Prosthetic Valve Thrombosis in the Acute Phase of the Stroke: Relevance of Detection and Follow-Up

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Background: Stroke may be the first symptom of prosthetic valve thrombosis (PVT); therefore, rapid diagnosis and therapy are crucial. We aimed to evaluate the prevalence, main predictors, and long-term clinical evolution of patients with PVT in the acute phase of stroke. *Methods:* We studied consecutive acute ischemic stroke patients with prosthetic heart valves who underwent emergent transesophageal echocardiography (TEE) during a 5-year period. Two groups were defined depending on the presence of PVT (PVT or non-PVT groups). Baseline characteristics, TEE findings, and international normalized ratios (INRs) at the stroke event were registered. Follow-up visits and TEE control examinations were performed. *Results:* Sixty-seven patients were registered. TEE was performed within the first week in 85% of patients (n = 57). PVT was diagnosed in 41.8% of cases (n = 28). Clinical severity and baseline INR level showed no differences when the PVT and non-PVT groups were compared. The presence of PVT was associated with the mitral valve location as compared with the aortic valve location (75% versus 25%, $P = .003$), the presence of spontaneous echocontrast (64.3% versus 35.9%, $P = .022$), and low ejection fraction (66.7% versus 32.7%, $P = .019$). The PVT group showed a trend toward higher percentage of recurrence (10.7% versus 2.5%, $P = .102$) in the follow up period (mean follow-up 25 months). *Conclusions:* The detection of PVT in the acute stroke phase was relevant, as the stroke recurrence rate was considerable. Therefore, all patients with prosthetic heart valve should undergo emergent TEE. **Key Words:** Ischemic stroke—prosthetic valve thrombosis—prognosis—transesophagic ecocardiography.

Introduction

Twenty percent of prosthetic heart valve carriers have a stroke despite anticoagulant treatment.[1] Prosthetic valve thrombosis (PVT) pathogenesis is based on a complex interaction between transprosthetic flow and prothrombotic factors.[2] According to New York Heart Association, PVT is classified according to valve leaflet mobility as nonobstructive prosthetic valve thrombosis (NOPVT) and obstructive prosthetic valve thrombosis (OPVT). Both types may cause embolic phenomena, but only OPVT is associated with hemodynamic instability.

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Stroke may be the first symptom of thrombosis in NOPVT cases.[3,4] Moreover, 25% of NOPVT patients have recurrent embolic events regardless of preventive treatment.[5] Transesophageal echocardiography (TEE) detects PVT by the visualization of hyperechogenic mass attached on the valve surface in a 2-dimensional modality. Spontaneous echocontrast (SE) in left atria and low left ventricle ejection fraction (low EF) are common findings related to PVT detection.[6]

The present study aimed to describe the prevalence and main predictors of PVT in acute stroke patients, and to describe its clinical and follow-up relevance.

Methods

We designed a retrospective single-center study from our prospective database registry of consecutive acute stroke patients with mitral or aortic heart valve prosthesis from 2010 to 2015. All patients were examined by a certified neurologist and underwent a complete workup evaluation (computed tomography or magnetic resonance imaging, Doppler ultrasound examination, blood test, and electrocardiogram) and a TEE examination. Patients with clinical suspicion of endocarditis, an atherotrombotic cause of stroke (>50% of extra- or intracranial vessel stenosis),[7] or carriers of biological heart valves were excluded. Every TEE was performed by an expert cardiologist following the same protocol test consisting of the multiphase array probe insertion inside the patients' esophagus, remaining in the left lateral decubitus. The standard 4-chamber view was obtained in 0° grades by positioning the probe in the mid-esophagus behind the left atrium to check the mitral prosthesis characteristics and sweeping the mitral prosthesis from 0° to 120°. Several echocardiography loops were obtained to observe the different chambers, the mitral and left ventricle walls. Aortic prosthesis was imaged in the longitudinal plane in 120° and in the transverse plane in 30°-40°, positioning the probe with the same method. Prosthetic valve mobility and structure were accurately evaluated. PVT was defined as mobile and pedunculated hyperechogenic structures, attached to the surface of the valve. Two groups were defined according to the presence of PVT (PVT group versus non-PVT group). OPVT was deemed if the hyperechogenic structure blocked leaflet motion.[6] SE was defined as hyperechogenic, smokelike images around the left atrium. Ejection fraction below 50% was considered low EF. Stroke severity was graded by the National Institutes of Health Stroke Scale (NIHSS).[8] Transient ischemic attack (TIA) and cortical symptoms (aphasia, hemianopia, gaze palsy, or neglect) were registered separately. International normalized ratios (INRs) at the stroke event (baseline INR) were determined, and prior-to-stroke INR levels were also analyzed. Patients were classified according to therapeutic anticoagulation (INR > 2.5) or subtherapeutic anticoagulation (INR < 2.5) depending on baseline INR level. Clinical follow-up visits were performed; in cases of recurrence or PVT detection, control TEE was ordered.

Statistical significance for intergroup differences for categorical variables was assessed by χ^2 test using SPSS 17.0 (SPSS Inc., Chicago, IL/USA). In the follow-up period, Kaplan–Meier test was used to assess the risk of stroke recurrence in the PVT and non-PVT groups. Multivariate analysis was performed using the Cox regression test, including the INR level at the stroke recurrent episode, SE, low EF, and atrial fibrillation.

Results

Sixty-seven patients were studied. The mean age was 65 years (standard deviation: 11.4) and 37.3% of the patients (n = 25) were male. The TIA rate was 32.8% (n = 22), and the median NIHSS score was 3 (interquartile range: 1-9). TEE was performed within the first week in 85% of the patients (n = 57). Seventy-three percent (n = 49) had aortic or mitral prosthesis and 26% (n = 18) had both. PVT was diagnosed in 41.8% of the patients (n = 28). Most PVTs occurred on the mitral valve (75%, n = 21) than in the aortic valve (25%, n = 7) (P = .003).

Comparing PVT and non-PVT groups, we did not find any difference in vascular risk factors and clinical pattern (TIA, cortical symptoms, or baseline NIHSSS score) (Table 1). With regard to echocardiographic findings, SE (64% [n = 18] versus 35.9% [n = 14], P = .022) and low EF (66.7% [n = 10] versus 32.7% [n = 16], P = .019), respectively, were associated with PVT.

We found the same rate of PVT detection in patients with therapeutic and subtherapeutic INR levels (PVT 35.7% [n = 10] versus non-PVT 35.9% [n = 14], P = .988) (Fig 1). Considering the INR level previous to stroke, we observed no differences neither (PVT 35% [n = 7] versus non-PVT 45.5% [n = 10], P = .491).

All PVT patients received unfractionated heparin or low–molecular-weight heparin, and 25% (n = 7) required also valve replacement surgery: in 3 cases due to nonresponsive OPVT and in 4 cases due to NOPVT progression. Eighty-two percent of patients (n = 23) underwent control TEE after PVT treatment, showing PVT resolution in 73.9% (n = 17) and persistence in 26.09% (n = 6). Patients with OPVT showed a trend toward higher mortality (40% [n = 2] versus 8.7% [n = 2], P = .07).

Fifty-nine percent of patients (n = 40) completed 25 months of median time of follow-up; 27 patients did not complete a year of follow-up (6 patients died with regard to stroke episode). During follow-up, 10% (n = 4) of the patients had stroke recurrence (Fig 2). There was a trend toward higher stroke recurrence in the PVT group (log rank P = .102), with a stroke recurrence cumulative risk of 22.1% in the PVT group versus 5.3% in the non-PVT group for a 30-month period. There were no differences in the multivariate analysis including INR level at the stroke recurrent episode, SE, low EF, and atrial fibrillation.