/CC-related CAT. Long-term follow-up for UAC- and EIC/CC-related CAT is performed by 83% and 67% of responders, respectively.

Conclusions: These data demonstrate that management of pediatric CAT varies considerably. These findings constitute an important rationale for the design of urgently required clinical trials.

OC 69.2 | Efficacy and Safety of Dabigatran in the Treatment and Secondary Prevention of Venous Thromboembolism in Children with Central Line or Implantable Device–related Thrombosis

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Background: Dabigatran etexilate (DE) has shown noninferiority versus standard of care (SOC) for treatment of acute venous thromboembolism (VTE), and a favorable safety profile in secondary VTE prevention in children. Further data on efficacy/safety of DE in the subgroup of children with a central venous catheter (CVC) or implantable device (ID) are of interest.

Aims: Subgroup analyses evaluating treatment of CVC/ID-related thrombosis and secondary VTE prophylaxis in children with continued CVC/ID use.

Methods: DIVERSITY trial: children (birth to <18 years) with objectively confirmed VTE initially treated with heparin were randomized (2:1) to receive up to 3 months of DE or SOC. Primary composite efficacy endpoint: complete thrombus resolution and freedom from VTE recurrence/VTE-related death. Secondary VTE prevention trial: children (>3 months to <18 years) with continued CVC/ID use received DE for up to 12 months. Eligible children had previous VTE treatment with SOC for ≥3 months or had completed either treatment in DIVERSITY. Primary endpoints: VTE recurrence and bleeding events (BEs).

Results: In DIVERSITY, 58 children (21.7%) had CVC/ID-related thrombosis. They were younger than the subgroup without CVC/ID thrombosis (mean 5.7 vs. 12.4 years for the DE cohort; mean 5.3 vs. 13.1 years for the SOC cohort). In those with CVC/ID thrombosis, 67.6% treated with DE versus 66.7% treated with SOC achieved the primary endpoint, whereas 40.6% versus 33.3%, respectively, met the primary endpoint in the non-CVC/ID subgroup (Table 1). In the secondary prevention trial, no recurrent VTE occurred in the 14 patients with CVC/ID (Table 2). Rates of major/clinically relevant nonmajor (CRNM) BEs were low.

Conclusions: In a cohort of children with CVC/ID-related VTE we found similar rates of efficacy endpoints with DE or SOC. Children with continued CVC/ID use and DE for secondary VTE prevention had no VTE recurrence and low rates of major and CRNM BEs.

TABLE 1 Acute VTE treatment trial: outcomes for CVC/ID* thrombosis subgroup analysis

DIVERSITY trial CVC/ID subgroup analysis	CVC/ID thrombosis yes, N = 58		CVC/ID thrombosis no, N = 209	
	DE	SOC	DE	SOC
Efficacy endpoints (randomized set), N	34	24	143	66
Primary endpoint: Complete thrombus resolution, freedom from recurrent VTE, freedom from VTE-related death, n (%)	23 (67.6)	16 (66.7)	58 (40.6)	22 (33.3)
Residual thrombotic burden at Day 84 or end of therapy				
Thrombus progression,† n (%)	0	0	5 (3.5)	4 (6.1)
Stabilization, n (%)	1 (2.9)	0	10 (7.0)	10 (15.2)
Partial resolution, n (%)	5 (14.7)	2 (8.3)	52 (36.4)	23 (34.8)
Complete resolution, n (%)	23 (67.6)	16 (66.7)	58 (40.6)	22 (33.3)
Missing, n (%)	5 (14.7)	6 (25.0)	18 (12.6)	7 (10.6)
Free from recurrent VTE or mortality related to VTE, n (%)	34 (100.0)	23 (95.8)	136 (95.1)	60 (90.9)
Partial or complete resolution and free from recurrent VTE or mortality related to VTE, n (%)	28 (82.4)	18 (75.0)	109 (76.2)	44 (66.7)
On-treatment any bleeding (treated set), N	34	24	142	66
Any bleeding, n (%)	3 (8.8)	1 (4.2)	35 (24.6)	21 (31.8)
Major bleeding, n (%)	1 (2.9)	0	3 (2.1)	2 (3.0)
CRNM bleeding, n (%)	0	0	2 (1.4)	1 (1.5)

*IDs were a portacath in four patients.
†Defined as any symptomatic or asymptomatic contiguous progression of the index thrombus.
CRNM, clinically relevant nonmajor; CVC, central venous catheter; DE, dabigatran etexilate; ID, implantable device; SOC, standard of care; VTE, venous thromboembolism.