Research letter

# Evaluation of Disease Progression in Arrhythmogenic Cardiomyopathy: The Change of Echocardiographic Deformation Characteristics Over Time

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**Text:**

Arrhythmogenic cardiomyopathy (AC) is an inherited cardiomyopathy characterized by progressive fibro-fatty replacement of the myocardium. Remarkably, previous studies suggest that progression of structural disease is uncommon during early stages of AC, while electrical disease progression is seen more frequently (1). One explanation for this discrepancy might be that conventional imaging methods have suboptimal sensitivity during early disease stages and may therefore be unable to detect subtle changes over time. Echocardiographic deformation imaging might be more sensitive than conventional imaging techniques for detection of structural disease progression in AC (2). We aimed to investigate the serial changes over time of echocardiographic deformation characteristics in AC.

We retrospectively included 86 subjects from the Netherlands AC registry who underwent two complete cardiac evaluations at our center, both including 2D-echocardiography. On the basis of baseline clinical evaluation, 50 subjects were classified as definite AC (fulfilling definite diagnosis according to the 2010 Task Force criteria [TFC]) and 34 subjects were classified as early AC (carrying a pathogenic mutation and having possible or borderline AC, but not fulfilling definite diagnosis). Mutations were predominantly desmosomal (32 [64%] in definite AC, 31 [86%] in early AC). The baseline findings of 49 subjects (57%) were described previously (3).

All echocardiograms were performed with Vivid 7 or Vivid E9 (GE Healthcare, Horten, Norway). At baseline and follow-up, we performed conventional echocardiographic measurements (as seen in **Figure 1A**). Additionally, 2D-speckle tracking was performed with EchoPAC version 202.39 (GE Healthcare, Horten, Norway). Regional deformation analyses were performed in the three segments of the right ventricular (RV) free wall (basal, mid and apical). As published previously, the regional deformation patterns were classified as type I (normal deformation), type II (delayed onset of shortening, reduced systolic peak strain and minor post-systolic shortening) or type III (predominantly systolic stretching and major post-systolic shortening) (3). Mechanical deterioration was defined as a change of the deformation pattern from type I to II/III, or from type II to III.

Overall, the mean follow-up duration was 6.6±3.1 years and did not differ significantly between definite AC and early AC. In definite AC subjects, all conventional echocardiographic measurements and deformation patterns deteriorated significantly between baseline and follow-up, which underlines the progressive character of this disease (**Figure 1**). In contrast, none of the conventional echocardiographic measurements changed significantly in early AC subjects. Relying only on these conventional parameters, one would conclude that structural disease progression is absent in early AC subjects. Strikingly, however, echocardiographic deformation imaging unmasked mechanical deterioration in 14 early AC subjects (39%). Mechanical deterioration was almost exclusively seen in the RV basal segment in this group (**Figure 1B**). These results strongly suggest that the first signs of structural disease progression can be unmasked by deformation imaging in this specific area. The deformation patterns that were found at baseline either remained stable or deteriorated, but did not reverse in any of the subjects, which implies that this is a stable marker of disease presence and progression.

Additionally, we studied the relation between mechanical deterioration and electrical disease progression. Fourteen early AC subjects had electrical disease progression during follow-up (defined as development of a new

electrical TFC which was absent at baseline). Interestingly, these subjects all had an abnormal deformation pattern in the RV basal segment after follow-up. These observations suggest that mechanical deterioration occurs in parallel with electrical disease progression. Remarkably, 6 subjects who did not have electrical disease progression also showed deterioration of the regional deformation pattern in the RV basal segment. This observation implies that mechanical deterioration may even precede electrical disease progression in early AC.

The present study is the first one to investigate the behavior of myocardial deformation in AC over time. The key finding is that echocardiographic deformation imaging unmasks progressive mechanical deterioration during the early stages of the disease, while conventional imaging measurements remain normal and unchanged. Our results suggest that mechanical deterioration develops in parallel with (or even prior to) electrical disease progression. We realize that the magnitude of disease progression in this study may potentially be overestimated due to selection bias.

Since the presence of structural disease identifies subjects who are at higher risk for adverse events, recognition of structural disease progression by deformation imaging may improve risk stratification during early stages of the disease (2). Accordingly, subjects with an unchanged deformation pattern may have a more benign disease course. Future studies should aim to investigate whether subjects with mechanical disease progression are at increased arrhythmic risk.

**References:**


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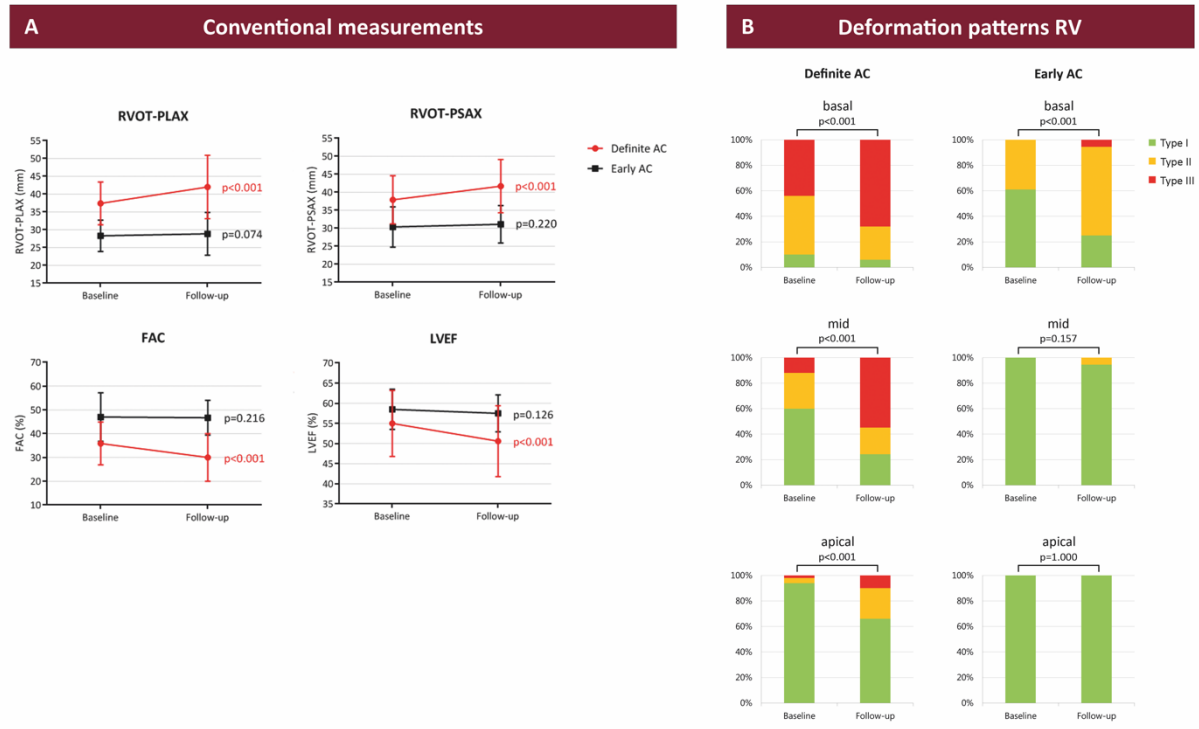
**Figure 1: The changes of echocardiographic measurements between baseline and follow-up.**




**(A)** The changes of conventional measurements in definite AC subjects (red) and in early AC subjects (black). **(B)** The changes of deformation patterns in definite AC subjects (left) and early AC subjects (right) in the three RV segments. AC=arrhythmogenic cardiomyopathy; FAC=fractional area change; LVEF=left ventricular ejection fraction; PLAX/PSAX=parasternal long/short axis view; RV=right ventricular; RVOT=right ventricular outflow tract.