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Letter to the Editor

Heart rate variability, but not heart rate, is associated with handgrip strength and mortality in older Africans at very low cardiovascular risk: A population-based study ☆

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A high heart rate and a low heart rate variability at rest are established predictors of various forms of functional impairment, morbidity, and mortality [1–6]. Two explanations can be given for these associations. On one hand, a high heart rate and a low heart rate variability are thought to reflect dysfunction of the flexible autonomic regulation of the heart rate in particular and of the body's functioning in general that arises during ageing [3–5]. On the other hand, a high heart rate and a low heart rate variability are brought about by cardiovascular risk factors, such as obesity, hyperlipidaemia, diabetes, hypertension, and physical inactivity [2,3,7–9]. Since research on heart rate and heart rate variability has almost exclusively been conducted in western populations with an affluent sedentary lifestyle and high prevalences of these risk factors, it has been difficult to determine whether or not heart rate and heart rate variability are associated with functional impairment, morbidity, and mortality independently of cardiovascular risk factors.

To disentangle the effects of ageing and the lifestyle-related cardiovascular risk factors, we investigated the associations of heart rate and heart rate variability with physical function and mortality among older persons in one of the least developed rural regions in Ghana. In this population, contrary to western populations, food is scarce, lifelong manual labour is necessary for subsistence agriculture, and obesity, hyperlipidaemia, diabetes, hypertension, and cardiovascular diseases are rare [10,11]. We measured physical function as handgrip strength, which strongly and independently predicts mortality in this population [12]. Elaborate descriptions of this population have been given elsewhere [10–12].

Ethical approval was given by the Ghana Health Services and the local chiefs and elders. Because of illiteracy, informed consent was obtained orally in the participant's own language. The study conforms to the ethical guidelines of the Declaration of Helsinki.

In 2009 and 2010 we registered demographic characteristics and conducted measurements of cardiovascular risk factors among 924 inhabitants of the Garu-Tempane District aged 50 years and older [10–12]. To ensure maximal participation, we set up a mobile research station and brought less mobile participants by car. Twelve-lead electrocardiograms (ECGs) were obtained as two sequential recordings of ten seconds in a lying and resting position (Schiller AT-104 PC). Three participants with atrial fibrillation were excluded from the analyses; the recordings of the other participants displayed sinus rhythm. The timing of the QRS complexes was automatically identified and verified manually. Recordings with ectopic complexes were excluded from the analyses, except for twelve participants with an ectopic complex in the last 2 s of the recording, in which cases all complexes from the ectopic complex onward were excluded. We determined heart rate in beats per minute (bpm) and heart rate variability in milliseconds (ms) as the standard deviation of normal RR intervals (SDNN) and as the root mean square of the differences between successive normal RR intervals (RMSSD).

Handgrip strength was measured using a Jamar dynamometer (Sammons Preston) while the participant was standing in an upright position with the arms parallel to the body. The highest handgrip strength of both hands was registered [12]. Follow-up for mortality after the measurements lasted until death, migration out of the research

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

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area, loss to follow-up, or our last visit to the research area in 2011. Data on follow-up were available for 814 (99.0%) participants and comprised 1396 person-years and 42 deaths.

Table 1 provides the demographic and cardiovascular characteristics of the Ghanaian study population. Of the 924 individuals who participated in the measurements, 822 could be included with data on heart rate, heart rate variability, and handgrip strength.

Fig. 1 shows the distributions of heart rate and heart rate variability over age. As age increased one year, heart rate increased with 0.15 bpm, SDNN decreased with 0.013 ln ms, and RMSSD decreased with 0.016 ln ms (all $p < 0.001$). Their variances were constant over age. Besides age, heart rate was higher in females, in individuals with a lower BMI, in individuals with a higher glucose level, and in individuals with a higher diastolic blood pressure. Both SDNN and RMSSD were higher in individuals with a higher wealth index and lower in individuals with a higher heart rate (Supplementary Table 1).

Handgrip strength was lower in individuals with a higher heart rate and higher in individuals with a higher SDNN or RMSSD (all $p < 0.001$). After adjustment for age, sex, tribe, and height, heart rate was not associated with handgrip strength, but handgrip strength remained higher in individuals with a higher SDNN ($p = 0.009$) or RMSSD ($p = 0.013$). After additional adjustment for other demographic and cardiovascular characteristics, these associations did not change ($p < 0.025$). The association of heart rate variability with handgrip strength was not different between males and females, individuals younger and older than 65 years, or individuals with and without underweight, defined as a BMI below 18.5 kg/m^2 (Supplementary Table 2).

Fig. 2 provides adjusted estimates of handgrip strength per tertiles of heart rate and heart rate variability. From the lowest to the highest tertile of heart rate, handgrip strength declined non-significantly with 0.57 kg. From the lowest to the highest tertile of SDNN, handgrip strength increased with 1.00 kg. From the lowest to the highest tertile of RMSSD, handgrip strength increased with 1.12 kg.

Heart rate was not associated with mortality. Heart rate variability and mortality were inversely associated with hazard ratios of 0.49 per ln ms increase in SDNN ($p = 0.006$) and 0.65 per ln ms increase in RMSSD ($p = 0.048$). After adjustment for age, sex, and tribe, these hazard ratios remained similar and remained significant for SDNN ($p = 0.021$), but lost significance for RMSSD ($p = 0.121$). After additional adjustment for other demographic and cardiovascular characteristics, the hazard ratios remained similar (Supplementary Table 3).

Table 1
Characteristics of the Ghanaian study population.

	Median (interquartile range) or *n* (%)
Individuals, *n*	822
Male sex, *n* (%)	421 (51.2)
Age, years	65 (56–72)
Tribe, *n* (%)	
Bimoba	572 (69.6)
Kusasi	195 (23.7)
Other	55 (6.7)
Household property value, US$	1085 (516–1944)
Safe drinking water, *n* (%)	721 (87.7)
Body mass index, kg/m^2	18.1 (16.6–19.6)
Waist circumference, cm	77 (72–81)
Capillary glucose, mmol/l	3.9 (3.4–4.4)
Diastolic blood pressure, mm Hg	70 (65–80)
Systolic blood pressure, mm Hg	120 (110–135)
Ankle–arm index	1.15 (1.08–1.23)
Heart rate, bpm	70 (62–78)
Heart rate variability, ms	
SDNN	19.6 (13.6–29.3)
RMSSD	18.0 (11.4–28.4)

Heart rate variability was calculated as the standard deviation of normal RR intervals (SDNN) and as the root mean square of the differences between successive normal RR intervals (RMSSD). Bpm: beats per minute.

Our results remained similar after exclusion of twelve participants who had shown ectopic complexes in the last 2 s of the ECG and after exclusion of 28 participants with sinus arrhythmia, defined as the presence of consecutive normal RR intervals differing by more than 120 ms.

This study is the first to investigate heart rate and heart rate variability in relation to physical function and mortality in rural Africa. Few studies have described their associations with cardiovascular risk factors in rural African populations, all in accordance with our results [13–16]. We showed that heart rate increased slightly over age and was dependent on cardiovascular risk factors, while heart rate variability decreased over age and was not dependent on cardiovascular risk factors. Heart rate was associated with neither handgrip strength nor mortality, while a lower heart rate variability was associated with lower handgrip strength and a higher risk of mortality independent of age, sex, tribe, and cardiovascular risk factors.

In western populations, conflicting results have been reported as to whether and how heart rate changes over age [8,9]. Our findings suggest that heart rate is dependent on lifestyle-related cardiovascular risk factors rather than age and that its association with functional impairment and mortality is predominantly mediated by these risk factors. Cardiovascular risk factors can increase heart rate by inducing haemodynamic alterations, cardiac conduction abnormalities, and sympathetic hyperactivation [3,7]. By contrast, heart rate variability decreases over age [2,8,9,17] and has been reported to be unaffected by cardiovascular risk factors in western populations as in rural African populations [17–19]. These findings suggest that heart rate variability is associated with functional impairment and mortality through mechanisms independent of cardiovascular risk factors. It is possible that heart rate variability declines during ageing as a result of a deteriorating autonomic regulation of the heart rate that occurs across populations with different lifestyles [3–5].

Since a high heart rate is a long-established predictor of cardiovascular disease and death, it is regarded as a potential therapeutic target [1,6]. While pharmacological lowering of the heart rate has been found to benefit patients with heart failure, it fails to do so in patients without heart failure [20]. Our study reinforces the explanation of others that the heart rate is accelerated not as a cause, but as an effect of cardiovascular disease [1,20]. It could be that in the detection and prevention of cardiovascular disease the role of heart rate is overrated, while that of heart rate variability has thus far remained underrated.

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Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

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JJEK, DvB, JBZ, RGJW, and JWJ conceived and designed this study. JJEK and DvB recruited the subjects and executed the measurements. ACM and ZL prepared the electrocardiographic data. JJEK executed the statistical analyses. JJEK and DvB drafted the manuscript. All authors interpreted the results, contributed intellectually, and critically revised the manuscript. The authors are grateful for the dedicated assistance of the local staff of the research team in the Garu-Tempane District in

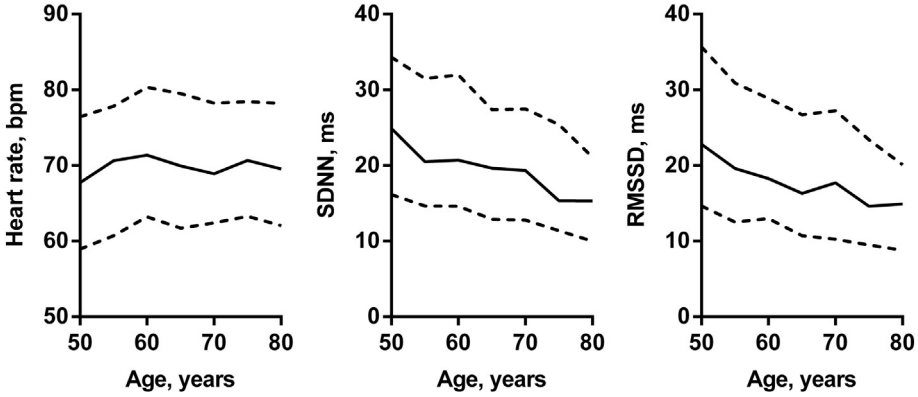

Fig. 1. Distributions of heart rate and heart rate variability over age in the Ghanaian study population. The data represent age-specific medians (continuous lines) and interquartile ranges (dashed lines) of heart rate and heart rate variability. Heart rate variability was calculated as the standard deviation of normal RR intervals (SDNN) and as the root mean square of the differences between successive normal RR intervals (RMSSD). Bpm: beats per minute.

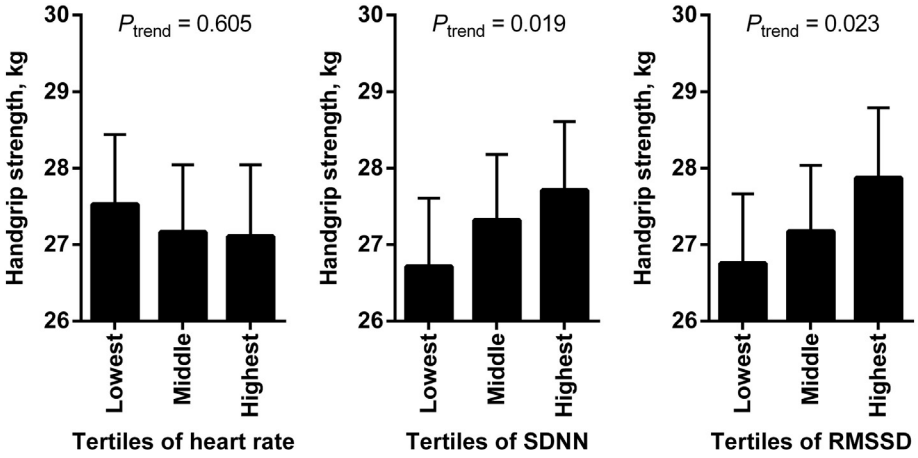

Fig. 2. Estimates of handgrip strength per tertiles of heart rate and heart rate variability in the Ghanaian study population. The data represent estimated means of handgrip strength per tertiles of heart rate and heart rate variability. Heart rate variability was calculated as the standard deviation of normal RR intervals (SDNN) and as the root mean square of the differences between successive normal RR intervals (RMSSD). The estimated means were fully adjusted for age, sex, tribe, height, drinking water source, body mass index, waist circumference, glucose level, diastolic and systolic blood pressure, ankle–arm index, and heart rate or heart rate variability. Bpm: beats per minute.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2015.03.383.

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