EDITORIAL

Resting Heart Rate: A Valuable Marker for Preventing Kidney Disease

Amr Abdin 💿, MD; Michael Böhm 💿, MD

esting heart rate (RHR) is an easily available biological parameter in clinical practice. Increased RHR is a known marker of increased mortality and the incidence of heart failure and other cardiovascular disease.^{1–3} The influence of elevated RHR on adverse outcomes and mortality in heart failure has been extensively studied, particularly in sinus rhythm with evidence that targeting an RHR <70 beats per minute (bpm) is beneficial.⁴ Therefore, in cardiovascular conditions in general, elevated RHR might be a useful risk indicator, while only in heart failure RHR represents a significantly modifiable risk factor.⁵ In addition, an association between high RHR and kidney disease has been established.⁶ High RHR may also predict kidney injury including microalbuminuria, independent of other cardiovascular risk factors.6-8

See Article by Tsai et al.

In this issue of the *Journal of the American Heart Association (JAHA*), Tsai et al examined the association between RHR and the risk of end-stage renal disease (ESRD) by studying 2504 patients with ESRD with a median follow-up of 13 years.⁹ They found that participants with an RHR of ≥80 bpm had a higher stage of chronic kidney disease, a lower estimated glomerular filtration rate, and more proteinuria than participants with an RHR of 60 bpm to 69 bpm. The risk of incident ESRD remained significantly elevated (HR 1.32, 1.10, 1.58 per 10-beat increase from 60 bpm). These results were consistent among all subgroups studied, including young and older people, men and women, and those with or without cardiovascular risk factors.

Tsai et al are to be congratulated on an important contribution to the evolving literature on the association between high RHR and kidney disease. Data from this study showed that even after excluding common cardiovascular risk factors such as smoking, hypertension, diabetes, hyperlipidemia, overweight, and obesity, high RHR continued to be significantly and independently associated with an increased risk of ESRD. A notable strength of the current analysis is that an increase in RHR between visits was also associated with an increased risk of ESRD. Even if RHR changed between 2 visits in the same patient, people with a higher RHR were at increased risk of ESRD.

Several mechanisms may underlie these effects. First, tachycardia is a recognized marker of the state of autonomic imbalance, sympathetic activation, and decreased vagal tone.^{1,7} During sympathetic overactivation, the production of vasodilators decreases and the production of vasoconstrictor factors increases.⁷ These autonomic imbalances lead to mitogenicity in the long-term effects on vascular smooth muscle and glomerular mesangial cells and consequently glomerular

Key Words: Editorials A heart rate kidney disease prevention

Correspondence to: Amr Abdin, MD, Klinik für Innere Medizin III-Kardiologie, Angiologie und Internistische Intensivmedizin Universitätsklinikum des Saarlandes, Kirrberger Street 100, 66421 Homburg, Germany. Email: amr.abdin@uks.eu

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

This article was sent to Yen-Hung Lin, MD, PhD, Associate Editor, for editorial decision and final disposition.

For Sources of Funding and Disclosures, see page 2.

^{© 2023} The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha

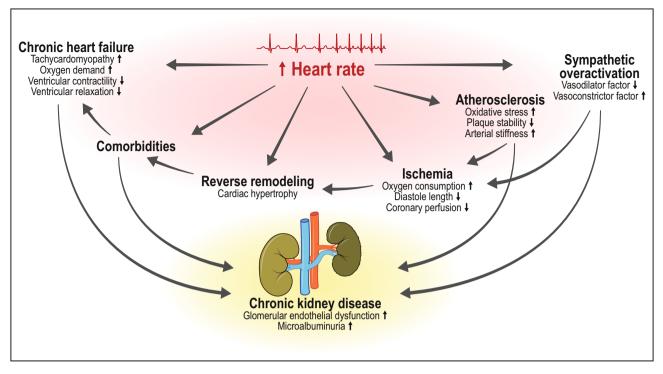


Figure Pathophysiological effects of heart rate on the cardiovascular disease continuum and chronic kidney disease.

endothelial dysfunction. Moreover, the progression of atherosclerosis and therefore nephrosclerosis due to changes in endothelial oxidative stress, which is sensitive to RHR reduction⁶ (Figure).

Fortunately, drugs that lower HR, such as β -blockers and ivabradine, can be used safely in ESRD. Furthermore, ivabradine can be safely used to reduce RHR in patients with heart failure with higher symptom burden and critically ill patients without lowering the blood pressure.¹⁰

Interestingly, in this analysis, the hazard ratios for ESRD displayed a *J-shaped* relationship. These findings indicate potential risks associated with RHR values <60 bpm in relation to ESRD. Some previous analyses suggest that bradycardia (RHR <60 bpm) may impede renal perfusion, thereby increasing the likelihood of kidney diseases.¹¹ Consequently, the authors designated the RHR range of 60 bpm to 69 bpm as the reference group, as they postulate that maintaining an RHR within this range might be preferable. Further investigation is warranted to determine whether the risk of adverse outcomes is heightened among individuals with an RHR <60 bpm.

These results suggest that monitoring and managing changes in RHR over time may be an important part of ESRD risk management. In addition, RHR may serve as a valuable marker for identifying high-risk individuals, which may help in the early detection of kidney disease and enable timely application of preventive strategies.

ARTICLE INFORMATION

Affiliation

Klinik für Innere Medizin III, Universitätsklinikum des Saarlandes, Saarland University, Homburg, Saar, Germany.

Sources of Funding

MB is supported by the Deutsche Forschungsgemeinschaft (German Research Foundation; TTR 219, project number 322900939).

Disclosures

AA reports speaker's honoraria from Boston Scientific and Bayer. MB reports personal fees from Abbott, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Cytokinetics, Medtronic, Novartis, Servier, and Vifor.

REFERENCES

- Ceconi C, Guardigli G, Rizzo P, Francolini G, Ferrari R. The heart rate story. *Eur Heart J Suppl*. 2011;13:C4–C13. doi: 10.1093/eurheartj/sur014
- Larsson SC, Drca N, Mason AM, Burgess S. Resting heart rate and cardiovascular disease. *Circ Genom Precis Med.* 2019;12:e002459. doi: 10.1161/CIRCGEN.119.002459
- Ho JE, Larson MG, Ghorbani A, Cheng S, Coglianese EE, Vasan RS, Wang TJ. Long-term cardiovascular risks associated with an elevated heart rate: the Framingham Heart Study. J Am Heart Assoc. 2014;3:e000668. doi: 10.1161/JAHA.113.000668
- Böhm M, Swedberg K, Komajda M, Borer JS, Ford I, Dubost-Brama A, Lerebours G, Tavazzi L; SHIFT Investigators. Heart rate as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomised placebo-controlled trial. *Lancet*. 2010;11:886–894. doi: 10.1016/S0140-6736(10)61259-7
- Abdin A, Anker SD, Cowie MR, Filippatos GS, Ponikowski P, Tavazzi L, Schöpe J, Wagenpfeil S, Komajda M, Böhm M. Associations between baseline heart rate and blood pressure and time to events in heart failure with reduced ejection fraction patients: data from the QUALIFY international registry [published online September 4, 2023]. *Eur J Heart Fail.* doi: 10.1002/ejhf.3023

- Böhm M, Schumacher H, Schmieder RE, Mann JF, Teo K, Lonn E, Sleight P, Mancia G, Linz D, Mahfoud F, et al. Resting heart rate is associated with renal disease outcomes in patients with vascular disease: results of the ONTARGET and TRANSCEND studies. *J Intern Med.* 2015;278:38–49. doi: 10.1111/joim.12333
- Inoue T, Iseki K, Iseki C, Ohya Y, Kinjo K, Takishita S. Heart rate as a risk factor for developing chronic kidney disease: longitudinal analysis of a screened cohort. *Clin Exp Nephrol.* 2009;13:487–493. doi: 10.1007/ s10157-009-0193-3
- Böhm M, Reil JC, Danchin N, Thoenes M, Bramlage P, Volpe M. Association of heart rate with microalbuminuria in cardiovascular risk patients: data from I-SEARCH. J Hypertens. 2008;26:18–25. doi: 10.1097/HJH.0b013e3282f05c8a
- Tsai MK, Gao W, Chien KL, Kyaw TW, Baw CK, Hsu CC, Wen CP. Resting heart rate independent of cardiovascular disease risk factors is associated with end-stage renal disease— a cohort study based on 476,347 adults. *J Am Heart Assoc.* 2023;12:e030559. doi: 10.1161/ JAHA.123.030559
- Abdin A, Komajda M, Borer JS, Ford I, Tavazzi L, Batailler C, Swedberg K, Rosano GMC, Mahfoud F, Böhm M, et al. Efficacy of ivabradine in heart failure patients with a high-risk profile (analysis from the SHIFT trial). ESC Heart Fail. 2023;10:2895–2902. doi: 10.1002/ ehf2.14455
- Farkas JD, Long B, Koyfman A, Menson K. BRASH syndrome: bradycardia, renal failure, AV blockade, shock, and hyperkalemia. *J Emerg Med.* 2020;59:216–223. doi: 10.1016/j.jemermed.2020.05.001