Mechanical Mitral Valve Thrombosis Secondary to Tinzaparin as an Anticoagulation Bridging Strategy

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For patients with mechanical heart valves, oral vitamin K antagonists effectively reduce the risk of valve thrombosis. Bridging strategies that use intravenous unfractionated heparin or subcutaneous low molecular weight heparin (LMWH) are required when reversal of anticoagulation is needed for invasive procedures or bleeding complications. There is limited data comparing anticoagulation efficacy between subtypes of LMWH and dosing regimens in this context. This report describes the case of a 45-year-old man with acute mechanical mitral valve thrombosis and suggests that the use of once daily dosing of subcutaneous tinzaparin may be an inappropriate anticoagulation bridging strategy.

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Acute thrombosis is an emergent complication of mechanical heart valves (MHVs) that involve accumulation of clot, subsequent leaflet restriction, and hemodynamic compromise [1, 2]. Oral vitamin K antagonists such as warfarin are used to anticoagulate MHV patients to minimize the risk of thrombosis [3]. Intravenous unfractionated heparin (UFH) and more recently subcutaneous low molecular weight heparin (LMWH) can be used to bridge patients when invasive procedures are required and anticoagulation must be stopped [3–5] In practice, LMWHs are increasingly used because they offer ease of administration, a better safety profile, and predictable therapeutic levels that eliminate the need for continuous monitoring which facilitates outpatient use, and they have been found to be efficacious in many studies [6–8]. However, there is a lack of comparative data between different LMWH subtypes and dosing regimens, and it is unknown if differences in efficacy exist. This report outlines the diagnosis and management of acute mechanical mitral valve (MV) thrombosis as a consequence of once daily subcutaneous tinzaparin as an anticoagulation bridging strategy.

A 45-year-old African Canadian man with rheumatic valve disease had mechanical aortic and MV prostheses implanted 12 years before. To investigate the cause of elevated transaminases in the presence of normal liver function, a percutaneous biopsy was performed. Periprocedurally, warfarin was discontinued, and the patient was placed on UFH with a partial thromboplastin time consistently maintained between 60 and 85 seconds. After the uncomplicated procedure, he was discharged on warfarin (international normalized ratio [INR] 1.1) and subcutaneous daily tinzaparin (175 U/kg) to be continued until the INR was greater than 2.5. Transthoracic echocardiography, performed at the time, was unremarkable with a mean MV gradient of 2.5 mm Hg, normal mechanical mitral leaflet motion, and an ejection fraction 50% to 55%.

Five days after starting tinzaparin the patient presented in acute heart failure preceded by 2 days of shortness of breath on exertion. Transesophageal echocardiography revealed abnormal mechanical MV function with one immobile leaflet and the other severely restricted (Video). The mean MV gradient was 19.0 mm Hg, and there was evidence of severe pulmonary hypertension and severe dysfunction of the right ventricle. With a diagnosis of acute mechanical MV thrombosis and progressive hemodynamic deterioration, emergency operation was performed.

After an uncomplicated redo sternotomy, the MV was exposed through a left atrial incision. It was apparent that the valve was thrombosed with a large clot immobilizing the leaflets (Fig 1). After explantation, the thrombosed

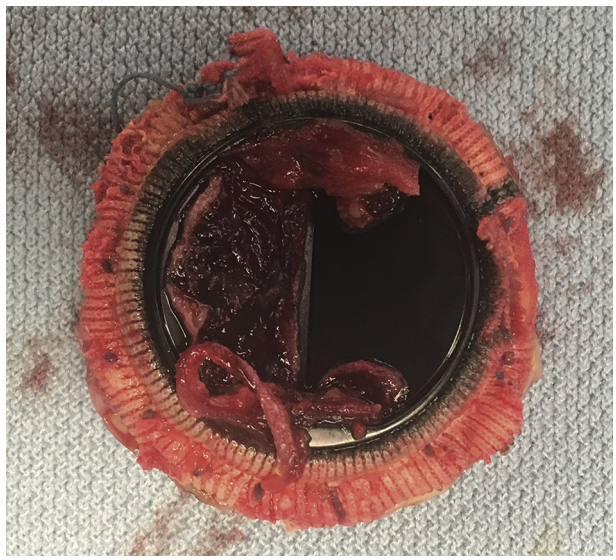

Fig 1. Thrombosed mechanical mitral valve prosthesis, likely secondary to inefficacy of daily dosed tinzaparin as a bridging strategy when resuming warfarin anticoagulation.

The Video can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2017.11.037] on http://www.annalsthoracicsurgery.org.

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valve was replaced with an On-X 25-mm prosthetic valve (On-X Life Technologies, Austin, TX). The postoperative echocardiogram showed improving ventricular function and a mean transvalvular gradient of 3 mm Hg.

The patient had an uncomplicated hospital stay and was bridged using UFH to a therapeutic INR. He was discharged 12 days after operation and remains well 2 months after discharge.

Comment

The use of LMWH as bridge therapy for MHV patients during times of temporary warfarin interruption is endorsed by both the American Heart Association/American College of Cardiology (AHA/ACC) and European Society of Cardiology (ESC) [4, 5]. There are no comparative data between different LMWHs and dose regimens, but most of the evidence supporting their use involves twice daily regimens [6, 7]. Accordingly, twice daily dosing is recommended by the ESC for all MHV patients and for patients at highest thrombotic risk (mitral MHV or aortic MHV with other thrombotic risk factors) by the AHA/ACC [3].

Our experience provides insight into the consequences of once daily LMWH dosing for bridging anticoagulation in MHV patients. Given the acute change in echocardiogram findings and the rapid deterioration in clinical status soon after starting tinzaparin, it is likely that the patient was inadequately anticoagulated. Target anti-Xa levels are 0.5 to 1.0 U/mL while using LMWH; the product monograph for tinzaparin (Innohep; LEO Pharma, Ballerup, Denmark) indicates there is no progressive accumulation with subsequent doses and a trough anti-Xa level of less than 0.3 U/mL is maintained [5]. Although twice daily dosing of enoxaparin (1 mg/kg) (Lovenox; Sanofi-Aventis, Paris, France) demonstrates accumulation and trough anti-Xa level of 0.5 U/mL at steady state. Thus, it is possible that patients dosed with daily tinzaparin have periods of insufficient anticoagulation that expose them to a higher risk of prosthetic valve thrombosis.

This case adds to the body of knowledge about anticoagulation bridging strategies in MHV patients who require short-term interruption of warfarin for procedures and illustrates the serious consequences of inappropriate bridging regimens. Our experience suggests tinzaparin dosed daily may not be as efficacious as other agents when used in MHV patients at high thrombotic risk, and we suggest UFH or twice daily LMWH dosing should be used preferentially in these patients.

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