Central Venous Catheter (CVC) - Related Thrombosis in Children with End Stage Renal Disease (ESRD) Undergoing Hemodialysis

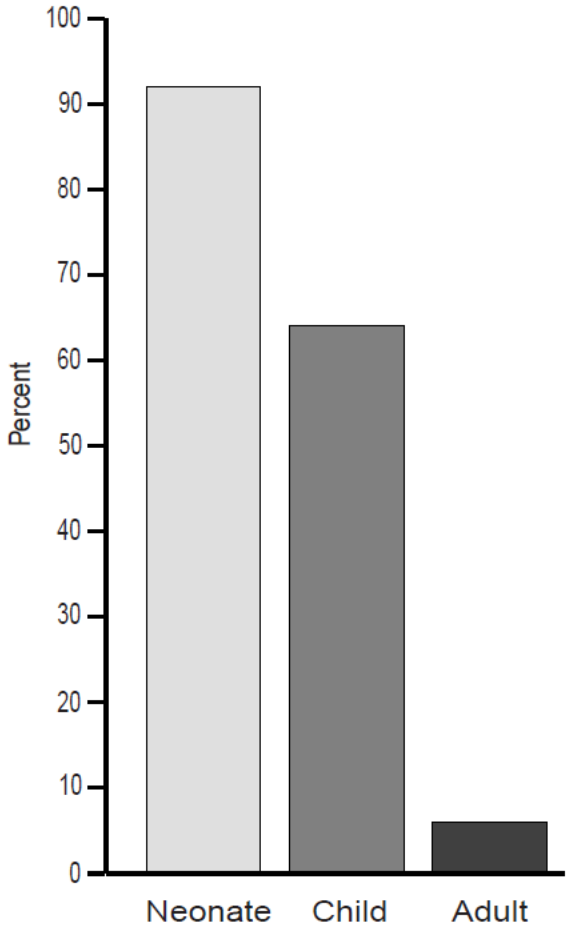
Noa Mandel-Shorer
Pediatric Hematology Oncology Division
Ruth Rappaport Children's Hospital
Rambam Medical Center

Ruth
Ruth Rappaport Children's Hospital
Rambam Health Care Campus

CVC - the single most important risk factor for VTE in the pediatric population

Irrespective of the underlying diagnosis and age,
the presence of CVC is the most important risk factor
for VTE in the pediatric population.

CVCs are associated with > 90% of neonatal VTE,
And > 60% of childhood VTE.

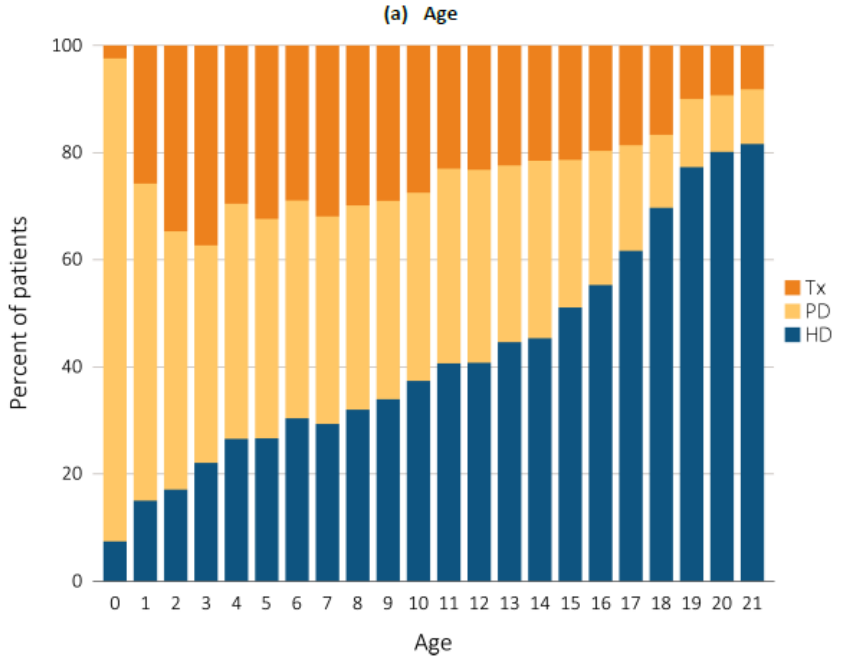


Andrew, Monagle and Brooker
Thromboembolic Complications During Infancy and Childhood, 2000

Most common medical conditions associated with pediatric CVC-VTE:

- Malignancy
- Congenital heart disease
- Systemic infection
- Neonates requiring NICU
- Critically ill children
- Gastrointestinal disease
- Cystic fibrosis
- **Renal disease:**
  - **ESRD requiring dialysis**
  - **Nephrotic syndrome**

Hemodialysis – most commonly used renal replacement modality in pediatric (0-21 y.o) patients awaiting a kidney transplant.



Venous access options:

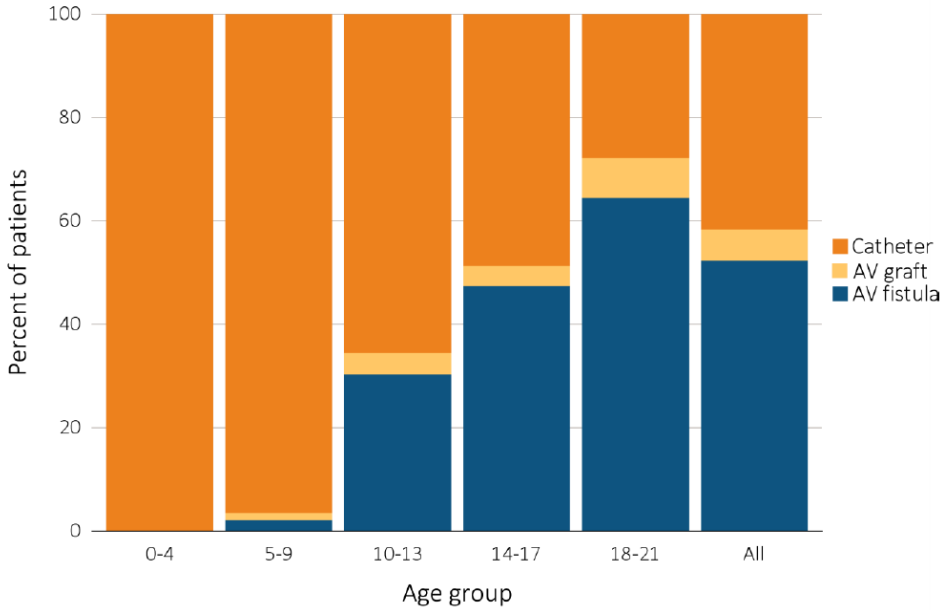
Arterivenous fistula **(AVF)** vs Central venous catheter **(CVC)**

Increased risk of complications associated with CVCs:

- Infection
- Fibrin sheath formation → CVC malfunction and failure
- Venous thrombosis/stenosis → future venous access loss

<u>European and American guidelines:</u>

AVF is preferable to CVC



Nevertheless, CVCs continue to predominate as hemodialysis access in children.

2016 USRDS annual data report

CVC-related VTE >>> significant morbidity and mortality.

Acute / short-term	Long-term
Death (2-4% in hospitalized children)	Post thrombotic syndrome (PTS)
Pulmonary embolism (PE)	Recurrent thrombosis
Superior vena cava (SVC) syndrome	Loss of future venous access
Chylothorax	
Paradoxical embolic stroke	
Cardiac arrest	
Infection and sepsis	
Repeated loss of CVC patency	

Hemodialysis Catheter Thrombotic Complications

- **Hemodialysis catheter failure** - in up to **80%** of CVCs.
- **Catheter occlusion and thrombosis** – in up to **60%** of failed CVCs.

↓

Frequent CVC removal and exchange

↓

Increased rates of venous thrombosis and stenosis:

- **Catheter-related venous thrombosis** – up to **30%** of hemodialysis patients.
- **Catheter-related central vein stenosis** – up to **40%** of patients.

↓

Preclusion of future hemodialysis d/t lack of venous access

A. Ma, Pediatr.Nephrol. 2013; M Adeb, J.Vasc.Interv.Radiol 2012; F Paglialonga, Hemodial.Int. 2012; I Eisenstein Clin.J.Am.Soc.Nephrol.2011; S.L. Goldstein, Pediatr. Nephrol 1997; FI Fadel, Urol.Nephrol 2008; B. Peynircioglu J.Vasc.Interv.Radiol 2007; I.J. Ramage Am.J.KidneyDis 2005; A. Sharma Pediatr.Nephrol 1999; R.D. Sheth Am.J.Kidney.Dis 2001; F. Paglialonga Pediatr. Nephrol 2016; P.J. Lopez J. Pediatr. Surg 2014; C. Quinlan; Pediatr. Nephrol 2013; R. Shroff Pediatr. Nephrol 2003

Diagnosis of CVC-related Thrombosis – High index of suspicion is required!

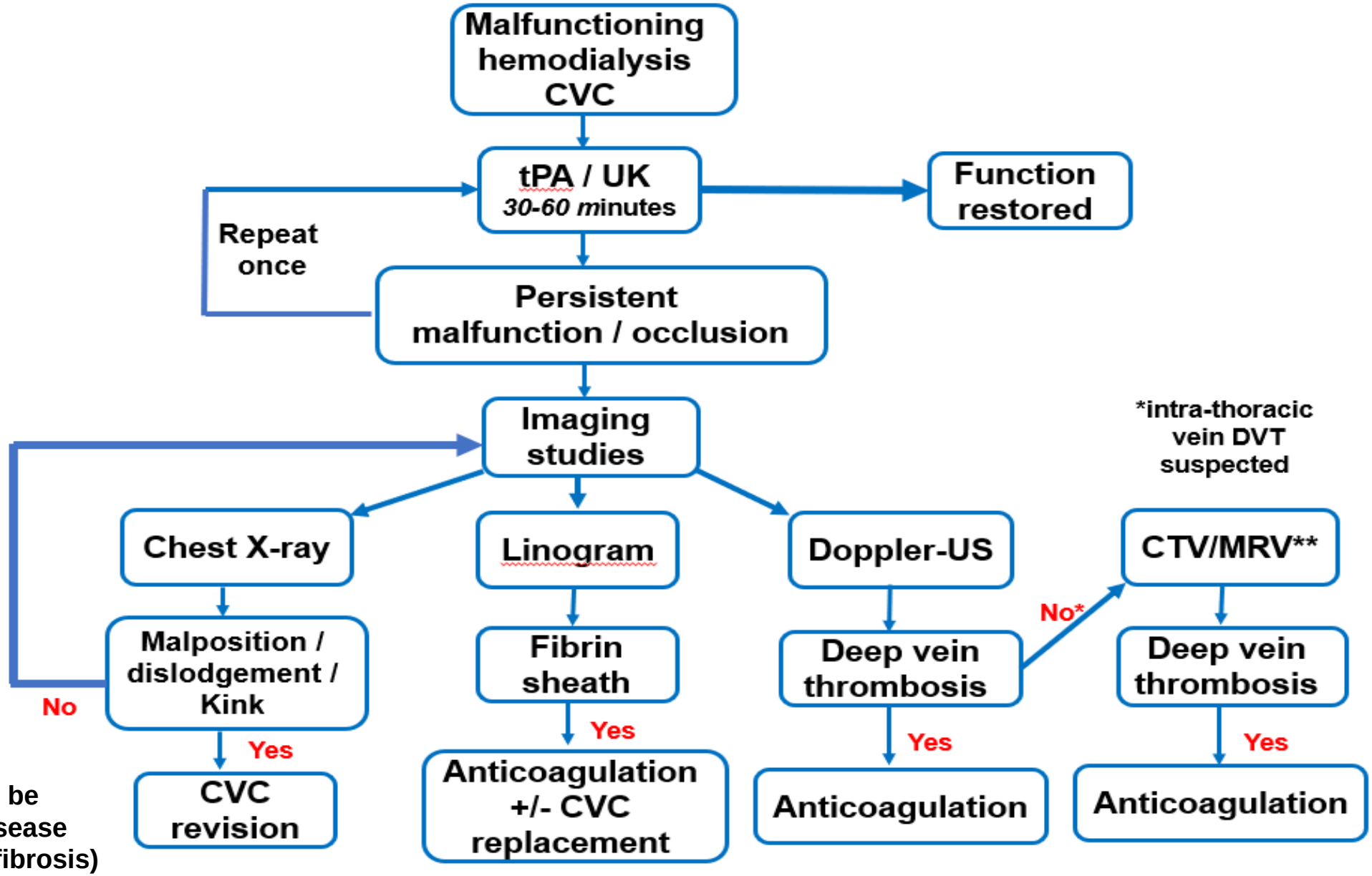
CVC occlusion / malfunction may be the sole manifestation of an underlying VTE of the associated vessels.

Current pediatric guidelines:

Investigate an occluded/malfunctioning CVC, especially when the occlusion/ malfunction persists despite the local installation of a thrombolytic agent.

E.Chalmers, BJH 2011

Suggested algorithm for investigation of malfunctioning hemodialysis CVC



** MRV with gadolinium should be avoided in advanced kidney disease (risk of nephrogenic systemic fibrosis)

Treatment - Catheter-related Thrombosis:

If catheter is no longer functional –

- Remove catheter following 3–5 days of therapeutic anticoagulation (diminish risk of embolization at removal).
- After removal of catheter, continue anticoagulation for 6wks-3mos.

If catheter remains functional –

- May remain in-situ.
- Therapeutic anticoagulation for 6 weeks to 3 months.
- After completion of therapeutic anticoagulation, continue prophylactic dosing for as long as the catheter is in situ.

P. Monagle et al, Chest 2012

Enoxaparin Treatment Protocol for Pediatric Hemodialysis Patients

- **Therapeutic anticoagulation for symptomatic fibrin sheath / deep venous thrombosis (DVT)** – following discussion with Hematology team:
- Start **dosing of Enoxaparin** at **1mg/kg once daily (q24hr).** On hemodialysis days, **administer post-dialysis**.
- **Subcutaneous administration** (not via hemodialysis line)
- **Monitor anti-Xa level** via **peripheral sampling** obtained **3-4 hours post administration**, aiming for **therapeutic levels (0.5-1**). May consult with Hematology team as for dose adjustments and timing of next Anti-Xa level.
- Consider drawing initially anti-Xa level also at 24h (or 48h, in cases when dialysis is done q72h) to exclude the need for change in dose/frequency in case through level is < 0.1-0.2.
- **Toxicity/accumulation monitoring** – **Trough anti-Xa level** obtained before hemodialysis – aim for Anti Xa **<0.1-0.2**.
- Following **three months of full anticoagulation**, assess patency of involved vein (doppler ultrasound) – if improvement / resolution of thrombus, consult with Hematology team re requirement for prophylactic treatment.

- **Secondary DVT Prophylaxis**:
- **Dose Enoxaparin at 1mg/kg once every two days (q48hrs)**, to be given post-dialysis.
- **Subcutaneous administration** (not via hemodialysis line)
- **Monitor Anti-Xa level** via **peripheral sampling** obtained **3 hours post administration** – aim for **0.3-0.5.**
- **Toxicity / accumulation monitoring** – **Trough Anti-Xa** level (48 hours post-administration) – aim for **< 0.1**
- In patients with a **history of thrombosis while on q48hr prophylaxis** or **high-risk patients** consider dosing prophylaxis at **0.5mg/kg q24hr**.
- **Continue prophylaxis for as long as the precipitating factor is present** (central venous catheter, significant proteinuria, etc.). Discussion of each case with Hematology team is recommended

Prevention of Hemodialysis CVC-related VTE

- **Control of catheter-related prothrombotic risk factors**
  - Accepatble: standard dual lumen, twin, or split catheters
  - Avoid PICCs
  - Avoid Subclavian vein cannulation
  - Preferred site: Rt Jugular vein
  - Femoral access – if no upper extremity venous access
  - Right atrial catheter tip positioning
  - Ultrasound-guided approach for CVC insertion

National Kidney Foundation 2006 updates, Am. J. Kidney Dis. 2006

- **Catheter locking solution –**
  - Heparin – optimal concentration?
  - tPA - superiority over heparin?

Hemmelgarn et al, NEJM 2011; Gittins et al, Arch. Dis. Child, 2007

Primary thromboprophylaxis for hemodialysis CVCs

Meta-analysis of pediatric studies on CVC-thromboprophylaxis:

No study has proven the efficacy of thromboprophylaxis against CVC-related VTE in children.

E.Vidal J.Thromb.Haemost. 2014

Meta-analysis of adult RCTs: No beneficial effect of VKAs on rates of CVC malfunction

Wang et al, Nephrol. Dial. Transplant. 2013

ACCP Guidelines for Antithrombotic Therapy in Neonates and Children, 9th ed (2012):

"2.46. For patients undergoing hemodialysis via CVAD, we suggest routine use of VKAs or LMWH for thromboprophylaxis as compared with no therapy (Grade 2C)"

The strategy is not widely employed by pediatric dialysis units.

Pilot study: VKAs in children with CVC on chronic haemodialysis -
Warfarin (INR target 2-3) for patients at high risk for CVC thrombosis (Active NS; Previous thrombosis)
CVC survival and malfunction-free survival rates were significantly higher in the warfarin-treated patient group, with no increased risk of bleeding. *Paglialonga et al, Pediatr. Nephrol. 2016*

Summary

- In pediatric ESRD patients, the provision of renal replacement therapy is a lifelong undertaking.
- Effective strategies for conservation of hemodialysis access are required.
- Access planning should take into account modifiable catheter-related prothrombotic risk factors.
- Prompt diagnosis and effective treatment of CVC-thrombosis are essential for CVC salvage, thereby reducing CVC exchanges and aiding in the conservation of future hemodialysis access sites.
- The identification of subpopulations of hemodialysis patients at high risk of CVC-related thrombosis will aid in the design and application of much needed multicenter prospective studies examining the risk and benefit of thromboprophylaxis.
- These much needed studies would optimally be designed and lead in collaboration between nephrologists and hematologists.

Thank You's…

Shoshi Revel-Vilk – Pediatric Hematology/Oncology
Shimrit Tzvi-Behr – Pediatric Nephrology

Suzan Williams – Pediatric Hematology/Oncology
Liz Harvey - Pediatric Nephrology

Pediatric Hematology/Oncology
Ayelet Ben-Barak
Myriam Ben-Arush

Pediatric Nephrology
Daniella Magen
Israel Eisenstein
Shirley Pollack