

## ALTERATION OF HEART RATE VARIABILITY AS A EARLY PREDICTOR OF CARDIOVASCULAR EVENTS: A LOOK AT CURRENT EVIDENCE

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PII: S0002-9149(19)31454-7  
DOI: <https://doi.org/10.1016/j.amjcard.2019.12.010>  
Reference: AJC 24337

To appear in: *The American Journal of Cardiology*

Received date: 3 December 2019  
Accepted date: 12 December 2019

Please cite this article as: Girolamo Manno , Giuseppina Novo , Salvatore Novo , Egle Corrado , Giuseppe Coppola , ALTERATION OF HEART RATE VARIABILITY AS A EARLY PREDICTOR OF CARDIOVASCULAR EVENTS: A LOOK AT CURRENT EVIDENCE, *The American Journal of Cardiology* (2019), doi: <https://doi.org/10.1016/j.amjcard.2019.12.010>



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**Reader's comment**

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**Conflict of interest: none.**

**No financial interest in this manuscript**

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We appreciated very much the paper by Habibi M. et al<sup>1</sup>, recently published in the Journal. Authors studied the association of baseline resting heart rate (RHR) and short-term heart rate variability (HRV) as surrogates of autonomic nervous system (ANS) with incident atrial fibrillation (AF) in individuals without previous cardiovascular disease<sup>2</sup>. A total of 6,261 participants of the Multi-Ethnic Study of Atherosclerosis (MESA) who were free of AF and diagnosed cardiovascular disease were enrolled. Three standard 10-second, 12-lead electrocardiograms (ECG) were used to measure RHR, the standard deviation of normal-to-normal intervals (SDNN) and the root mean square of successive differences in RR intervals (RMSSD). It was found that cardiac ANS dysregulation indicated as higher RHR and lower HRV is associated with incident AF independent of known cardiovascular risk factors. Not only that, these results demonstrate how HRV and SNN can be considered as direct indicators of ANS dysregulations, especially when they are at a subclinical level, leading to AF, independently of other cardiovascular risk factors.

HRV is defined as the oscillation in both the interval between consecutive heartbeats (considered RR intervals) and the consecutive measures of instantaneous heart rates. HRV provides indirect insight into autonomic nervous system tone. In the last decades brought an increasing interest in HRV assessment as a diagnostic tool in detection of autonomic impairment, and prediction of prognosis in several cardiac disorders. Recently, 2019 ESC Guidelines on diabetes and pre-diabetes underlined the importance of low HRV (a marker of diabetic CV autonomic neuropathy)<sup>3</sup>. In fact it has been associated with an increased risk of fatal and non-fatal CAD<sup>4,5</sup>.

Our study group also recently conducted a retrospective study on 85 patients referred for suspected angina to the Cardiology Unit of the University Hospital “Paolo Giaccone”, in Palermo, who underwent coronary angiography (CA) in the period between May 2015 and June 2017<sup>6</sup>. We observed that the group with higher levels of Homeostatic Model Assessment

of Insulin Resistance (HOMA-IR) index, showed significantly reduced HRV parameters (SDANN, SDNN index and RMSSD) compared to subject with normal insuline sensitivity ( $91.6 \pm 22.5$  vs.  $116.1 \pm 25.32$ ,  $p = 0.001$ ;  $70.9 \pm 12.52$  vs.  $85 \pm 21.13$ ,  $p=0.007$  and  $27 \pm 8.27$  vs.  $40.11 \pm 20.66$ ,  $p= 0.004$ ) (Table 1). Accordingly, greater values of HOMA-IR were associated with a reduction in HRV indices at Simple Linear regression, and this relationship was confirmed for all the parameters taken into consideration, in particular for RMSSD ( $p<0.001$ ). Multivariate regression analysis showed an independent association of both RMSSD and SDNN with HOMA-IR. Our study demonstrated an association between reduced HRV and IR. Being HRV impaired in patients with IR even in the absence of overt metabolic syndrome it could be speculated that the autonomic impairment, highlighted with HRV reduction, can be an early event of cardiovascular events and chronotropic incompetence, so it could become a non-invasive marker to identify high risk patients deserving early treatment for organ damage prevention in IR condition<sup>7</sup>.

In conclusion, Habibi M. et al.<sup>1</sup> should be congratulated for their comprehensive study which contributes to found an independent association of high RHR and low or high HRV, as surrogates of ANS function, with new onset AF in a multiethnic population. Whether frequent rhythm surveillance in this population would be beneficial for early diagnoses of AF or whether modulation of ANS will decrease the risk of future AF needs further studies. This very interesting study will help to fill a knowledge gap in a currently evidence-poor field and that needs more clinical evidences.

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Journal Pre-proof