CLINICAL IMAGE

Rivaroxaban twice daily for lysis of left atrial appendage thrombus: a potential new therapeutic option

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Rivaroxaban is a direct factor Xa inhibitor used in the treatment and prevention of thromboembolic events. In patients with atrial fibrillation (AF), a single daily dose is recommended,[1] whereas in those with acute deep vein thrombosis or pulmonary embolism, rivaroxaban should be used twice daily for 3 weeks. Considering the relatively short half-life of rivaroxaban (7–11 hours) and rare but known cases of a persistent thrombus in the left atrial appendage (LAA) despite the use of rivaroxaban once daily,[2] the question arises of whether some patients with AF should receive the drug twice daily.

We present a case of a 45-year-old obese man with hypertension and persistent AF with a CHA_2DS_2-VASc score of 1 and a HAS-BLED score of 0, who was admitted to our center for AF ablation. The patient had been on chronic therapy with rivaroxaban (20 mg once daily), β-blockers, and angiotensin-converting enzyme inhibitors. Routine preablation transesophageal echocardiography (TEE) revealed a thrombus in the LAA (FIGURE 1A), and ablation was postponed. The patient entered the ongoing Riva-Twice study (approved by a local ethics committee; No. 49/PB/2015), and the dose of rivaroxaban was increased to 15 mg twice daily. After 8 weeks, the patient underwent the second TEE, which excluded the presence of the LAA thrombus (FIGURE 1B). Moreover, on the day before ablation, intracardiac echocardiography was performed and confirmed no thrombus in the LAA (FIGURE 1C).

Blood samples were taken during both treatment regimens 3, 12, and 24 hours after the morning dose of rivaroxaban to measure the activity of the anti-Xa factor. We used the anti-factor Xa chromogenic method (Diagnostica Stago, Asnières-sur-Seine, France), with the therapeutic range of plasma rivaroxaban levels between 20 and 500 ng/ml, which is sufficient to define the therapeutic level of rivaroxaban during its administration. The measurements showed a markedly higher activity of anti-Xa factor at the studied time points during treatment with rivaroxaban, 15 mg twice daily, compared with a standard dose of 20 mg once daily (FIGURE 1D). No bleeding complications occurred.

In the available literature, there are single case reports demonstrating the efficacy of the recommended once-daily dose of rivaroxaban in dissolving LAA thrombi.[3,4] An ongoing multicenter study[5] evaluates the efficacy of oral rivaroxaban (once daily) in dissolving an LAA thrombus in patients with nonvalvular AF. However, there are patients in whom the thrombus persists despite therapy.

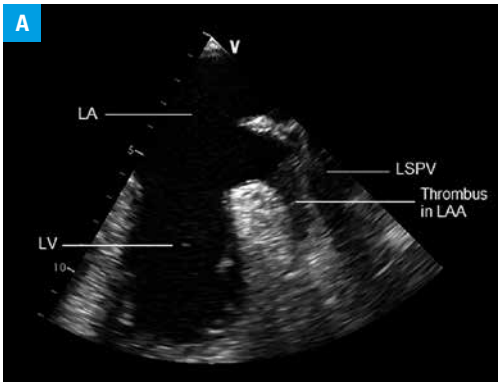

FIGURE 1 **A** – Transesophageal echocardiography (TEE) showing a thrombus in the left atrial appendage (LAA) during rivaroxaban therapy (once-daily regimen); **B** – TEE showing the LAA without a thrombus during rivaroxaban therapy (twice-daily regimen); **C** – intracardiac echocardiography from the pulmonary artery, showing the resolution of the thrombus in the LAA after rivaroxaban therapy (twice-daily regimen); **D** – anti-factor Xa activity expressed as rivaroxaban concentrations (once-daily and twice-daily regimens)
Abbreviations: LA, left atrium; LSPV, left superior pulmonary vein; LV, left ventricle; PA, pulmonary artery

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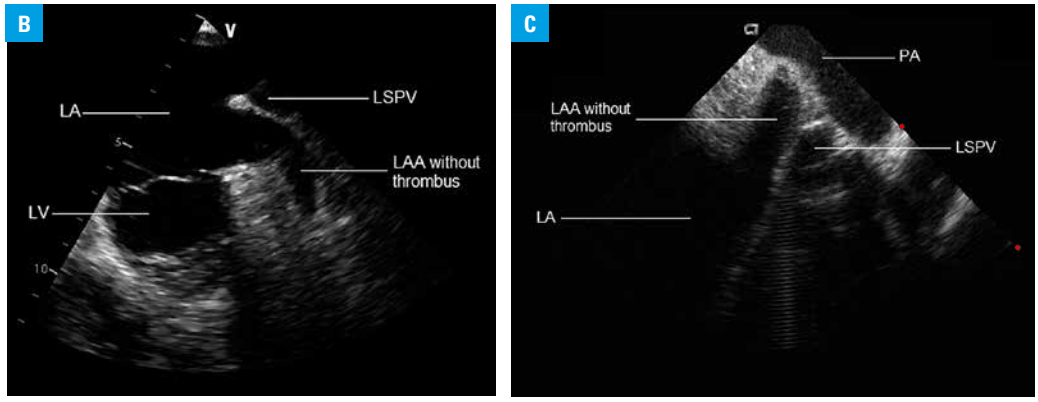

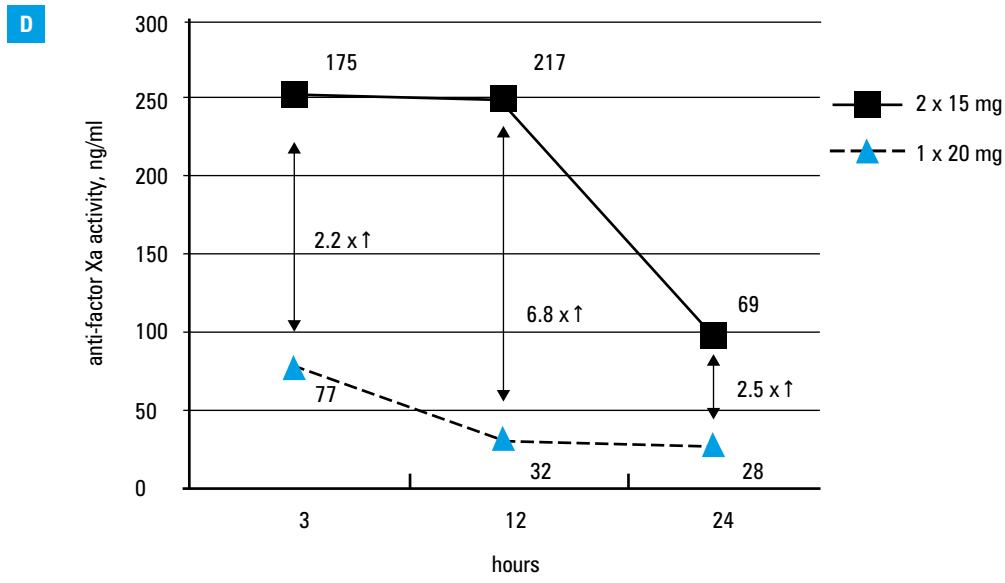

To our knowledge, this is the first report showing that the use of rivaroxaban twice daily may be effective in dissolving an LAA thrombus in this patient group. Increased anti-Xa factor levels during rivaroxaban therapy (twice-daily regimen) were associated with the resolution of the thrombus. In our patient, the relatively low plasma levels of rivaroxaban (once daily) may by partially attributed to the rapid elimination of the drug (a young and healthy patient without renal or hepatic impairment). It may be speculated that especially in such patients, the once-daily regimen may be insufficient for the prevention of thromboembolic events. Further prospective studies are needed to confirm our preliminary findings.

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