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Resting Heart Rate and its Effect on All-Cause Morbidity and Mortality

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Abstract

- According to the American College of Cardiology (ACA 2019), approximately every 40 seconds an individual has a myocardial infarction (MI).
- While the ACA reports a decrease in death rate from cardiovascular disease by 18.6% (2006-2016) and a decrease in death rate from coronary artery disease by 31.8% (2006 – 2016); Heart disease remains the leading cause of death, affecting approximately 5.7 million American adults.
- A literature review was conducted through systematic reviews, meta-analyses, randomized controlled trials (RCTs), and peer-reviewed medical journals, The Journal of the American Medical Association (JAMA), and The Journal of the American College of Cardiology (ACC), to evaluate the effects of variation in resting heart rate and its effect on cardiovascular morbidity and mortality.
- Literature shows a reduction in resting heart rate to 80 beats per minute or lower has a significant reduction in deposition of plaque within the cardiovascular system, reducing the risk of complications such as coronary artery disease, myocardial infarction, stroke, and death. Additionally, no benefit is found in reduction of resting heart rate below 60 beats per minute, through any method or than natural occurrence.
- *Keywords*: resting heart rate, resting tachycardia, resting bradycardia, atherosclerosis, cardiovascular disease, morbidity, and mortality.

Introduction

- According to the American Heart Association (2016), heart failure affects approximately 5.7 million adults in the United States, with the number of heart failure diagnosis increasing each year.
- This study focuses on resting heart rate and its effects on morbidity and mortality.
- Resting heart rate groups include: <60 beats per minute. 60-80 beats per minute, and >80 beats per minute.

Statement of the Problem

- In the United States, heart disease is the leading cause of death in men and women of most ethnicities, accounting for approximately 610,000 deaths annually according to the CDC (2019). With guidelines aiming to reduce blood pressure and reduce atherosclerosis (plaque deposits in the blood vessels), how closely is heart rate, especially resting tachycardia, being looked at in the development of heart disease, associated morbidity and mortality? All major contributing factors of cardiovascular disease need to be addressed if heart disease, associated morbidity and mortality are to be significantly reduced, this includes bradycardia, resting tachycardia and their effect on cardiovascular disease.

Research Questions

- In the general population, does variation in heart rate reduce chance of cardiovascular disease, morbidity and mortality in those with bradycardia?
- Does tachycardia increase the risk for cardiovascular disease, morbidity and mortality, compared to those with a heart rate in target range?

Literature Review

- **Bradycardia and its associated risk of cardiovascular disease and mortality.**
  - Messerli et al (2016) concluded that in those with heart failure, the use of negative chronotropic drugs (beta blocker, calcium channel blocker) reduced cardiovascular events and exacerbations by reducing oxygen demand of the cardiovascular system. Adversely, in patients with hypertension, reduction of resting heart rate increases the chance of cardiovascular event, through increased central systolic blood pressure and decreased brachial blood pressure, causing a ventricular – vascular mismatch
  - Dharod et al. (2016) found that patients with a resting heart rate of <60 bpm, regardless of ethnicity and not on heart rate modifying medications, had similarities including lower BMI, less likely to have diabetes, increased physical activity and of male sex. In addition, these individuals were more likely to have changes represented on EKG. Patients who are on a heart rate modifying medication and have a resting heart rate of <60 bpm showed an increased risk of mortality due to cardiovascular disease, compared to those who are not on heart rate modifying medication. Table 4 shows correlation of heart rate categories, hazard ratios for cardiovascular disease and the associated mortality rate.
  - Makita et al. (2014) compared the effects of bradycardia and the development of cardiovascular disease to the well-established findings of tachycardia and its known comorbidity of cardiovascular disease events in men. In the study, 17,766 men and women were studied with the results of the study based on a mean follow-up time frame of 5.6 years. Noted cardiovascular events occurred 213 times in men and occurred 186 times in women. Of the groups based on resting heart rate, increased risk of cardiovascular disease events was greatest in men with a resting heart rate of <60 beats per minute, as well as the group of men and women whose resting heart rate was equal to or >80 beats per minute
- **Target heart range and its associated cardiovascular risk.**
  - Steward et al. (2017) focused on lifestyle and their modification according to the guideline references noted in the methods portion. Lifestyle modifiers focused on areas including; exercise, diet, alcohol consumption, weight, smoking cessation. Additional modifiers considered that involve medical therapy include; anti-hypertensive therapy, lipid lowering therapy, anti-platelet therapy and blood glucose control. An important factor when considering lifestyle change is the effect on systolic and diastolic blood pressure, as well as BMI. Those who have a blood pressure >115/75, where each 20mmHg rise in systolic blood pressure (115) or a 10mmHg rise in diastolic blood pressure (75) doubles an individual's risk for cardiovascular disease event occurrence. Additionally, those with a BMI >25 show increased risk for development of cardiovascular disease, while those with a BMI <20 have an increased all cause mortality. Optimal BMI is 20-25.

Literature Review Cont.

- **Tachycardia and its associated risk of cardiovascular disease.**
  - . Palatini (1999) notes a study conducted on Army officers correlating a two to three times higher frequency of developing hypertension in those with transient tachycardia, as compared to those who had heart rate within target, dating back to 1945. Levy, White, Stroud (1945) were the first to publish in the Journal of American Medical Association a found correlation between resting tachycardia and increase in cardiovascular mortality.
  - In the elderly, Sutton-Tyrrell, Alcorn, Herzog, et al studied 187 patients with systolic hypertension. In the studied patients, a correlation between those with a resting heart rate and development of carotid stenosis was evident (p=0.013).
  - In patients with hypertension, cardiovascular relative risk was adjusted for those who smoke, factored in total cholesterol, and those with left ventricular hypertrophy. With previous mentioned risk factors considered, incidence for cardiovascular mortality was 1.68 in males and 1.70 in females. For sudden death the adjusted odds ratios were 1.93 and 1.37, respectively, in the men and women with hypertension. (Palatini, 1999).
  - A meta-analysis of 29 trials in which patients were assigned to early treatment with β-blockers revealed a 13% reduction in overall mortality (p = 0.02). (Teo, Yusuf, Furberg, 1993). Clear benefit of beta-blocker administration was seen in those whose heart rate decreased by 14 beats per minute. In those whose heart rate didn't decrease by at least eight beats per minute, no benefit of beta-blocker administration was observed. (Kjekshus 1986).

Discussion

- In those with resting bradycardia (<60 bpm), benefits are seen in select populations. The population that benefit the most are those with a resting heart rate of 60 bpm or less, who are not on heart rate modifying medication.
- Individuals whose HR is 60-80 benefit from lifestyle modification to reduce BP to <120/180, lower BMI to 20-25, cessation of smoking and alcohol intake, and reduction of HDL/LDL ratio to <5 (3.5 optimal). These lifestyle modifications greatly reduce the risk of CVD development.
- Reduction in tachycardia through pharmacotherapy (beta blocker, calcium channel blocker) show the greatest benefit in prevention of CVD and associated risks (MI, stroke, death) when rate is reduced by at least 8-14 points.

Table 4. Hazard Ratios for Incident Cardiovascular Disease (CVD) and Mortality by Heart Rate (HR) Category[a]

HR Category, beats per minute	Model 1 Hazard Ratio (95% CI)	*P* Value for Trend	Model 2 Hazard Ratio (95% CI)	*P* Value for Trend	Model 3 Hazard Ratio (95% CI)	*P* Value for Trend	Model 4 Hazard Ratio (95% CI)	*P* Value for Trend
Incident CVD								
Participants not taking HR-modifying drugs								
<50	1.10 (0.73-1.67)		1.03 (0.68-1.57)		1.02 (0.67-1.55)		1.07 (0.71-1.63)	
50-59	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
60-69	1.26 (1.00-1.59)	<.001	1.17 (0.93-1.48)	.13	1.17 (0.93-1.48)	.14	1.19 (0.94-1.51)	.16
70-79	1.41 (1.08-1.84)		1.26 (0.96-1.66)		1.26 (0.96-1.65)		1.27 (0.96-1.67)	
≥80	2.05 (1.46-2.89)		1.59 (1.11-2.27)		1.57 (1.10-2.24)		1.55 (1.08-2.22)	
Participants taking HR-modifying drugs								
<50	1.32 (0.71-2.47)		1.28 (0.68-2.40)		1.28 (0.68-2.39)		1.27 (0.68-2.37)	
50-59	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
60-69	1.88 (1.22-2.87)	.04	1.88 (1.22-2.90)	.06	1.89 (1.22-2.92)	.06	1.84 (1.19-2.86)	.10
70-79	1.58 (0.87-2.86)		1.58 (0.86-2.92)		1.59 (0.86-2.92)		1.58 (0.85-2.92)	
≥80	2.27 (0.99-5.22)		2.17 (0.91-5.14)		2.20 (0.92-5.22)		1.80 (0.75-4.29)	
Mortality								
Participants not taking HR-modifying drugs								
<50	0.71 (0.47-1.09)		0.74 (0.49-1.13)		0.72 (0.47-1.10)		0.71 (0.41-1.09)	
50-59	0.82 (0.66-1.02)		0.85 (0.69-1.07)		0.85 (0.68-1.06)		0.83 (0.67-1.04)	
60-69	1 [Reference]	<.001	1 [Reference]	.002	1 [Reference]	.002	1 [Reference]	.002
70-79	1.21 (0.97-1.52)		1.21 (0.97-1.53)		1.22 (0.97-1.53)		1.21 (0.96-1.52)	
≥80	1.58 (1.16-2.15)		1.51 (1.10-2.07)		1.52 (1.11-2.08)		1.49 (1.08-2.05)	
Participants taking HR-modifying drugs								
<50	2.39 (1.41-4.06)		2.36 (1.36-4.09)		2.43 (1.39-4.22)		2.42 (1.39-4.20)	
50-59	1.54 (0.99-2.40)		1.60 (1.02-2.52)		1.62 (1.03-2.54)		1.65 (1.05-2.59)	
60-69	1 [Reference]	.001	1 [Reference]	.001	1 [Reference]	.001	1 [Reference]	.002
70-79	1.39 (0.75-2.56)		1.36 (0.74-2.52)		1.36 (0.74-2.52)		1.35 (0.73-2.50)	
≥80	4.38 (2.14-8.94)		3.91 (1.83-8.32)		3.87 (1.82-8.25)		3.55 (1.65-7.65)	

Abbreviation: HR, heart rate.

[a] Model 1 adjusts for age, sex, race, education, alcohol use, smoking, and any vigorous activity. Model 2: model 1 plus diabetes mellitus, total cholesterol level, high-density lipoprotein cholesterol level, lipid-lowering drug use, body mass index, creatinine level, systolic blood pressure, and diastolic blood pressure. Model 3: model 2 plus hypertension drugs. Model 4: model 3 plus coronary artery calcium prevalence and major electrocardiographic abnormalities.

Table 4 from " Association of asymptomatic bradycardia with incident cardiovascular disease and mortality" by Dharod, A., Soliman, E., Dawood, F., Chen, H., Shea, S., Nazarian, S., & Bertoni, A. (2016. *Journal of American Medical Association Internal Medicine*, *176*(2), 219.

Applicability to Clinical Practice

- Information from the literary review allows medical providers to take the benefits shown in reducing resting tachycardia in the patient population and apply it to cardiovascular disease prevention and apply it to those with subsequent morbidities to reduce overall mortality.
- Information shows the limitation of heart rate reduction and its limited benefits in certain patient populations, such as those already in target range heart rate, and those whose heart rate and correlating blood pressure are optimized for their current health status

References

- Messerli, F., Rimoldi, S., Bangalore, S., Bavishi, C., & Laurent, S. (2016). When an increase in central systolic pressure overrides the benefits of heart rate Lowering. *Journal of the American College of Cardiology*, *68*(7), 754–762. http://dx.doi.org/10.1016/j.jacc.2016.03.610.
- Dharod, A., Soliman, E., Dawood, F., Chen, H., Shea, S., Nazarian, S., & Bertoni, A. (2016). Association of asymptomatic bradycardia with incident cardiovascular disease and mortality. *Journal of American Medical Association Internal Medicine*, *176*(2), 219. http://dx.doi.org/10.1001/jamainternmed.2015.7655
- Makita, S., Onoda, T., Ohsawa, M., Tanno, K., Tanaka, F., Omama, S., Nakamura, M. (2014). Bradycardia is associated with future cardiovascular diseases and death in men from the general population. *Atherosclerosis*, *236*(1), 116–120. http://dx.doi.org/10.1016/j.atherosclerosis.2014.06.02.
- Stewart, J., Manmathan, G., & Wilkinson, P. (2017). Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. *Journal of Royal Society of Medicine Cardiovascular Disease*, *6*, 204800401668721. http://dx.doi.org/10.1177/2048004016687211.
- Kubota, Y., Chen, L., Whitsel, E., & Folsom, A. (2017). Heart rate variability and lifetime risk of cardiovascular disease: The atherosclerosis risk in communities' study. *Annals of Epidemiology*, *27*(10). http://dx.doi.org/10.1016/j.annepidem.2017.08.024.
- Fyfe-Johnson, A., Muller, C., Alonso, A., Folsom, A., Gottesman, R., Rosamond, W., Maclehose, R., (2016). Heart rate variability and incident stroke. *Stroke*, *47*(6), 1452–1458. http://dx.doi.org/10.1161/strokeaha.116.012662
- Perret-Guillaume, C., Joly, L., & Benetos, A. (2009). Heart rate as a risk factor for cardiovascular disease. *Progress in Cardiovascular Diseases*, *52*(1), 6–10. http://dx.doi.org/10.1016/j.pcad.2009.05.003
- Shabtaie, S. A., Witt, C. M., & Asirvatham, S. J. (2019). Natural History and Clinical Outcomes of Inappropriate Sinus Tachycardia. *Journal of Cardiovascular Electrophysiology*. http://dx.doi.org/10.1111/jce.14288
- Williams, B., & Lacy, P. S. (2009). Impact of heart rate on central aortic pressures and hemodynamics. *Journal of the American College of Cardiology*, *54*(8), 705–713. http://dx.doi.org/10.1016/j.jacc.2009.02.088.
- Heart Disease Facts & Statistics. (n.d.). Retrieved from https://www.cdc.gov/heartdisease/facts.htm#targetText=About 610,000 people die of, for both men and women.
- Mozzafarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation*. 2016;133: e38-e360.
- Williams B., Lacy P.S. (2009*) CAFE and the ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) Investigators. Impact of heart rate on central aortic pressures and hemodynamics: analysis from the CAFE (Conduit Artery Function Evaluation) study: CAFE-Heart Rate*. J Am Coll Cardiol 54:705–713.
- Kjeldsen S.E., Hedner T., Syvertsen J.O., et al., NORDIL Study Group (2002*) Influence of age,sex and blood pressure on the principal endpoints of the Nordic Diltiazem (NORDIL) Study*. J Hypertension 20:1231–1237.
- (1990) *Effect of verapamil on mortality and major events after acute myocardial infarction (the Danish Verapamil Infarction Trial II–DAVIT II*). Am J Cardiol 66:779–785.
- Swedberg K., Komajda M., Böhm M., (2010*) Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study*. Lancet 376:875–885.
- Belz G.G. (1995) *Elastic properties and Windkessel function of the human aorta*. Cardiovasc Drugs Ther 9:73–83.
- Flaa A., Mundal H.H., Eide I., et al. (2006) *Sympathetic activity and cardiovascular risk factors in young men in the low, normal, and high blood pressure ranges*. Hypertension 47:396–402..
- Mancia G., De Backer G., Dominiczak A., *et al.ESH-ESC Task Force on the Management of Arterial Hypertension. 2007 ESH-ESC Practice Guidelines for the Management of Arterial Hypertension: ESH-ESC Task Force on the Management of Arterial Hypertension* J Hypertens, 25 (2007), pp. 1751-1762.
- Benetos A., Rudnichi A., Thomas F., *et al. Influence of heart rate on mortality in a French population: role of age, gender and blood pressure* Hypertension, 33 (1999), pp. 44-52 .
- Morcet J., Safar M., Thomas F., *et al. Associations between heart rate and other risk factors in a large French population* J Hypertens, 17 (1999), pp. 1671-1676.
- Gillum R.F., Makuc D.M., Feldman J.J. *Pulse rate, coronary heart disease, and death; the NHANES I Epidemiologic Follow-Up Study* Am Heart J, 121 (1991), pp. 171-177.
- Sutton-Tyrrell K, Alcorn HG, Herzog H, et al. *Morbidity, mortality, and antihypertensive treatment effects by extent of atherosclerosis in older adults with isolated systolic hypertension*. Stroke 1995; 26: 1319-24.
- Teo KK, Yusuf S, Furberg CD. *Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials*. JAMA 1993; 270: 1589-95.
- Kjekshus JK. *Importance of heart rate in determining betablocker efficacy in acute and long-term acute myocardial infarction intervention trials*. Am J Cardiol 1986; 57: 43F-9F.
- Teo KK, Yusuf S, Furberg CD. *Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials*. JAMA 1993; 270: 1589-95.
- Benjamin, E. J., Muntner, P., & Alonso, A. (2019, February 19). AHA 2019 Heart Disease and Stroke Statistics. Retrieved February 6, 2020, from https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/02/15/14/39/aha-2019-heart-disease-and-stroke-statistics

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