Journal Pre-proof

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

Girolamo Manno, Giuseppina Novo, Salvatore Novo, Egle Corrado, Giuseppe Coppola

 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 2019Accepted 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

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2019 Elsevier Inc. All rights reserved.

The American Journal of Cardiology		
January	1, 2017	
Comparison of Kerly Star Countys Retween Jaturations and Swachnuckluting Stem Unity/Optical Coherence Interapophy Data of Source and No. on Relaxander Stein Ando	Wate-Andysis of the Balatice of Echocorolographic Epicential Adjoine Teace Tealeries and the Mendodic Synchronic Development of a Method to Etab Seath Patients With	.n
Beins of Server K3 is not Polynomical Tany Acids Retrict on Coronary Manusclarus's in Statis Trackel Patients With Coronary Antary Traceae &	Destigrant of a Markal to Kat Southy Reserve With Haut Fallura for 20Dey Rasdiniasion Using Inglimitable Destar Tragmatics	.70
Comparison of These Place Discovers Alter Thinkoy Persistences Construct Internetistics in Patients With Left Ventricular Equation Frankrise ACEV Venue 140% (Frankrise INCECIPIEANE True). UP Solity and Elicopy of Sectional Place Texas. JP Solity and Elicopy of Sectional Place Venue. JP	Redicting and Researing Neon Tables Minophillisations: Is These a data for Inglisestate Device Degeosthol Comparison of Wardslee in New Yerses Warner Debegring "Device New York: Valor Inglisestan for Searce Rome, Services Scien Nation Maleseer Confliction Report.	.85
Proprietic Guildines of Serial Citizative Public Resumments in ST Devotor Acute Myscendral Infection	Report (Rechild South Anadhatis Managament With Conscious Sedators in Patients Undergang Transathere Asris Yahre Inscienting	
Darbitess of Helicite and Charantee Project Concentrations for Pandrices of Outcome Acate Concentry Underson State Mends Register of Acate 25/Devotor Net-SEConstan Mysocietud Velenitor 2423402 21	Incidence and Elect of Acore Kalway Injury After Transcelene Acet, Value Replacement Varie Network Value Academic Research Construct Online Cell Vantische Research Rescalifies in Long Term	100
Processed Worksholm on Handling in Anal World Parlers	Edit Farmande Konnen Bernberge in Jong Den Dr.12 Read European With Magainia Distant Condumygraphy Role of Server Witherstein Realization Reaction	106
Mactor 45 Orical Candidas and Programs Value of Film Mediated	Wetscretest in Despose of Cardioc Inchesters' in	m
Dilaton in Patanis With Nord? Segment Devotor Acute Conversy Syndrome. 31 Gender Differences in Calls to 911 During or Acute	Electroconforgeneille, Sported OES7, Angle and Incident Conforcementer Orientere in HV/Informed Parlame, Brann Re- Strategies for the Monogeneent of Antioetrocical Decays (2004)01 Study.	
Coronary Syndrome		
Runan Innormalificancy Visualificited Patients With Point Tana Acute Coronary Tyndroma	No the samples halo of Contests, the page AL AL AN antissian And Taxtu www.ajaandine	
Andjais of the Panolance of Cardiovascular Diaeses and Associated Balk Spotter for Europeon-American-and Advance-American-Reputations in the State of Peringhnesis 2007 – 2009 68	22	-

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

Reader's comment

Girolamo Manno^{a,#}, Giuseppina Novo^a, Salvatore Novo^a, Egle Corrado^a, Giuseppe Coppola^a.

 a. Cardiology Unit, University Hospital P. Giaccone, Department of Excellence of Sciences for Health Promotion and Mothernal-Child Care, Internal Medicine and Specialities (ProMISE) "G. D'Alessandro", Palermo, Italy

Conflict of interest: none.

No financial interest in this manuscript

#Corresponding author:

Dr. Girolamo Manno

Via Verona, 37 Raffadali (AG) 92015; +39 3683482563

Email: girolamomanno@hotmail.it

Journal Pre-proof

We appreciated very much the paper by Habibi M. et al¹, 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 autonomical nervous system (ANS) with incident atrial fibrillation (AF) in individuals without previous cardiovascular disease². 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-tonormal 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 consecutives 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)³. In fact it has been associated with an increased risk of fatal and non-fatal CAD^{4,5}.

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 2017⁶. We observed that the group with higher levels of Homeostatic Model Assessment

Journal Pre-proof

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 condition⁷.

In conclusion, Habibi M. et al.¹ 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.

REFERENCES

- Habibi M, Chahal H, Greenland P, Guallar E, Lima JAC, Soliman EZ, Alonso A, Heckbert SR, Nazarian S. Resting Heart Rate, Short-Term Heart Rate Variability and Incident Atrial Fibrillation (from the Multi-Ethnic Study of Atherosclerosis (MESA)). Am J Cardiol. 2019 Dec 1;124(11):1684-1689.
- Skov MW, Bachmann TN, Rasmussen PV, Olesen MS, Pietersen A, Graff C, Lind B, Struijk JJ, Kober L, Haunso S, Svendsen JH, Gerds TA, Holst AG, Nielsen JB. Association between heart rate at rest and incident atrial fibrillation (from the Copenhagen Electrocardiographic Study). Am J Cardiol 2016;118:708–713.
- 3. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, Federici M, Filippatos G, Grobbee DE, Hansen TB, Huikuri HV, Johansson I, Jüni P, Lettino M, Marx N, Mellbin LG, Östgren CJ, Rocca B, Roffi M, Sattar N, Seferović PM, Sousa-Uva M, Valensi P, Wheeler DC; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2019 Aug 31. pii: ehz486.
- Liao D, Carnethon M, Evans GW, Cascio WE, Heiss G. Lower heart rate variability is associated with the development of coronary heart disease in individuals with diabetes: the atherosclerosis risk in communities (ARIC) study. Diabetes. 2002;51(12):3524-31.
- 5. Pop-Busui R, Evans GW, Gerstein HC, Fonseca V, Fleg JL, Hoogwerf BJ, Genuth S, Grimm RH, Corson MA, Prineas R; ACCORD Study Group. Effects of cardiac autonomic dysfunction on mortality risk in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. Diabetes Care. 2010;33(7):1578-84.

- Novo G, Manno G, Levantino P, Cangemi S, Evola V, GiustinaVitale, Evola S, Luparelli M, Novo S. Long-term parameters of heart rate variability in patients with insulin-resistance. J Cardiovasc Med (Hagerstown). 2019 Nov;20(11):792-793.
- Björkander I, Forslund L, Ericson M, Rehnqvist N, Hjemdahl P, Kahan T. Longterm stability of heart rate variability in chronic stable angina pectoris, and the impact of an acute myocardial infarction. Clin Physiol Funct Imaging. 2009 May;29(3):201-8. doi: 10.1111/j.1475-097X.2009.00857.