Cardioversion of persistent atrial flutter in non-anticoagulated patients at low risk for thromboembolism

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Key words:
Atrial flutter cardioversion; Transesophageal atrial overdrive pacing; Thromboembolism; Anticoagulation.

Background. **The true risk of thromboembolic events after cardioversion of atrial flutter was not addressed carefully. Nevertheless, thromboembolic events were thought to be rare and less likely to occur after cardioversion of atrial fibrillation. The aim of this study was to prospectively evaluate if the interruption of persistent typical atrial flutter could be safely performed without anticoagulation in a group of patients at low risk for thromboembolic events.**

Methods. **We studied 64 subjects selected among 138 consecutive patients with persistent typical atrial flutter (minimal duration 72 hours) in whom a transesophageal atrial pacing was performed in our electrophysiology laboratory from October 1994 to May 1999. Exclusion criteria included: anticoagulation therapy during the previous 4 weeks; previous history of atrial fibrillation; recent (< 1 month) myocardial infarction; history of thromboembolic events; left ventricular ejection fraction < 40%; presence of moderate or severe mitral regurgitation or stenosis; induction of sustained (> 6 hours) atrial fibrillation during transesophageal atrial pacing. Patients in whom atrial flutter persisted in spite of transesophageal atrial pacing underwent external direct current cardioversion or right atrial overdrive pacing within 24 hours. Thromboembolic events were checked for 4 weeks after the restoration of sinus rhythm.**

Results. **Sinus rhythm was restored in 54 patients by transesophageal atrial pacing, in 8 patients by electrical cardioversion, and in 2 by right atrial pacing. The mean duration of atrial flutter was 18 ± 19 days, the mean left atrial size 41.3 ± 6.2 mm, and the mean left ventricular ejection fraction 54.8 ± 7.3%. During the study period no episodes of thromboembolism were recorded.**

Conclusions. **Cardioversion of persistent typical atrial flutter in non-anticoagulated patients at low risk for thromboembolic events appears safe.**

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Introduction

Atrial flutter is a frequently observed cardiac arrhythmia, almost as common as all other regular combined supraventricular tachycardias[1]. It is usually symptomatic, with the most common symptom being palpitations, due to the abrupt, striking increase in the ventricular response rate[2]. In these cases a quick interruption of the arrhythmia is mandatory. Less often the ventricular response rate is lower and symptoms are moderate or absent. Thus, cardioversion is delayed for days and atrial flutter becomes chronic.

The true risk of thromboembolic events after cardioversion of atrial flutter was not addressed carefully. Nevertheless, thromboembolic events were thought to be rare and less likely to occur after cardioversion of atrial fibrillation[3-8]. So, current recommendations by the American College of Chest Physicians suggest that anticoagulation is not required in the pericardioversion period for patients with atrial flutter without a previous history of atrial fibrillation[3]. This approach has been discussed in recently published studies[9-13]. These authors have suggested that patients with atrial flutter are at a substantially increased risk for thromboembolism, and have recommended full anticoagulation for these patients. However, oral anticoagulation could be hazardous by itself. Bleeding is the most serious complication: annual incidence of major/fatal bleeding is 1.35%[14].

The aim of this study was to prospectively evaluate if interruption of persistent typical atrial flutter could be safely performed without anticoagulation in a group of patients at low risk for thromboembolic events.

Methods

Patients. Our study population was chosen among 138 consecutive patients with persistent typical atrial flutter (minimal duration 72 hours) in whom a transesophageal atrial pacing was performed in our electrophysiology laboratory from October 1994 to May 1999. Exclusion criteria were: anticoagulation therapy during the previous 4 weeks; previous history of atrial fibrillation; recent (< 1 month) myocardial infarction; history of thromboembolic events; left ventricular ejection fraction < 40%; presence of moderate or severe mitral regurgitation or stenosis; induction of sustained (> 6 hours) atrial fibrillation during transesophageal atrial pacing. Patients in whom atrial flutter persisted in spite of transesophageal atrial pacing underwent external direct current cardioversion or right atrial overdrive pacing within 24 hours.

Transesophageal atrial pacing. After giving informed consent, patients underwent the stimulation in the postabsorptive and non-sedated state. A hexapolar catheter with an interelectrode distance of 2 cm (model TOEC 6 Medico, Padua, Italy) was advanced through the nostril and positioned to the point where we observed the largest amplitude of transesophageal atrial deflection; the lead was then taped to the nose. Surface electrocardiographic leads I, II, III and V_1, and bipolar transesophageal electrogram were recorded at a paper speed of 25 mm/s. Pacing was performed by connecting two of the six electrodes to a programmable stimulator (model TECS II Medico, Padua, Italy). The pulse duration of the stimulator was set at 20 ms. Pacing was initiated using a stimulus intensity of 10 mA, and increased in 1-mA increments until a stable capture was achieved with overdrive.

Echocardiographic analysis. Transthoracic two-dimensional imaging and pulsed Doppler echocardiography were performed using Hewlett-Packard Sonos 1500 or 2000 ultrasound machines equipped with 2.5 and 3.5 MHz phased-array transducers before atrial flutter termination. Left ventricular ejection fraction was determined by calculating the end-diastolic and end-systolic volumes according to Folland. Left atrial size was measured at end-systole in the parasternal long-axis views.

Follow-up. Four weeks after the restoration of the sinus rhythm each patient underwent an outpatient visit in order to check thromboembolic events, and an electrocardiogram for the determination of cardiac rhythm.

Definitions. Typical atrial flutter. Atrial flutter characterized by negative flutter waves in leads II, III, aVF, and V_6, and positive in V_1 (counterclockwise flutter) or positive flutter waves in leads II, III, aVF, and V_6, and negative in V_1 (clockwise flutter)[15,16].

Thromboembolic event. Thromboembolic events were coded as to whether they occurred in the cerebral, pulmonary or peripheral circulation. Determination of a thromboembolic event was based on clinical findings and had to be supported by radiologic studies, including computerized axial tomographic scan, ventilation-perfusion scanning and angiography.

Statistical analysis. Data are expressed as mean ± SD for continuous variables and rates (%) for categoric variables.

Results

Among the 138 enrolled patients, 67 were excluded from the study: 1 patient with moderate mitral regurgitation; 2 patients with a left ventricular ejection fraction < 40%; 23 patients who were assuming anticoagulation therapy in the 4 weeks before the interruption; 4 patients with previous documented episodes of atrial fibrillation; 37 patients converted to sustained atrial fibrillation or atypical atrial flutter by transesophageal atrial pacing.

Sinus rhythm was restored by transesophageal atrial pacing in 54 patients. Among the patients in whom atrial flutter persisted in spite of transesophageal atrial pacing, 8 underwent an external direct current cardioversion and 2 a right atrial overdrive pacing within 24 hours, while 7 patients refused to undergo any other procedure.

Baseline data of the 64 patients of our study group are listed in table I. The mean duration of atrial flutter was 18 ± 19 days (range 3-90 days) in 56 cases, whereas it was not possible to identify the exact time of onset of the arrhythmia in 8 patients. In 9 patients atrial flutter lasted for more than 1 month. At the echocardiographic analysis the mean left atrial size was 41.3 ± 6.2 mm (range 31-55 mm), the mean left ventricular end-di-

Table I. Baseline data of the study group.

Age (years)	68 ± 8 (range 49-85)
Men/women	58/6
Duration of AFL (days)	18 ± 19 (range 3-90)
Cycle length of AFL (ms)	240 ± 34 (range 180-300)
Heart rate (b/min)	102 ± 38 (range 45-200)
Antiarrhythmic drugs (%)	64
LVEDV (ml/m^2)	63.5 ± 10.5 (range 50-90)
LVEF (%)	54.8 ± 7.3 (range 40-67)
LA size (mm)	41.3 ± 6.2 (range 31-55)
Associated disease (%)	56
Hypertension (%)	30
Ischemic heart disease (%)	14
Dilatative cardiomyopathy (%)	1.5
Congenital heart disease (%)	1.5
Chronic lung disease (%)	9

Data are presented as mean ± SD. AFL = atrial flutter; LA = left atrial; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction.

astolic volume 63.5 ± 10.5 ml/m² (range 50-90 ml/m²), and the mean left ventricular ejection fraction 54.8 ± 7.3% (range 40-67%). An associated disease was present in 56% of patients: hypertension in 30%, ischemic heart disease in 14%, chronic lung disease in 9%, dilatative cardiomyopathy in 1.5%, congenital heart disease in 1.5%.

No convincing clinical findings for thromboembolism were recorded in the 4 weeks after the restoration of sinus rhythm. At the end of the study period sinus rhythm was present in 55 patients (86%), while atrial flutter resumed in 8 cases (12%) and atrial fibrillation appeared in 1 patient (2%).

Table II. Previous studies.

Author	No.	Mean EF (%)	TE	AFL interruption (%)
Arnold et al.[28]	122	–	0	ECV
Chalasani et al.[29]	98	–	0	ECV
Metha and Baruch[9]	41	34	7.3	ECV
Wood et al.[10]	86	51	4.6	ECV, RF, AP
Lanzarotti and Olshansky[11]	46	43	7.5	ECV
Seidl et al.[13]	191	52	2.1	ECV, RF, AP

AFL = atrial flutter; AP = atrial pacing; ECV = electrical cardioversion; EF = ejection fraction; RF = radiofrequency ablation; TE = thromboembolic events.

Discussion

This is the first prospective study in which the incidence of thromboembolism in a cohort of non-anticoagulated patients at low risk for thromboembolic events requiring cardioversion of persistent typical atrial flutter was evaluated. Cardioversion of atrial flutter was never associated with an embolic event during a follow-up of 4 weeks.

Thromboembolic risk. Considering the common occurrence of atrial flutter, little information is available to determine the true risk of thromboembolic events in the pericardioversion period. The major clinical trials of anticoagulation therapy for atrial fibrillation excluded patients with atrial flutter[3-8]. In several small-sized published studies of cardioversion, patients with atrial fibrillation, atrial flutter and supraventricular arrhythmias were pooled together, making interpretation difficult[17-20]. Nevertheless, thromboembolic risk was thought to be low in atrial flutter due to the organized atrial contraction: the synchronous activity was presumed to prevent blood stasis and thrombus formation.

The low thromboembolic risk of atrial flutter was not confirmed by transesophageal echocardiographic studies which reported a combined prevalence of left atrial thrombus and spontaneous left atrial echo contrast in non-anticoagulated patients with atrial flutter from 6 to 43%[12,21-24]. Moreover, left atrial appendage stunning and the development of new or increased left atrial spontaneous echo contrast after conversion to sinus rhythm, previously reported for patients with atrial fibrillation, were detected also in patients with atrial flutter[12,25-27].

Up till now, the incidence of thromboembolism in atrial flutter has been analyzed by retrospective studies (Table II)[9-11,13,28,29]. Arnold et al.[28] reported no embolic events in 122 direct current cardioversions in patients with atrial flutter, 26% of whom received anticoagulation. The minimal duration of the arrhythmia was 48 hours. All patients were followed up for evidence of embolism for at least 2 weeks, postoperative patients for 6 weeks. This series was characterized by a high prevalence of patients with a postoperative atrial flutter (67%) and with a normal o mild depressed left ventricular function (70%). Chalasani et al.[29] reviewed 98 direct current cardioversions in 85 patients, 12% of whom received anticoagulation. No thromboembolic events were reported up to 24 hours after cardioversion. The duration of atrial flutter was unknown in 73 of 98 episodes and was not reported in the remaining 25 cases. An underlying heart disease was present in 57% of patients. Data about left ventricular function were unknown. More recently these optimistic data were discussed by several published papers. Mehta and Baruch[9] found a neurologic ischemic event in 3 of 41 (7.3%) patients within 48 hours of direct current cardioversion of atrial flutter. One patient had a global left ventricular systolic dysfunction, and the other 2 had episodes of atrial fibrillation after the onset of thromboembolic events. These patients were non-anticoagulated and had undergone transesophageal echocardiography immediately prior to cardioversion without evidence of intracardiac thrombi. Wood et al.[10] reported an incidence of systemic or pulmonary embolism after cardioversion in 4 of 86 non-anticoagulated patients (4.6%) with chronic or recurrent atrial flutter and a mean left ventricular ejection fraction of 51%. Lanzarotti and Olshansky[11] reported a 3% incidence of thromboembolic events after interruption of chronic atrial flutter by right atrial pacing, direct current cardioversion, or radiofrequency ablation in 100 patients. Excluding the 54 patients who received effective anticoagulation therapy, in whom no thromboembolic events occurred, the incidence increased up to 7.5%. This series included patients with a high prevalence of underlying heart disease, a low left ventricular ejection fraction (mean 42%), and an atrial flutter duration of > 6 months.

Very interesting data could be obtained from the complex paper of Seidl et al.[13]. Interruption of chronic or recurrent atrial flutter was obtained in 191 patients (35% receiving warfarin) by electrical cardioversion, medical cardioversion, overdrive stimulation, or catheter ablation. Excluding patients who underwent a catheter ablation, the incidence of acute embolic events was 1.8%. Excluding patients with a history of thromboembolic events or transient ischemic attack, the overall embolic risk became 5% during a mean follow-up of 26

± 18 months, yielding an annual risk of approximately 1.8%. Using a logistic regression model, hypertension was the only independent predictor of embolic risk.

Our data are in accordance with those of Arnold et al.[28] and Chalasani et al.[29] but strikingly in contrast with those of the more recent studies[9-11,13]. These discrepancies may probably be explained by the different clinical characteristics of the study groups: patients with both typical and atypical atrial flutter, with atrial flutter of different duration, with or without anticoagulant therapy, with different prevalence of heart disease and left ventricular dysfunction were included. Moreover, efforts to exclude patients with transient atrial fibrillation were not always made. Instead, we enrolled a homogeneous series of consecutive non-anticoagulated patients with typical atrial flutter who can be generally defined at low risk for thromboembolic events: patients without any history of atrial fibrillation, thromboembolic events, recent acute myocardial infarction, without mitral valve disease, and with left ventricular ejection fraction > 40%. According to our results, these patients do not seem to be at increased risk for embolic events.

Our results probably are not influenced by the mode of cardioversion because atrial stunning is a possible result of the arrhythmia itself and not of the mode of cardioversion[30].

Benefit/risk ratio of oral anticoagulation. Bleeding is the most serious complication of oral anticoagulation. The hemorrhagic risk during oral anticoagulation in outpatients monitored by INR in specialist anticoagulation clinics was prospectively estimated by the ISCOAT study[14]. The rate of fatal, major, and minor bleeding events was 0.25, 1.1, and 6.2 per 100 patients-years of follow-up, respectively. The hemorrhagic risk was significantly higher during the first 90 days of treatment (40.5% of all hemorrhagic events happened during this period), and in patients > 70 years. Instead, the target INR (• 2.8 or > 2.8) did not affect the rate of bleeding.

Review of the literature and results of our study allow us to draw some conclusions: 1) the rate of acute embolism after atrial flutter interruption in an unselected population is still uncertain[9-11,13,28,29]; 2) the rate of bleeding complications during oral anticoagulation therapy is not negligible (the risk of major/fatal bleeding during 8 weeks of anticoagulation therapy is 0.50%); 3) a certain rate of thrombotic events is expected despite anticoagulation therapy; 4) the rate of acute embolism after atrial flutter interruption in a selected population at low risk for thromboembolic events is low (< 2%)[13].

Our future efforts should be directed towards recognizing those patients at high risk for thromboembolism in whom a pericardioversion period of oral anticoagulation is mandatory, rather than to anticoagulating all patients with atrial flutter.

Study limitations. Some limitations are present in this study. The screening for thromboembolic events was based on clinical findings. Neurological exam, ophthalmological exam, urinalysis were not performed in all patients. Thus, clinically silent emboli cannot be excluded.

This study includes a limited number of patients generally considered at low risk for thromboembolic events. Thus, our results cannot be extended to all patients with persistent or chronic atrial flutter.

In conclusion, cardioversion of persistent typical pure atrial flutter in non-anticoagulated patients at low risk for thromboembolic events appears safe. However, the mechanisms responsible for thromboembolism in atrial flutter are multiple and complex, thus large-scale, randomized trials are necessary.

References

1. Jolly WA, Ritchie WJ. Auricular flutter and fibrillation. Heart 1910-1911; 2: 177-221.
2. Olshansky B, Wilber D, Hariman RJ. Atrial flutter - update on the mechanism and treatment. Pacing Clin Electrophysiol 1992; 15: 2308-35.
3. Laupacis A, Albers G, Dalen J, Dunn M, Feinberg W, Jacobson A. Antithrombotic therapy in atrial fibrillation. Chest 1995; 108: 352S-359S.
4. Peterson P, Boyson G, Godfredson J, Anderson ED, Anderson B. Placebo-controlled randomised trial of warfarin and aspirin for the prevention of thromboembolic complications in chronic atrial fibrillation: the Copenhagen AFASAK study. Lancet 1989; 1: 175-9.
5. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. N Engl J Med 1990; 323: 1505-11.
6. Stoke Prevention in Atrial Fibrillation Study Group Investigators. Stroke prevention in atrial fibrillation study: final results. Circulation 1991; 84: 527-39.
7. Connaly SJ, Laupacis A, Gent M. Canadian Atrial Fibrillation Anticoagulation (CAFA) study. J Am Coll Cardiol 1991; 18: 349-55.
8. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. N Engl J Med 1992; 327: 1406-12.
9. Mehta D, Baruch L. Thromboembolism following cardioversion of "common" atrial flutter. Risk factors and limitations of transesophageal echocardiography. Chest 1996; 110: 1001-3.
10. Wood KA, Eisenberg SJ, Kalman JM, et al. Risk of thromboembolism in chronic atrial flutter. Am J Cardiol 1997; 79: 1043-7.
11. Lanzarotti CJ, Olshansky B. Thromboembolism in chronic atrial flutter: is the risk underestimated? J Am Coll Cardiol 1997; 30: 1506-11.
12. Irani WN, Grayburn PA, Afridi I. Prevalence of thrombus, spontaneous echo contrast, and atrial stunning in patients undergoing cardioversion of atrial flutter. A prospective study using transesophageal echocardiography. Circulation 1997; 95: 962-6.
13. Seidl K, Hauer B, Schwick NG, Zellner D, Zahn R, Senges J. Risk of thromboembolic events in patients with atrial flutter. Am J Cardiol 1998; 82: 580-3.
14. Palareti G, Leali N, Coccheri S, et al. Bleeding complications

of oral anticoagulant treatment: an inception-cohort, prospective collaborative study (ISCOAT). Lancet 1996; 348: 423-8.
15. Lesh MD, Kalman JM. To fumble flutter or tackle "tach"? Toward updated classifiers for atrial tachyarrhythmias. J Cardiovasc Electrophysiol 1996; 7: 460-6.
16. Kalman JM, Olgin JE, Saxon LA, Lee RJ, Scheinman MM, Lesh MD. Electrocardiographic and electrophysiologic characterization of atypical atrial flutter in man. Use of activation and entrainment mapping and implications for catheter ablation. J Cardiovasc Electrophysiol 1997; 8: 121-44.
17. Navab A, La Due JS. Postconversion systemic arterial embolism. Am J Cardiol 1965; 16: 52-3.
18. Morris JM, Peter RH, McIntosh HD. Electrical conversion of atrial fibrillation: immediate and long-term results and selection of patients. Ann Intern Med 1966; 65: 216-31.
19. Lown B. Electrical reversion of cardiac arrhythmias. Br Heart J 1967; 29: 469-89.
20. Bjerkleund C, Orning O. The efficacy of anticoagulant therapy in preventing embolism related to DC electrical cardioversion of atrial fibrillation. Am J Cardiol 1969; 23: 208-16.
21. Black IW, Hopkins AP, Lee LC, Walsh WF. Evaluation of transesophageal echocardiography before cardioversion of atrial fibrillation and atrial flutter in nonanticoagulated patients. Am Heart J 1993; 126: 375-81.
22. Santiago D, Warshofsky M, Li Mandri G, et al. Left atrial appendage function and thrombus formation in atrial fibrillation-flutter: a transesophageal echocardiographic study. J Am Coll Cardiol 1994; 24: 159-64.
23. Feltes TF, Friedman RA. Transesophageal echocardiographic detection of atrial thrombi in patients with nonfibrillation atrial tachyarrhythmias and congenital heart disease. J Am Coll Cardiol 1994; 24: 1365-70.
24. Bikkina M, Alpert MA, Mulekar M, Shakoor A, Massey CV, Covin FA. Prevalence of intraatrial thrombus in patients with atrial flutter. Am J Cardiol 1995; 76: 186-9.
25. Jordaens L, Missault L, Germonprè E, et al. Delayed restoration of atrial function after conversion of atrial flutter by pacing or electrical cardioversion. Am J Cardiol 1993; 71: 63-7.
26. Grimm RA, Stewart WJ, Arheart KL, Thomas JD, Klein AL. Left atrial appendage "stunning" after electrical cardioversion of atrial flutter: an attenuated response compared with atrial fibrillation as the mechanism for lower susceptibility to thromboembolic events. J Am Coll Cardiol 1997; 29: 582-9.
27. Sparks PB, Jayaprakash S, Vohra JK, et al. Left atrial "stunning" following radiofrequency catheter ablation of chronic atrial flutter. J Am Coll Cardiol 1998; 32: 468-75.
28. Arnold AZ, Mick MJ, Mazurek RP, Loop FD, Trohman RG. Role of prophylactic anticoagulation for direct current cardioversion in patients with atrial fibrillation or atrial flutter. J Am Coll Cardiol 1992; 19: 851-5.
29. Chalasani P, Cambre S, Silverman M. Direct-current cardioversion for the conversion of atrial flutter. Am J Cardiol 1996; 77: 658-60.
30. Sparks PB, Kalman JM, Vohra J, et al. Effect of direct current shocks on atrial mechanical function in patients with structural heart disease. J Am Coll Cardiol 1998; 31: 1395-9.