

# Heart Rate Variability Is a Predictor of Mortality in Chronic Kidney Disease: A Report from the CRIC Study

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## Commentary

By Professor Richard Glasscock

Heart rate variability (HRV), as assessed by the standard deviation of R-R intervals on EKG, has been repetitively demonstrated to show an association with all-cause mortality in the general population. Low values for HRV are associated with higher mortality. Cardiac autonomic neuropathy (sympathetic and/or parasympathetic) are believed to underlie these associations. Since patients with CKD and/or ESRD can have alterations in sympathetic tone and parasympathetic abnormalities, it seems logical that an association of HRV and mortality might be seen, even in an exaggerated form, in such subjects. The Chronic Renal Insufficiency Cohort (CRIC) investigators examined the association of HRV (in a 10-second EKG taken at enrollment) in 3244 CRIC participants followed for a median of 4.2 years. HRV was measured by two methods: standard deviation of all R-R intervals (SDNN), and the root mean square of successive differences between R-R intervals (RMSSD). Not unexpectedly, the baseline HRV was associated with a number of factors, such as age, heart failure and low eGFR. More importantly, an increased hazard ratio for renal events (ESRD or a 50% decrease in eGFR) or cardiovascular events were not associated with low HRV as assessed by SDNN or RMSSD in multi-variable adjusted analysis. HRV did not seem to add much to prediction of risk for these outcomes over and above the 'usual suspects'. There was a significant non-linear ('U'-shaped) relationship

of RMSSD (but not for SDNN) and all-cause mortality – with both high and low HRV associated with an increased risk for all-cause mortality. This association may be due to increased sympathetic and decreased parasympathetic tone in CKD, but the relative contributions of these two patho-physiological states have not yet been teased out. Unfortunately, the precise cause of the deaths is unknown in this cohort or the implication of the finding for possible intervention is mainly speculative. Disease-specific mortality rates would have been very useful in order to relate the 'U'-shaped curve of HRV by RMSSD and HR for mortality. Thus, until we know more about the basis of the apparent adverse effect of low and high HRV on mortality in CKD, the prognostic utility of determining HRV in patients with CKD is still to be determined.

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