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Original Article

Left atrial thrombus and prognosis after anticoagulation therapy in patients with atrial fibrillation

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Summary
Background: Anticoagulation therapy reduces the risk of thromboembolic events by two-thirds in patients with atrial fibrillation (AF). The prevalence of left atrial thrombus (LAT) in AF patients with anticoagulation therapy has not been fully investigated.
Purpose: To investigate the prevalence of LAT and its impact on the outcomes in patients with nonvalvular AF after anticoagulation therapy.
Methods: This study consisted of 231 patients with nonvalvular AF who had transthoracic (TTE) and transesophageal echocardiographic (TEE) examinations more than 3 weeks after anticoagulation therapy. The clinical and echocardiographic characteristics were evaluated.
Results: LAT was observed in 13 (8.8%) of 148 patients with sub-therapeutic anticoagulation, and in 3 (3.6%) of 83 patients with sufficient anticoagulation. The presence of LAT was associated with higher $CHADS_2$ score, decreased LA volume changes and the presence of spontaneous echocardiographic contrast (SEC) in patients with sub-therapeutic anticoagulation.

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Patients with LAT after sufficient anticoagulation were male with permanent AF who had decreased left ventricular systolic and diastolic function and dilated LA on TTE and SEC, and reduced appendage flow velocity on TEE. Patients with LAT had worse cardiovascular outcomes compared with those without LAT ($p = 0.02$).

Conclusions: We demonstrated that LAT was a univariate risk factor associated with worse cardiovascular outcomes, which was observed in 8.8% of patients with sub-therapeutic anticoagulation and 3.6% of patients with sufficient anticoagulation.

Introduction

Nonvalvular atrial fibrillation (AF) increases in prevalence as the population ages [1], which increases the long-term risk of stroke and mortality from all causes [2—4]. Anticoagulation therapy reduces the risk of thromboembolic events by two-thirds in patients with AF [5,6] indicating that, in some AF patients, it may not be effective in preventing thromboembolic events. The left atrium (LA), especially its appendage, is the presumed site of thrombus formation as a result of blood stasis, which is thought to cause stroke in patients with AF [7—12]. Anticoagulation therapy is controlled for international normalized ratio (INR) of 2.0 in elderly patients and 2.5 for younger patients in Western countries [13,14]. In contrast, anticoagulation therapy is controlled for INR between 2.0 and 3.0 in patients with ages of younger than 70 years, and between 1.6 and 2.6 in patients with ages of 70 years or older in the Japanese population. However, the incidence of LA thrombus (LAT) in AF patients with anticoagulation therapy has not been fully investigated, especially in association with whether sufficient anticoagulation therapy with INR greater than or equal to 2.0 for at least 3 weeks is achieved or failed. Furthermore, the impact of the presence of LAT on the outcomes has not been fully determined. Therefore, the purpose of this study was to investigate the clinical and echocardiographic characteristics of AF patients with LAT after more than 3 weeks of anticoagulation therapy and to compare the outcomes in patients with and without LAT.

Methods

Study population

The records of 231 patients with AF who had transthoracic (TTE) and transesophageal echocardiographic (TEE) examinations more than 3 weeks after anticoagulation therapy were reviewed at Osaka Ekisaikai Hospital and the Sakakibara Heart Institute. Their data were abstracted from the clinical and echocardiography databases from October 2005 to September 2010, and retrospectively analyzed. Patients were excluded if they had (1) history of prior cardiac surgery, (2) moderate or more severe valvular diseases, or (3) congenital heart disease. Patients were referred to TEE examination for decisions with regard to cardioversion. No patients had probable thrombus on a previous TEE examination.

The clinical risk factors, including ages of 75 years or older, hypertension, diabetes, congestive heart failure, and history of cerebral ischemia, were evaluated in each individual, and then the $CHADS_2$ score was calculated [15]. Based on the results of laboratory examinations, patients were divided into 2 groups: sufficient anticoagulation and sub-therapeutic anticoagulation. When 2 consecutive laboratory examinations with the interval of more than 3 weeks showed INR greater than or equal to 2.0, anticoagulation therapy was considered as sufficient. Other patients were classified into the group with sub-therapeutic anticoagulation. The INR value just before TEE examination (2 ± 5 days) was also provided. This study was approved by the ethics committees of Osaka Ekisaikai Hospital and the Sakakibara Heart Institute, respectively.

Transthoracic echocardiography

Two-dimensional TTE was performed in the standard manner with several commercially available echocardiographic systems with tissue Doppler echocardiographic capabilities; Sonos 5500 and IE-33 (Philips Medical Systems, Andover, MA, USA), Sequoia 512 (Siemens, Mountainview, CA, USA), Vivid 7 (GE Medical Systems, Milwaukee, WI, USA), or Aplio SSA-770 (Toshiba Medical Systems, Tokyo, Japan). Echocardiographic images were obtained in standard parasternal and apical views and digitally stored. After carefully choosing the highest possible quality image and regular preceding R-R intervals using the digital storing system, echocardiographic measurement was reviewed to obtain the following echocardiographic parameters for this study.

1. Left ventricular (LV) end-diastolic and end-systolic volumes were obtained to calculate LV ejection fraction using Simpson's method from apical 4- and 2-chamber views.
2. LV mass was calculated based on the area—length formula [16].
3. Maximum and minimum LA volumes were measured by the Simpson's rule methods from apical 4- and 2-chamber views. LA volume change was calculated as (maximum volume − minimum volume)/maximum volume × 100.
4. Pulsed-wave Doppler examination of mitral inflow was performed to measure peak velocity (E) and deceleration time of the early diastolic flow. Early diastolic mitral annular velocity (e') was also measured from tissue Doppler imaging in the septal wall. The ratio of E to e' was then calculated (E/e').
5. After recording the tricuspid systolic velocity with continuous-wave Doppler, right ventricular (RV) systolic pressure was calculated using the simplified Bernoulli equation [17], adding the right atrial pressure estimated