

Original articles

The ALPHA study (T-wave ALternans in Patients with Heart failure): rationale, design and endpoints

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Background. Sudden death and pump failure are the main causes of death in patients with heart failure. Patients with ischemic and non-ischemic cardiomyopathy are at similar risk of arrhythmic mortality; however, standard non-invasive and invasive tests are not routinely available for non-ischemic patients. T-wave alternans (TWA) has been proposed as a potential marker of susceptibility to ventricular tachycardia-fibrillation in several groups of patients.

Methods. The ALPHA study was designed to evaluate the independent predictive value of the measurement of microvolt TWA on the combined occurrence, after 18 months of follow-up, of cardiac death and life-threatening arrhythmias in a population of patients with non-ischemic dilated cardiomyopathy and NYHA class II and III. This is a multicenter prospective observational study. A total of 370 patients, with measurable TWA, will be enrolled during routine follow-up for heart failure treatment; a logbook will be used to collect basic information on the whole screened population. Patients will be enrolled during a 2-year period and will be followed up for 18 months. The primary endpoint of the study will be the combined incidence of cardiac death and life-threatening ventricular arrhythmias. The study will complete recruitment by mid 2004 and report in 2006.

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Introduction

Heart failure (HF) is a syndrome that affects over 6.5 million Europeans with 580 000 new cases diagnosed annually¹. Left ventricular dysfunction, reduced exercise tolerance, and ventricular arrhythmias are all associated with this condition². The prognosis is typically poor, with a 1-year all-cause mortality of approximately 12-15%³⁻⁵. Sudden death and pump failure due to progressive HF are the main causes of death in these patients. The goals of therapy are to minimize symptoms, improve functional capacity, and increase survival⁶. However, despite the continuous progress in the medical treatment of patients with HF, the mortality remains extremely high. Notably, a significant proportion of the mortality among patients in NYHA class II and III is due to ventricular tachyarrhythmias. Among antiarrhythmic drugs, amiodarone is the only agent that has been shown not to increase mortality⁵. However,

large randomized placebo-controlled clinical trials of amiodarone in patients with severe HF have yielded mixed results^{5,7}. Device therapy has been shown to reduce the total mortality in patients with ventricular tachyarrhythmias in randomized clinical trials comparing antiarrhythmic drugs and implantable cardioverter-defibrillators (ICD)^{8,9}. Among patients with ischemic heart disease, both non-invasive and invasive predictors of arrhythmic events have been identified; specifically, in post-infarction patients with left ventricular dysfunction clinical evidence shows a survival benefit with the use of an ICD^{8,9}. Although patients with non-ischemic dilated cardiomyopathy are similarly at high risk of arrhythmic mortality, the current screening methods have been shown to have a very low positive predictive value and are of limited value in the identification of those patients who could benefit from an ICD. Microvolt T-wave alternans (TWA) has been proposed as a potential marker of susceptibility to