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Research Letter

Association between pulse pressure and the risk of sudden cardiac death in middle-aged men: A 22-year follow-up population-based study

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Introduction

Sudden cardiac death (SCD) affects approximately 1 in every 7 adults in the United States.[1] A similarly high burden is reported globally with estimates of 4-5 million cases of SCD per year.[2] Hypertension increases the risk for SCD, suggesting that blood pressure (BP) is an important risk factor for SCD.[3] Pulse pressure (PP) is defined as the numeric difference between systolic and diastolic BP. With advancing age, there are increases in systolic BP with slight decreases in diastolic BP resulting in a widening of PP and associated negligible changes in mean arterial pressure (MAP). Increases in PP are attributable to large artery stiffening and have been shown to be more predictive of adverse cardiovascular outcomes than other BP components, particularly in middle-aged and older adults.[4, 5] It remains unclear whether PP predicts the risk SCD in the general population. The purpose of this study was to investigate whether PP is associated with the risk of SCD, independently of MAP in middle-aged men.

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Methods

Participants were part of the Kuopio Ischaemic Heart Disease Risk Factor Study, which is a prospective population-based study designed to investigate risk factors for CVD and related outcomes in randomly selected sample of men from eastern Finland. At baseline, examinations were conducted on 2,682 men (82.9% of the potential eligible) who resided in the town of Kuopio or its surrounding rural communities between March 1984 and December 1989. Complete data was available on 2,356 participants (aged 42-60) at baseline in this analysis.

Resting systolic and diastolic BP were measured using a sphygmomanometer and was expressed as the mean value from 6 different measurements (3 while supine, 1 while standing, and 2 while sitting). Brachial PP was defined as the difference between systolic and diastolic BP. The participants were divided into PP quartiles as follows; quartile 1: <37 mmHg, quartile 2: 37-43 mmHg, quartile 3: 43-51 mmHg, and quartile 4: >51 mmHg.

SCD was defined as a fatal event that occurred within 1 h after the onset of symptoms or within 24 h when autopsy data did not reveal a non-cardiac cause of SCD or after a fatal cardiac arrest following successful resuscitation from ventricular tachycardia and/or ventricular fibrillation. Diagnostic classification of events was based on symptoms, electrocardiographic (ECG) findings, cardiac enzyme elevations, autopsy findings (80% of the SCDs), and history of coronary heart disease (CHD) combined with relevant clinical and ECG findings. Data on SCDs were derived from interviews with family members, hospital records, death certificates, autopsy reports and medico-legal documents.

We used Cox proportional hazard models adjusted for age, body mass index (BMI), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), C-reactive protein (CRP), diabetes mellitus (DM), hypertension (HTN), family history of CHD, previous myocardial infarction (MI), physical activity, and MAP to determine the hazard ratios (HRs) and 95% confidence intervals (CIs) of PP for SCD. Statistical analyses were conducted using SPSS version 21.0 (SPSS, Armonk, NY).

Results

A total of 253 (10.7%) SCDs occurred during an average of 22 years of follow-up. Cumulative hazard curves demonstrated higher survival among males in the lowest quartile of PP levels compared to those in the highest quartile (*P*=xxx for log-rank test; **Figure 1**). The HR of SCD in men within the highest quartile of PP (>51mmHg) versus men with the lowest quartile of PP (<37mmHg) was 1.80 (95% confidence interval, 1.18-2.76) after multivariable adjustment. Each unit increment in PP was associated with a 2% (HR, 1.02, 95% CI, 1.01-1.03) increased risk of SCD following adjustment for potential confounders (**Table 1**).

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Discussion

These results suggest that increased PP is associated with a higher risk of SCD in the general population and this is independent of MAP as well as several established and emerging risk factors. The widening of PP with advancing age and CVD is mechanistically linked to large artery stiffness. Increased large artery stiffness detrimentally alters ventricular-vascular coupling and cardiac energetics such that afterload is increased (i.e. increased oxygen demand) and myocardial perfusion reduced (i.e. reduced oxygen supply). Subendocardial ischemia may serve as the substrate for lethal arrhythmogenesis. Large artery stiffness may also hasten the atherosclerotic process, contributing to plaque rupture and myocardial infarction. Atherosclerotic CVD is a notable cause of SCD and responsible for ~50-80% of all cases.[6]

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Diagnosis, treatment and management of CVD and hypertension-related target organ

damage relies exclusively on the assessment of extreme BP values during the cardiac cycle; the peak (i.e. systolic) and trough (i.e. diastolic). Examination of the BP curve with attention to the pulsatile component of BP (i.e. PP) offers insight on CVD risk extending beyond the assessment of the steady component of the curve (i.e. MAP) or individual extreme values (systolic or diastolic BP). Elevated PP has been shown to be associated with increased risk of incident atrial fibrillation,[7] heart failure, coronary artery disease and cardiovascular mortality.[8] Our novel findings add to the literature on the role of PP as an indicator of heart health. Further studies are required to replicate these findings and evaluate if brachial PP may help to identify patients who are at increased risk for SCD and therefore aid in early therapeutic decision-making.

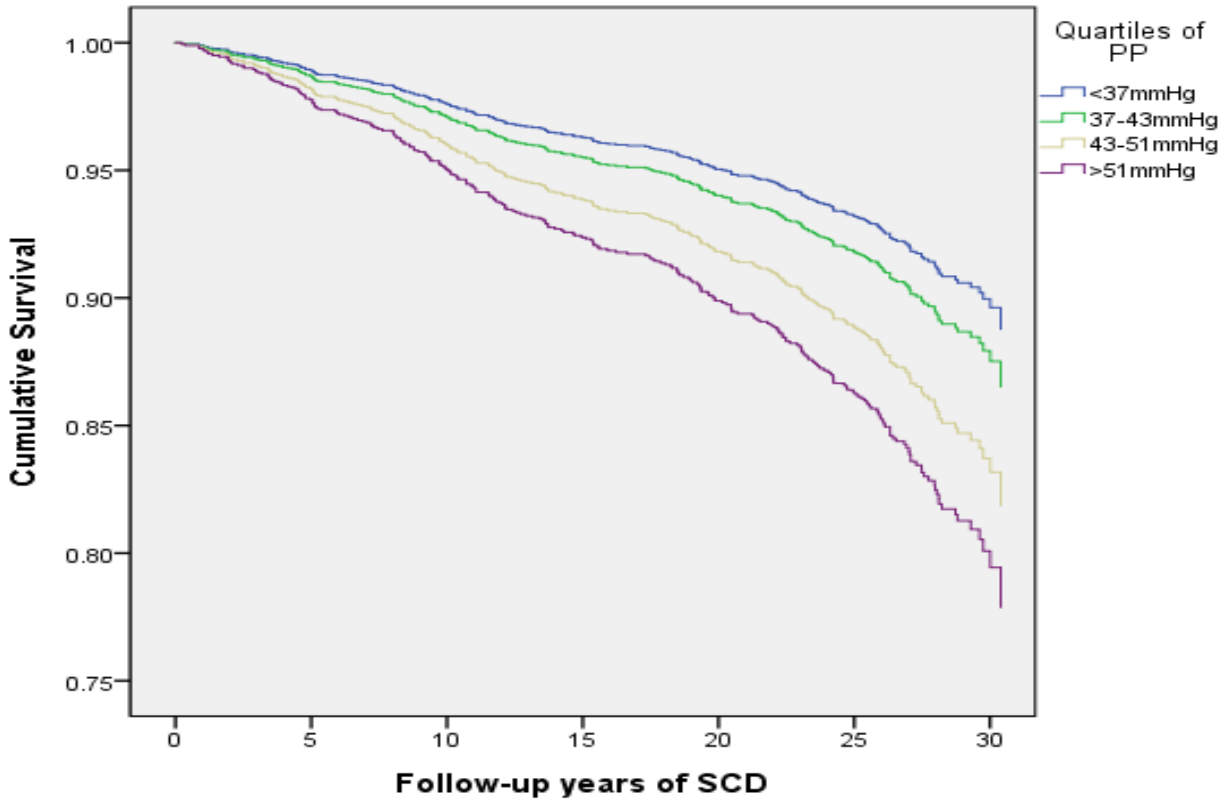
Table 1. Hazard ratio (HR) and 95% confidence interval (CI) for risk of sudden cardiac death by pulse pressure quartiles.

Variables	Case/n (% incident)	Unadjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)
<37 mmHg	41/567 (7.2%)	1 (ref)	1 (ref)	1 (ref)
37-43 mmHg	50/579 (8.6%)	1.24 (0.82-1.87)	1.16 (0.75-1.78)	1.11 (0.72-1.71)
43-51 mmHg	75/628 (11.9%)	1.77 (1.21-2.59)	1.85 (1.25-2.74)	1.67 (1.12-2.50)
>51 mmHg	87/582 (14.9%)	2.43 (1.68-3.53)	2.17 (1.47-3.22)	1.80 (1.18-2.76)
Each 1 mmHg	253/2,356 (10.7%)	1.03 (1.02-1.04)	1.02 (1.01-1.03)	1.02 (1.01-1.03)

Model 1: Adjusted for age, body mass index, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, C-reactive protein, history of diabetes mellitus, history of hypertension, family history of coronary heart disease, previous myocardial infarction, and physical activity

Model 2: model 1 plus mean arterial pressure

Figure 1. The age and examination year adjusted survival curves of sudden cardiac death according to quartiles of pulse pressure.



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