International Journal of Cardiology 171 (2014) e42–e45

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Gender differences in the interaction between heart rate and its variability — How to use it to improve the prognostic power of heart rate variability ☆

Jerzy Sacha [a,*], Szymon Barabach [a], Gabriela Statkiewicz-Barabach [b], Krzysztof Sacha [c], Alexander Müller [d], Jaroslaw Piskorski [e], Petra Barthel [d], Georg Schmidt [d]

[a] Department of Cardiology, Regional Medical Center, Opole, Poland
[b] Institute of Physics, Wroclaw University of Technology, Wroclaw, Poland
[c] Instytut Fizyki imienia Mariana Smoluchowskiego and Mark Kac Complex Systems Research Center, Uniwersytet Jagiellonski, ulica Reymonta 4, PL-30-059 Krakow, Poland
[d] 1.Medizinische Klinik und Deutsches Herzzentrum München der Technischen Universität München, Munich, Germany
[e] Institute of Physics, University of Zielona Gora, Zielona Gora, Poland

ARTICLE INFO

Article history:
Received 5 September 2013
Accepted 30 November 2013
Available online 7 December 2013

Keywords:
Heart rate
Heart rate variability
Autonomic nervous system
Myocardial infarction
Mortality

Accelerated heart rate (HR) as well as reduced heart rate variability (HRV) are commonly recognized risk factors for different adverse outcomes in various diseases [1,2]. Yet, there is a growing body of evidence that elevated HR is mainly a significant predictor of such outcomes in men but not in women [3]. Moreover, HR and HRV are associated with each other but this relationship is both physiologically and mathematically determined [4–6]. Recently, we have shown that the association between HR and HRV may be mathematically modified, i.e. one may strengthen or weaken the HRV dependence on HR [7]. By using this method, we have demonstrated that HR contributes to the prognostic power of HRV in patients after myocardial infarction (MI), albeit, this contribution is different for different outcomes, i.e. it is positive for cardiac death but negative for non-cardiac one [8]. Indeed, if HRV becomes more dependent on HR, its predictive ability increases for cardiac mortality but decreases for non-cardiac one — conversely, when losing this dependence, HRV is losing its power for predicting cardiac death but gaining its power for non-cardiac one [8]. However, this phenomenon has never been tested in males and females separately. The goal of the study was to explore the HR impact on the prognostic value of HRV in different genders.

We analyzed the post-MI patients recruited between January 1996 and December 2000 (i.e. the exploratory sample, n = 1455; 1154 males) and then validated the results by studying another post-MI population recruited between January 2001 and December 2005 (i.e. the validation sample, n = 946; 782 males). Both cohorts took part in earlier studies and were followed up for 5 years—the details have been published elsewhere [9]. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee and all participants gave their informed consent.

Each of the patients underwent Holter recording during the second week after the index infarction. Spectral HRV indices were estimated from 512 RR interval segments and then averaged for every patient. Power spectra were calculated by means of the fast Fourier transform and the following indices were distinguished: very low frequency (VLF, 0.003–0.04 Hz), low frequency (LF, 0.04–0.15 Hz), high frequency (HF, 0.15–0.6 Hz) and total power (TP, 0.003–0.6 Hz). Seven classes of spectral HRV indices with different dependence on HR were obtained by either division or multiplication of average standard indices of each patient by different powers of the corresponding average RR interval (avRR), i.e.: hrv1—by division of standard HRV indices by avRR to the power 4; hrv2—by division of standard HRV indices by avRR squared; hrv3—consisted of standard HRV indices; hrv4—by multiplication of standard HRV indices by avRR squared; hrv5—by multiplication of standard HRV indices by avRR to the power 4; hrv6—by multiplication of standard HRV indices by avRR to the power 8; and hrv7—by multiplication of standard HRV indices by avRR to the power 16. Their respective average Spearman correlation coefficients with HR were: −0.001, −0.4, −0.64, −0.78, −0.85,−0.93, and −0.97 (all statistically significant except for hrv1). In the hrv1 and hrv2 classes the HRV dependence on HR was weakened, but it was strengthened in the hrv4, hrv5, hrv6 and hrv7 classes. During the follow-up period 135 patients (104 males) and 49 patients (42 males) died in the exploratory and validation group, respectively. The exact description of the method, analyzed population and protocol has been published elsewhere [7,8].

☆ All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Regional Medical Center - Department of Cardiology, Al. Witosa 26, 45-418 Opole, Poland. Tel.: +48 77 452 06 60; fax: +48 77 452 06 99.
E-mail address: sacha@op.pl (J. Sacha).

http://dx.doi.org/10.1016/j.ijcard.2013.11.116

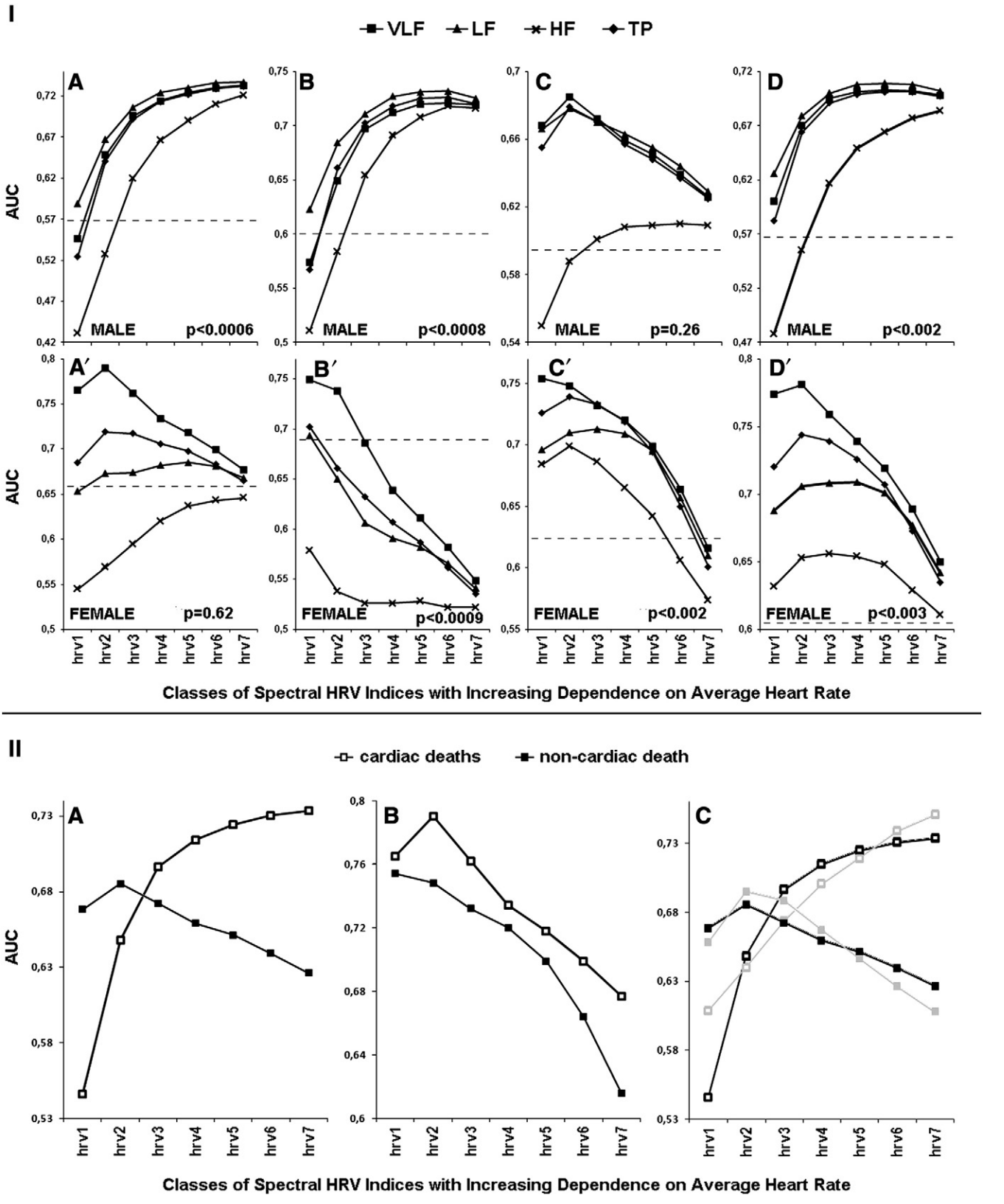

Fig. 1. Exploratory study: panel I presents the prognostic powers (AUC, area under receiver–operator characteristic curves) of spectral indices from various HRV classes for different modes of death in males and females, i.e.: cardiac death (A, A′); sudden cardiac death (B, B′); non-cardiac death (C, C′); and all-cause death (D, D′), (p-values refer to Friedman ANOVA test for differences between classes). All AUC above dashed lines are significantly different from 0.5, those below are not. Panel II depicts the predictive powers (AUC) of VLF for cardiac versus non-cardiac death in men (A) and women (B) from the exploratory sample, and in men from both exploratory and validation sample (C) — data corresponding to the exploratory sample are marked with black color but those of validation one with gray color. Of note, in men, VLF from hrv1 is a stronger predictor of non-cardiac than cardiac death and conversely, VLF from hrv7 is more powerful in predicting cardiac than non-cardiac death. However, in women VLF from hrv1, which is completely HR-independent, is as good in predicting cardiac death as non-cardiac one. The diagram in panel II C represents data from male subgroups in the exploratory and validation samples — one can see a very good correspondence between prognostic powers of VLF for cardiac and non-cardiac death in men from both samples (compare black and gray lines in panel II C). Such a comparison was not possible in women, since in the validation sample, only 3 of them died from cardiac causes and 4 from non-cardiac ones and consequently all AUCs were not different from 0.5.