Long Term Fate of Left Atrial Thrombi and Incidence of Cerebral Embolism under Continuous Anticoagulation Therapy

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Background: Patients (pts) with atrial fibrillation (AF) and atrial thrombi are known to have an increased risk for cerebral embolism. However, there is little known about the clinical course of atrial thrombi and the incidence of cerebral embolism in those patients during anticoagulation therapy. The high sensitivity of diffusion-weighted imaging (DWI) suggests that this technique could provide an improved estimate of cerebral ischemic events associated with the presence of left atrial thrombi.

Purpose: The aims of this prospective study were 1. to evaluate the incidence of clinically silent and apparent cerebral embolism in patients with newly diagnosed atrial fibrillation and atrial thrombi by using DWI, to assess 2. the long term fate of atrial thrombi under continued anticoagulation therapy and 3. the incidence of cerebral embolism during a follow-up period of 12 months with continuous anticoagulation therapy.

Material and methods: Study group inclusion criteria were: 1. newly diagnosed AF with evidence of left atrial thrombi detected by TEE and 2. new start of anticoagulation therapy [International Normalized Ratio (INR) 2.0-3.0]. The study group consisted of 32 pts (18 males, 14 females) with a mean age of 63 +/- 10 years. 19 pts (12 males, 7 females; mean age 55 +/- 12 years) with 1. newly diagnosed AF but no evidence of atrial thrombi and 2. equivalent anticoagulation regimen as in study group served as control group. The following procedures were performed in a serial and prospective manner at the beginning of the study, at 1, 3, 4 and 12 months in both groups: a) Magnetic resonance imaging (MRI) studies of the brain including a diffusion-weighted, single-shot, spin-echo echoplanar sequence at a 1.5 Tesla Gyroscan ACS-NT scanner [Philips Medical Systems; maximal gradient strength 21 mT/m, increase time 0.2 ms, maximal slew rate 105 T/m s; diffusion gradient b values of 0, 500, and 1000 s/mm^2; repetition time (TR) 4000 ms; echo time (TE/TEd) 120 ms/85 ms; slice thickness 6 mm; matrix 101 x 256)], b) transesophageal echocardiographic studies (TEE) for detection of thrombi in the left atrium (LA) or LA appendage, and assessment of thrombus echogenity, left ventricular ejection fraction, LA volume, and peak emptying velocities of the LA appendage and c) clinical neurologic assessment.

Results: 11 out of 32 pts (34%) had bright diffusion lesions on the initial MR studies consistent with acute cerebral emboli; in 10/11 pts (91%) emboli were clinically silent. In 4 out of 32 pts (13%) DWI depicted new or additional cerebral emboli (n=9) during the follow-up period despite continuous anticoagulation therapy. 2 (50%) of these patients had clinically apparent neurologic deficits. In the control group 1 out of 19 pts (5%) had evidence of cerebral embolism as assessed by DWI at the beginning of the study while no embolism occurred during the 12 month follow-up. 16% (5/32) of left atrial thrombi in the study group resolved completely under anticoagulation therapy within 4 weeks, 53% (17/32) resolved within 12 months. Pts with cerebral embolism revealed by DWI had significantly larger thrombi (as assessed by TEE on the initial TEE: 3.2 +/- 2.2 cm^2 vs. 1.0 +/- 0.6 cm^2; p=0.003) and lower thrombus echogenity (p=0.04) compared to pts without embolism. No significant correlation existed between peak emptying velocities of the LA appendage, left ventricular ejection fraction and LA volume with cerebral embolism (p<0.05).

Conclusion: 1. The incidence of clinically inapparent cerebral emboli in pts with newly diagnosed AF and atrial thrombi is much higher than the incidence of clinically apparent emboli and has been underestimated in the past. 2. Only 53% of atrial thrombi disappear within 12 months under anticoagulation therapy. 3. New cerebral embolism may occur even with continued effective anticoagulation therapy in 13% of pts. 4. Larger thrombus size and low thrombus echogenity are associated with a significant (p<0.05) higher risk for cerebral embolism.

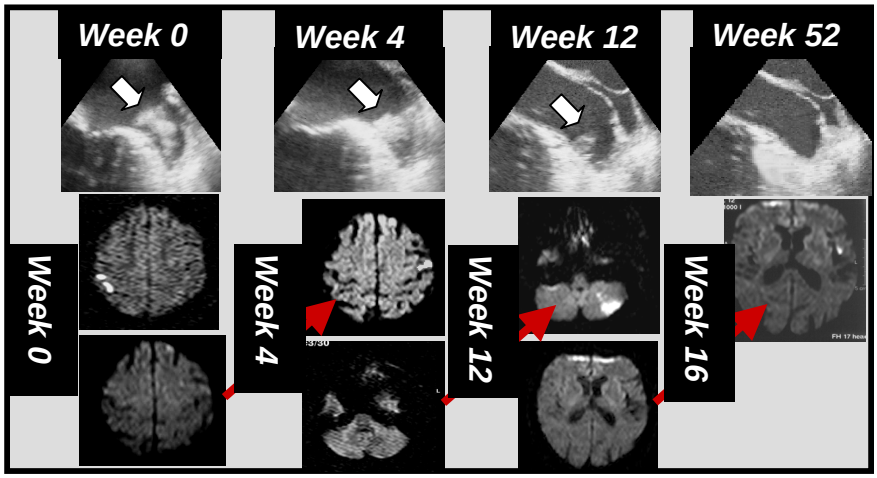

Fig. 1 Thrombus in the LA appendage (white arrows) resolving under continuous anticoagulation from week 0 to week 52 detected by TEE (upper row), associated with multiple cerebral infarcts as assessed by serial DWI exams (middle und lower row).