

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 34545

Title: Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study

Reviewer's code: 00058696

Reviewer's country: United States

Science editor: Li-Jun Cui

Date sent for review: 2017-06-16

Date reviewed: 2017-06-19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

I have carefully evaluated this new manuscript. This is a confirmatory study, but the manuscript is not organized as such. GS Hillis has published: i. a multicenter study; ii. there was a large number of patients; iii. the patients' medication list was better evaluated; iv. the patients rested for a minimum of 5 minutes in the seated position prior to obtaining resting heart rate; v. increased heart rate was associated with increased cardiovascular deaths; but vi. the median follow up was only 4.4 years. In the authors' present manuscript: 1) No hypothesis is presented. 2) There must be a problem to solve. The authors do not provide a clear contrast between the results of the Hillis study and the similar results of Stettler (reference 23), in comparison to the results of Anselmino (reference 19) who identified no increased cardiovascular risk in diabetic patients. The authors then need to explain how the organization of their present study helps to understand the differences in these previously reported results. 3) In this present study, there is no clear evidence for increased cardiovascular risk (see Table 2) in

individuals with increased heart rate; is this because the number of participants is much lower than the number included in the Hillis study or perhaps the Hillis study is too short to judge the risk of death from non-cardiovascular causes? 4) Abstract, Results: final sentence is not supported by the Authors' results. 5) Abstract, Conclusion: "additional prognostic information can be gleaned from this". This statement has to be removed; the authors do not provide a specific heart rate that can be applied uniformly to judge any risk using a heart rate obtained in a diabetic patient. The heart rates in this study were taken from ECG reports. There was no uniform rest period described prior to these ECGs. 6) In blood chemistries, was a thyroid blood test obtained? 7) In the Methods, the authors need to state that the patients' medication lists were not complete. 8) Results: "Those with resting heart rate greater than the median had higher BMI". In the discussion, this is not well considered. In a systematic approach, was this finding in part related to deconditioning (e.g. less physical activity), heart failure with edema, or metabolic disorders in diabetic patients (i.e. thyroid dysfunction or B vitamin deficiencies). 9) Discussion: "preventive efforts such as aggressive control of hyperglycemia to minimize the prevalence of"; if the authors have some data to demonstrate that improved control of the blood sugar prevents the complication of neuropathy, please put in the data or the reference. 10) In the discussion, one would prefer the authors to provide some idea how they would organize future studies of potential mechanisms for an increased heart rate in diabetic patients. If this mechanism were better understood, then the causes of death might be better understood. At that point, preventive medical care could be considered.

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 34545

Title: Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study

Reviewer's code: 03429673

Reviewer's country: United States

Science editor: Li-Jun Cui

Date sent for review: 2017-06-16

Date reviewed: 2017-06-25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a retrospective data analysis of 1,315 patients with type 2 diabetes to determine the association between resting heart rate (RHR) and all-cause and cardiovascular disease mortality. The authors used Cox proportional hazards regression to calculate HR with adjustment for certain confounders. They concluded that heart rate is an independent predictor of all-cause and cardiovascular disease mortality in this diabetic study population. Overall the manuscript is well written. The main results are clearly expressed in the tables and figures. There are a few concerns about the limitations of this study: 1. This is a retrospective cohort study conducted in a single center. The results suggest association, not causality. 2. The proposed underlying mechanism that affects RHR is cardiac autonomic dysfunction in diabetic patients. This may be influenced by not only A1c (a surrogate marker for diabetes control) and duration of diabetes, but also the presence of diabetic complications such as diabetic neuropathy, nephropathy and retinopathy. Adjusting for those diabetic complications may be helpful and relevant. It

would be better if the authors could retrieve data on diabetic complications and adjust for those confounders. 3. RHR could be significantly affected by certain medications, e.g. beta-blockers and non-hydro-pyridine calcium channel blockers. It would be much better if the authors could retrieve pharmacy data and adjust for certain medications as confounders. The association between higher RHR and the presence of type 2 diabetes was documented by analysis of data from the 2010-2013 Korea National Health and Nutrition Examination Survey (KNHANES). (PLoS One. 2016 Dec 16;11(12):e0168527. doi: 10.1371/journal.pone.0168527. eCollection 2016.) The predictive value of RHR for CV morbidity and mortality and all-cause mortality has been reported in diabetic patients: (Eur J Prev Cardiol. 2016 Aug;23(12):1298-306.) (Diabetes Care. 2012 Oct;35(10):2069-75.). The findings from this manuscript would not contribute to the existing literature. In addition, higher RHR has been reported to be associated with both cardiovascular and non-cardiovascular mortality In general population. This association suggests that RHR probably is a marker of overall well-being, rather than a specific disease marker. (Am J Cardiol 2017;119:1003-7).

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 34545

Title: Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study

Reviewer's code: 03699916

Reviewer's country: Denmark

Science editor: Li-Jun Cui

Date sent for review: 2017-06-16

Date reviewed: 2017-06-26

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This study is a well-design observational study. In this study, authors investigate the association of resting heart rate with all-cause and cardiovascular disease (CVD) mortality in the Diabetic patients from analyses of 4 different models. Authors demonstrate that heart rate is an independent predictor of all-cause and CVD mortality in this population with type 2 diabetes. The only limitation is that in all models the factor of medication is not possible to include, however the authors provide a reasonable explanation. Furthermore, the conclusions of the study come from the whites and blacks, therefore the results may not be extended to other race/ ethnicities as authors suggestion. However the results of this study may be suggested that the same study should be done in other race/ ethnicities. The manuscript is well written and the English is good, and it is relevant for the readership of WJD. It is suggested to be accepted for publication in WJD.

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 34545

Title: Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study

Reviewer's code: 00506294

Reviewer's country: Spain

Science editor: Li-Jun Cui

Date sent for review: 2017-06-16

Date reviewed: 2017-06-28

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> [Y] Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> [] High priority for publication
<input checked="" type="checkbox"/> [Y] Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> [Y] No	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

The article: "Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study" is an interesting clinical research based on data of the Diabetes Heart Study with many subjects and the authors demonstrate that heart rate is an independent predictor of all-cause mortality in this population with type 2 diabetes mellitus and they show the relationship between heart rate increase and the degree of mortality. The study is well designed and the statistical methodology is correct and the conclusion can to be considered.

PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 34545

Title: Heart Rate is an independent predictor of all-cause mortality in Individuals with Type 2 Diabetes: The Diabetes Heart Study

Reviewer's code: 02446566

Reviewer's country: Japan

Science editor: Li-Jun Cui

Date sent for review: 2017-06-16

Date reviewed: 2017-07-01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript describes simple and interesting result that high resting heart rate predict mortality even in diabetics who frequently have neuropathy in sympathetic and/or para-sympathetic nervous system. The author has found that older participants had lower heart rate. Then, for an elderly patient, 1SD increase from median may have more risk as compared with the result from the whole age group. If data available, I want a table of median resting heart rate for several age groups. Increased resting heart rate may result from small stroke volume and shift of pressure-volume curve. minor point Page 5 third line from the bottom "HBA1c" may be "HbA1c". Page 6 line 15 "if all-cause" may be "of all-cause"