Tissue velocity imaging of the left atrium predicts response to flecainide in patients with acute atrial fibrillation

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BACKGROUND Acute atrial fibrillation (AF) is often treated with the administration of intravenous flecainide; however, this treatment may not always be successful and is potentially hazardous. Previous studies suggest that electro-echocardiographic tissue velocity imaging (TVI) of the atrial wall may reflect atrial remodeling.

OBJECTIVE To study whether atrial TVI can be used to identify nonresponders of flecainide administered intravenously in patients with acute AF.

METHODS We used atrial TVI to measure atrial fibrillatory cycle length determined by using tissue velocity imaging (AFCL-TVI) and atrial fibrillatory wall motion velocity determined by using tissue velocity imaging (AFV-TVI) in the left atrium in 52 (55%) patients presenting with acute AF in the emergency department. These 2 parameters reflect electrical and structural remodeling, respectively. Standard baseline characteristics were recorded.

RESULTS Patients were predominantly men (76%) and 64 ± 11 years old. Thirty-six (69%) patients had successful cardioversion after flecainide infusion. There were no significant differences in baseline characteristics between responders and nonresponders. Patients with a successful cardioversion had a longer mean AFCL-TVI and higher median (interquartile range) AFV-TVI compared with patients with failed cardioversion: 172 ± 29 ms vs 137 ± 35 ms ($P < .001$) and 4.2 (3.3–6.2) cm/s vs 2.3 (1.9–3.5) cm/s ($P = .001$).

CONCLUSIONS Electro-echocardiographic atrial TVI measurement is a promising noninvasive tool for predicting outcome of pharmacological cardioversion. A short AFCL-TVI and a low AFV-TVI are related to failure of cardioversion of AF using flecainide.

KEYWORDS Atrial fibrillation; Echocardiography; Pharmacological cardioversion; Flecainide; Tissue Velocity Imaging

ABBREVIATIONS **AF** = atrial fibrillation; **AFCL** = atrial fibrillatory cycle length; **AFCL-TVI** = atrial fibrillatory cycle length determined by using tissue velocity imaging; **AFV** = atrial fibrillatory wall motion velocity; **AFV-TVI** = atrial fibrillatory wall motion velocity determined by using tissue velocity imaging; **ARP** = atrial refractory period; **ECG** = electrocardiogram/electrocardiographic; **LA** = left atrium/atrial; **LVEF** = left ventricular ejection fraction; **ROC** = receiver-operating characteristic; **SR** = sinus rhythm; **TVI** = tissue velocity imaging

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia.[1] Patients presenting with acute AF can be treated with flecainide, a class 1C antiarrhythmic drug, administered intravenously or by the oral pill-in-the pocket approach.[2,3] Flecainide administered intravenously results in cardioversion to sinus rhythm (SR) in 56%–90% of the patients.[4–6] Unfortunately, the success rate of pharmacological cardioversion with flecainide rapidly declines with the duration of the current AF episode.[7–9] Furthermore, the administration of intravenous flecainide can result in complications including ventricular proarrhythmia, bradycardia, advanced conduction block, and heart failure.[10] Patients may also face the risk of atrial proarrhythmia including sinus pauses and atrial flutter with 1:1 atrioventricular conduction and extreme QRS widening.[11,12] Therefore, ideally, only responders should be selected for flecainide infusion as this reduces the incidence of side effects to an absolute minimum. Therefore, ideally, all nonresponders should be identified to reduce the incidence of unnecessary side effects. The atrial fibrillatory cycle length (AFCL) could be a useful parameter for this selection because it reflects the atrial refractory

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period (ARP) as well as the extent of atrial electrical remodeling, and it is readily available by means of noninvasive atrial fibrillatory cycle length determined by using tissue velocity imaging (AFCL-TVI) echocardiography.[13,14] More electrical remodeling results in shortening of the refractory period and consequently a shorter AFCL-TVI.[13] The shorter the refractory period, the shorter the AFCL and the more frequent AF is persistent.[14–16] In addition, AF is associated with structural remodeling that can be assessed by using TVI. The velocity of the atrial fibrillatory wall motion as determined by using tissue velocity imaging (AFV-TVI) is inversely related to the extent of structural atrial remodeling.[13,17] We hypothesize that AFCL-TVI and AFV-TVI can be used to identify nonresponders of flecainide administered intravenously in patients with acute AF.

Methods

In this study in 2 centers, we included consecutive daytime patients presenting with acute AF (<48 hours) at the emergency department and were undergoing pharmacological conversion using flecainide intravenously. The duration of the current episode of paroxysmal AF was based on the onset of complaints as reported by the patients. Exclusion criteria were age <18 years, atrial flutter, and contraindications for flecainide infusion including reduced left ventricular function, heart failure symptoms, Brugada electrocardiogram (ECG), QRS duration >120 ms or bundle branch block, hypokalemia, acute ischemia, known hypersensitivity to flecainide, and known sinus node dysfunction. Anticoagulation was administered per hospital protocol. Written informed consent was obtained from all patients, and the institutional review boards of the participating hospitals approved the study.

Echocardiography

Before the administration of flecainide, a transthoracic echocardiography was performed with a Vivid 7 Ultrasound System (GE Healthcare, Little Chalfont, United Kingdom). Echocardiography was repeated 5 minutes after the administration of flecainide infusion. The frame rate was set above 100 Hz. The color TVI images were recorded in an apical 4-chamber view while the patient was lying in supine to a left-lying position and during the end-expiratory phase in order to avoid respiratory artifacts. By using commercially available software (Q-analysis, GE Healthcare), we offline analyzed the color TVI curves obtained in the late diastole from the lateral wall of the left atrium (LA) immediately above the mitral annulus, as validated and reported previously (Figure 1). The AFCL-TVI and AFV-TVI were measured from at least 3 heart cycles. Patients were excluded if the number of heart cycles available for TVI analysis was less than 3. On average, 4 cycles were measured per patient. The *AFCL-TVI* was defined as the time interval between 2 consecutive negative deflections of the late diastolic atrial tissue velocity curve and the average of at least 3 AFCL-TVIs was reported. The *AFV-TVI* was defined as the

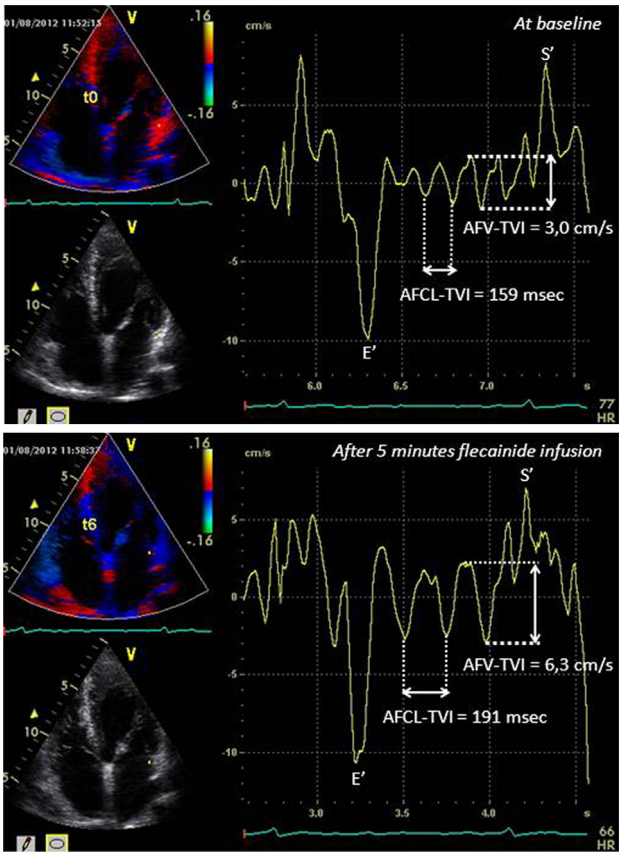

Figure 1 Change in AFCL-TVI and AFV-TVI after 5 minutes of flecainide infusion. AFCL-TVI = atrial fibrillatory cycle length determined by using tissue velocity imaging; AFV-TVI = atrial fibrillatory wall motion velocity determined by using tissue velocity imaging.

difference in the velocity of negative and positive deflections of the late diastolic atrial tissue velocity curve; the highest value found was reported. In addition, all patients underwent standard echocardiography determining left ventricular and atrial dimensions according to the recommendations as described in the American Society of Echocardiography guidelines.[18] The LA volume was indexed to body surface area (LA volume index). Patients were excluded from further analysis if patients had inadequate echocardiograms for TVI analysis owing to interference with ventricular motion. Patients who had inadequate echocardiograms had a higher median heart rate compared with patients in whom TVI measurement was feasible (120 ± 25 beats/min vs 102 ± 22 beats/min; $P < .001$).

Flecainide treatment

Under continuous ECG monitoring, all patients received infusion of 2 mg/kg (maximal 150 mg) of flecainide in 10 minutes. If there was conversion to SR, the infusion was terminated. Flecainide infusion was discontinued in case of side effects (such as excessive QRS widening, ventricular arrhythmias or compromise of AV conduction, or hypotension). The patient's rhythm was monitored, and blood pressure was measured for 1 hour after the administration