Prosthetic heart valve thrombosis (PVT) is a serious complication with high morbidity and mortality [1], the incidence vary depending on the type of valve (0.03% in biological and up to 20% in mechanical valves) [2,3,5,6]. Surgery is the first therapeutic option in patients with PVT [4], but some patients have a high risk for complications and cannot be taken into this procedure.

Thrombolysis has emerged as a treatment strategy for PTV in patients who are not candidates for surgery. Despite limited evidence surrounding this treatment, some centers use an ultra-slow infusion protocol. In our center, a low-dose tissue plasminogen activating factor (rTPA) protocol is used (1 mg/h for 25 h, repeating the same protocol according to STS score. Three patients had thrombus greater than 1 cm in length (Table 1).

Successful results were considered when the mean transvalvular gradients were normalized (3 patients) or when the shock status resolved and the echocardiogram reported recovery of valve function and function (1 patient) (Table 1). One patient had a bleeding episode (thoracic wall hematoma) requiring transfusion of blood cell components. At discharge all patients were alive, three receiving warfarin and one receiving low molecular weight heparin.

PVT has a mortality rate between 6% and 69%, even with surgical management [4]. Patients not candidates for surgery can be considered for thrombolytic treatment [7]. The evidence for this management is controversial technique in critically ill patients not candidates for surgery.
used safely. Özcan et al. reported the use of this intervention in 114 patients, with a mortality rate of 0.83% and 6.7% of adverse events, including stroke, embolism and gastrointestinal bleeding. This protocol was related to a gradual thrombus lysis, lower incidence of secondary embolisms and mortality [4,8,9]. In our case series, one patient presented an adverse event (thoracic wall hematoma) with no evidence of secondary embolisms.

Altay et al. reported a patient with a large mobile thrombus (8 × 10 mm) attached to the atrial side of a mechanical mitral valve who received an infusion of 25 mg of rTPA within 25 min and 6 h of intravenous infusion of unfractioned heparin in-between two rTPA doses. After four sets of rTPA infusion (100 mg), successful valve motion and decreased valve gradient were achieved [11]. This case is similar to one of the patients described above, which required a higher dose (50 mg) to recover valvular function.

Rapid thrombolysis protocols are associated with increased embolic risk, especially with larger thrombus (area greater than 0.8 cm²) [10]. Ozkan et al. described a 3-hour infusion protocol of streptokinase 1.5 million units, with no difference in recovery of valve function compared with ultra-slow protocols (15–24 h), but the rapid infusion group developing major complications [12]. Pape et al. reported a case of early massive embolism and death after thrombolysis of a mechanical mitral valve with a bolus of 20 mg of rTPA followed by an infusion of 10 mg/h for 3 h. Those cases may have discouraged the use of rapid protocols [13]. Contraindications for thrombolysis infusions are related to the risk of bleeding, but not related to the clinical condition (we included all patient with cardiogenic shock) [3,4,12].

The ultra-slow protocol can be implemented in other clinical scenarios as in pulmonary thromboembolism (PTE). Yilmaztepe et al. reported a case of a 72-year-old woman with PTE after knee surgery and a right atrial mobile mass within the tricuspid valve with high bleeding risk who received a slow infusion of rTPA (25 mg in 24 h), presenting minor bleeding from surgical site after 18 h of thrombolytic therapy.

Table 1

| Patient | Age (years) | Gender | Clinical onset at admission | INR at admission/time since prosthetic heart valve surgery | Thrombus size (cm) | ICU stay (days) |
|---------|-------------|--------|-----------------------------|----------------------------------------------------------|--------------------|----------------|
| A       | 78          | Female | Sudden dyspnea, pulmonary edema, cardiogenic shock | NA/15 months | 1.3 × 0.8 | 12 |
| B       | 59          | Male   | Progressive dyspnea and cardiogenic shock | 1.3/12 months | 1.2 × 0.8 | 10 |
| C       | 51          | Female | Progressive dyspnea and cardiogenic shock | NA/6 months | 0.7 × 0.9 | 14 |
| D       | 22          | Male   | Progressive dyspnea, respiratory failure and cardiogenic shock | NA/120 months | 1.4 × 0.9 | 21 |

Fig. 1. Biological prosthetic heart valves. Patients with biological prosthetic heart valve on mitral position. Images corresponds to patients A,C and D; A2 during systole, A2 during diastole, C1 during systole, C2 during diastole, D in diastole and D-3D corresponds to tridimensional reconstruction.
Echocardiographic control revealed a normal right ventricular function and the mass disappeared. [14]

One hypothesis considered for developing PVT is subtherapeutic anticoagulation control (low INR level). The evaluation of INR at the time of hospital admission may not represent the previous anticoagulation status related to the onset of thrombus formation [7].

Our study has inherent limitations and the results should be interpreted with caution. First, we reported a small series of patients and second, there were no for surgical management to make possible comparisons. Several centers have reported their own experience, which represent more visibility to this technique. [4]

In our study, there was no adverse cerebrovascular or embolic systemic events even though the thrombus was classified as large (greater than 1 cm). There were no cases of mortality even though the patients included were critically ill.

Although controversial, ultra-slow thrombolysis is presented as an available, feasible, safety and effective treatment option for patients with PVT with large thrombus who are not considered for cardiac surgery. This intervention helps to recover the valve function and compensate the heart failure. It must be performed under intensive monitoring and with echocardiographic surveillance. More evidence is required to have an adequate level of recommendation.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

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