Periodic repolarization dynamics in a patient with subacute myocarditis

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Introduction
Periodic repolarization dynamics (PRD) is a novel electrocardiography (ECG)-based biomarker referring to sympathetic activity–associated low-frequency oscillations of cardiac repolarization.1 Electrophysiological as well as experimental studies showed that PRD presumably reflects the effect of phasic sympathetic activity on the ventricular myocardium.1,2 There is a large body of evidence supporting that alterations of the sympathetic branch of the autonomic nervous system play a crucial role in the development of arrhythmic as well as nonarrhythmic complications.3,4 Previous studies were able to demonstrate the strong prognostic value of increased PRD levels in various diseases including in post–myocardial infarction patients as well as patients with chronic ischemic and nonischemic cardiomyopathy.1,5–7 However, patients with acute, subacute, or chronic myocarditis have not been studied particularly. Despite an improved understanding of its pathophysiology, myocarditis still shows limited therapy options and can lead to sudden cardiac death. Recently, the link between autonomic nervous function, predominantly with an increase in sympathetic tone, and inflammation has become of great interest in research and a close connection has been found, especially for myocarditis.8

Here, we describe the case of a man with subacute myocarditis showing distinct increases in the autonomic biomarker PRD compared to levels measured before the development of the disease.

KEY TEACHING POINTS
• Inflammatory cardiac processes such as myocarditis have been linked to dysfunctional states of the autonomic nervous system.
• To objectify autonomic nervous function, different heart rate– and electrocardiography-based biomarkers have been developed over the years. Periodic repolarization dynamics (PRD) is one of those biomarkers most likely reflecting the effect of efferent sympathetic activity on the level of the ventricular myocardium.
• PRD shows strong prognostic power in patients with ischemic as well as nonischemic cardiomyopathy.
• This case shows distinct elevation of PRD levels in a patient with myocarditis during the diseased state compared to levels obtained before developing the myocarditis.
• PRD changes might point to an increased risk for the development of malignant arrhythmias in patients with myocarditis.

KEYWORDS Autonomic function; ECG; Myocarditis; PRD; Repolarization instability

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All vital signs were within normal range. Laboratory testing revealed no signs of inflammation and cardiac biomarkers hsTnI and CK were not elevated. Resting ECG showed normal sinus rhythm without any repolarization abnormalities. In a long-term ECG we detected an increased number of symptomatic monomorphic premature ventricular contractions (168 beats in 24 hours). The patient stated that he has never experienced palpitations before; the premature ventricular contractions thus have to be considered as new and myocarditis-related. Echocardiography revealed a preserved left ventricular function with an ejection fraction of approximately 53% without relevant valve abnormalities. Speckle-tracking analysis revealed pathologic strain patterns predominantly inferolaterally (Figure 1A). Coronary artery disease was ruled out by computed tomography angiography. Cardiac magnetic resonance imaging demonstrated subepicardial late gadolinium enhancement in the inferior and inferolateral myocardial ventricular wall (Figure 1B) consistent with the diagnosis of a subacute myocarditis.

To investigate autonomic biomarkers, we additionally performed a high-resolution (1000 Hz) digital ECG in Frank-lead configuration in supine and resting condition for 20 minutes. The PRD level was significantly increased (8.19 deg²) when compared to the cut-off value of 5.75 deg² established in previous large trials. Since the patient coincidentally participated as a healthy volunteer in previous studies approximately 2 months before the development of the myocarditis, we had several recorded PRD values (1.87 deg² and 1.84 deg²) serving as baseline values for comparison (Figure 2A). The patient had excellent ECG quality for PRD measurement (ECG traces, Figure 2B). The patient was started on bisoprolol 2.5 mg once daily, and PRD levels measured 4 days later were suppressed (0.70 deg²) and remained at this low level afterwards (0.71 deg² and 1.12 deg²) (Figure 2).

Discussion

Several disease entities have been found to be associated with an autonomic dysbalance. Particularly in cardiologic diseases, an overactivity of the sympathetic nervous system increases the risk for the development of life-threatening arrhythmias. PRD as an ECG-based biomarker captures the effect of sympathetic activity on the level of the ventricular myocardium. Numerous previous studies have shown its strong prediction of adverse outcome in patients with acute and chronic myocardial infarction as well as with nonischemic cardiomyopathy.

Myocarditis is linked to autonomic dysfunction and this is associated with a higher incidence of arrhythmias. However, the validity of findings of increased autonomic biomarker in an acute disease state is often limited, as no prior measurements in the same patient are available. In our case, the patient coincidentally was part of a different trial as a healthy volunteer, and PRD measurements were obtained about 2 months before his myocarditis. Therefore, we are able to provide longitudinal data before and during the disease as well as after starting...
treatment with beta-blockers. As a result, the high PRD levels we observed can be clearly linked to the underlying myocarditis.

These changes in sympathetic activity–mediated repolarization instability during myocarditis might contribute to the occurrence of malignant cardiac arrhythmias. Clearly, systematic future studies are needed to further explore clinical implications.

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