The role of thrombolytic therapy in mechanical heart valve thrombosis.

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Abstract

Prosthetic Valve Thrombosis (PVT) is rare but serious complication of prosthetic valve replacement, clinically it can be obstructive or non-obstructive with Thrombolytic Therapy (TT) being increasingly used for obstructive mechanical PVT given its similar efficacy compared with surgery. However, best TT protocol is virtually unknown. In this short communication, I would like to discuss the clinical issues with available evidence on TT in PVT, our study on the role of tenecteplase in the management of O-PVT and clinical questions that need to be addressed in future studies.

Keywords: Prosthetic valve thrombosis, Thromboembolic events, Thrombolytic therapy, Cardiogenic shock, Imaging.

Accepted on 25 August, 2021

Introduction

Prosthetic Valve Thrombosis (PVT) is associated with significant morbidity and mortality. The risk of PVT and Thromboembolic Events (TE) events is higher with MHVs than with BHVs. The reported rates of PVT are highly variable and is influenced by the intensity and timing of serial imaging follow-up, and it is likely that many cases of thrombus formation remain undetected because imaging is usually done only for patients presenting with symptoms; thus, underestimating the true incidence [1]. When considered in terms of clinically relevant obstruction, the annual incidence with MHV ranges from 0.5% to 6.0% and TE has an estimated annual incidence of 2.5% to 3.7%. In BHVs, reported annual rates and TE were 0.03% and 0.38%, respectively [1]. These rates are particularly high in developing countries and reaching an incidence of 6% in first 6 months after surgery [2]. For any prosthetic valve the greatest risk of TE is seen in first 3 months after surgery due to the lack of endothelialisation and absence of therapeutic anticoagulation is reported to be an independent predictor of TE [1].

Thrombolytic Therapy for Mechanical Valve Thrombosis

Clinical studies suggest that patients with non-O-PVT should be managed with optimization of anticoagulant treatment (Short-term IV Unfractionated Heparin (UFH)) followed by warfarin adjustment for small thrombi (length of <5-10 mm). If thrombus size is increasing or is complicated by embolism or if thrombus is large (>10 mm), Thrombolytic Therapy (TT) with low dose tPA may be considered. After resolution of the event, these patients may be considered to have a higher risk of new cardio embolic events. Therefore, scientific societies recommend adding antiplatelet therapy with aspirin besides increasing the therapeutic range of anticoagulation though the data on this practice is controversial [3,4]. The optimal treatment of O-PVT is controversial, and to date no randomized clinical trials have been conducted to assist in decision making. Systematic review of observational studies [5] that compared the two therapies had suggested that surgery do not offer any mortality benefit over TT and hence later can be an alternative to surgery in O-PVT but at the cost of the higher bleeding and TE rates. Whereas another review with indirect comparison [6] of studies that used TT and/or surgery for O-PVT, had showed that mortality in patients treated by TT for PVT is lower than in patients treated surgically, but again with higher incidence of bleeding and TE.

Though, TT have similar efficacy and may have similar mortality atleast compared to surgery in short term, the major drawback is its associated morbidity. It should be noted majority of older studies on which bulk of the data is based, used Streptokinase (STK) which is shown to be associated with higher bleeding rates compared to newer agents like Tenecteplase (TNK) [7]. So, the use of next generation thrombolytic agents may mitigate this morbidity (bleeding and TE events) and may improve patient outcomes. In fact, we in our single center study [8] had observed that TNK infusion is associated with statistically better safety profile compared to STK. Even in our mini-review [8] of 19 studies (863 left sided O-PVT episodes with 85% involving mitral position) TNT use was associated with a lower composite rate of bleeding, TE and death compared to STK (at least numerically). Recently based on single center studies and series, due to lower rates of TE and bleeding, guidelines had proposed that treatment with slow-infusion low-dose TT can be considered as an alternative to emergency surgery in patients with a left-sided mechanical obstructive O-PVT [9]. But it should be noted that slow infusion may not be relevant in patients with NYHA IV class or in cardiogenic shock and at the same time surgical mortality also increases with NYHA class [6]. In our study [8] of 84 O-mitral PVT episodes with about 90% being in NYHA class III or class IV had shown that complete clinical success with TT remains >80% and TNT use was associated with faster clinical and hemodynamic recovery. Hence, TT with TNT is still a reasonable option in patients with poor hemodynamics.

Future Directions

Given the improvements in surgical techniques, patient management and wide spread use of newer generation thrombolytic, the first priority of clinical studies is to identify best TT protocol in terms of efficacy and safety for PVT patients. Secondly, trials evaluating the various thrombolytic agents should use uniform definition for "thrombolytic success" such that multiple studies comparisons can be more meaningful. Third, given the occurrence of TE events and recurrence of O-PVT after hospital discharge in patients who received TT therapy in the background of good data [10] suggesting that reoperation is associated with better survival compared to TT on long-term follow-up; the question of TT vs. surgery should be answered beyond in-hospital outcomes. Fourth, though studies with tissue Plasminogen Activator (tPA) had shown its safety and efficacy in O-PVT, what actually is "low-dose" and "slow-infusion" need to be well defined to other newer thrombolytic agents too. Finally, techniques and role of percutaneous manipulation of prosthetic valves should be adequately defined.

Conclusion

Based on available clinical literature and easier feasibility it may be suggested that TT may be considered as first line therapy in patients with O-PVT and also in non-O-PVT with larger thrombus burden (>10 mm). Though ideal TT is unknown, data from small scale clinical studies suggests that newer generation thrombolytic may be preferable to STK. Low dose, slow infusion of tPA and TNT infusion should be considered in asymptomatic, NYHA I, II, III patients. Also, TNT infusion can be considered even in patients with NYHA IV or cardiogenic shock. Further research in the ideal TT and its comparison with re-surgery is need of the hour.

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