

Normalised Heart Rate Variability After Sacubitril/Valsartan

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We present the case of a patient with heart failure and reduced ejection fraction. After changing from candesartan to sacubitril/valsartan, we saw a normalised heart rate variability.

Keywords

Heart rate variability (HRV), heart failure, implantable cardioverter-defibrillator (ICD), sudden cardiac death.

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We report the case of a 44-year-old woman with a history of chronic heart failure with reduced ejection fraction (HFrEF) due to ischemic cardiomyopathy (New York Heart Association [NYHA] class II). In 2010, she had a myocardial infarction with thrombotic occlusion of the left anterior descending coronary artery, alleged in the context of an essential thrombocythaemia. The patient had an ejection fraction of 35% and received a primary prevention subcutaneous defibrillator. Holter monitoring documented reduced heart rate variability (HRV) with a standard deviation of the normal-to-normal interval (SDNN) of 82 ms (*Figure 1*). The patient was switched to sacubitril/valsartan for prognostic purposes. After 4 months of angiotensin receptor/neprilysin inhibitor (ARNi) therapy we documented a normalised SDNN (162 ms, *Figure 2*). Furthermore, the rate of premature ventricular contraction (PVC) was greatly reduced to 0.1% after ARNi (41 PVC of 74,480 QRS complexes) compared to 1.7% (1,030 PVC of 62,268 QRS complexes) before. Interestingly, the left ventricular systolic function did not change.

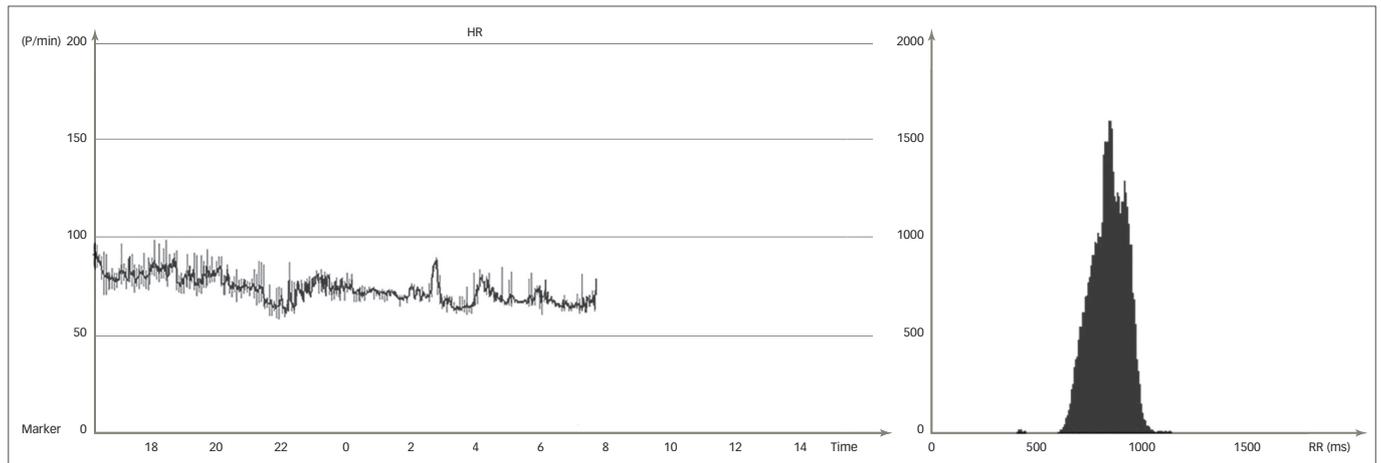
Discussion

Sacubitril/valsartan is indicated for treatment of symptomatic HFrEF. Its market approval was based on results of the pivotal PARADIGM-HF (Prospective Comparison of ARNi with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) study. This trial included 8,442 patients and was terminated early as it demonstrated a greater benefit of sacubitril/valsartan compared to enalapril in decreasing cardiovascular mortality and hospitalisations for heart failure.¹

Sacubitril/valsartan reduced cardiovascular mortality through a similar reduction in pump failure and sudden cardiac death (heart rate 0.80; 95% confidence interval; 0.73–0.87; $p < 0.001$).¹ Previous studies showed a correlation between myocardial wall stress with elevated natriuretic peptide and ventricular arrhythmias.^{2,3} De Diego et al. recently demonstrated a reduction of ventricular arrhythmias in 120 patients with implantable cardioverter-defibrillator (ICD) and HFrEF largely due to ischemic origin (82%). After 9 months of therapy with conventional renin-angiotensin-aldosterone system inhibition, patients were switched to sacubitril/valsartan.⁴ This study found reduced incidence of ventricular arrhythmias and demonstrated an increase in left ventricular ejection fraction by 8%. Natriuretic peptides may contribute to a reduction in sympathetic tone, and HRV is impaired in patients with HFrEF at risk of sudden cardiac death.⁵⁻⁷ Future studies will need to address the value of ICD implantation on top of optimal medical therapy with sacubitril/valsartan.⁸

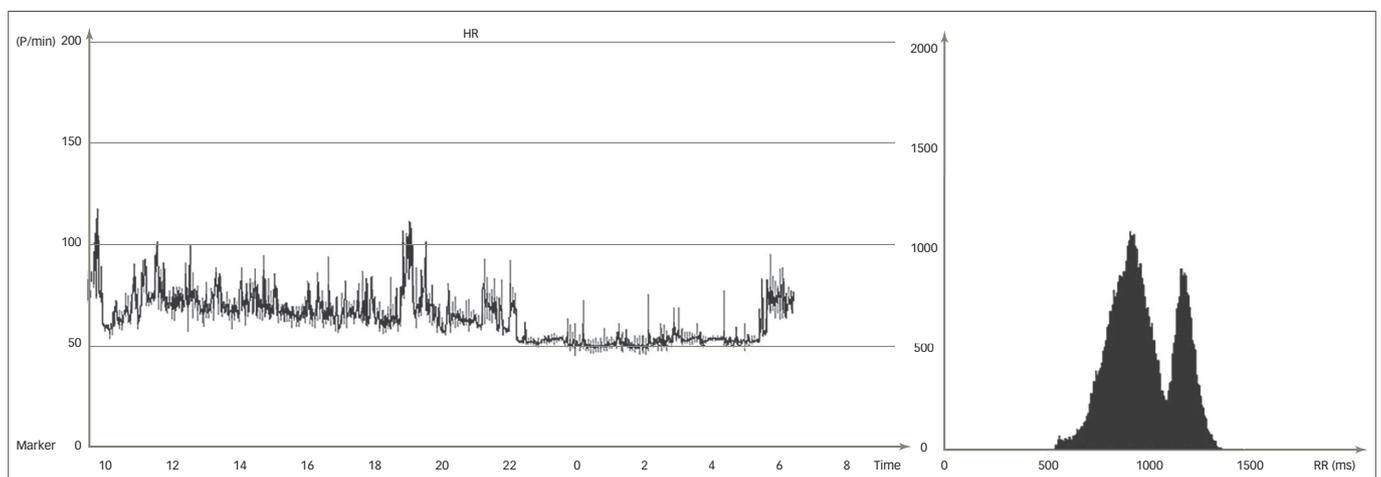
Our case is the first report of an increase in HRV after therapy with sacubitril/valsartan. Thus, the development of HRV in our patient emphasises the potential beneficial effect of ARNi regarding a risk of sudden cardiac death. The fact that these findings are independent from the left ventricular function underpins this assumption. □

Figure 1: Circadian heart rate and RR interval histogram of the Holter electrocardiogram prior to sacubitril/valsartan



Standard deviation of the normal-to-normal interval = 82 ms.

Figure 2: Circadian heart rate and RR interval histogram of the Holter electrocardiogram after sacubitril/valsartan



Standard deviation of the normal-to-normal interval = 162 ms.

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