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British Intestinal Failure Alliance (BIFA) Guidelines

Detection and Treatment of Catheter-Related Thrombosis in Patients Receiving Home Parenteral Support*

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Aims of the guideline

1. To help the recognition of acute catheter/central vein thrombosis and appreciate that it is a medical emergency.
2. To outline the short and long-term prevention and treatment/of catheter/central vein thrombosis.
3. To prevent chronic central vein stenosis/occlusion from occurring, and when it does to show methods of treating it.

Background

Catheter-related thrombosis can include central venous thrombosis (CVT) in the vein in which the catheter is located, as well as thrombus attached to the end of the catheter (attached to a fibrin sheath). Central venous stenosis or occlusion can occur as a result.

Catheter-related thrombosis (CRT) is a serious complication of home parenteral support (HPS) (1). Recurrent CRT can lead to a loss of venous access, which is essential for delivery of HPS to patients with intestinal failure (IF). Providing and maintaining central venous access is vital in this group of patients. There is a wide range of reported incidence, ranging from 0.01-0.40 per 1000 catheter days in adults (2–11)(12–14). Patent central veins are crucial for patients on HPS and the loss of 2 or more central veins is an indication for consideration of intestinal transplantation (15).
There is little evidence based guidance and the treatment algorithms below are largely based on expert opinion and clinical experience. In this guidance evidence is drawn from the literature and if not available from expert opinion.

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Catheter Related Thrombosis

Risk factors

The presence of a central venous catheter is the most important risk factor for the development of CRT. Several mechanisms play a role in the development of CRT including compromised blood flow, vessel wall injury by the catheter or parenteral nutrition, increasing number of lumens (16), catheter/vessel ratio (17), use of power injectable devices (18), site of catheter insertion (19), CVC tip position (16,20), catheter related bloodstream infection (21,22), parenteral nutrition osmolality (23), prothrombotic tendencies and hypercoagulable states.

A provoked thrombosis can be caused by sepsis and venous trauma.

1. If there is a history of recurrent thrombosis, a family history of thrombosis or no clear factor causing the thrombosis (unprovoked), then tests should be performed to look for an underlying coagulation disorder (Table 1).
2. Catheter tip position is crucial for long term catheters. The tip position for long term catheters (usually made of polyurethane or silicone) should be in the lower SVC or at the entry to the right atrium. CVT rates increase exponentially as the tip becomes located proximally (20).
3. It is important that for all patients on HPS that the current status of their central veins are clearly documented. This is often overlooked.
4. Ultrasound is recommended for all PICC insertions.
5. External diameter of the catheter should not exceed ⅓ of the internal diameter of the vein (17).

Symptoms and signs

The majority of CRT are thought to be asymptomatic, perhaps even as high as two thirds (12). Symptomatic CRT can present with a wide range of symptoms and signs, including CVC dysfunction, formation of visible collateral vessels, head or upper extremity pain and swelling (when the CVC accesses a vein leading to the SVC) or pain and swelling in the back, pelvis or legs (when the CVC accesses a vein leading to the IVC).

Symptoms and signs occur when the thrombosis is acute. However, in patients where the thrombosis is more indolent or longstanding then there can be no symptoms or signs, although on close inspection there are often enlarged superficial veins in the territory that the thrombosis affects.

Often the flow rate through the catheter is not compromised but sometimes there can be occlusion alarms occurring from the pump, or patients may notice some stiffness and/or discomfort when flushing the catheter. For patients where the catheter is used on a regular basis to withdraw blood or an antimicrobial lock a persistent withdrawal occlusion (PWO) may also be present.

Diagnosis

6. A diagnosis of CVT can be made by CT venogram, MR venogram or contrast venogram. Ultrasound with doppler can be used but this is only reliable to detect subclavian, jugular or femoral thromboses. It is not reliable when the thrombosis is more central.

Management

Where investigations reveal the presence of a new thrombus.

7. Do not remove CVC immediately; take bloods to test for a coagulation disorder (Table 1) and start thrombolysis if within 14 days of onset of symptoms. If >14 days since onset of symptoms then consider anticoagulation only.
8. There should be an early discussion of the patient with the vascular radiological team. Thrombolysis should be offered in accordance with the available interventional radiological expertise. This is initiated by interventional radiology and the patient should then be monitored in an HDU bed.
9. Subsequently venography is repeated every 24 hours (see flowchart). If the thrombus disperses without any central venous distortion, then subsequently the patient should be anticoagulated prior to discharge.
10. If there is a residual central venous stenosis then balloon venoplasty can be considered (with or without stenting) and subsequently antiplatelet therapy should be given for 3-6 months, with anticoagulation after this.
11. If thrombolysis does not result in any improvement in the thrombosis with a persistent occlusion, then the CVC should be replaced via a different route and subsequently anticoagulation should be offered. Occasionally, if very difficult venous access, interventional radiology can access the same site and place a new catheter beyond the thrombus.
12. In some centres central venous recannalisation (venoplasty with or without placement of a venous stent) can be considered when there is a chronic stenosis/occlusion. This will depend on the venous anatomy as well as the available expertise.
13. Long-term anticoagulation must be considered, with any decision to cease determined on a case-by-case basis involving discussions with an expert in intestinal failure/parenteral support.
14. When 2 of the 4 major supra-diaphragmatic veins have been lost there should be consideration for a small bowel transplant.

Central venous thrombosis with a coexistent catheter related infection

A CVT can occur together with a CVC infection in 10% cases (24,25).

15. As sepsis can be occult, some units recommend blood cultures in all patients with a suspected central vein thrombosis as for suspected CRBSI (26,27). If the patient presents with a fever together with the thrombosis then antibiotics should be started (according to a CVC infection protocol) together with thrombolysis, otherwise a bacteraemia and septicaemia may develop.

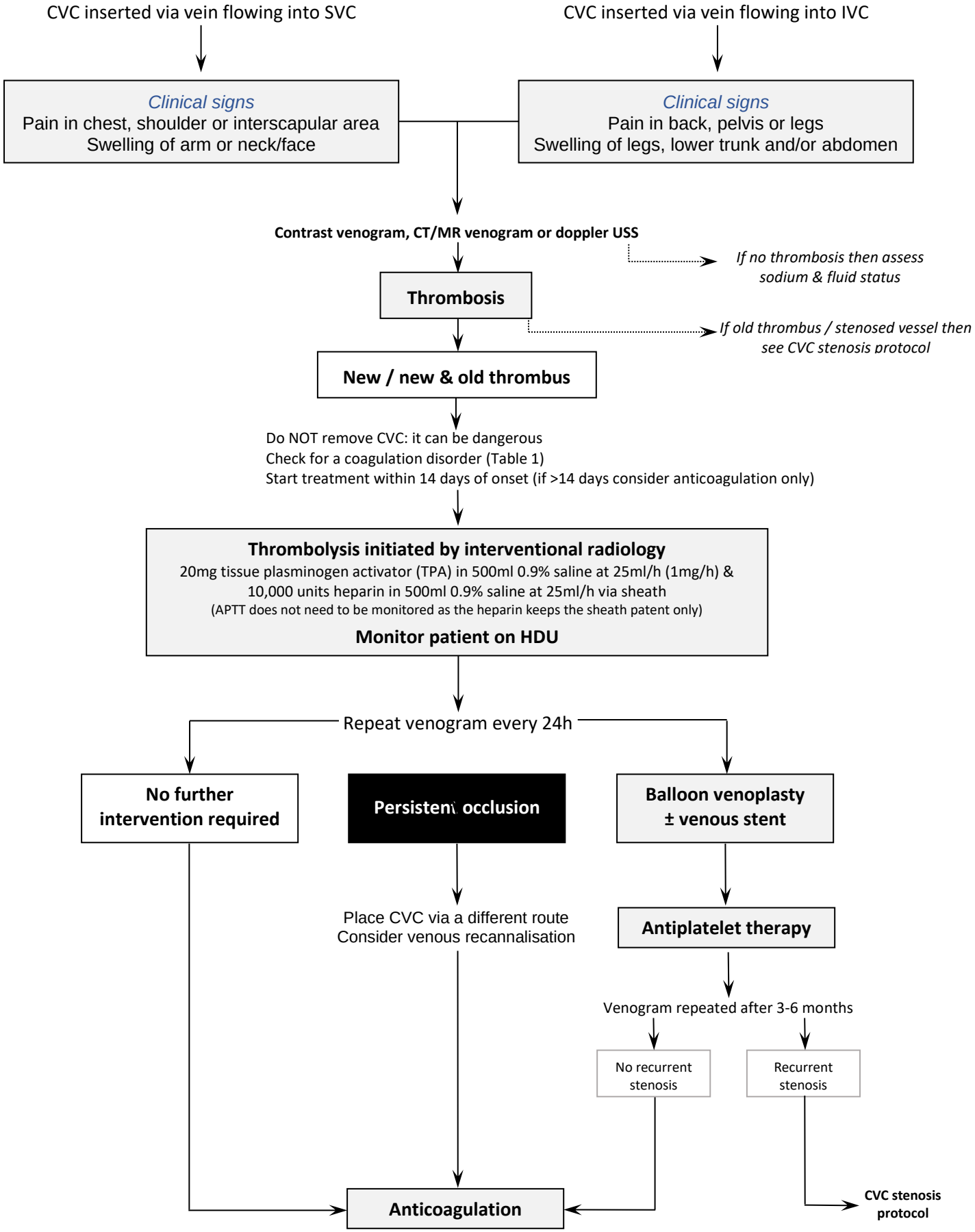
Bilateral thrombosis

16. If the patient has a new thrombosis that extends bilaterally then thrombolysis may need to be applied to both sides (either at the same time or sequentially). This should be discussed with the radiologist.

Table 1: Checking for a coagulation disorder

Provoked thrombosis (sepsis, venous trauma)	No specific investigations required	
Unprovoked thrombosis, family history or recurrent thrombosis	Initial tests	Measure - Autoantibodies (ANA, anticardiolipin & B2GPI antibodies) - Lupus anticoagulant - Factor V leiden - Antithrombin III - Test for paroxysmal nocturnal haemaglobinuria - Protein gene 20210A mutation - If mesenteric or portal thrombosis in the past, check JAK2 mutation (if positive for lifelong anticoagulation) Consider underlying malignancy (breast examination or PSA, tumour markers, CT scan)
	After 3 months (by haematology)	Protein C Free protein S

Flowchart 1: Catheter related thrombosis flowchart



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Thrombus at the end of the CVC

Symptoms and signs

In itself thrombus at the end of the CVC is asymptomatic. However, if there are emboli that come from the thrombus these may present with symptoms of pulmonary emboli (chest pain, SOB, palpitations, haemoptysis).

Diagnosis

This is usually an incidental finding after CTV, MRV or echocardiogram.

Management

17. The management depends on the size of the thrombus. This can be divided into small, medium or large thrombus attached to the end of the CVC. Arbitrarily small is <10mm, medium is 10-50mm and large is >50mm.
18. Small thrombi: withdraw the CVC. This will not result in a clinically significant pulmonary embolus.
19. Medium thrombi: start thrombolysis via the CVC [20mg TPA in 500ml 0.9% saline at 25ml/h (1mg/h)] and monitor the patient on HDU. If the CVC is blocked then a thrombolysis catheter can be placed by interventional radiology adjacent to the thrombus. The imaging should be repeated every 24h until the thrombus is <10mm and then the CVC can be removed.
20. Large thrombi: the patient should be referred to a cardiothoracic unit for thrombectomy.
21. The subsequent management for all patients is elective CVC replacement & anticoagulation.

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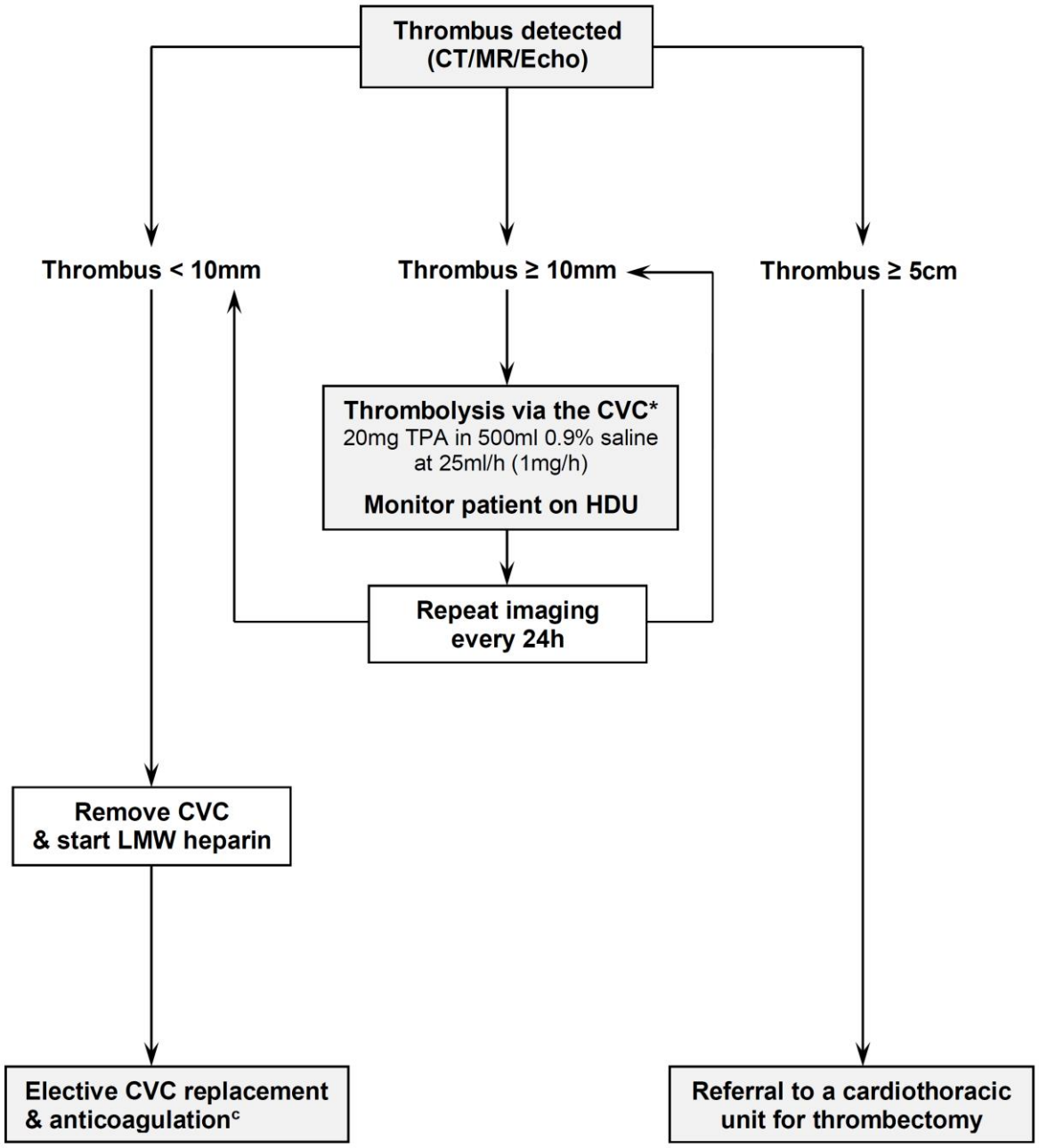
Flowchart 2: clinical practice based algorithm for thrombosis at the end of the CVC



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Central venous stenosis

A central venous stenosis may be present in patients who have had an indwelling central venous catheter over a long period of time. In addition, central venous stenosis can often occur treatment for a central venous thrombosis.

Symptoms and signs

The clinical signs are similar to those for a central venous thrombosis but are much less acute. Often there are subtle signs with dilated veins over the chest or neck, dilated collateral veins or mild signs of swelling when an infusion is running.

Diagnosis

A diagnosis of CV stenosis can be made by CT venogram, MR venogram or contrast venogram. Ultrasound with doppler can be used but this is only reliable to detect subclavian, jugular or femoral stenoses. It is not reliable when the thrombosis is more central.

Management

22. Once diagnosed, the decision to treat will depend upon symptoms, the location of the stenosis as well as local interventional or vascular expertise. The most appropriate treatment requires close discussion with the interventional radiologists and, if necessary, the vascular surgeons.
23. Patients with a CV stenosis who are not undergoing any interventional procedures should be anticoagulated to prevent a subsequent thrombosis
24. Patients with a CV stenosis who undergo an interventional procedure should receive antiplatelet therapy for 3-6 months and subsequently receive anticoagulation if no other procedures are being considered

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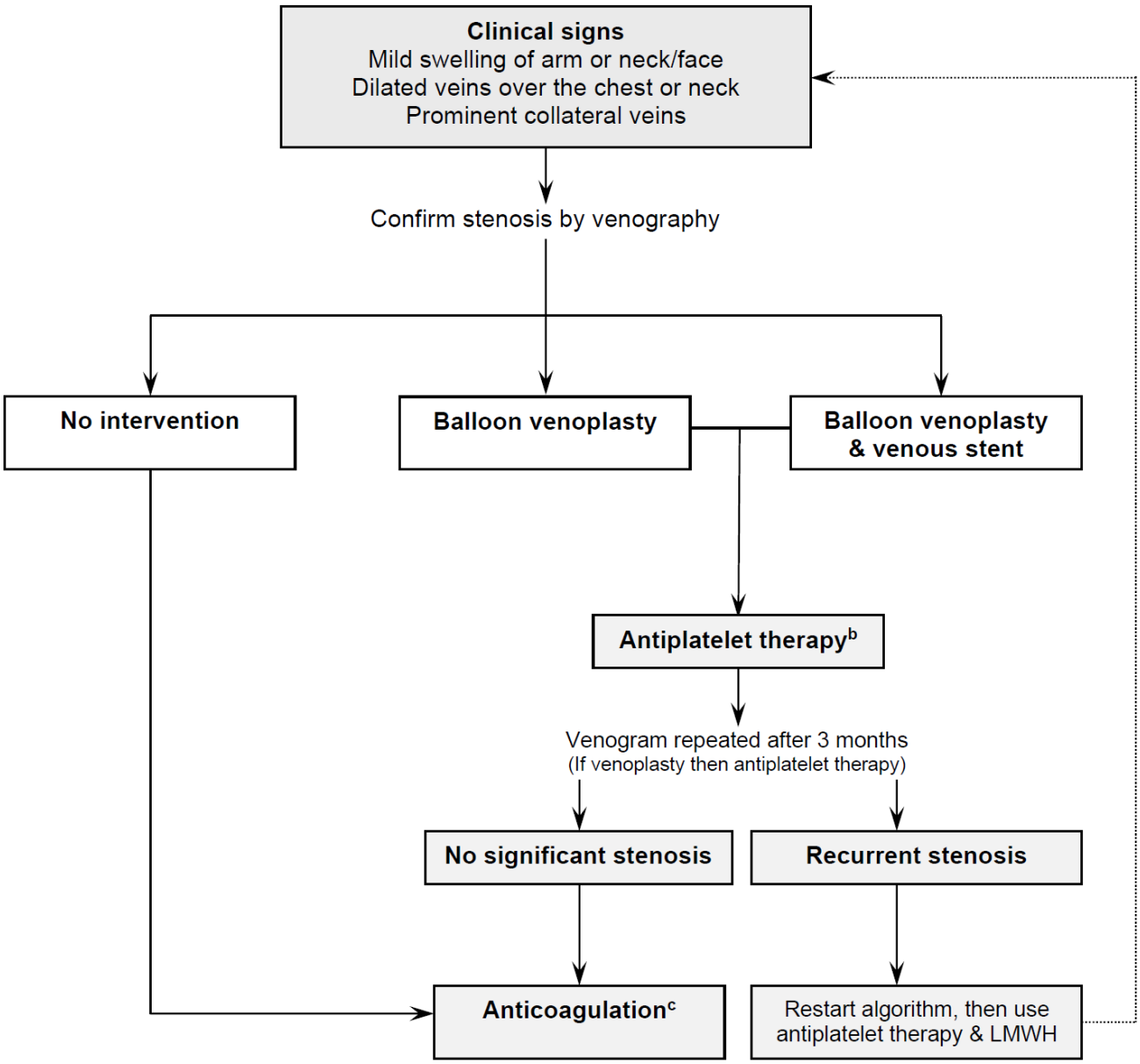
Flowchart 3: clinical practice-based algorithm for CV stenosis



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References

1. Dibb M, Lal S. Home Parenteral Nutrition: Vascular Access and Related Complications. Nutr Clin Pract Off Publ Am Soc Parenter Enter Nutr. United States; 2017 Dec;32(6):769–76.
2. Brandt CF, Hvistendahl M, Naimi RM, Tribler S, Staun M, Brobech P, et al. Home Parenteral Nutrition in Adult Patients With Chronic Intestinal Failure: Catheter-Related Complications Over 4 Decades at the Main Danish Tertiary Referral Center. J Parenter Enter Nutr [Internet]. 2016;(Cvc):1–10. Available from: http://pen.sagepub.com/cgi/doi/10.1177/0148607116655449
3. Christensen LD, Holst M, Bech LF, Drustrup L, Nygaard L, Skallerup A, et al. Comparison of complications associated with peripherally inserted central catheters and Hickman??? catheters in patients with intestinal failure receiving home parenteral nutrition. Six-year follow up study. Clin Nutr. 2016;
4. Bozzetti F, Mariani L, Bertinet DB, Chiavenna G, Crose N, De Cicco M, et al. Central venous catheter complications in 447 patients on home parenteral nutrition: an analysis of over 100.000 catheter days. Clin Nutr. 2002;21:475–85.
5. Mukau L, Talamini MA, Sitzmann J V, Burns RC, McGuire ME. Long-term central venous access vs other home therapies: complications in patients with acquired immunodeficiency syndrome. JPEN J Parenter Enteral Nutr. United States; 1992;16(5):455–9.
6. Bakker H, Bozzetti F, Staun M, Leon-Sanz M, Hebuterne X, Pertkiewicz M, et al. Home parenteral nutrition in adults: a european multicentre survey in 1997. ESPEN-Home Artificial Nutrition Working Group. Clin Nutr [Internet]. 1999;18(3):135–40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10451476
7. Lorentsen R, Munck LK, Wildt S. Parenteral therapy and complications in patients with intestinal failure in a regional unit. Scand J Gastroenterol. England; 2017 Dec;52(12):1326–30.
8. Durkin MJ, Dukes JL, Reeds DN, Mazuski JE, Camins BC. A Descriptive Study of the Risk Factors Associated With Catheter-Related Bloodstream Infections in the Home Parenteral Nutrition Population. JPEN J Parenter Enteral Nutr [Internet]. 2015/01/16. 2016 Sep;40(7):1006–13. Available from: https://pubmed.ncbi.nlm.nih.gov/25596210
9. Szeinbach SL, Pauline J, Villa KF, Commerford SR, Collins A, Seoane-Vazquez E. Evaluating catheter complications and outcomes in patients receiving home parenteral nutrition. J Eval Clin Pract. England; 2015 Feb;21(1):153–9.
10. Touré A, Duchamp A, Peraldi C, Barnoud D, Lauverjat M, Gelas P, et al. A comparative study of peripherally-inserted and Broviac catheter complications in home parenteral nutrition patients. Clin Nutr. 2015;34(1).
11. Cotogni P, Pittiruti M, Barbero C, Monge T, Palmo A, Boggio Bertinet D. Catheter-related complications in cancer patients on home parenteral nutrition: a prospective study of over 51,000 catheter days. JPEN J Parenter Enteral Nutr. United States; 2013;37(3):375–83.
12. Cuerda C, Joly F, Corcos O, Concejo J, Puiggrós C, Gil C, et al. Prospective study of catheter-related central vein thrombosis in home parenteral nutrition patients with benign disease using serial venous Doppler ultrasound. Clin Nutr. England; 2016 Feb;35(1):153–7.
13. Harrison E, Herrick AL, Dibb M, McLaughlin JT, Lal S. Long-term outcome of patients with systemic sclerosis requiring home parenteral nutrition. Clin Nutr. 2015;34(5):991–6.

14. Lloyd DAJ, Vega R, Bassett P, Forbes A, Gabe SM. Survival and dependence on home parenteral nutrition: Experience over a 25-year period in a UK referral centre. Aliment Pharmacol Ther. 2006;24(8):1231–40.
15. Matsumoto CS, Subramanian S, Fishbein TM. Adult Intestinal Transplantation. Gastroenterol Clin North Am. 2018 Jun;47(2):341–54.
16. Eastridge BJ, Lefor AT. Complications of indwelling venous access devices in cancer patients. J Clin Oncol Off J Am Soc Clin Oncol. United States; 1995 Jan;13(1):233–8.
17. Spencer TR, Mahoney KJ. Reducing catheter-related thrombosis using a risk reduction tool centered on catheter to vessel ratio. J Thromb Thrombolysis 2017; 44(4):427-434.
18. Baxi SM, Shuman EK, Scipione CA, Chen B, Sharma A, Rasanathan JJK, Chenoweth CE. Impact of postplacement adjustment of peripherally inserted central catheters on the risk of bloodstream infection and venous thrombus formation. Infect Control Hosp Epidemiol 2013; 34(8):785-92.
19. Gould JR, Carloss HW, Skinner WL. Groshong catheter-associated subclavian venous thrombosis. Am J Med. United States; 1993 Oct;95(4):419–23.
20. Cadman A, Lawrance JAL, Fitzsimmons L, Spencer-Shaw A, Swindell R. To clot or not to clot? That is the question in central venous catheters. Clin Radiol. England; 2004 Apr;59(4):349–55.
21. Crowley AL, Peterson GE, Benjamin DKJ, Rimmer SH, Todd C, Cabell CH, et al. Venous thrombosis in patients with short- and long-term central venous catheter-associated Staphylococcus aureus bacteremia. Crit Care Med. United States; 2008 Feb;36(2):385–90.
22. van Rooden CJ, Schippers EF, Barge RMY, Rosendaal FR, Guiot HFL, van der Meer FJM, et al. Infectious complications of central venous catheters increase the risk of catheter-related thrombosis in hematology patients: a prospective study. J Clin Oncol Off J Am Soc Clin Oncol. United States; 2005 Apr;23(12):2655–60.
23. Berea-Baltierra R, Rivas-Ruiz R, Vela-Martinez E, Sevilla-Gonzalez M de la L, Talavera-Pina JO, Valencia-Jimenez E, et al. Risk factors for subclavian vein thrombosis in cancer patients with total parenteral nutrition. J Clin Med Res [Internet]. 2014/07/28. Elmer Press; 2014 Oct;6(5):345–53. Available from: https://pubmed.ncbi.nlm.nih.gov/25110538
24. Buchman AL, Misra S, Moukarzel A, Ament ME. Catheter thrombosis and superior/inferior vena cava syndrome are rare complications of long term parenteral nutrition. Clin Nutr. England; 1994 Dec;13(6):356–60.
25. van Ommen CH, Tabbers MM. Catheter-related thrombosis in children with intestinal failure and long-term parenteral nutrition: how to treat and to prevent? Thromb Res. United States; 2010 Dec;126(6):465–70.
26. Lal S, Chadwick P, Nightingale J and the BIFA Committee. Diagnosis of catheter related blood stream infections (CRBSIs). April 2018. https://www.bapen.org.uk/pdfs/bifa/recommendations-for-crbsi-diagnosis.pdf
27. Lal S, Chadwick P, Nightingale J and the BIFA Committee. Management of catheter related blood stream infections (CRBSIs). January 2019. https://www.bapen.org.uk/pdfs/bifa/recommendations-on-management-of-crbsi.pdf

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