Prosthetic Valve Thrombosis in Pregnancy
A Promising Treatment for a Rare and Mostly Preventable Complication

Patricia Casais, MD, PhD; Florencia Rolandi, MD, MSc

Prosthetic heart valve thrombosis (PVT) is a rare complication, with an estimated incidence of 0.1% to 5.7% per patient-year.1 However, during pregnancy, changes in the hemostatic system lead to a procoagulant state that increases the risk of PVT up to 10%.2 This maternal and fetal life-threatening complication is mostly preventable with long-term adequate anticoagulation therapy. When anticoagulation fails, treatment focuses on choosing between cardiac surgery and thrombolysis, 2 therapeutic strategies with risks and benefits for the mother and fetus that are difficult to assess.

The authors’ conclusions on the superiority of thrombolysis over surgery and the redefinition of the lytic option as a first-line therapy in pregnant patients with PVT require careful evaluation. Previous studies of cardiac surgery showing maternal and fetal mortality rates of 6% and 30%, respectively, were published a decade ago and were based mostly on coronary revascularization procedures. Since then, some recommendations have been included, such as appointing the procedure during the second trimester of pregnancy when possible, monitoring intraoperative fetal heart rate and uterine contractions, and maintaining normothermia during the surgery. In fact, results of more recent series of surgical management of valvular diseases in pregnant women seem to have improved.4,5 It is noteworthy that 4 of the 28 events were rethrombosis; 3 of them were recurrent obstructive thrombi occurring during the same pregnancy. The intervals between the first PVT treated with thrombolysis and the recurrence were 3, 6, and 10 weeks; the doses of tissue-type plasminogen activator used in the first event ranged from 25 to 100 mg. These observations raise the question of whether the first treatment should be considered indeed successful or whether the definition of thrombolytic success should include some time free of thrombosis besides the echocardiography and clinical criteria. However, an adequate anticoagulant treatment after thrombolysis is essential to achieve time free from thrombosis. After thrombolysis, anticoagulant treatments in these 3 patients were warfarin, low-molecular-weight heparin (LMWH) at a lower dose (than the dose at the time of the first event), and no anticoagulation at all. For clinicians, this is an important learning point from this study: PVT either de novo or recurrent requires optimizing anticoagulation after thrombolysis.

The observations by Özkan et al are in agreement with previous reports showing that risk factors for valve thrombosis during pregnancy are the same as in nonpregnant women, which are a prosthetic valve in the mitral position and subtherapeutic anticoagulation. These facts highlight the need for careful evaluation of the thrombotic risks in each particular patient and the importance of prevention with adequate anticoagulation.

Although evaluation of the efficacy of an anticoagulant treatment requires the assessment of time spent within the therapeutic range during follow-up, data not provided in the present study, anticoagulation was subtherapeutic in 93% of the patients at the time of PVT diagnosis regardless of the regimen used. Moreover, 3 episodes occurred in patients receiving no anticoagulant treatment at all, 1 of them in a 25-year-old woman with a previous PVT while on LMWH at 6 weeks’ gestation who recurred at the 12th week.

There is no optimal anticoagulant regimen during pregnancy for patients with mechanical heart valve prostheses because every therapeutic option has its drawbacks. Anticoagulant regimens in pregnant patients with prosthetic valve leaflets are associated with similar risks of maternal bleeding but with different embolic risks.

Warfarin throughout the entire pregnancy with an intended international normalized ratio of 2.5 to 3.5 is the safest for the mother, with an incidence of PVT <4%. LMWH twice daily with a target anti–factor Xa level of 0.7 to 1.2 IU/mL at 4 hours after injection is associated with an embolic risk of 7% to 16%. Unfractionated heparin twice daily to maintain activated partial thromboplastin time values twice the control or to achieve an anti–factor Xa level of 0.35 to 0.70 IU/mL is associated with the highest risk of thromboembolic complications (33%).6 However, published reports include very heterogeneous populations, different risk factors for thromboembolism, different valve types and position, unreported time

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Instituto de Investigaciones Epidemiológicas, Academia Nacional de Medicina de Buenos Aires, Buenos Aires, Argentina (P.C.); and Hospital Italiano de Buenos Aires, Buenos Aires, Argentina (F.R.).

Correspondence to Patricia Casais, MD, PhD, Pacheco de Melo 3081, C1425ASU, Buenos Aires, Argentina. E-mail casais@epidemiologia.anm.edu.ar

(Circulation. 2013;128:481-482.)

© 2013 American Heart Association, Inc.

Circulation is available at http://circ.ahajournals.org
DOI: 10.1161/CIRCULATIONAHA.113.004259

481
in therapeutic range, and unassessed compliance with anticoagulation in many studies.\(^7\)\(^9\)

Although warfarin was associated with the lowest risk of PVT, there is concern about its safety for the fetus. Unlike heparins, warfarin crosses the placenta and is associated with early fetal loss and with teratogenesis (0.6% to 10%), although embryopathy and spontaneous abortions might be dose-dependent with a very low risk when the dose is \(<5\) mg/d. Even though some authors recommend intravenous heparin before delivery (week 35–36),\(^10\) currently, one of the most accepted anticoagulant regimens for pregnant patients with prosthetic valves is switching to therapeutic doses of LMWH during the first trimester and restarting warfarin in the 13th week until the 35th to 36th week, when it is substituted with LMW again.

Still, American and European recommendations for anticoagulation in this scenario are not in full agreement. European Society of Cardiology guidelines discourage the use of LMWH during the entire pregnancy because of the thrombotic risks and consider the use of warfarin throughout pregnancy when the dose is \(<5\) mg/d (or phenprocoumon \(<3\) mg/d or acenocoumarol \(<2\) mg/d).\(^11\)

The American College of Chest Physicians’ antithrombotic therapy and prevention of thrombosis evidence-based clinical practice guidelines and American College of Cardiology/American Heart Association guidelines recommend (grade 2 recommendations) that low-dose aspirin be added in pregnant patients with mitral valve prostheses and with other high-risk factors (such as prior thromboembolic event or atrial fibrillation).\(^5\)\(^12\) In the study by Özkan et al, only 2 patients were receiving low-dose aspirin, and none of the patients with recurrent PVT were on aspirin after the first event.

Patients should be informed about the risks and benefits of each alternative, and they should be aware that compliance with the chosen treatment is essential to prevent complications. Factors to be considered when deciding on the best anticoagulant treatment include patient preferences, physician expertise, costs, and availability of monitoring.\(^13\)

Neonatal mortality in the series by Özkan et al was 20%, similar to the incidence reported in other studies. All abortions occurred before the 11th week of gestation (weeks 6, 9, and 11), in patients on both warfarin and LMWH, and between 1 and 5 weeks after thrombolysis. The small number of early abortions (only 5) precludes any conclusions being drawn on a causal effect of anticoagulation or thrombolysis. In addition, because early spontaneous miscarriages occur in 15% to 25% of pregnancies and are caused by random karyotype abnormalities of the embryo in 50% of the cases, chance cannot be ruled out.\(^14\)

In conclusion, the low-dose slow-infusion regimen of tissue-type plasminogen activator is promising because it seems safe for the mother and the fetus, but further research is needed to determine its efficacy. Thus, there is currently no evidence to recommend it as the first therapeutic choice in PVT because other factors such as gestational age at diagnosis, contraindications for thrombolytics, and hospital resources should be considered. Finally, focus on an adequate anticoagulation treatment, probably including low-dose aspirin in mitral valves, and patient compliance are crucial to avoid this severe complication.

**Disclosures**

None.

**References**


**Key Words:** Editorials ■ anticoagulants ■ pregnancy ■ heart valves ■ thrombolysis
Prosthetic Valve Thrombosis in Pregnancy: A Promising Treatment for a Rare and Mostly Preventable Complication
Patricia Casais and Florencia Rolandi

_Circulation_. 2013;128:481-482; originally published online June 28, 2013;
doi: 10.1161/CIRCULATIONAHA.113.004259

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/128/5/481

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/