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Between a Rock and a Hard Place: Systemic Thrombolysis for Obstructive Mechanical Valve Thrombosis

Michael A Campbell MBChB BMedSci

Cardiology Specialist Registrar

Northern Ireland Medical Dental Training Association (NIMDTA), 42 Beechill Rd, BT8 7RL

Introduction

Whilst obstructive mechanical valve dysfunction has a wide differential diagnosis encompassing pannus formation, valve degeneration and endocarditis, clinicians must maintain a high index of suspicion for mechanical valve thrombosis (MVT), particularly in acute presentations. Management options for MVT include optimisation of anticoagulation, thrombolytic therapy (TLT), transcatheter therapies (TCT) and surgery. (1)

Take Home Messages

- Obstructive mechanical valve thrombosis (MVT) is associated with high morbidity and mortality and the role of thrombolytic therapy (TLT) in treating MVT is debated
- Contemporary observational and randomised evidence demonstrate low-dose, slow, image guided TLT achieves high rates or valve re-opening and low complication rates
- These data support TLT as a reasonable first line alternative to surgery in selected patients with obstructive MVT
- Larger, multi-centre studies with long term follow up are required before TLT and surgery are regarded as equivalent treatment strategies

In patients presenting with symptoms or signs of heart failure in the presence of obstructive MVT (see figure 1), optimisation of anti-coagulation alone is not recommended. (2,3)

Mortality with surgical therapies is high (10-15%) and increasing evidence suggests that TLT is a safe and efficacious treatment option. (2) The focus of this review is the approach to TLT in patients with obstructive MVT.

Surgery versus Thrombolysis

Previous recommendations favouring surgery for obstructive MVT were derived from retrospective observational studies indicating similar efficacy in restoring valve function, but lower rates of thrombotic and bleeding complications. (4,5) Evidence supporting TLT for right sided heart valves was limited to case series. (6) The HATTUSHA study was a multi-centre, prospective observational study comparing low-dose, slow infusion alteplase without concomitant unfractionated heparin (UFH) as first treatment (n=83) versus surgery (n=75) for obstructive MVT. Most participants included had left sided prostheses (n=119 mitral, 75.3%; n=26 aortic, 16.5%) and a small minority had right sided protheses (n=13 tricuspid, 8.2%). Treatment allocation was determined by the local HEART team with similar baseline surgical risk, although mitral prostheses were more common in the surgical arm. Technical success of TLT, assessed by 12-hourly transthoracic echocardiograms (TTE), required normalisation of valve haemodynamics, ≥75% thrombus reduction and symptomatic improvement and was achieved in 90.4% with a median dose of tPA of 59mg. Although no formal inferential comparisons were performed, point estimates of major complications (6% vs 41.3%), major bleeding (2.4% vs 9.3%), embolic events (2.4% vs 5.3%) and 3 month mortality (2.4% vs 18.7%) favoured TLT(7)

SAFE-PVT randomised 79 patients with imaging-confirmed left sided obstructive MVT to TLT or surgery. TLT regimens mirrored HATTUSHA, with repeat dosing permitted up to 200mg. Most patients had mitral prostheses (72%) and 43% were NYHA III/IV. Only 82% of patients randomised surgery underwent the procedure, and just 53% within 48 hours. Rates of the primary endpoint, defined as discharge with restored valve function and no major complications, were similar between groups. Residual valve dysfunction was more frequent with TLT, but major adverse events occurred less frequently, driven by lower mortality. SAFE-PVT supports low-dose, slow infusion thrombolysis in selected patients while underscoring the need for multicentre data and longer term follow up.(3)

Reflecting the residual uncertainty, ESC/EACTS guidance prioritises surgery for operable patients with obstructive left-sided MVT, reserving TLT for selected scenarios,(3)whereas ACC/AHA guidelines place surgery and TLT on more equal footing, emphasising individualised HEART team decision making. (Table 1). (2)

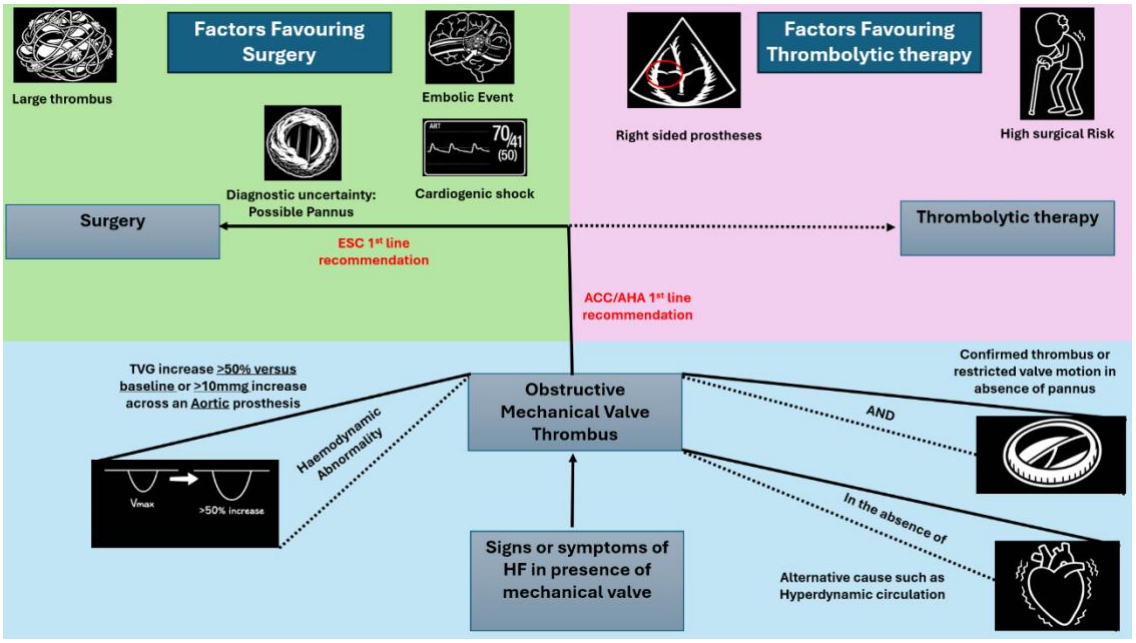

Figure 1. Original figure (produced by the author) demonstrating conceptual decision framework for the management of obstructive mechanical valve thrombosis, illustrating clinical and imaging factors that favour surgical intervention versus thrombolytic therapy. ACC/AHA guidelines have the therapies as equivalent with decision making according to the HEART team assessment of individual factors, whereas, ESC guidelines favour surgery as the first treatment with thrombolytic therapy offered if surgery is felt to be unfavourable.

Low, slow dose versus high dose thrombolysis

Early experience with TLT for MVT relied on high-dose regimens incorporating an initial bolus, largely extrapolated from STEMI protocols, and was associated with unacceptably high rates of major bleeding and systemic embolisation. (8) This approach was subsequently challenged by studies evaluating low-dose, slower infusion strategies guided by imaging. The TROIA trial was a prospective observational study in which patients with MVT were allocated to one of five thrombolytic regimens differing in agent, dose and infusion rate, with serial transoesophageal echocardiography (TOE) used to guide repeat dosing and assess thrombus resolution. Low-dose, slow-infusion alteplase (25 mg over 6 hours) achieved rates of valve reopening comparable to higher-dose strategies, while substantially reducing major bleeding and embolic complications, establishing that thrombolytic efficacy can preserved at lower doses with image guidance.(9)

This concept was extended in the PROMETEE study, which evaluated an ultra-slow infusion protocol using alteplase 25 mg over 25 hours, repeated as required based on repeat imaging, with a median total dose of 50 mg. High rates of thrombus resolution were achieved with very low rates of major bleeding or thrombotic complications. A randomised study comparing ultra-slow, low-dose thrombolysis (25mg/25 hours) with a faster, higher dose (50mg/6 hours) regimen demonstrated similar efficacy but fewer bleeding events with the ultra-slow protocol. (10) Additional observational data in pregnancy further support image-guided slow-infusion TLT, where avoiding surgery and bleeding is particularly desirable. (11) Collectively, these studies support low-dose, slow or ultra-slow TLT as an effective strategy that reduces bleeding risk without compromising efficacy.

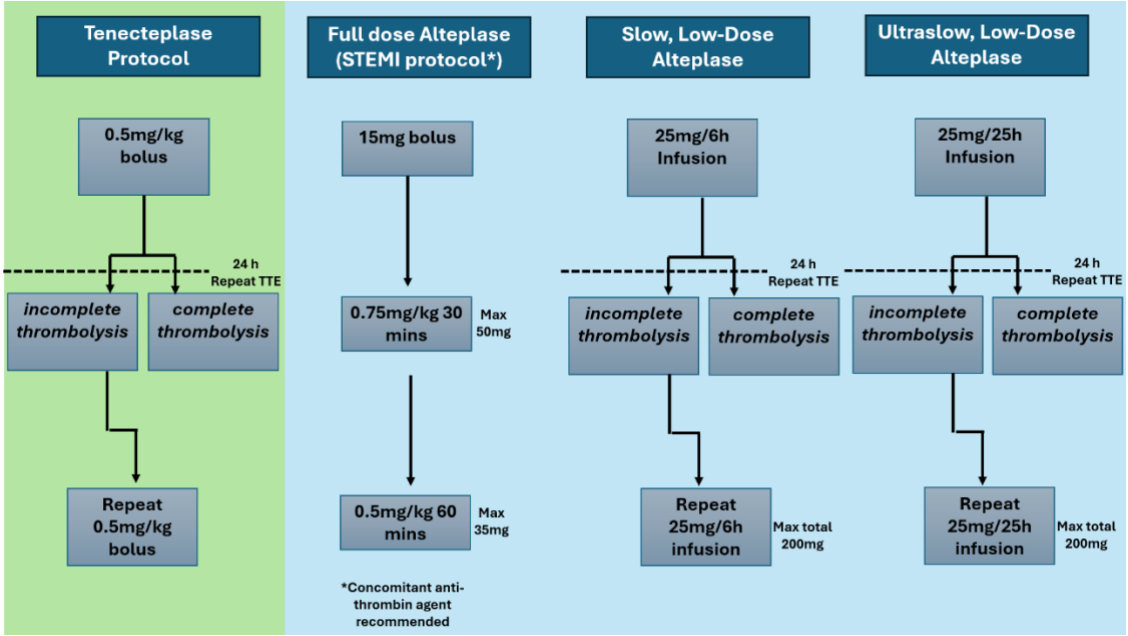

Figure 2. Original figure (produced by the author) comparing differing thrombolytic protocols.

Thrombolytic Agent

Tenecteplase, an alternative fibrinolytic agent with greater fibrin specificity and single-bolus administration, is now recognised by the European Stroke Organisation (ESO) as an alternative to alteplase for acute ischaemic stroke.(12) However, its role in MVT had not been prospectively evaluated prior to the TENET trial. TENET randomised 83 patients with obstructive left sided MVT in an open-label fashion to slow, low dose alteplase (25mg/6 hours up to total of 150mg) or tenecteplase (0.5mg/kg bolus dose, with repeat dose allowed after 24h) examining a primary efficacy outcome of thrombolytic success (normalisation of haemodynamics on echo, symptom improvement and normalisation of leaflet motion on fluoroscopy) and a composite safety outcome of death, major bleeding or systemic embolisation at discharge. Patients with cardiogenic shock were excluded. Tenecteplase was non-inferior and superior to alteplase with respect to the efficacy outcome and was non-inferior with respect to safety. Major complications were rare in both groups. Given single-centre design, TENET is hypothesis generating but supports a TLT-first strategy for obstructive MVT and selective use of Tenecteplase as an alternative to slow, low-dose alteplase.

Conclusions

In conclusion, contemporary evidence and international guideline recommendations support slow, low-dose thrombolytic therapy as a reasonable first line alternative to surgery for selected patients with obstructive mechanical valve thrombosis. However, long term follow up in larger, multicentre populations is required before these strategies can be regarded as equivalent. Future research should focus on whether the rates of higher residual valve dysfunction observed after TLT translate into adverse clinical outcomes, or whether a hybrid approach, utilising TLT as a stabilising intervention and surgery downstream might be the optimal treatment strategy.

Table 1. Summary of International Guideline Recommendations pertaining to TLT for MVT

Guideline Society	1st Line	TLT Regimen	Specific Indications for TLT	Specific Indications for surgery
ESC/EACTS (2025)	Heart Team Evaluation (Class 1) Surgery if large thrombus or embolic event (class IIa).	Slow, low-dose alteplase where surgery not favoured. No dose stated.	• High surgical risk • Right sided valve	• Large thrombus (>10mm) • Thromboembolic event • CI to TLT • Cardiogenic shock • Possible pannus • Recurrent thrombus
AHA/ACC (2020/2024 update)	Surgery and TLT equally recommended (1b) individualising according to clinical factors and local expertise after Heart Team evaluation.	Slow-infusion, low dose (Alteplase 25mg/6hours without bolus, or 25mg/25hours, repeated as needed)	• High surgical risk • First-time episode • NYHA I-III • Small thrombus (≤0.8 cm2) • Thrombus visualised	• Low surgical risk • Contraindication TLT • Recurrent thrombus • NYHA IV • LA thrombus • Concomitant severe CAD or other valve disease • Possible Pannus

(Abbreviations) MVT – mechanical valve thrombosis, TLT – thrombolytic therapy, CI – contraindication, AHA- Amercian Heart Association, ACC – American College of Cardiology, ESC – European Society of Cardiology, EACTS – European Association of Cardiothoracic Surgery

Disclosures

None to declare

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