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Poor R-wave progression as a predictor of sudden cardiac death in the general population and subjects with coronary artery disease

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BACKGROUND Poor R-wave progression (PRWP) is a common clinical finding on the standard 12-lead electrocardiogram (ECG), but its prognostic significance is unclear.

OBJECTIVE The purpose of this study was to examine the prognosis associated with PRWP in terms of sudden cardiac death (SCD), cardiac death, and all-cause mortality in general population subjects with and without coronary artery disease (CAD).

METHODS Data and 12-lead ECGs were collected from a Finnish general population health examination survey conducted during 1978–1980 with follow-up until 2011. The study population consisted of 6854 subjects. Main end points were SCD, cardiac death, and all-cause mortality. PRWP was defined as R-wave amplitude $\leq$ 0.3 mV in lead V_3 and R-wave amplitude in lead $V_2 \leq$ R-wave amplitude in lead V_3.

RESULTS PRWP occurred in 213 subjects (3.1%). During the follow-up period of 24.3 $\pm$ 10.4 years, 3723 subjects (54.3%) died. PRWP was associated with older age, higher prevalence of heart failure and CAD, and β-blocker medication. In multivariate analyses, PRWP was associated with SCD (hazard ratio [HR] 2.13; 95% confidence interval [CI] 1.34–3.39), cardiac death (HR 1.75; 95% CI 1.35–2.15), and all-cause mortality (HR 1.29; 95% CI 1.08–1.54). In the subgroup with CAD, PRWP had a stronger association with cardiac mortality (HR 1.71; 95% CI 1.19–2.46) than in the subgroup without CAD, while the association with SCD was significant only in the subgroup with CAD (HR 2.62; 95% CI 1.38–4.98).

CONCLUSION PRWP was associated with adverse prognosis in the general population and with SCD in subjects with CAD.

KEYWORDS Electrocardiography; Coronary artery disease; Epidemiology; R-wave; Sudden cardiac death

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Introduction

Sudden cardiac death (SCD) is a major cause of death and in many cases the first manifestation of heart disease. Coronary artery disease (CAD) is the most common underlying condition leading to SCD.[1] In the current treatment guidelines, the primary prevention of SCD with implantable cardioverter-defibrillator therapy primarily relies on reduced left ventricular ejection fraction (LVEF) in echocardiography, since the risks associated with other individual markers are typically only modest.[2] However, most SCD victims do

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not present with an indication for implantable cardioverter-defibrillator before the fatal event. Therefore, improvements in SCD risk stratification methods are needed. Multiple electrocardiographic (ECG) patterns have been associated with SCD risk in previous studies both in general populations and in patient populations with cardiac disorders,[3] and the presence of several ECG abnormalities has been suggested to improve the identification of subjects at high SCD risk in the general population.[4,5]

Poor R-wave progression (PRWP) in the precordial leads is a relatively frequent finding on the standard ECG, but its physiological background and clinical significance are still not fully understood. Although PRWP is often found in patients with cardiac disorders, it is not an uncommon finding in individuals without a history of preexisting cardiac disease.[6] The prognostic significance of PRWP has been studied mostly in specific patient populations with cardiac disorders with a prevalence of 8%–10%.[7] In a previous study in the general adult population, PRWP was a common ECG finding with a prevalence of 5.1% and was associated with increased total and cardiovascular mortality in women.[8]

To our knowledge, the risk of SCD associated with PRWP on the resting ECG has not been previously studied. Therefore, the aim of the present study was to examine the risk of SCD and overall prognosis associated with PRWP in general population subjects with and without CAD.

Methods

Study population

The study population comprised 7217 subjects participating in the Social Insurance Institution's Mini-Finland Health Survey in 1978–1980. Subjects were 30 years or older, and the survey population reflects the Finnish general population. Participants were interviewed regarding their health status, medications, diseases, symptoms, and lifestyle. Participants underwent health examinations, including measurements of blood pressure, body mass index, and total serum cholesterol level, in addition to the recording of an ECG and a posterior-anterior and a lateral chest radiograph. The previous medical records provided by participants were also reviewed as a part of the diagnostic assessment. The Mini-Finland Health Survey methods have been reported comprehensively previously.[9,10]

The Mini-Finland Health Survey preceded the current legislation on ethics in medical research. All participants were fully informed about the study; they participated in the study voluntarily; and the use of the information for medical research was explained to them. Agreeing to participate in the baseline health examination was taken to indicate informed consent. Participants were free to unconditionally withdraw their consent at any time, in which case their data were deleted. The study protocol and the practice of the subject's voluntary participation indicating informed consent were approved by the Institutional Review Board (IRB 00007085) of the National Institute for Health and Welfare.

ECG measurement and analyses

A standard 12-lead ECG was recorded from all study participants during the health examination in 1978–1980, with a paper speed of 50 mm/s and a calibration of 1 mV/10 mm. ECGs were classified according to the revised Minnesota code after the baseline examinations.[11] Later, the original paper ECGs were digitized and digitally assessed in 2015–2016, as described previously.[10] In brief, the original paper ECGs were scanned and subsequently the scanned ECG recordings were converted to a digital signal using custom-made software. Finally, the digitized ECG signals were measured digitally using another custom-made software. Subjects with missing health examination data (n = 20) and subjects with missing or unreadable ECGs (n = 213) were excluded from the analyses. Additionally, subjects with left or right bundle branch block (n = 98), second- or

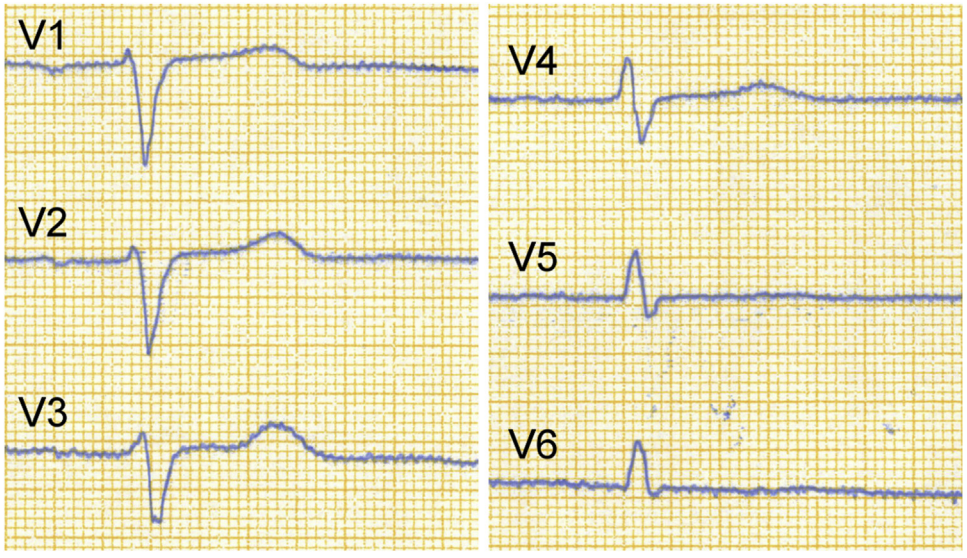

Figure 1 Electrocardiographic leads V_1 through V_6 of a subject presenting with poor R-wave progression. Paper speed is 50 mm/s.

Table 1 Baseline characteristics of subjects

Characteristic	All (N = 6854)			No CAD (n = 6047)			CAD (n = 807)		
	Normal R-wave progression (n = 6641 [96.9%])	PRWP (n = 213 [3.1%])	Difference (*P* value)	Normal R-wave progression (n = 5882 [97.3%])	PRWP (n = 165 [2.7%])	Difference (*P* value)	Normal R-wave progression (n = 759 [94.1%])	PRWP (n = 48 [5.9%])	Difference (*P* value)
Male sex*	3044 (45.8)	69 (32.4)	<.001	2681 (45.0)	41 (24.8)	<.001	396 (52.2)	28 (58.3)	.24
Age (y)†	51.1 ± 14.0	55.1 ± 14.2	<.001	49.5 ± 13.5	51.8 ± 13.3	.10	63.5 ± 10.5	66.3 ± 11.3	.05
Systolic blood pressure (mm Hg)‡	143 ± 23	144 ± 23	.07	142 ± 22	142 ± 24	.46	156 ± 25	151 ± 21	.07
Diastolic blood pressure (mm Hg)‡	87 ± 12	87 ± 11	.65	87 ± 11	87 ± 11	.69	89 ± 12	87 ± 10	.26
Hypertension‡	3850 (58.0)	144 (67.6)	.21	3187 (54.2)	98 (59.4)	.48	663 (87.4)	46 (95.8)	.11
Total serum cholesterol level (mmol/L)‡	7.0 ± 1.4	6.9 ± 1.4	.02	6.9 ± 1.4	6.9 ± 1.4	.23	7.4 ± 1.5	6.8 ± 1.4	.03
Body mass index (kg/m^2)‡	25.9 ± 4.1	25.6 ± 4.6	.06	25.8 ± 4.1	25.3 ± 4.7	.07	27.1 ± 4.1	26.7 ± 4.2	.84
Heart failure‡	593 (8.9)	38 (17.8)	.003	290 (4.9)	12 (7.3)	.66	303 (39.9)	26 (54.2)	.14
CAD‡	759 (11.4)	48 (22.5)	<.001	–	–	–	–	–	–
Diabetes‡	349 (5.3)	20 (9.4)	.07	227 (3.9)	10 (6.1)	.33	122 (16.1)	10 (20.8)	.53
Smoking‡	1501 (22.6)	35 (16.4)	.51	1349 (23.0)	30 (18.2)	.95	152 (20.1)	5 (10.4)	.09
β-Blocker medication‡	433 (6.5)	23 (10.8)	.04	244 (4.1)	9 (5.5)	.57	189 (24.9)	14 (29.2)	.31
LVH‡	922 (13.9)	29 (13.6)	.98	756 (12.9)	17 (10.3)	.73	166 (21.9)	12 (25.0)	.80
Heart rate (beats/min)‡	68 ± 14	68 ± 14	.13	68 ± 13	68 ± 14	.11	70 ± 16	69 ± 14	.70
QRS duration (ms)‡	85 ± 11	84 ± 14	.40	84 ± 11	82 ± 11	.15	86 ± 14	93 ± 17	.002
QTc interval (ms) ‡	409 ± 29	406 ± 34	.08	408 ± 28	404 ± 30	<.001	412 ± 37	417 ± 44	.37
LAHB‡	59 (0.9)	7 (3.3)	.23	43 (0.7)	4 (2.4)	.46	16 (2.1)	3 (6.3)	.44

Values are presented as mean ± SD or n (%).

CAD = clinical diagnosis made in baseline examinations or Q waves on the electrocardiogram (Minnesota code 1.1 or 1.2).

CAD = coronary artery disease; LAHB = left anterior hemiblock; LVH = left ventricular hypertrophy; PRWP = poor R-wave progression; QTc = corrected QT.

*Between-group comparisons were adjusted for age.

†Between-group comparisons were adjusted for sex.

‡Between-group comparisons were adjusted for age and sex.

Table 2 HRs for cardiac death, SCD, and death from any cause

Variable	All (N = 6854)		
	Normal R-wave progression (n = 6641 [96.9%])	Poor R-wave progression (n = 213 [3.1%])	Poor R-wave progression × CAD interaction (*P* value)
Cardiac death			
No. of cardiac deaths (% of subjects)	1546 (23.3)	75 (35.2)	
Age and sex adjusted HR (95% CI)	1	1.71 (1.35−2.15)	.73
Multivariate adjusted HR (95% CI)	1	1.75 (1.39−2.21)	.47
SCD			
No. of SCDs (% of subjects)	355 (5.3)	19 (8.9)	
Age and sex adjusted HR (95% CI)	1	1.97 (1.24−3.12)	.21
Multivariate adjusted HR (95% CI)	1	2.13 (1.34−3.39)	.12
Death from any cause			
No. of deaths (% of subjects)	3592 (54.1)	131 (61.5)	
Age and sex adjusted HR (95% CI)	1	1.25 (1.05−1.49)	.53
Multivariate adjusted HR (95% CI)	1	1.29 (1.08−1.54)	.31

Multivariate models of all subjects were adjusted for age, sex, systolic blood pressure, heart rate, total serum cholesterol level, diabetes, smoking, left ventricular hypertrophy on the electrocardiogram, β-blocker usage, heart failure, and CAD.

CAD = coronary artery disease; CI = confidence interval; HR = hazard ratio; SCD = sudden cardiac death.

third-degree atrioventricular block (n = 3), preexcitation pattern (n = 5), or pacemaker rhythm (n = 8) were excluded, because these subjects were considered to not represent the general population owing to preexisting conduction abnormality. Finally, after excluding subjects with other major ECG abnormalities (n = 16), a total of 6854 subjects remained for the analyses. *PRWP* was defined as R-wave amplitude $\leq$ 0.3 mV in lead V_3 and R-wave amplitude in lead $V_2 \leq$ R-wave amplitude in lead V_3.[12] An example of PRWP is shown in Figure 1.

Baseline diagnoses

Trained nurses screened the participants for the following diagnoses and symptoms, and even a slightest sign or symptom for a cardiovascular morbidity in the screening was followed by a clinical assessment by a physician.

A diagnosis of myocardial infarction (MI) was defined if at least one of the following criteria was met: (1) pathological Q waves indicating transmural infarction on the study ECG, (2) ECG findings consistent with possible MI and previous hospitalization because of MI with elevated cardiac enzyme levels, or (3) typical history of MI and previous hospitalization because of MI with elevated cardiac enzyme levels. *Angina pectoris* was defined as a history of typical exercise-related chest pain relieved within minutes of rest or with use of sublingual nitroglycerin substrates. *Hypertension* was defined if at least one of the following criteria was met: (1) systolic blood pressure above 140 mm Hg, (2) diastolic blood pressure above 90 mm Hg, or (3) blood pressure medication (diuretics, β-blocker medication, or other blood pressure medication).

Subjects were regarded to have CAD if they in the baseline health examinations met the structured criteria for MI or angina pectoris.[11]

Follow-up

Participants were followed from the baseline examination in 1978–1980 until the end of 2011 by using the nation-wide Causes of Death Register maintained by Statistics Finland, which records every death in the country. A total of 1077 subjects (27% of all deceased) of all the Mini-Finland survey participants were autopsied during the follow-up period, of whom 194 were SCD cases (48% of SCD cases). SCD cases were determined by 2 experienced cardiologists by using the modified Cardiac Arrhythmia Suppression Trial criteria based on death certificates, hospital records, and autopsy records,[13] in which *SCD* was defined as death of cardiac origin that occurred unexpectedly within 1 hour of the onset of new symptoms or a death that was unwitnessed and unexpected, unless a specific noncardiac cause of death was confirmed. In cases with lack of uniformity, a third experienced cardiologist reviewed the case and made the final classification. SCD was the primary end point, and cardiac death and death from any cause were the secondary end points. The full follow-up time was used in the primary analyses, while a secondary analysis was performed with a shorter follow-up time of 10 years to control for potential changes in cardiovascular risk profile during a longer follow-up period and assess the significance of PRWP in a more clinically meaningful time frame.

Statistical analysis

The general linear model was used for comparison of age- and sex-adjusted mean values for continuous variables and the prevalence of categorical variables. The Cox proportional hazards model was used for the calculation of hazard ratios (HRs) and 95% confidence intervals (CIs). In the entire study population, the multivariate models were adjusted with age, sex, systolic blood pressure, heart rate, total serum cholesterol level, diabetes, active smoking, β-blocker medication, left ventricular hypertrophy (LVH) on the ECG on the basis of the Sokolow-Lyon criterion, heart failure diagnosis, and CAD. In the subgroup analysis of subjects with and without CAD, the multivariate models were adjusted with same factors excluding the presence of CAD. The survival of subjects

in different groups was illustrated using Kaplan-Meier plots. The statistical significance of effect modification was tested using the Wald test by entering an interaction term of PRWP and the presence of CAD. All reported *P* values are 2-sided, and $P < .05$ was considered statistically significant. All statistical analyses were performed using SPSS version 27 (IBM Corporation, Armonk, NY).

Results

Baseline characteristics of subjects

The baseline characteristics of subjects are presented in Table 1. Altogether, there were 213 subjects with PRWP on their resting ECG, resulting in a prevalence of 3.1% in the study population (6854). Of the 213 subjects with PRWP, 69 were men (2.2% of all men) and 144 were women (3.8% of all women). Subjects with PRWP were older, had more heart failure and CAD, had lower levels of total serum cholesterol, and were more often on β-blocker medication. However, no significant differences in body mass index or the prevalence of LVH or left anterior hemiblock were observed in subjects with or without PRWP. In the subgroup with CAD, the prevalence of PRWP was 5.9%, while the prevalence of PRWP was 2.7% in the subgroup without CAD.

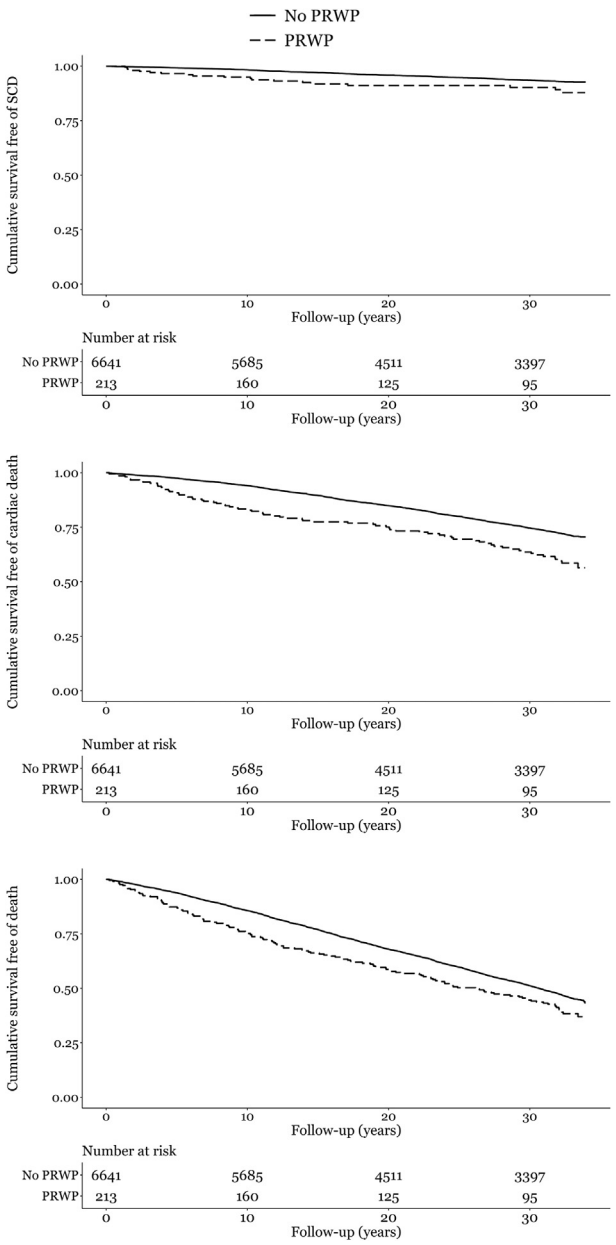

Figure 2 Kaplan-Meier survival plots for cardiac death, sudden cardiac death (SCD), and death from any cause in subjects with normal R-wave progression and poor R-wave progression (PRWP).

Mortality and fatal cardiac events

During the follow-up period of 24.3 ± 10.4 years, 3723 subjects (54.3%) died. Cardiac deaths amounted to 1621 deaths (43.5% of all deaths) and SCD to 374 deaths (10.0% of all deaths). After adjusting for multiple clinical variables, the risk of all-cause mortality (HR 1.29; 95% CI 1.08–1.54; $P = .004$), the risk of cardiac mortality (HR 1.75; 95% CI 1.39–2.21; $P < .001$), and the incidence of SCD (HR 2.13; 95% CI 1.34–3.39; $P = .001$) were higher in the group with PRWP than in the group without PRWP (Table 2). PRWP was associated with SCD and cardiac mortality in both men and women, but not with all-cause mortality in women (see the Online Supplement). The Kaplan-Meier curves for all-cause mortality, cardiac death, and SCD in subjects with and without PRWP are presented in Figure 2.

Risk of death in CAD

The Cox proportional hazards models with SCD, cardiac death, and all-cause mortality as end points were also used in subjects with and without CAD (Table 3). In the subgroup with CAD (n = 807), 48 subjects had PRWP, while in the subgroup without CAD (n = 6047), 165 subjects had PRWP. As shown in Figure 3, cardiac mortality, SCD, and all-cause mortality were higher in patients with CAD than in patients without CAD during the follow-up period.

In the subgroup with CAD, PRWP had a strong association with cardiac mortality (HR 1.71; 95% CI 1.19–2.46; $P = .004$) and SCD (HR 2.62; 95% CI 1.38–4.98; $P = .003$). Of the 807 subjects in the subgroup with CAD, 157 (19.5%) also presented with Q waves. After exclusion of these subjects, the PRWP finding remained significantly associated with a higher risk of SCD (HR 2.96; 95% CI 1.38–6.32; $P = .005$), cardiac mortality (HR 1.89; 95% CI 1.24–2.90; $P = .003$), and all-cause mortality (HR 1.50; 95% CI 1.05–2.14; $P = .026$) in the multivariate adjusted analysis.

In the subgroup without CAD, PRWP was associated with only an increased risk of cardiac mortality (HR 1.64; 95% CI 1.20–2.23; $P = .002$) in the multivariate adjusted models. The possible interaction of PRWP and CAD was assessed, with the results showing no statistically significant effect modification ($P > .05$).

Table 3 HRs for cardiac death, SCD, and death from any cause for subjects with and without CAD

Variable	No CAD (n = 6047)		CAD (n = 807)	
	Normal R-wave progression (n = 5882 [97.3%])	Poor R-wave progression (n =165 [2.7%])	Normal R-wave progression (n = 759 [94.1%])	Poor R-wave progression (n = 48 [5.9%])
Cardiac death				
No. of cardiac deaths (% of subjects)	1133 (19.3)	42 (25.5)	413 (54.4)	33 (68.8)
Age and sex adjusted HR (95% CI)	1	1.49 (1.09−2.02)	1	1.51 (1.06−2.16)
Multivariate adjusted HR (95% CI)	1	1.64 (1.20−2.23)	1	1.71 (1.19−2.46)
SCD				
No. of SCDs (% of subjects)	274 (4.7)	8 (4.8)	81 (10.7)	11 (22.9)
Age and sex adjusted HR (95% CI)	1	1.26 (0.62−2.56)	1	2.28 (1.21−4.30)
Multivariate adjusted HR (95% CI)	1	1.48 (0.73−2.99)	1	2.62 (1.38−4.98)
Death from any cause				
No. of deaths (% of subjects)	2908 (49.4)	87 (52.7)	684 (90.1)	44 (91.7)
Age and sex adjusted HR (95% CI)	1	1.15 (0.93−1.42)	1	1.22 (0.90−1.66)
Multivariate adjusted HR (95% CI)	1	1.20 (0.97−1.49)	1	1.37 (1.00−1.86)

Multivariate models in subgroup analyses were adjusted for age, sex, systolic blood pressure, heart rate, total serum cholesterol level, diabetes, smoking, left ventricular hypertrophy on the electrocardiogram, β-blocker usage, and heart failure.

CAD = coronary artery disease; CI = confidence interval; HR = hazard ratio; SCD = sudden cardiac death.

10-Year follow-up

A secondary analysis was performed with a shorter follow-up time of 10 years. After multivariate adjustment, the HR for all-cause mortality in individuals with PRWP was 1.57 (95% CI 1.19–2.08; $P = .001$) during the 10-year follow-up period. For cardiac death, the HR for PRWP was 2.41 (95% CI 1.69–3.46; $P < .001$), while for SCD, the HR for PRWP was 2.74 (95% CI 1.41–5.31; $P = .003$).

In the subgroup with CAD, PRWP had an association with cardiac mortality (HR 2.27; 95% CI 1.44–3.57; $P < .001$) and SCD (HR 3.50; 95% CI 1.61–7.62; $P = .002$) in the multivariate adjusted models. In the subgroup without CAD, PRWP was associated with only cardiac mortality (HR 2.62; 95% CI 1.46–4.70; $P = .001$) while not being associated with SCD (HR 1.46; 95% CI 0.35–5.98; $P = .60$).

Discussion

The risk of SCD associated with PRWP on the resting ECG has not been studied previously in the general adult population or in patients with or without CAD. The results of this study demonstrated that PRWP was associated with SCD, cardiac death, and all-cause mortality in the general population after adjusting for several cardiac risk factors. The risk of SCD and cardiac mortality was especially pronounced in subjects with established CAD, while in subjects without CAD, PRWP was associated only with cardiac death and not with SCD.

To our knowledge, the prevalence and prognosis of PRWP in the general population have been studied previously by only 1 study but this did not include SCD as an end point. In that study, on the basis of the Finnish Health 2000 general population cohort, PRWP was a relatively common ECG finding and predicted a risk of total and cardiovascular mortality in women but not in men during the 6-year follow-up period[8]; in men, PRWP was more strongly associated with CAD and MI. In the present study, PRWP was significantly associated with cardiac death in both sexes during the follow-up period of up to 30 years even after adjusting for multiple clinical risk factors. Moreover, the presence of PRWP on the ECG was associated with a twofold risk of SCD in both men and women. The prevalence of PRWP in the present study (3.1%) was slightly lower than that in the Health 2000 study (5.1%). In both studies, women were more prone to have PRWP than men. In the present study, the prevalence of PRWP between sexes was more even (2.2% of men and 3.8% of women) than that in the Health 2000 study (2.7% of men and 7.0% of women). The Mini-Finland Health Survey involved a larger population and a longer follow-up time as compared with the Health 2000 study, which possibly explains some of the differences in the results. Furthermore, the baseline characteristics of subjects as well as the prevalence of heart diseases and their treatment are not fully comparable between these 2 studies as the 2 studies describe population cohorts of different times, with Mini-Finland survey baseline examinations performed in 1978–1980 and Health 2000 in 2001.

In the subgroup with established CAD, PRWP was a more frequent finding than in subjects without CAD (5.9% vs 2.7%, respectively). Moreover, in the subgroup with CAD, PRWP had a stronger association with cardiac mortality and SCD than in the subgroup without CAD. These results indicate that the combination of PRWP and CAD presents a higher risk of SCD and cardiac death. As Q-wave MI is a well-documented etiology of PRWP,[6] further analyses were performed in the CAD group by excluding subjects with Q waves. The PRWP finding remained significantly associated with a higher risk of SCD, cardiac mortality, and all-cause mortality even after exclusion of subjects with Q waves, suggesting that previous large MI presenting with anterior Q waves may not be the sole explanation for the association between PRWP and adverse outcome.

Even though PRWP was not associated with SCD or death from any cause in the non-CAD subgroup, it was associated with an increased cardiac mortality, possibly suggesting some underlying structural or functional heart abnormalities also in these subjects. However, despite the long follow-up time, the event rate of SCD in subjects with PRWP with no CAD was fairly low, with only 2 events in the first 10 years of follow-up and 8 events during the full follow-up period. The observed event rate in this relatively young and low-risk population may be too low to enable accurate risk estimates.

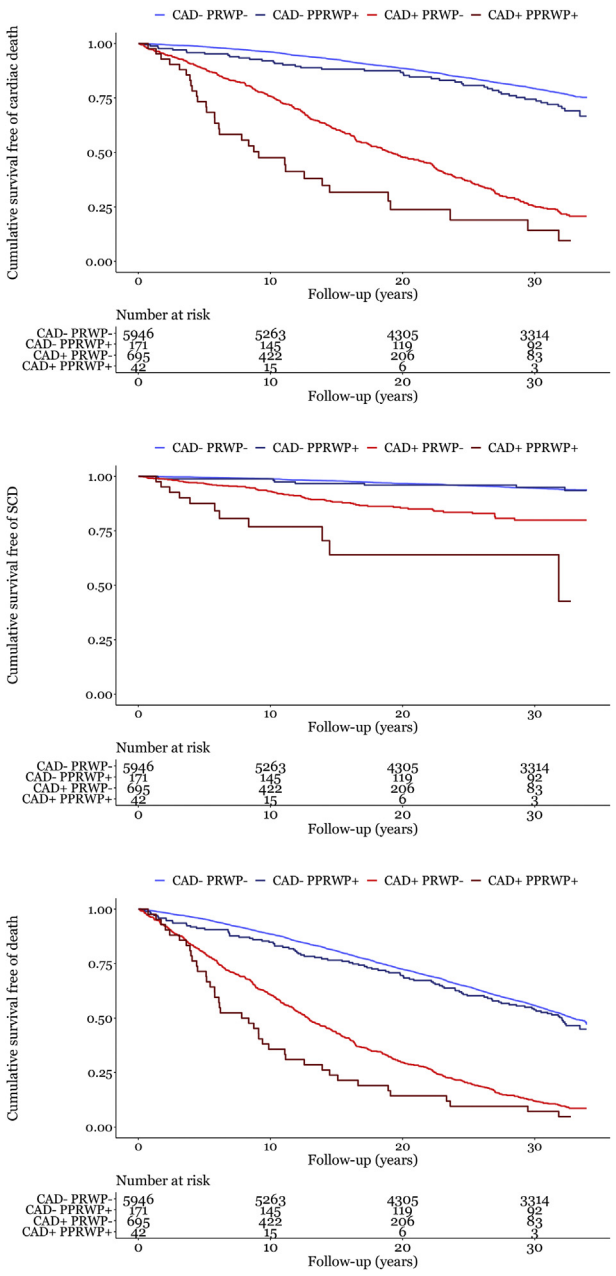

Figure 3 Kaplan-Meier survival plots for cardiac death, sudden cardiac death (SCD), and death from any cause in subjects with normal R-wave progression and poor R-wave progression (PRWP) divided into coronary artery disease (CAD) and no-CAD subgroups.

Delayed QRS transition in the precordial ECG leads, or clockwise rotation of the QRS complex, may accompany PRWP in some cases. This ECG finding of delayed QRS transition has earlier been associated with increased mortality and an increased risk of SCD.[14] A recent study further reported that delayed QRS transition at lead V_5 or later was associated with an increased risk of SCD independent of cardiac function.[15] However, although these conditions may in some cases overlap, in PRWP the loss of anterior depolarization forces is more prominent and the clinical outcome worse compared with isolated delayed QRS transition. A relative decrease in the amplitude of anteriorly directed cardiac electrical forces may also be caused by left bundle branch block or Wolff-Parkinson-White syndrome,[6] but subjects with left bundle branch block and Wolff-Parkinson-White syndrome were excluded in the present study.

In addition, PRWP may be caused by LVH or may occur in otherwise normal subjects,[12] but in the present study, subjects with PRWP did not have a significantly higher prevalence of LVH on the ECG than those without PRWP. The loss of anterior depolarization forces caused by anterior MI can lead to Q-wave formation, loss of normal precordial R-wave progression, or delayed QRS transition. However, PRWP was also detected in asymptomatic subjects in the present study, and exclusion of subjects with anterior Q waves did not change the results. Thus, PRWP may also be a marker of unrecognized structural or electrical abnormalities in the myocardium, which lead to an increased risk of ventricular arrhythmias in the presence of ischemia or other predisposing condition. Thus, an alert clinician should notice PRWP, look for other signs or symptoms of heart disease, and initiate necessary preventive measures. However, further studies are needed to establish whether PRWP, maybe in combination with other risk markers, could be useful in SCD risk stratification in specific patient populations.

Limitations

The number of end points was relatively small particularly in terms of SCD in general population subjects without CAD, leading to wide CIs and making statistical inference uncertain. Although subjects underwent comprehensive interviews and health examinations, no echocardiography was performed for subjects; hence, no data were available regarding the cardiac structure or left ventricular function. It is also possible that some patients could have had prior silent MI or asymptomatic LV dysfunction. Since the current criteria for primary prevention of SCD rely on reduced LVEF,[1,2] further analysis should be performed with data on LVEF also being available. Furthermore, exercise stress test or coronary angiography was not systematically performed on the study subjects, and the CAD diagnosis was based on ECG findings and structural interviews about symptoms and previous diagnoses followed by the clinical assessment by a physician.

PRWP was not one of the predefined ECG abnormalities that led to further examinations or interventions. Hence, the study setup does not allow to determine how many patients

with PRWP were referred to seek medical assistance because of a new CAD or heart failure diagnosis and whether such medical assistance could have altered the prognosis or outcomes.

Finally, although this study is based on a large nationally representative cohort in Finland, the baseline examinations were performed in 1978–1980 and thereby the middle-aged population of this study may differ from today's populations. Also, because of the mostly Caucasian origin of the population, there may be limitations in applying the results to other populations.

Conclusion

The main finding of the present study is that PRWP in an ECG is associated with increased mortality and a markedly elevated risk of adverse cardiac events in the general adult population. The risk of SCD was pronounced in subjects with CAD, indicating that diagnostic measures regarding underlying CAD in subjects with PRWP may be warranted. The future role of PRWP in SCD risk stratification is still to be determined.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2022.02.010.

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