Diagnostic Accuracy of the Electrocardiogram for Heart Failure With Reduced or Preserved Ejection Fraction

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Research Letter

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To the Editor:

Current heart failure (HF) guidelines recommend electrocardiography (ECG) as an essential initial investigation in a patient's workup.[1] However, these recommendations were based on studies primarily including patients with HF with reduced ejection fraction (HFrEF).[1–3] Guidelines do not distinguish HFrEF from HF with preserved and mid-range ejection fraction (HFpEF and HFmrEF) in their ECG recommendations. We hypothesized that a normal ECG does not exclude HFpEF and has a considerably lower sensitivity for diagnosing HFpEF than HFrEF.

The current study was performed with data from the Singapore Heart Failure Outcomes and Phenotypes (SHOP) study, which included 1093 patients with HF (22% HFpEF) recruited from 6 centers in Singapore and 962 community-dwelling controls without HF. We validated our results in the independent Asian neTwork for Translational Research and Cardiovascular Trials (ATTRaCT) cohort, which consisted of 515 patients with HF (27% HFpEF) and 174 controls without HF, also recruited from these same centers in Singapore. ATTRaCT and SHOP had a similar study design previously described.[4] All patients were aged >18 years presenting with a primary diagnosis of HF or attending a hospital clinic for management of HF within 6 months of decompensated HF. Patients with severe valve disease as the primary cause of HF, a primary diagnosis of acute coronary syndrome, end-stage renal failure (estimated glomerular filtration rate <15 mL/min/m^2), isolated right-sided HF or specific HF subgroups (eg, constrictive pericarditis, hypertrophic cardiomyopathy) were excluded. The full inclusion and exclusion criteria of the SHOP study, which were the same for the ATTRaCT study, were reported previously.[4] All participants provided informed consent, and the ethics committee approved the study from each participating institution in compliance with the declaration of Helsinki.[4] Resting 12-lead ECGs performed at recruitment were interpreted by a blinded qualified reader. Echocardiography was performed, and plasma N-terminal pro-B-type NP (NT-proBNP) was measured in all participants at baseline. HFrEF was defined as a left ventricular ejection fraction (LVEF) of <40%, HFmrEF as an LVEF of 40%−49% and HFpEF as an LVEF of ≥50%. An abnormal ECG had ≥1 of the following characteristics: QRS >120 ms, left/right bundle branch blocker or interventricular conduction delay, left ventricular hypertrophy (LVH), right ventricular hypertrophy, any QRS axis deviation, ST segment or T wave abnormalities, or any arrhythmia (heart block, atrial or ventricular arrhythmia). When all of these ECG abnormalities were absent and the patient was in sinus rhythm, the ECG was considered normal.

Patients in the ATTRaCT cohort were slightly younger (58 ± 12 years vs 62 ± 12 years; $P < .001$) and more often men (80% vs 76%) than patients in the SHOP cohort, despite having the same inclusion and exclusion criteria. Among patients with HF from SHOP, 869 (80%) of ECGs were abnormal versus 116 (12%) in non-HF participants ($P < .001$). The ECG was more often abnormal in patients with HFrEF (84%) and HFmrEF (82%) than HFpEF (65%). In SHOP and ATTRaCT, QRS axis deviation (prevalence ratio [PR] >1.5 in both cohorts), LVH (PR in both cohorts >1.7), STT abnormalities (PR in both cohorts >1.4), and QRS >120 ms (PR in both cohorts >4.4) were more common in HFrEF than HFpEF ($P < .05$ for all). The sensitivity for distinguishing HF from non-HF controls was lower in patients with HFpEF (sensitivity 65%, specificity 88%) than HFrEF (sensitivity 84%, specificity 88%) (Fig. 1A). In the ATTRaCT study, the percentage of abnormal ECGs was higher in HFrEF than HFpEF (76% vs 57%; $P < .001$). Sensitivity was lower for detecting HFpEF (57%) than HFrEF (75%) (Fig. 1B). The proportion of false negatives (patients with a normal ECG but HFpEF) was 43% in ATTRaCT and 35% in SHOP. Results remained similar when restricting analyses to patients with an NT-proBNP of >125 ng/L. In secondary analyses, we compared patients with HFpEF and a normal ECG from SHOP with age- and sex-matched hypertensive (systolic blood pressure >140 mm Hg) controls without HF to address any concern that patients with HFpEF and a normal ECG might not have HF. LVH (left ventricular mass index ≥115 g/m^2 for men and ≥95 g/m^2 for women) on echocardiography was present in 71% of patients with HFpEF and a normal ECG compared with 17% of hypertensive controls with a normal ECG ($P < .001$) and 5% of

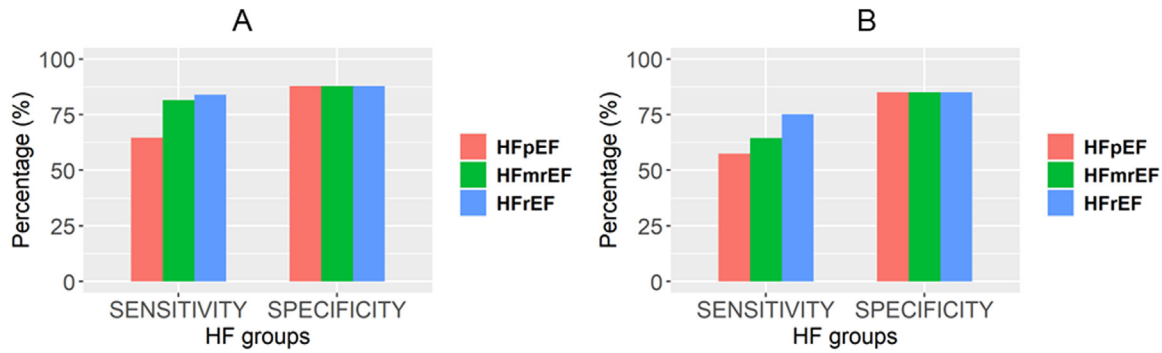

Fig. 1. (A) Barplots showing the sensitivity and specificity for heart failure (HF) left ventricular ejection fraction (LVEF) subtypes in the Singapore Heart Failure Outcomes and Phenotypes (SHOP) cohort. **(B)** Barplots showing the sensitivity and specificity for heart failure LVEF subtypes in the Asian neTwork for Translational Research and Cardiovascular Trials (ATTRaCT) cohort. HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

patients with HFpEF and a normal ECG died within 1 year compared with 0% of age- and sex-matched hypertensive controls with a normal ECG.

Our results indicate that an abnormal ECG's sensitivity is lower for diagnosing HFpEF than HFrEF. The sensitivity of an abnormal ECG for the diagnosis of HFrEF was similar to earlier studies.[2,3] Only 16% of patients with HFrEF in SHOP and 25% with HFrEF in ATTRaCT had a normal ECG. In contrast, one-third of patients with HFpEF had a normal ECG in SHOP and 43% in ATTRaCT. Despite using the same inclusion and exclusion criteria, patients in the ATTRaCT cohort were slightly younger and more often women than those in the SHOP cohort. This difference might have been caused by sampling bias and could influence some of the different observations between the two cohorts. An extended QRS duration and LVH were more common in HFrEF than HFpEF. Data from the Multi-Ethnic Study of Atherosclerosis (MESA) study showed that diffuse myocardial fibrosis, a hallmark of HFpEF, masks ECG signals of LVH and extended QRS duration, possibly explaining the lower sensitivity.[5] Our findings suggest that other diagnostic modalities should be considered to diagnose HFpEF, such as NT-proBNP or echocardiography. Our data showed cardinal features of HFpEF in patients with a normal ECG, including cardiac structural abnormalities and worse mortality than age- and sex-matched hypertensive controls. Our results should be viewed in light of several limitations, including a post hoc study design, inclusion of only healthy (nondyspnoeic) controls, and inclusion of only patients and controls of Asian ethnicity.

In conclusion, our data show that a normal ECG might not exclude a HF diagnosis, especially in HFpEF. Future guidelines need to consider the differential sensitivity of the ECG in ruling out HFrEF versus HFpEF.

Disclosures

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