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CARDIOLOGY Rounds™

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Transesophageal Echocardiographic-Guided Cardioversion of Atrial Fibrillation

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Introduction

Atrial fibrillation, the most common sustained tachyarrhythmia is characterized by disorganized electrical and mechanical activity of the atria. From a clinical standpoint and particularly in patients with structural heart disease, this results in impaired functional capacity, and an increased risk of congestive heart failure, embolic events, and death. Direct current electrical cardioversion may be used to restore sinus rhythm, with the intention of improving functional capacity and of obviating the increased thromboembolic risk associated with chronic atrial fibrillation.[1] However, electrical cardioversion itself carries risk of embolism, which in the non-anticoagulated patient, is estimated to be as high as 5-6%.[2] Similarly, chemical cardioversion is also known to be associated with an embolic risk.[3-6] It is presumed that the resumption of organized atrial contraction, achieved by electrical, by chemical or by spontaneous cardioversion, results in expulsion into the arterial circulation of an existing minimally adherent thrombus within the atrium or appendage. According to the recommendations of the American College of Chest Physicians, patients with atrial fibrillation lasting longer than two days should receive warfarin to achieve a therapeutic INR (2.0 to 3.0) for three weeks before elective cardioversion, and should continue for four weeks after reversion to normal sinus rhythm.[7] This approach is intended to minimize the embolic risks associated with cardioversion; however, compared to an approach of earlier cardioversion without therapeutic anticoagulation, it is associated with longer treatment duration, increased risk of bleeding complications, delayed cardioversion, and increased cost. This approach is based upon previous non-randomized and non-controlled studies.

The recently published ACUTE Pilot Study[8] has suggested feasibility and safety of a transesophageal echocardiographic-guided cardioversion approach in which exclusion of a

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pre-existing left atrial thrombus (by TEE) enables early cardioversion without the need for the standard three weeks of systemic anticoagulation. Another recently published study[9] suggests that transesophageal echocardiographic-guided cardioversion, without transthoracic echocardiography, may be cost-effective, and particularly beneficial for patients with increased bleeding risk.

Mechanism of Cardioversion related Cardio-Embolism

The mechanism responsible for new cardio-embolic events after cardioversion has been traditionally related to dislodgment of a pre-existing left atrial appendage or atrial cavitary thrombus.[3] The reported incidence of left atrial thrombus as visualized by transesophageal echocardiography in patients with atrial fibrillation is approximately 13 percent.[10-15] Since the incidence of post-cardioversion embolic events appears to be less than half of that (in the order of 2 to 5%), it is probable that not all pre-existing left atrial appendage thrombi embolize subsequent to cardioversion.

Most reported cardioversion related embolic events do not occur at the time of successful cardioversion and the resumption of normal sinus rhythm. The interval of time between cardioversion and embolic events may range from a few hours to a few weeks following cardioversion.[16] There are a number of explanations for this delayed occurrence. The resumption of mechanical atrial activity lags behind electrical sinus rhythm, resulting in delayed expulsion of left atrial appendage thrombus. Secondly, electrical cardioversion may temporarily "stun" the atria (for hours-days), such that they have resumed normal electrical activity, but are without contractile function, and are therefore potentially a more thrombogenic milieu.[17,18] Echocardiographic imaging of atria post-cardioversion documents that approximately one quarter of patients have atrial stunning.[18]

Experience with TEE Guided Cardioversion (Table 1)

If left atrial appendage thrombus is excluded by transesophageal echocardiography, then, from the perspective of preventing embolism of a pre-existing thrombus, pre cardioversion anti-coagulation may be unnecessary. Several groups of investigators have examined the safety of such a transesophageal echocardiographic-guided approach to elective cardioversion in conjunction therapeutic anti-coagulation. Manning et al., studied the safety of this transesophageal echocardiographic-guided approach in 230 patients undergoing electrical or chemical cardioversion who were screened with transesophageal echocardiography.[10] In thirty-four patients (15%), atrial thrombi were detected, and cardioversion was subsequently deferred. Patients without atrial thrombus underwent electrical and/or pharmacological cardioversion while receiving systemic anticoagulation which continued for one month. No embolic events were reported using this approach. Reports by Orsinelli et al[19], also supported the safety of a transesophageal echocardiographic-guided approach.

Table 1

Study	Number of patients	Number of atrial thrombi detected (%)	Number of embolic events
Grimm et al[2]	40	1 (2.5)	0
Stoddard et al[14]	82	11 (13)	0
Black et al[16]	156	12 (8)	1
Orsinelli et al[19]	39	9 (23)	1
Manning et al[10]	230	34 (15)	0

Although these results are promising, there are concerns about widespread applicability of such an approach until more studies, especially larger studies, confirm safety and efficacy. The apparent safety and the lack of clinical events in these patients could well have been due to inadequate power in the studies. These studies have provided no information in the relative efficacy of this approach compared to conventional treatment. Disconcertingly, there have been reports of patients with apparently normal transesophageal echocardiographic studies experiencing systemic embolism following cardioversion. The reasons are unclear, but may pertain to technical echocardiographic reasons (such as failure to visualize a small thrombus or atypical atrial appendage configuration), or potentially to formation of thrombus in an electrical cardioversion "stunned" atrium or appendage, with subsequent embolization when mechanical activity resumed. Lastly, in the approach of empirical anti-coagulation then cardioversion, some patients undergo spontaneous reversion to sinus rhythm, and therefore do not need admission for this procedure.

Recent studies suggest that atrial thrombus, spontaneous echo contrast and atrial stunning may be seen more commonly in patients with chronic atrial flutter than was previously recognized.[18]

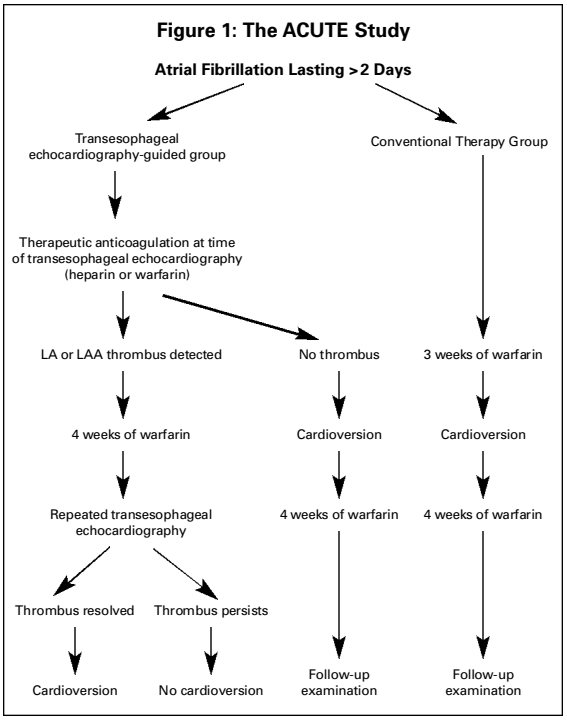
Advantages of Early Cardioversion

Early, versus deferred, cardioversion enables early return of atrial mechanical function with its physiological benefits. A shortened duration of atrial fibrillation increases the likelihood of successful cardioversion. Both transesophageal echocardiography and cardioversion can be performed during a single hospital admission. Repeated blood tests during the three week period of anticoagulation required by the conventional method are avoided. The risk of serious bleeding may be reduced by shortening the duration of anticoagulation from seven to four weeks. However these benefits remain to be demonstrated in randomized controlled trials.

Randomized Controlled Trials

The Assessment of Cardioversion Utilizing Trans-Esophageal echocardiography (ACUTE) pilot study randomized 126 patients: 62 to the TEE guided arm, and 64 to the conventional arm.[8] There were no recognized emboli in the TEE group, and there was a single recognized embolus in the conventional therapy group. The results suggested that the TEE guided approach may be safer, more convenient, and associated with fewer bleeding complications. Although the ACUTE pilot study was underpowered to detect real differences between the two treatments arms, it has shown the feasibility of a larger scale randomized controlled trial and has confirmed the safety of the TEE guided approach.

The ACUTE trial is a presently ongoing multicentre prospective randomized controlled trial and expected to include a total of 3000 patients. Patients with atrial fibrillation of greater than two days duration who are not on chronic anticoagulation and are considered possible candidates for electrical cardioversion are eligible for the study. Patients are either randomized to the transesophageal echocardiography-guided anticoagulation management arm or a conventional arm (figure 1). Patients randomized to the transesophageal echocardiography arm receive heparin or warfarin anticoagulation and undergo transesophageal echocardiography. If atrial thrombus can be excluded by trans-



esophageal echocardiography, patients will then undergo cardioversion immediately thereafter. Therapeutic anticoagulation will be achieved and maintained during and for four weeks after cardioversion. Patients randomized to the conventional arm will undergo transesophageal echocardiography, get three weeks of anticoagulation prior to cardioversion and for four weeks thereafter. The primary endpoints are the occurrence of stroke, peripheral embolism, or major bleeding at eight weeks after randomization. The secondary endpoints are deaths, transient ischemic attacks, or other minor bleeding complications. The cost-effectiveness of the two treatment strategies will be assessed. Further follow-up examination will be performed six months after randomization.

Prolonged anticoagulation of all patients undergoing elective cardioversion is not without problems. The use of warfarin in this predominantly elderly group of patients with atrial fibrillation is associated with a significant risk of bleeding. Delayed cardioversion may necessitate repeated admissions or clinic visits. Due to these problems, the conventional approach to elective cardioversion is not universally practiced.

Transesophageal echocardiography has proven efficacy and safety in visualizing the left atrial appendage and is suited for exclusion of thrombi before elective cardioversion. If left atrial and left atrial appendage thrombus can be excluded, the three weeks of anticoagulation before cardioversion may not be necessary. If this approach is shown to besafe and effective, then the duration of treatment can be shortened and elective cardioversion can be expedited. The ACUTE pilot study has yielded preliminary evidence of the feasibility and safety of performing a larger study. The results of the ACUTE study will yield important information on the cost-effectiveness of the transesophageal echocardiographic-guided approach to anticoagulation and optimal method of treatment of patients with atrial fibrillation who require cardioversion.

Summary

Pilot studies suggest that transesophageal-guided cardioversion of atrial fibrillation may be a cost-effective and feasible strategy, particularly in patients with increased bleeding risks. These studies are preliminary and should not change the current standard of practice of empirical anticoagulation (when not contraindicated), then subsequent cardioversion. The results of the larger ACUTE multicenter trial are awaited.

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Abstracts of Interest

A Survey of Atrial Fibrillation in Family Practice: the West Birmingham Atrial Fibrillation Project

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To investigate the prevalence, clinical features and management of patients with atrial fibrillation (AF), we surveyed patients in 2 family practices (serving a patient population of 16,519) where 4,522 subjects (27.4%) were aged ≥50 years. Of the latter, 111 patients (2.5%) were found to have AF (42 males; mean age 76.6, s.d. 9.1): 0.77% of AF patients were age 50-60 years, 2.78% age 61-70 years, 9.68% age 71-80 years, 9.68% age 81-85 years, and 11.9% age > 85 years old. Female patients were significantly older than males (79.0 vs 72.7 years, t-test p < 001). 81 patients (73%) had chronic AF, whilst 30 patients (27%) had paroxysmal AF. The commonest aetiological factors were hypertension (36.9%), ischaemic heart disease (28.8%, with a previous myocardial infarction in 12), valvular heart disease (25.2%), hyperthyroidism (15.3%), alcohol excess (5.4%) and cardiomyopathy (5.4%); with no obvious cause for AF in 6 patients. Cardiac failure was associated with AF in 34 patients (30.6%), and stroke in 29 patients (18%). Although 40 patients (36.1%) had a latest blood pressure measurement > 160/90 mmHg, only 20 patients were recorded as having had hypertension. Only 20 patients (18%) had an echocardiogram and 26 (23.4%) a chest x-ray. 58 patients (52.3%) had their thyroid function test measured at any time. Warfarin was prescribed to 40 patients (36%), with anticoagulation intensity monitoring by the family practitioner in 3 cases (7.5%), hospital clinic in 30 (75%) and by both family practioner and hospital in 7 cases (17.5%). Of those not anticoagulated (n = 71), only 12 patients (16.9%) had contraindications to warfarin therapy, including dyspepsia (n = 5), dementia (3), and chronic renal failure (1). Patients treated with warfarin were younger than those who were not prescribed warfarin (71.3 vs 79.6 years, unpaired t test p < 0.001). Aspirin was being prescribed in 21 patients (18.9%), primarily for previous myocardial infarction in 7. Only 30.6% (34/101) had ever presented to hospital practice. In conclusion, AF is a common arrhythmia in family practice, and is commonly associated with hypertension, ischaemic heart disease and heart failure. Few patients had ever presented to hospital practice; and there was a suboptimal application of standard investigations and use of antithrombotic therapy, especially warfarin, for the prophylaxis for stroke. This survey has considerable implications for the efficient management of patients with atrial fibrillation in the primary care setting, and suggests that guidelines for the treatment of this common arrhythmia in family practice are required.

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Echocardiographic Assessment of Left Atrial Appendage Function Immediately Before and 24 Hours After Successful Cardioversion for Atrial Fibrillation.

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Persistent mechanical dysfunction of left atrial appendage (LAA) after successful cardioversion in patients with atrial fibrillation may be associated with LAA thrombus development and embolization. However, LAA function after cardioversion has not been investigated systematically. We assessed LAA and left atrial function by transesophageal echo (TEE), immediately before and 24 hours after cardioversion to sinus rhythm, in 42 patients with nonvalvular atrial fibrillation (39-79 years, mean 64; male 64%).

Left atrial function, assessed by ECG-P wave and Doppler transmitral flow velocity profile, returned to normal after cardioversion in each of the 42 study patients. Left atrial appendage function, assessed as ejection flow velocity signal synchronized with ECG-P wave, returned to normal in 29 of the 42 patients (69%) and remained impaired in the remaining 13 (31%). At pre-cardioversion TEE, maximal LAA area was significantly larger in the patients with persistent LAA dysfunction compared to those with restored LAA function (maximal LAA area: 5.0 ± 1.6 and 3.8± 1.2 cm^2, respectively; $p<0.02$). None of the other variables examined, including age, duration of atrial fibrillation, left atrial size, and left ventricular fractional shortening, differed significantly in the two groups.

Conclusions: Our findings indicate that: 1) Mechanical function of LAA is restored in the majority of patients 24 hours after successful cardioversion for atrial fibrillation; 2) Size of LAA is inversely correlated with probability of restoration of normal LAA function. Our observations also suggest that TEE, performed 24 hours after cardioversion to sinus rhythm, may permit identification of patients with restored LAA function in whom post-cardioversion anticoagulation could be unnecessary.

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