EDITORIAL COMMENT

Is Atrial Flutter a Risk Factor for Stroke?*

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Large prospective, randomized, controlled trials have demonstrated the efficacy of anticoagulation for the prevention of cardioembolic stroke in atrial fibrillation. Anticoagulation with warfarin is associated with a 70% relative risk reduction in thromboembolic events for certain high risk groups and this can be accomplished without a substantive risk of major bleeding (1–3). Whether chronic atrial flutter carries a similar risk to atrial fibrillation for cardioembolic stroke and whether anticoagulation reduces that risk remain controversial. To our knowledge, no randomized trials of anticoagulation for stroke prevention in chronic atrial flutter have been performed and uniform recommendations regarding anticoagulation in atrial flutter have not been established (4). Our knowledge regarding cardioembolic stroke in this area has been derived in part from the large prospective, randomized trials of atrial fibrillation that have included patients with atrial flutter, observational studies of the prevalence of left atrial thrombus in atrial flutter, mechanistic studies that have examined the development of left atrial mechanical stunning and thrombus formation following the cardioversion of atrial flutter and various case reports and retrospective studies of embolic stroke that have complicated the cardioversion of atrial flutter to sinus rhythm (1–3,5–17).

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In this issue of the Journal, Schmidt et al. (18) have made a significant contribution to our expanding knowledge of chronic atrial flutter and its associated thromboembolic potential. Transesophageal echocardiography was used to assess the prevalence of left atrial thrombus and left atrial spontaneous echo contrast in 139 patients with chronic atrial flutter undergoing 202 electrophysiologic interventions—curative radiofrequency ablation, pace termination of atrial flutter or electrical cardioversion. Twenty-four hours prior to cardioversion, 15 patients (7.4%) demonstrated dense left atrial spontaneous echo contrast (LASEC) at transesophageal echocardiography and 2 patients (1.4%) had existing left atrial thrombus. Diabetes, hypertension and a decreased left ventricular ejection fraction (<40%) were associated with LASEC. Seven patients (5%) had a history of thromboembolism, all of whom also had paroxysmal atrial fibrillation. All patients received full heparinization for at least 24 h following cardioversion and in 35% it was continued until warfarin had achieved an international normalized ratio of >2.0.

Using this approach, following 200 separate cardioversions in 137 patients, there were no clinical embolic events over a subsequent 4-week period. The authors suggest that for patients with pure atrial flutter, it may be reasonable to perform cardioversion using only short-term anticoagulation but they are appropriately cautious to point out that this may not be applicable in high risk patients. Should we, on the basis of this large cohort of patients, recommend that some patients with chronic atrial flutter receive only short duration anticoagulation at the time of cardioversion?

An assessment of the thromboembolic risk and of the prevalence of thrombus in patients with atrial flutter is confounded by the varying rate of anticoagulation in published studies perhaps reflecting the absence of definitive recommendations (5–9,13,14). In the current study, 35% of patients underwent anticoagulation and in only 1.4% was thrombus identified. In a recent study of unselected patients with chronic atrial flutter not receiving anticoagulation, left atrial thrombus was observed in 11% and significant LASEC in 34% (6). In addition, thromboembolic stroke may complicate chronic atrial flutter and its cardioversion to sinus rhythm. Several nonrandomized studies incorporating over 450 patients undergoing cardioversion of chronic atrial flutter without anticoagulation have identified a thromboembolic event rate of 2% to 6% (5,13,15–17). Furthermore, it has also been suggested that the thromboembolic incidence during chronic atrial flutter has been underestimated. Lanzarotti and Olshansky (13) found an embolic incidence of 15% in patients with chronic atrial flutter who did not undergo effective anticoagulation compared to 0% in those who did.

Although no patients in the present large cohort developed a stroke following cardioversion, one must ask just what sample size is sufficient to provide definitive information particularly in a nonrandomized study. A review of the literature surrounding the cardioversion of atrial fibrillation demonstrates over 25 studies with over 5,000 patients which taken as a whole suggest the thromboembolic event rate may be approximately 5% in unanticoagulated patients (22). However, among this group, several large studies (62 patients and 152 patients, respectively) found a 0% incidence of stroke following cardioversion of atrial fibrillation even in patients who were not anticoagulated (23,24). Yet in the current era, the need for anticoagulation of atrial fibrillation at the time of cardioversion is clearly established.

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As Schmidt et al. (18) are careful to observe, when assessing the thromboembolic risk associated with atrial flutter, it is important to consider the relationship between flutter and fibrillation and their frequent coexistence. All seven patients (5%) in the present study with a history of thromboembolism had prior documented paroxysmal atrial fibrillation. The authors conclude that the presence of atrial fibrillation is a risk factor for stroke in atrial flutter and indeed this clinical observation parallels their previous work demonstrating more severe left atrial mechanical dysfunction in patients with combined atrial flutter and fibrillation compared with pure atrial flutter (7). However, even here conflicting evidence exists. Atrial fibrillation was not found to be an independent risk factor for stroke in chronic atrial flutter in a recent retrospective study suggesting that atrial flutter alone conferred some risk of thromboembolic stroke (14).

Whether the mere presence of a single bout of atrial fibrillation is sufficient to substantially increase the risk of stroke in atrial flutter is unknown. Previous studies have demonstrated both organization of atrial fibrillation to atrial flutter and disorganization of atrial flutter to atrial fibrillation (25–27). Substantial evidence suggests atrial fibrillation and atrial flutter are linked through common anatomic/electrophysiologic substrates and triggers and so it is likely that many patients with atrial flutter have had paroxysms of atrial fibrillation. It may be very difficult to determine whether a patient with atrial flutter also has had episodes of atrial fibrillation as both types of arrhythmia may confer similar symptoms and indeed many episodes of atrial fibrillation are asymptomatic (28). Although patients with atrial fibrillation will certainly require anticoagulation, the absence of documented fibrillation may not necessarily convey low risk.

Transesophageal echocardiography studies have demonstrated that when taken as a group, atrial mechanical dysfunction is more pronounced during atrial fibrillation than in atrial flutter and the same may be true immediately following cardioversion (9). Nevertheless, there is considerable overlap and a proportion of atrial flutter patients will have severe postreversion mechanical remodeling or “stunning” with left atrial appendage velocities of <20 cm/s and even with rapid development of appendage thrombus (Fig. 1). These latter observations are consistent with the knowledge that both electrical and mechanical remodeling of the atria occur as a result of rapid atrial rates whether this be atrial fibrillation, atrial flutter or rapid atrial pacing (29). This postreversion left atrial mechanical dysfunction will occur irrespective of the mode of reversion and is seen after spontaneous, pace termination, electrical, pharmacologic and surgical cardioversion and radiofrequency ablation termination of chronic atrial arrhythmias (Fig. 1). Risk factors for the development of atrial mechanical stunning and hence left atrial thrombus are ill-defined but structural heart disease and the chronicity of the preceding arrhythmia appear to be important (30). Furthermore, while stunning does appear to have reversed by three weeks in the majority of patients, it is unclear whether this is also true at 24 h (10,11,30). Thus it is difficult to be certain that 24 h of postprocedural heparin will be sufficient unless one can identify low risk patients with a high degree of confidence.

The present study helps to dichotomize atrial flutter patients into low and high risk groups for thromboembolism. Diabetes, hypertension and a decreased left ventricular ejection fraction (<40%) were associated with what was termed a “thrombogenic milieu”—severe LASEC or the presence of left atrial appendage thrombus. This finding is certainly in agreement with other studies and strongly argues a case for anticoagulation in chronic atrial flutter.
associated with these risk factors (5). Perhaps surprisingly, a previous history of thromboembolism, paroxysmal atrial fibrillation and a left atrial diameter of \( > 40 \) mm were not associated with a thrombogenic milieu but as the authors suggest, this may represent a type 1 error due to relatively small subgroup numbers.

The current study excluded patients with atrial flutter occurring soon after myocardial infarction and in the postoperative period following cardiothoracic surgery. Whether this group of patients is at high risk is uncertain, but indirect evidence regarding the risk of thromboembolism during this acute period suggests that precardioversion anticoagulation is probably warranted as it is in atrial fibrillation unless transesophageal echocardiography excludes thrombus (31).

**RECOMMENDATIONS**

What then should be our approach to anticoagulation for chronic atrial flutter and should transesophageal echocardiography be used at the time of cardioversion in all patients? The present study suggests that there may be a low risk group of patients in whom only short-term periprocedural anticoagulation is required. It is important to recall, however, that in atrial fibrillation, much larger randomized trials were needed before it was shown that anticoagulation had a major effect on decreasing stroke risk. In addition, evidence from studies evaluating atrial mechanical function clearly demonstrate that significant left atrial mechanical stunning and thrombus formation may develop following cardioversion of chronic atrial flutter and argues strongly in favor of anticoagulation to prevent thromboembolism (9–12). In the light of these recent insights into the dynamic changes in left atrial mechanical function at the time of cardioversion and in the absence of a randomized, prospective, controlled study, we believe that a conservative approach to reversion of atrial flutter be followed with adherence to the atrial fibrillation anticoagulation guidelines.

In our own practice, all patients with chronic atrial flutter undergo anticoagulation. If cardioversion is planned, all patients undergo anticoagulation for 3 weeks and all receive warfarin for 3 weeks following cardioversion. Where radiofrequency ablation is the mode of cardioversion, low molecular weight heparin therapy is commenced on cessation of warfarin therapy 5 days prior to the procedure and unfractionated heparin is administered periprocedurally. Transesophageal echocardiography is performed at the time of radiofrequency ablation as it may provide complementary information to that obtained through clinical risk stratification and may identify patients with severe LASEC and left atrial mechanical dysfunction in whom the risk of postcardioversion stunning and thrombus formation may be high. In the light of recent evidence, the performance of transesophageal echocardiography prior to cardioversion may even obviate the requirement for three weeks of prereversion anticoagulation (32).

In patients with pure atrial flutter, on the basis of the present study, it would seem appropriate to strongly consider anticoagulation when atrial flutter is associated with left ventricular dysfunction, hypertension, prior atrial fibrillation or diabetes. Other patients with significant structural heart disease and those with a history of thromboembolism may be added to these categories. This will then involve a large proportion of patients with atrial flutter.

**FUTURE DIRECTIONS**

As curative radiofrequency ablation is fast becoming first-line therapy for chronic atrial flutter, a randomized, prospective, controlled trial of long-term anticoagulation for chronic atrial flutter is unlikely to be performed where access to electrophysiologic interventions is freely available. Whether a 3-week period of anticoagulation should be routine following cardioversion of chronic atrial flutter is perhaps more likely to be the subject of a randomized, prospective, controlled study. Whether the curative ablation of atrial flutter has any important effect on stroke prevention will be an important area for future research and an analysis of large prospective databases of ablation procedures may shed some light on this issue. The true prevalence of atrial fibrillation in patients with atrial flutter is not known and a more accurate assessment of this may guide our recommendations for anticoagulation. The pathophysiologic mechanisms responsible for left atrial mechanical stunning in atrial arrhythmias require elucidation and whether this can be prevented or attenuated may be the subject of further research. Finally, a more precise determination of the clinical risk factors for atrial stunning is required which may help us in the selection of patients warranting anticoagulation in the absence of randomized trial evidence.

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**REFERENCES**


