Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice, affecting slightly less than 1% of the general population. Patients with AF suffer from a decrease in functional capacity secondary to a combination of palpitations, dyspnea, myocardial ischemia, congestive heart failure and hypotension. In addition, unorganized atrial electrical and mechanical activity result in blood stasis and the formation of atrial thrombi placing the patient at risk of systemic thromboembolism. It is therefore important, if feasible, to attempt cardioversion (CV) to normal sinus rhythm (NSR) in these patients.

The most concerning complication of CV in AF is systemic thromboembolism, and more specifically stroke. In 1960, Goldman reported a 1.5% embolization event rate in 400 AF patients undergoing chemical CV who had not received anticoagulation. This study proposed for the first time that anticoagulant therapy initiated prior to CV could stabilize pre-existing thrombus allowing it to organize and adhere to the atrial wall. The first report of thromboembolism associated with electrical CV occurred in 1963 when Lown et al. examined 50 AF patients undergoing chemical CV who had not received anticoagulation. This study proposed for the first time that anticoagulant therapy initiated prior to CV could stabilize pre-existing thrombus allowing it to organize and adhere to the atrial wall. The first report of thromboembolism associated with electrical CV occurred in 1963 when Lown et al. examined 50 AF patients undergoing chemical CV who had not received anticoagulation.
determine if early TEE-guided CV was safer than conventional therapy. The Assessment of Cardioversion Using Transesophageal Echocardiography (ACUTE) pilot study was the first prospective, randomized trial to examine patients with AF of > 2 days duration undergoing clinically indicated CV. A total of 126 patients from 10 international clinical sites were randomized to conventional anticoagulation or a TEE-guided approach with short-term anticoagulation. CV was postponed in 7 (13%) patients due to atrial thrombi identified on TEE. The TEE-guided strategy resulted in early CV without embolization in all patients without atrial thrombi detected on TEE. In addition, CV was performed much earlier with this strategy than with the conventional method (0.6 weeks vs. 4.7 weeks). Based on the results of this pilot study, the ACUTE multicenter trial prospectively enrolled 1222 patients with AF of > 48 h duration and assigned them to TEE-guided (n = 619) or conventional therapy (n = 603). Although there was no difference in the rate of embolization at 8 weeks follow-up, the TEE-guided group had a significantly lower rate of hemorrhagic events. In addition, this group had a significantly shorter time to CV compared to the conventional-therapy group (3.0 ± 5.6 vs. 30.6 ± 10.6 days, p < 0.001). At 8 weeks follow-up, there were no differences in the rates of death, maintenance of NSR, or in functional status between the two groups. This randomized trial suggested that a TEE-guided approach with a short period of anticoagulation may be considered a clinically efficacious alternative to conventional therapy in AF patients scheduled for electrical CV.

The current study by Corrado et al. showed that prior to electrical CV of AF, subtherapeutic levels of anticoagulation using the conventional anticoagulant approach may expose patients to systemic thromboembolism. The study is important because it demonstrates the difficulties in maintaining therapeutic anticoagulation prior to CV using conventional-therapy guidelines. Left atrial appendage (LAA) thrombus was identified on TEE in 4 (9.8%) of 41 patients with at least 1 subtherapeutic INR, a disturbingly high prevalence. However, this value is very consistent with the findings of Shen et al. who retrospectively examined the prevalence of atrial thrombi in 182 AF patients who were anticoagulated for ≥ 3 weeks with at least 1 subtherapeutic INR. On pre-CV TEE, LAA thrombi were identified in 18 (9.9%) patients. In the current study by Corrado et al., patients with thrombi were found to have lower INR values, a higher prevalence of atrial spontaneous echo contrast (SEC) and lower LAA emptying velocities. It is important to note that the mere presence of atrial thrombus on TEE portends a poor prognosis as shown previously. Of the 4 patients with atrial thrombus in this study, follow-up at 1 year documented 2 TIA's, 2 major bleeds and 2 deaths compared to only 1 TIA in the 37 patients without atrial thrombus.

Based on this study, it is therefore essential to maintain therapeutic levels of anticoagulation in the 3 weeks preceding CV. When conventional guidelines are used, subtherapeutic INR values are extremely common and frequently result in prolongation of prophylactic anticoagulation prior to CV. Schlicht et al. demonstrated a widespread failure to follow the ACCP’s Third Consensus Conference of Antithrombotic Therapy recommendations. In 51 retrospectively identified patients who underwent elective CV, 14 (27.5%) patients failed to receive a complete 3-week course of anticoagulation prior to their procedure. Similarly, in 1152 patients undergoing CV, Carlsson et al. have shown that the ACCP guidelines are not followed in 59% of patients ≥ 65 years of age. The ACUTE trial highlighted some of the difficulties in following the conventional approach. Only 33 (55.2%) of 603 patients in the conventional-treatment group ever underwent electrical CV. Of the remaining 270 patients who did not undergo CV, 127 (47%) had a spontaneous or chemical CV. The other 143 (53%) patients never underwent CV of any kind often due to subtherapeutic anticoagulation. Subtherapeutic levels of anticoagulation unnecessarily expose patients to an increased risk of systemic thromboembolization. There is also no consensus on how patients with subtherapeutic INR values during the 3 weeks prior to CV should be managed. Although many physicians will “reset the 3-week clock” of anticoagulation, this may lead to an increased risk of bleeding and an escalated cost of therapy. Recently in an economic evaluation of the ACUTE Trial, Klein et al. showed that conventional therapy resulted in 24% higher cumulative costs than TEE-guided therapy, primarily due to bleeding complications. Although no guidelines on patient selection for TEE in AF of > 48 h duration currently exist, it has been suggested that patients with a subtherapeutic INR should undergo TEE and immediate CV if atrial thrombi are not present (Table 1).

When considering the results of this study, it is important to bear in mind several significant limitations. Most importantly, this was a single center retrospective study consisting of a very small group of patients. It is, therefore, much more difficult to accurately characterize the cohort in question. In addition, the nature of this study prevents assessment of INR values at regularly scheduled
In summary, this study stresses the importance of therapeutic INR values in patients undergoing CV for AF. Clinicians must remain cognizant of the fact that subtherapeutic INR values prior to CV are associated with a relatively high prevalence of atrial thrombi. It is, therefore, essential to strictly follow the current ACCP anticoagulation guidelines for CV of AF greater than 48 h duration. Alternatively, patients who unsuccessfully complete 3 weeks of conventional anticoagulation therapy may be considered for early TEE-guided therapy.

### References


