

Electrocardiographic Predictors of Heart Failure With Reduced Versus Preserved Ejection Fraction: The Multi-Ethnic Study of Atherosclerosis

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Background—Several markers detected on the routine 12-lead ECG are associated with future heart failure events. We examined whether these markers are able to separate the risk of heart failure with reduced ejection fraction (HFrEF) from heart failure with preserved ejection fraction (HFpEF).

Methods and Results—We analyzed data of 6664 participants (53% female; mean age 62 ± 10 years) from MESA (Multi-Ethnic Study of Atherosclerosis) who were free of cardiovascular disease at baseline (2000–2002). A competing risks analysis was used to compare the association of several baseline ECG predictors with HFrEF and HFpEF detected during a median follow-up of 12.1 years. A total of 127 HFrEF and 117 HFpEF events were detected during follow-up. In a multivariable adjusted model, prolonged QRS duration, delayed intrinsicoid deflection, left-axis deviation, right-axis deviation, prolonged QT interval, abnormal QRS-T axis, left ventricular hypertrophy, ST/T-wave abnormalities, and left bundle-branch block were associated with HFrEF. In contrast, higher resting heart rate, abnormal P-wave axis, and abnormal QRS-T axis were associated with HFpEF. The risk of HFrEF versus HFpEF was significantly differently for delayed intrinsicoid deflection (hazard ratio: 4.90 [95% confidence interval (CI), 2.77–8.68] versus 0.94 [95% CI, 0.29–2.97]; comparison $P=0.013$), prolonged QT interval (hazard ratio: 2.39 [95% CI, 1.55–3.68] versus 0.52 [95% CI, 0.23–1.19]; comparison $P<0.001$), and ST/T-wave abnormalities (hazard ratio: 2.47 [95% CI, 1.69–3.62] versus 1.13 [95% CI, 0.72–1.77]; comparison $P=0.0093$).

Conclusions—Markers of ventricular repolarization and delayed ventricular activation are able to distinguish between the future risk of HFrEF and HFpEF. These findings suggest a role for ECG markers in the personalized risk assessment of heart failure subtypes. (*J Am Heart Assoc.* 2017;6:e006023. DOI: 10.1161/JAHA.117.006023.)

Key Words: electrocardiography • epidemiology • heart failure

Heat failure (HF) is a major public health problem. Despite advances in treatment and improved survival in recent decades, the annual mortality for HF remains high, reaching proportions of all adult deaths of 40.5% in men and 59.5% in women.¹ The diagnosis of HF is frequently made late, only when patients develop acute symptoms,² making non-invasive, accurate, and cost-effective means of detection a priority.

Approximately 50% of patients hospitalized for HF have preserved ejection fraction (HFpEF).^{2,3} The management of HFpEF differs from the management of HF with reduced ejection fraction (HFrEF). Recent clinical trials have demonstrated that neurohormonal antagonists, such as β -blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers, are effective in HFrEF.^{4,5} However, the benefit of these therapies in HFpEF is unclear,⁶ suggesting

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Clinical perspective

What Is New?

- Several markers detected on the routine 12-lead ECG are predictive of future HF events.
- Whether these ECG markers are able to distinguish between the risk of HF with reduced versus preserved ejection fraction is currently unknown.
- This analysis from MESA (Multi-Ethnic Study of Atherosclerosis) shows that markers of ventricular repolarization and delayed ventricular activation are able to distinguish between the future risk of HF with reduced versus preserved ejection fraction.

What Are the Clinical Implications?

- Identifying specific ECG markers that separate the risk of heart failure with reduced versus preserved ejection fraction highlights the unique pathophysiological differences between these conditions and suggests a potential use of these markers in personalized risk assessment of specific types of HF.

that fundamental differences exist in the pathophysiology of both conditions.⁷

A number of studies have demonstrated that several markers detected on the routine ECG are associated with future HF events^{8–17}; however, it is currently unknown if a differential risk profile exists for these ECG markers in the prediction of HF_{rEF} versus HF_{pEF}. The ability to identify specific predictors for HF_{rEF} and HF_{pEF} is an important step to target appropriate preventive strategies for each HF subtype. Consequently, we conducted a competing risks analysis to identify specific ECG predictors that separate the risk of HF_{rEF} from HF_{pEF} in MESA.

Methods

Study Population

Details of MESA have been reported previously.¹⁸ Briefly, between July 2000 and September 2002, a total of 6814 persons were recruited at 6 field centers (Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles, California; New York, New York; and St. Paul, Minnesota). Participants between 45 and 84 years of age with no clinical cardiovascular disease were recruited. All participants provided informed consent, and the study protocol was approved by the institutional review board at each participating institution. For the purpose of this analysis, participants were excluded if they were missing baseline ECG data, baseline characteristics, or HF follow-up data.

Baseline Characteristics

Participant characteristics were collected during the initial MESA visit. Age, sex, race/ethnicity, income, and education were self-reported. Annual income was categorized as <\$20 000 or ≥\$20 000, and education was categorized as *high school or less* or *some college or more*. Smoking was defined as ever (current or former) versus never smoker. Blood samples were obtained after a 12-hour fast, and measurements of total cholesterol, high-density lipoprotein cholesterol, and plasma glucose were used. Diabetes mellitus was defined as fasting glucose values ≥126 mg/dL or a history of diabetes medication use. Blood pressure was measured for each participant after 5 minutes in the seated position, and systolic measurements were recorded 3 separate times, and the mean of the last 2 values was used. The use of aspirin, statins, and antihypertensive medications was self-reported. Body mass index was computed as the weight in kilograms divided by the square of the height in meters. Resting heart rate was obtained from baseline ECGs.

ECG Measurements

In MESA, 12-lead digital ECGs were obtained by trained technicians using GE MAC 1200 electrocardiographs with standardized procedures. ECGs were transmitted electronically to the MESA ECG Reading Center located at the Epidemiological Cardiology Research Center (Wake Forest School of Medicine, Winston-Salem, NC). According to MESA protocol, all filters in the ECG machines were disabled to provide unfiltered measurements. All ECGs were automatically processed, after visual inspection for technical errors and inadequate quality, using the 2001 version of the GE Marquette 12-SL program. As part of routine quality control measures regarding ECG data processing, trained staff performed visual inspection of main ECG waveforms and confirmed computer-detected ECG abnormalities.

Abnormal P-wave duration, PR interval, and QRS duration were defined as values >120, >200, and >100 ms, respectively. Prolonged QT interval was defined as ≥460 ms for women and ≥450 ms for men using the Framingham formula: $QT_F = QT + 0.154 \times [1 - (60/\text{heart rate})]$.¹⁹ Abnormal P-wave axis was defined as values outside the range of 0° and 75°. ^{20,21} Left-axis deviation was defined as QRS axis less between −90° and −30°, and right-axis deviation was defined as QRS axis between −90 and +90°. Abnormal QRS-T angle was defined as values greater than the sex-specific 95th percentile values (men: >88°; women: >77°). Abnormal P-wave terminal force in lead V₁ (PTFV₁) was defined as values >4000 μV×ms.²² Time to peak R wave (intrinsicoid deflection [ID]) was automatically measured from V5 and V6 (the left ventricular chest leads), and the maximum of both values was

used in the main analysis. Time to ID values >50 ms were considered abnormal.²³ Left ventricular hypertrophy was defined by the Cornell criteria (R wave amplitude AV_L plus S wave amplitude $V_3 \geq 2.8$ mV in men and ≥ 2.0 mV in women).²⁴ Low QRS voltage, ST/T-wave abnormalities, right bundle-branch block, and left bundle-branch block were defined using Minnesota Code Criteria.²⁵

Heart Failure

The ascertainment of incident HF events in MESA has been described previously.²⁶ Participants were followed for incident cardiovascular events from baseline through December 31, 2013. At intervals of 9 to 12 months, a telephone interviewer contacted each participant to inquire about all interim hospital admissions, cardiovascular outpatient diagnoses, procedures, and deaths. In addition, MESA occasionally identified medical encounters through cohort clinic visits, participant call-ins, medical record abstractions, or obituaries. Next-of-kin interviews for out-of-hospital cardiovascular deaths also were used.

The outcome of interest for this analysis was the composite of probable and definite HF events. Definite or probable HF required symptoms, such as shortness of breath or edema, because asymptomatic disease is not a MESA end point. In addition to symptoms, probable HF required a previous physician diagnosis and the patient to be receiving medical treatment for HF. Definite HF required ≥ 1 other criteria, such as pulmonary edema or congestion by chest x-ray, dilated ventricle or poor left ventricular function by echocardiography or ventriculography, or evidence of left ventricular diastolic dysfunction. HF events were stratified by type as HFrEF or HFpEF. HFpEF events were defined as cases with ejection fraction $\geq 50\%$.

Statistics

Baseline characteristics were compared by HF status. Categorical variables were reported as frequency and percentage, whereas continuous variables were recorded as mean \pm SD. Statistical significance for categorical variables was tested using the χ^2 method and the ANOVA procedure for continuous variables.

Follow-up time was defined as the time between the baseline ECG measurement until a diagnosis of HF, death, loss to follow-up, or end of follow-up (December 31, 2013). Cox regression was used to compute hazard ratios (HRs) and 95% confidence intervals for the association between each ECG measurement and HF. *P* values for the HRs were computed using the likelihood ratio method. Separate analyses were conducted for HFrEF and HFpEF. Multivariable models were constructed as follows: model 1 adjusted for age, sex, race/ethnicity, income, and education; model 2 adjusted for model

1 covariates plus systolic blood pressure, heart rate, smoking, diabetes mellitus, body mass index, total cholesterol, high-density lipoprotein cholesterol, aspirin, statins, and antihypertensive medications. A competing risks analysis was used to compare the association of several ECG predictors with HFrEF and HFpEF. Specifically, we used the Lunn–McNeil method to test whether ECG predictors that were significantly associated with each HF type were associated with a differential risk for HFrEF versus HFpEF.²⁷ The proportional hazards assumption was not violated in our analyses. Statistical significance was defined as $P < 0.05$. SAS version 9.4 was used for all analyses.

Results

A total of 6664 participants (mean age 62 ± 10 years, 53% women, 38% white, 12% Chinese American, 28% black, 22% Hispanic) were included in the final analysis. Baseline characteristics stratified by the development of HF are shown in Table 1. As shown, participants who did not develop HF were more likely to be young, to be female, to have higher educational attainment and income, and to have fewer cardiovascular risk factors compared with those who developed HFrEF or HFpEF. Compared with HFrEF, participants with HFpEF were more likely to be older, to be female, to report smoking, and to have higher systolic blood pressure and cholesterol values. Almost none of those with HFpEF had left bundle-branch block, and those with HFrEF tended to have a higher prevalence of prolonged QRS duration, abnormal time to ID, prolonged QT duration, and ST/T-wave abnormalities.

Over a median follow-up of 12.1 years (25th–75th percentiles: 11.6–12.7 years), a total of 244 HF cases (incidence rate per 1000 person-years: 3.33; 95% confidence interval, 2.94–3.77) were identified. Of these, 127 (52%) were HFrEF and 117 (48%) were HFpEF. Among the ECG markers examined, higher resting heart rate, prolonged QRS duration, abnormal time to ID, left-axis deviation, abnormal QRS-T angle, left ventricular hypertrophy, ST/T-wave abnormalities, and left bundle-branch block were significantly associated with all HF events (Figure).

Table 2 shows the multivariable HRs for the development of HFrEF and HFpEF associated with each ECG measurement separately. As shown, prolonged QRS duration, delayed time to ID, left-axis deviation, right-axis deviation, prolonged QT interval, abnormal QRS-T axis, left ventricular hypertrophy, ST/T-wave abnormalities, and left bundle-branch block were associated with HFrEF. In contrast, higher resting heart rate, abnormal P-wave axis, and abnormal QRS-T axis were associated with HFpEF. The risk of HFrEF versus HFpEF was different for abnormal time to ID (comparison $P = 0.013$), prolonged QT interval (comparison $P < 0.001$), and ST/T-wave abnormalities (comparison $P = 0.0093$).

Table 1. Baseline Characteristics by HF Subtype

Characteristic	No HF (n=6420)	HFrEF (n=127)	HFpEF (n=117)	P Value*
Age, mean±SD, y	62±10	67±8.9	70±8.5	<0.001
Men, %	2996 (47)	91 (72)	58 (50)	<0.001
Race/ethnicity				0.023
White, %	2446 (38)	50 (40)	50 (43)	
Chinese American, %	782 (12)	3 (2)	12 (10)	
Black, %	1769 (28)	46 (36)	32 (27)	
Hispanic, %	1423 (22)	28 (22)	23 (20)	
Education, high school or less, %	2328 (36)	51 (40)	49 (42)	0.31
Income <\$20 000, %	1703 (27)	47 (37)	40 (34)	0.0060
Ever smoker, %	3156 (49)	73 (57)	69 (59)	0.021
Diabetes mellitus, %	866 (13)	39 (31)	36 (31)	<0.001
Body mass index, kg/m ² , mean±SD	28±5.4	29±5.5	30±6.4	<0.001
Systolic blood pressure, mm Hg, mean±SD	126±21	137±22	139±23	<0.001
Total cholesterol, mg/dL, mean±SD	194±36	187±36	189±33	0.017
HDL cholesterol, mg/dL, mean±SD	51±15	47±13	50±14	0.0083
Antihypertensive medications, %	2329 (36)	76 (60)	65 (56)	<0.001
Aspirin, %	1496 (23)	46 (36)	37 (32)	<0.001
Statin, %	938 (15)	25 (20)	17 (15)	0.28
Heart rate, mean±SD, bpm	63±9.6	64±11	66±10	0.0014
P-wave duration, >120 ms, %	699 (11)	27 (21)	21 (18)	<0.001
PR interval, >200 ms, %	492 (7.6)	19 (15)	15 (13)	0.0014
PTFV ₁ , >4000 ms, %	940 (15)	30 (24)	30 (26)	<0.001
Abnormal P-wave axis, %	548 (8.5)	11 (8.7)	18 (15)	0.033
QRS duration, >100 ms, %	1239 (19)	56 (44)	34 (29)	<0.001
Time to ID, >50 ms, %	113 (1.8)	14 (11)	3 (2.6)	<0.001 [†]
Left-axis deviation, %	367 (5.7)	21 (17)	14 (12)	<0.001
Right-axis deviation, %	23 (<1)	2 (1.6)	0 (0)	0.15 [†]
Prolonged QT interval, %	481 (7.5)	28 (22)	6 (5.1)	<0.001
Abnormal QRS-T axis, %	293 (4.6)	22 (17)	19 (16)	<0.001
Left ventricular hypertrophy, %	236 (3.7)	12 (9.5)	8 (6.8)	0.0017 [†]
Low voltage, %	124 (1.9)	1 (<1)	3 (2.6)	0.55 [†]
ST/T-wave abnormalities, %	852 (13)	44 (35)	25 (21)	<0.001
Right bundle-branch block, %	145 (2.3)	6 (4.7)	7 (5.9)	<0.001 [†]
Left bundle-branch block, %	16 (<1)	5 (3.9)	1 (<1)	<0.001 [†]

bpm indicates beats per minute; HDL, high-density lipoprotein; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; PTFV₁, P-wave terminal force in V1.

*Statistical significance for continuous data was tested using the ANOVA procedure, and categorical data were tested using the χ^2 test.

[†]Statistical significance tested using the Fisher exact test because of low cell frequencies.

Discussion

In this analysis from MESA, we demonstrated that several ECG markers are associated with both HFrEF and HFpEF. In addition, markers of ventricular repolarization and delayed ventricular activation were able to distinguish between

HFrEF and HFpEF events. These findings suggest that distinct ECG profiles exist in the prediction of HFrEF and HFpEF.

Although several reports have shown that findings on the routine ECG are associated with future HF events,⁸⁻¹⁷ few

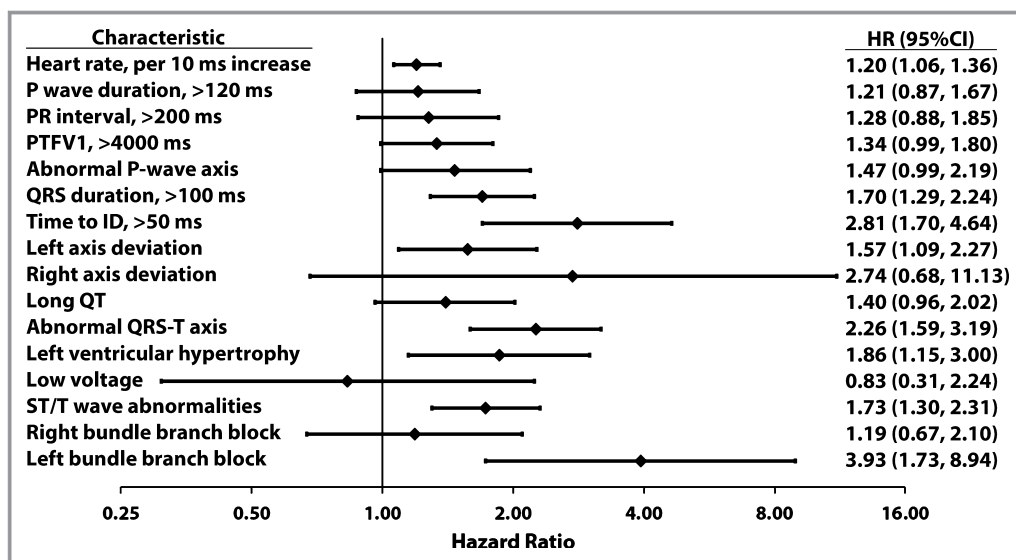


Figure. Association between electrocardiographic abnormalities and heart failure. Model adjusted for age, sex, race/ethnicity, education, income, systolic blood pressure, smoking, diabetes mellitus, body mass index, cholesterol, high-density lipoprotein cholesterol, aspirin, statins, and antihypertensive medications. CI indicates confidence interval; HR, hazard ratio; ID, intrinsicoid deflection; PTFV1, P-wave terminal force in V1.

have explored whether ECG predictors vary in their ability to distinguish between HF_{rEF} and HF_{pEF}. A recent examination from the Framingham Heart Study has shown that left ventricular hypertrophy and left bundle-branch block are associated with HF_{rEF} and that atrial fibrillation is associated with HF_{pEF}.²⁸ In that study, which was limited to white participants, the aforementioned markers were the only ECG abnormalities examined.

Similar to findings from the Framingham Heart Study, our data confirm that left ventricular hypertrophy is associated with HF_{rEF}.²⁸ The reason for this finding possibly is related to the fact that left ventricular hypertrophy detects abnormal left ventricular mass,²⁹ which is a well-known risk factor for HF_{rEF}. In addition, men dominate the HF_{rEF} population and, on average, have significantly higher left ventricular mass than women.³⁰ Consequently, it is possible that sex differences in left ventricular mass contribute to the predilection of ECG left ventricular hypertrophy for HF_{rEF} events. Furthermore, similar to findings from the Framingham Heart Study, left bundle-branch block was associated with HF_{rEF} and not HF_{pEF}.

The current analysis represents the most comprehensive study to examine the differential predictive abilities of ECG abnormalities to distinguish between HF_{rEF} and HF_{pEF} risk. In our study, markers of abnormal ventricular depolarization (QRS duration, delayed time to ID), axis deviation (left and right), abnormal ventricular repolarization (ST/T-wave abnormalities), and conduction disease (left bundle-branch block) were associated with HF_{rEF}. In contrast, higher resting heart rate and abnormal P-wave axis were associated with HF_{pEF}. Abnormal QRS-T axis was associated with both subtypes.

However, only abnormalities of ventricular depolarization (delayed time to ID) and repolarization (prolonged QT interval and ST/T-wave abnormalities) were statistically different in terms of associations with HF subtypes. Overall, the unique findings presented support a role for the 12-lead ECG to separate HF risk by subtype (eg, HF_{rEF} versus HF_{pEF}).

Delayed time to ID is thought to represent conduction delay secondary to increases in left ventricular cavity size and increases in left ventricular end-diastolic volume.^{31,32} Similarly, abnormalities of left ventricular repolarization possibly detect structural abnormalities that predispose to HF_{rEF} rather than HF_{pEF}.^{29,33,34} This is supported by data that have shown that ST/T-wave abnormalities are not associated with diastolic dysfunction that would be expected in the development of HF_{pEF}.³⁵ Therefore, abnormal ECG measures of ventricular repolarization would be expected to differentially predict HF_{rEF} compared with HF_{pEF}. Overall, these data suggest that delayed time to ID, prolonged QT interval, and ST/T-wave abnormalities detect subclinical anatomical abnormalities that predispose to HF_{rEF} instead of events with normal ejection fraction.

By 2030, the prevalence of HF is projected to increase by 23%, with medical costs increasing to nearly \$53.1 billion.³⁶ Accordingly, the identification of at-risk individuals by low-cost, noninvasive cardiac assessment is of paramount importance due to the large burden that HF will place on the healthcare system. Our results suggest that simple markers detected on routine ECG are able to distinguish between persons who will develop HF_{rEF} and HF_{pEF}. In addition, the distinctive associations between certain ECG markers with

Table 2. Electrocardiographic Predictors of HFrEF Versus HFpEF

ECG Predictor*	HFrEF (n=127)			HFpEF (n=117)			P Comparison [§]
	Model 1 [†] HR (95% CI)	P Value	Model 2 [‡] HR (95% CI)	P Value	Model 1 [†] HR (95% CI)	P Value	
Heart rate, per 10-ms increase	1.15 (0.97–1.37)	0.11	1.09 (0.91–1.30)	0.34	1.43 (1.20–1.71)	<0.001	1.34 (1.12–1.60)
P wave duration, >120 ms	1.52 (0.98–2.35)	0.059	1.32 (0.85–2.05)	0.21	1.30 (0.80–2.10)	0.29	1.09 (0.67–1.78)
PR interval, >200 ms	1.50 (0.91–2.46)	0.11	1.36 (0.83–2.23)	0.23	1.33 (0.77–2.31)	0.31	1.19 (0.69–2.08)
PTFV ₁ , >4000 ms	1.57 (1.04–2.37)	0.033	1.32 (0.87–1.99)	0.20	1.65 (1.09–2.51)	0.019	1.35 (0.88–2.07)
Abnormal P-wave axis	0.83 (0.44–1.55)	0.56	1.00 (0.53–1.89)	0.99	1.64 (0.99–2.72)	0.056	2.04 (1.22–3.42)
QRS duration, >100 ms	2.45 (1.70–3.53)	<0.001	2.14 (1.48–3.09)	<0.001	1.53 (1.01–2.32)	0.048	1.28 (0.84–1.95)
Time to ID, >50 ms	5.67 (3.25–9.90)	<0.001	4.90 (2.77–8.68)	<0.001	1.22 (0.39–3.83)	0.74	0.94 (0.29–2.97)
Left-axis deviation	2.08 (1.29–3.36)	0.0028	1.86 (1.15–3.02)	0.012	1.47 (0.83–2.60)	0.19	1.29 (0.73–2.28)
Right-axis deviation	4.94 (1.22–19.95)	0.025	4.98 (1.22–20.40)	0.025	N/A	N/A	N/A
Prolonged QT interval	2.55 (1.66–3.90)	<0.001	2.39 (1.55–3.68)	<0.001	0.52 (0.23–1.19)	0.12	0.48 (0.21–1.11)
Abnormal QRS-T axis	3.30 (2.06–5.28)	<0.001	2.52 (1.56–4.05)	<0.001	2.66 (1.61–4.39)	<0.001	2.01 (1.21–3.33)
Left ventricular hypertrophy	3.36 (1.82–6.22)	<0.001	2.56 (1.36–4.82)	0.0036	1.70 (0.82–3.54)	0.15	1.31 (0.62–2.76)
Low voltage	0.45 (0.06–3.19)	0.42	0.43 (0.06–3.09)	0.40	1.28 (0.40–4.04)	0.68	1.20 (0.38–3.81)
ST/T-wave abnormalities	3.04 (2.09–4.43)	<0.001	2.47 (1.69–3.62)	<0.001	1.33 (0.85–2.08)	0.22	1.13 (0.72–1.77)
Right bundle-branch block	1.16 (0.51–2.67)	0.72	1.03 (0.45–2.36)	0.95	1.63 (0.75–3.55)	0.22	1.38 (0.63–3.02)
Left bundle-branch block	9.29 (3.78–22.83)	<0.001	6.75 (2.70–16.86)	<0.001	1.95 (0.27–14.02)	0.51	1.28 (0.17–9.30)

CI indicates confidence interval; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio; ID, intrinsicoid deflection; PTFV₁, P-wave terminal force in V₁.

*Selected from the list of ECG predictors that showed significant associations with total heart failure events in a model similar to model 2.

[†]Adjusted for age, sex, race/ethnicity, education, and income.

[‡]Adjusted for model 1 covariates plus systolic blood pressure, smoking, diabetes mellitus, body mass index, cholesterol, high-density lipoprotein cholesterol, aspirin, statins, and antihypertensive medications.

[§]P value comparison computed using effect estimates from model 2 for the variables that showed a significant P value in at least 1 of the heart failure subtypes.

^{||}Hazard ratio not computed due to 0% prevalence of the abnormality in HFpEF.

different patterns of HF, which further emphasizes the unique differences between HFpEF and HFpEF,²⁸ suggest that the ECG may have a role to guide targeted preventive strategies for each HF subtype. The ECG also could be a useful tool to select patients for clinical trials with aims to prevent specific HF subtypes. Further research, however, is needed to determine the cost-effectiveness of using the ECG to characterize HF risk by subtype before recommendations regarding clinical practice or research applications are made.

The current study should be interpreted in the context of several limitations. Although rigorous methods were used to account for all HF cases, some events may have been missed. It is unlikely, however, that the resulting bias would have been differential in nature rather than merely reducing effect estimates toward the null. Because of the limited number of HF event subtypes, we were unable to explore whether racial or ethnic variation exists regarding the differential prediction of ECG abnormalities for HF subtype events. In addition, although numerous covariates were included in our multivariable models, we acknowledge that residual confounding remains a possibility.

In conclusion, our results indicate that HFrEF and HFpEF are preceded by distinct profiles on the routine 12-lead ECG, suggesting a role for ECG recordings to better characterize the risk of HF by subtype. Further research is needed to confirm our findings and to determine whether these markers are able to identify individuals in whom targeted preventive therapies are warranted to reduce the current and future burden of HF.

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Disclosures

None.

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