Thrombosis in Continuous Flow Left Ventricular Assist Devices: Our Clinical Experience With Medical and Surgical Management

U. Köksel*, O. Erbasan, Ö. Bayezid, C. Kemaloğlu, S. Özçobanoğlu, İ. Gölbaşı, and C. Türkay

Department of Cardiovascular Surgery, Akdeniz University Hospital, Antalya, Turkey

ABSTRACT

Background. Continuous-flow left ventricular assist devices (CF-LVADs) such as the HeartMate II and HeartWare left ventricular assist device are important alternatives to heart transplantation. Thrombosis is a serious complication in both devices and we present our approach to treating thrombosis and analysis of predisposition factors.

Methods. Our center's CF-LVADs database was retrospectively reviewed for pump thrombosis between January 2011 and January 2015. The patients were grouped for pump thrombosis (n = 13) and nonpump thrombosis (n = 85). Patients with pump thrombosis were further divided by device type (n = 5 HeartMate II and n = 8 HeartWare left ventricular assist device). Predisposition factors for pump thrombosis, our treatment approach, and patient outcomes were evaluated.

Results. Pump thrombosis was diagnosed in 13 of 98 patients. The rate of pump thrombosis did not differ between the 37 HeartMate II and 61 HeartWare left ventricular assist device patients. High mean arterial blood pressure ($P < .01$) and noncompliance with the anticoagulation regimen ($P = .04$) were associated significantly with thrombosis. Twelve patients with stable hemodynamics were treated initially with intravenous tissue plasminogen activator and 1 patient who had end-organ damage underwent pump exchange. Two patients failed to respond to medical treatment and underwent pump exchange. Two patients with recurrent thrombosis were administered intracardiac tissue plasminogen activator. Five patients died after medical treatment and 4 deaths were due to cerebral hemorrhage.

Conclusions. Avoiding increased mean arterial blood pressures and ensuring optimal anticoagulation may help to decrease pump thrombosis. In patients with pump thrombosis, thrombolytic therapy is an alternative that is less invasive than pump exchange, but carries the risk of hemorrhage and thromboembolism.

DESPITE advances in medical therapy, mortality and morbidity in patients with advanced heart failure remains high [1]. With an increasing number of patients with advanced heart failure and an ever-limited supply of donor organs, use of continuous-flow left ventricular assist devices (CF-LVADs) for bridge to transplant, bridge to recovery, or destination therapy has increased [2] along with the complications associated with CF-LVADs [3]. The HeartMate II (HMII) ventricular assist device (Thoratec Corp., Pleasanton, CA) and the HeartWare left ventricular assist device (HVAD; HeartWare Inc. Framingham, MA) are the most commonly used CF-LVADs.

Pump thrombosis is a serious complication that is potentially fatal owing to obstruction of blood flow and risk of thromboembolism. Even though the exact mechanism of thrombus formation is not known, a possible cause could be contact of blood components with the artificial surface of the device [4]. Moreover, inadequate anticoagulation or antiplatelet therapy may precipitate a thrombus event.

*Address correspondence to Umut Köksel, Department of Cardiovascular Surgery, Akdeniz University Faculty of Medicine, Antalya 07070, Turkey. E-mail: umutkoksel@hotmail.com

0041-1345/16
http://dx.doi.org/10.1016/j.transproceed.2016.04.025

Table 1. Baseline Characteristics of Pump Thrombosis and Nonthrombosis Groups, Pump Thrombosed HMII and HVAD*

Variables	HMII Thrombus (n = 5)	HVAD Thrombus (n = 8)	P*	All device Thrombus (n = 13)	All Device No Thrombus (n = 85)	P*
Demographics (preoperative)						
Age (y)	57.2 ± 10	48.5 ± 8.5	.1	51.8 ± 9.7	53.9 ± 1.1	.34
Male sex (%)	4 (80)	8 (100)	.38	12 (92)	71 (83)	.68
Ischemia etiology (%)	2 (40)	6 (75)	.29	8 (61)	37 (43)	.22
Body mass index (kg/m^2)	27.3 ± 1.7	28.9 ± 3.3	.3	28.3 ± 2.8	27.8 ± 3	.44
Left ventricular ejection fraction	20.2 ± 1.6	20.6 ± 2.6	.94	20.4 ± 2.2	21.3 ± 2.6	.2
Creatinine (mg/dL)	1.42 ± 0.4	1.35 ± 0.4	.66	1.37 ± 0.4	1.45 ± 0.6	.37
INTERMACS profile level (%)						
1	1 (20)	1 (12.5)	.95	2 (15.4)	12 (14.1)	.98
2	2 (40)	3 (37.5)	.98	5 (38.5)	21 (24.7)	.32
3	2 (40)	3 (37.5)	.98	5 (38.5)	37 (43.5)	.73
4–7	0	1 (12.5)	.95	1 (7.7)	15 (17.6)	.68
Comorbidities (%)						
Diabetes	2 (40)	2 (25)	.93	4 (30.8)	27 (31.8)	.98
Hypertension	2 (40)	4 (50)	.94	6 (46.2)	37 (43.5)	.98
History of smoking	4 (80)	6 (75)	.96	10 (76.9)	48 (56.5)	.22
Cardiac surgery history	1 (20)	2 (25)	.96	3 (23.1)	19 (22.4)	.98
Postimplantation						
Postoperative mean blood pressure (mm Hg)	83.2 ± 4	82.6 ± 5.6	.76	82.8 ± 4.8	74.4 ± 5.5	<.01†
Noncompliance with anticoagulation regimen	1 (20)	3 (37.5)	.94	4 (30.8)	9 (10.6)	.04†
Time to event (d)‡	264 ± 158	532 ± 206	.1	395 ± 216	-	-
Recurrent thrombosis‡	0 (0)	2 (25)	.48	2	-	-

Continuous data are presented as mean value ± standard deviation and categoric data as the percentage.

The baseline parameters are reported for thrombosis patients with HMII (n = 5) in the first column, with HW (n = 8) in the second column, for all thrombosis patients (n = 13) in the fourth column and nonpump thrombosis patients (n = 85) in the fifth column. *P* values between thrombosis patients with HMII and HW implants are reported in the third column, and between all thrombosis patients and nonthrombosis patients in the sixth column.

Abbreviation: INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support

*Statistical testing for significance was performed using Fisher's exact test for categoric data, 2 independent samples *t* tests for parametric data and Mann–Whitney *U* test for nonparametric data.

†Statistically significant.

‡Time to event and recurrent thrombosis were not used for nonthrombosis patients.

Hemolysis, heart failure, abnormal pump parameters, and abnormal auscultation findings are potential indications of pump thrombosis. Serum lactate dehydrogenase >2.5 times the upper limit of normal at 72 hours after implantation can be an indication of pump thrombosis [5,6]. As hemolysis progresses, the patient may develop hemoglobinuria, anemia, and hyperbilirubinemia. In addition, pump thrombosis can be observed at the tip of pump inflow cannula on echocardiography, or blood inflow and outflow can be evaluated with Doppler sonography.

Medical therapy treatment for pump thrombosis often consists of unfractionated heparin (UFH), intravenous (IV) or intracardiac tissue plasminogen activator (tPA), and glycoprotein IIb/IIIa inhibitors such as eptifibatide used individually or in combination. Surgical pump exchange is an alternative to medical treatment. Successful treatment of pump thrombosis is defined as clinical resolution of symptoms, improving hemolytic markers, and return to normal pump parameters.

METHODS

In this study, we present our clinical experience in the diagnosis, treatment, and prevention of pump thrombosis in HMII or HVAD patients. The CF-LVAD database of our center was retrospectively reviewed to determine patients with pump thrombosis between January 2011 and January 2015. Pump thrombosis was diagnosed based on abnormal pump parameters, an increase in lactate dehydrogenase owing to hemolysis, recurrent symptoms of heart failure, and transthoracic echocardiography. Of the 98 CF-LVAD bridge to transplant and destination therapy patients (37 HMII, 61 HVAD), 13 had pump thrombosis. Patients with pump thrombosis were further grouped based on device—HMII (n = 5) and HVAD (n = 8). Factors that may predispose to pump thrombosis were compared among pump thrombosis and nonpump thrombosis groups and also among HMII and HVAD groups with thrombosis. Treatment modalities and their outcomes were also evaluated.

All patients with HMII and HVAD implants received the same anticoagulation (target international normalized ratio [INR] of 2–3) and antiplatelet therapy (acetylsalicylic acid 100 mg). For patients with symptoms of pump thrombosis who were stable hemodynamically and had no end-organ damage, our stepped approach included first treating with IV tPA and UFH. IV tPA consisted of a bolus of 15 mg, then a 0.75 mg/kg (maximum 50 mg) infusion over 30 minutes, followed by a 0.5 mg/kg (maximum 35 mg) infusion over 1 hour. The total maximum tPA dose was 100 mg. If no resolution was observed despite a maximum tPA dose, patients underwent pump exchange. In patients who presented with onset of end-organ damage or with unstable hemodynamics, emergency pump exchange was the chosen treatment.

Patients with recurring thrombosis received intracardiac tPA, which is more invasive compared with IV treatment. Intracardiac