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Electrocardiogram as a screening tool to exclude chronic systolic heart failure with reduced left ventricular ejection fraction

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ABSTRACT

INTRODUCTION. In recent years, the waiting time for outpatient echocardiography has been increasing. This has potential consequences for patients with de novo systolic heart failure (HF). Thus, screening methods for HF are needed. One method may be electrocardiogram (ECG). We assessed the diagnostic value of the ECG in identifying HF with reduced left ventricle ejection fraction (LVEF) in patients referred from primary care.

METHODS. A 2020-2021 observational retrospective study was conducted on patients referred from primary care on suspicion of HF. All patients had ECG performed before LVEF was documented by echocardiography.

RESULTS. In total, 248 patients (61.5%) presented with an abnormal ECG. Among these patients, 4.8% had LVEF 41-49% and 7.7% had LVEF ≤ 40%. An abnormal ECG was found to be associated with reduced LVEF. The negative predictive value of the ECG was 99%, regardless of whether the ECG was interpreted by the cardiologist or automatically. Adding the ECG to a logistic model with traditional risk factors, the ECG increased the area under curve from 0.72 to 0.79.

CONCLUSION. This study is the first study to assess the value of automatic ECG interpretation compared with a cardiologist's interpretation. The normal ECG can safely exclude HF with LVEF < 50% and may serve as a gatekeeping tool to further assist the primary care physician in identifying patients with de novo systolic HF.

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Chronic systolic heart failure is a condition with an increasing prevalence and incidence [1, 2]. Regardless of any treatment given, heart failure causes increasing morbidity, mortality and decreasing quality of life [1]. However, timely treatment may potentially increase quality of life and reduce or postpone morbidity and mortality.

In recent years, the waiting time for outpatient echocardiography has increased due to a growing number of referrals [2, 3] and downscaling of the outpatient clinic during the COVID-19 pandemic [4]. The rising waiting time has direct and possibly fatal consequences for patients with heart failure. This calls for simple screening methods to prioritise referrals. For this purpose, the electrocardiogram (ECG) is an inexpensive, accessible and non-invasive way to examine these patients.

According to European Society of Cardiology guidelines for chronic systolic heart failure [5], a normal ECG and low levels of N-terminal pro-brain natriuretic peptide (NT-pro-BNP) make the diagnosis of heart failure unlikely. However, the guidelines do not mention whether a normal ECG may exclude chronic systolic heart failure without the contribution of NT-pro-BNP. In Danish primary care, NT-pro-BNP is not measured routinely [6].

The primary aim of this study was to examine whether a normal ECG may exclude chronic systolic heart failure with left ventricular ejection fraction (LVEF) < 50% and serve as a gatekeeping tool in patients referred to the cardiac outpatient clinic from primary care on suspicion of heart failure. Furthermore, in relation to interpretation of the ECG, we wanted to explore whether there was any difference between a cardiologist and an automated interpretation. Lastly, the aim was to assess whether a model predicting heart failure from risk factors may benefit from addition of ECG.

METHODS

Study population

The population consisted of adults living in any of six municipalities served by Odense University Hospital Svendborg in Svendborg, Denmark. All patients referred from 31 October 2020 to 1 November 2021 from primary care on suspicion or symptoms of heart failure were evaluated.

Inclusion criteria

Suspicion of heart failure in the referral

and/or

Description of symptoms/signs of heart failure: dyspnoea and/or fatigue and/or fluid retention.

Exclusion criteria

Missing ECG or echocardiography in medical records

History of heart failure.

One of five senior cardiologists in the department read each referral, evaluated the ECG in the referral and noted whether the ECG was normal or abnormal.

Subsequently, the patients attended the cardiac outpatient clinic for an echocardiography and LVEF was documented. The cardiologists performing echocardiography did not have access to either the referral ECG or the ECG evaluation done by the first cardiologist.

Retrospectively, we collected data on comorbidities with relation to heart failure and on other conditions causing symptoms seen in heart failure.

Data collection

Electrocardiogram

All patients enrolled had a 12-lead ECG performed prior to echocardiographic assessment. For most patients, ECG was performed in primary care. The remaining patients had a 12-lead ECG performed in the hospital. During initial evaluation of the ECG, the senior cardiologist only reported whether the ECG was normal or abnormal.

An ECG was classified as abnormal if the rhythm was abnormal (atrial/ventricular fibrillation, atrial/ventricular flutter or atrial rhythm), if conduction abnormalities were discovered (all degrees of atrioventricular block, both types of bundle branch block and fascicular block), whether there were R-wave, Q-wave or T-wave changes, significant ST-deviations (> 1 mm and ≥ 2 contiguous leads) or if the patient had prolonged QT [7, 8]. Thus, any significant ECG change was noted. Classification of ECG changes was documented retrospectively.

After classification, patients were divided into groups depending on the type of ECG abnormality found.

Echocardiography

Following current recommendations [9, 10], recommending Simpson biplane method for LVEF estimation, echocardiography was performed by a skilled senior cardiologist blinded to the first cardiologist ECG findings. The time of echocardiography varied from a few weeks to months after referral depending on the severity of the symptoms and findings presented in the referral.

Retrospectively, at baseline, patients were divided into two groups; a group of patients with normal ECG and a group with abnormal ECG. Subsequently, the group with ECG changes was stratified into three groups by LVEF (LVEF 50-60%, LVEF 41-49% or LVEF < 40%).

Statistical analysis

The T-test was used to compare parametric variables. For nonparametric variables, the χ^2 test or (two-tailed) Fisher's exact test was used.

We estimated sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and positive likelihood ratio (LR+) as well as negative likelihood ratio (LR–) for the ECG as interpreted by the cardiologist and the machine.

Using multivariable logistic regression, it was possible to build two receiver-operation characteristics (ROC) curves to predict heart failure with reduced LVEF < 50% and estimate the area under curve (AUC), thereby assessing whether addition of the ECG would increase the AUC. In one model, heart failure with reduced LVEF < 50% was predicted from traditional risk factors. In the other model, the ECG was added to the traditional risk factors.

All statistical analyses were performed in Stata/BE 17.0 (StataCorp LLC, College Station, TX, USA). A p value of less than 0.05 was considered statistically significant.

Trial registration: not relevant.

RESULTS

At baseline, 461 patients were screened for enrollment in the study. Among these, 58 patients were excluded; 24 patients (41.4%) had a history of heart failure, 21 patients (36.2%) had a missing ECG or echocardiographic assessment and seven (12.1%) patients had no substantiated suspicion of heart failure (four patients referred for echocardiography before administering antipsychotics and three patients referred because of personal wishes). The final study population consisted of 403 patients.

In the study population, 155 patients presented with normal ECG and 248 patients presented with abnormal ECG. In general, patients with abnormal ECG were significantly older males with ischaemic heart disease, type II diabetes and hypercholesterolaemia. See **Table 1** for baseline characteristics.

TABLE 1 Baseline characteristics and echocardiographic findings for the electrocardiogram groups as well as overall characteristics.

	Overall	Normal ECG	Abnormal ECG	p value
Age, mean ± SD, yrs	70.7 ± 12.8	67.0 ± 14.0	73.1 ± 13.7	< 0.001
Patients, total, n (%)	403 (100)	155 (38.5)	248 (61.5)	-
Male sex, n (%)	200 (49.6)	57 (36.8)	143 (57.7)	< 0.001
Symptoms/signs of heart failure, n (%)				
Dyspnoea	356 (88.4)	141 (91.0)	215 (86.7)	NS
Fatigue	48 (11.9)	13 (8.4)	35 (14.1)	0.084
Fluid retention	159 (39.5)	57 (36.8)	102 (41.1)	NS
Ischaemic heart disease, n (%)	59 (14.6)	9 (5.8)	50 (20.2)	< 0.001
Type 2 diabetes, n (%)	56 (13.9)	11 (7.1)	45 (18.1)	0.002
Hypercholesterolaemia, n (%)	162 (40.2)	52 (33.5)	110 (44.4)	0.031
Hypertension, n (%)	258 (64.0)	96 (61.9)	162 (65.3)	NS
Smoking history, n (%)				
Ever smoker	209 (51.9)	81 (52.3)	128 (51.6)	NS
Never smokers	194 (48.1)	74 (47.7)	120 (48.4)	NS

ECG = electrocardiogram; NS = not significant; SD = standard deviation.

Distribution of electrocardiogram abnormalities in the three left ventricular ejection fraction groups

Table 2 shows the distribution of ECG abnormalities in the three LVEF groups.

TABLE 2 Distribution of electrocardiogram abnormalities overall and in the three left ventricle ejection fraction groups. The values are n (%).

		LVEF			
	Overall	50-60%	41-49%	≤ 40%	p value
Patients, total	403 (100)	370 (91.8)	14 (3.5)	19 (4.7)	-
Abnormal ECG	248 (61.5)	217 (58.6)	12 (85.7)	19 (100)	< 0.001
Atrial flutter/fibrillation	53 (13.2)	46 (12.4)	2 (14.3)	5 (26.3)	NS
AV block	22 (5.5)	20 (5.4)	1 (7.1)	1 (5.3)	NS
LBBB	26 (6.5)	17 (4.6)	1 (7.1)	8 (42.1)	< 0.001
RBBB	22 (5.5)	20 (5.4)	2 (14.3)	0	NS
Fascicular block	24 (6.0)	22 (5.9)	2 (14.3)	0	NS
T-wave changes	40 (9.9)	34 (9.2)	4 (28.6)	2 (10.5)	.059
ST-segment deviation	36 (8.9)	26 (7.0)	6 (42.9)	4 (21.1)	< 0.001
Left ventricular hypertrophy	9 (2.2)	9 (2.4)	0	0	NS
Q-wave abnormalities	28 (6.9)	24 (6.5)	2 (14.3)	2 (10.5)	NS

AV = atrioventricular; ECG = electrocardiogram; LBBB = left bundle branch block; LVEF = left ventricle ejection fraction; RBBB = right bundle branch block.

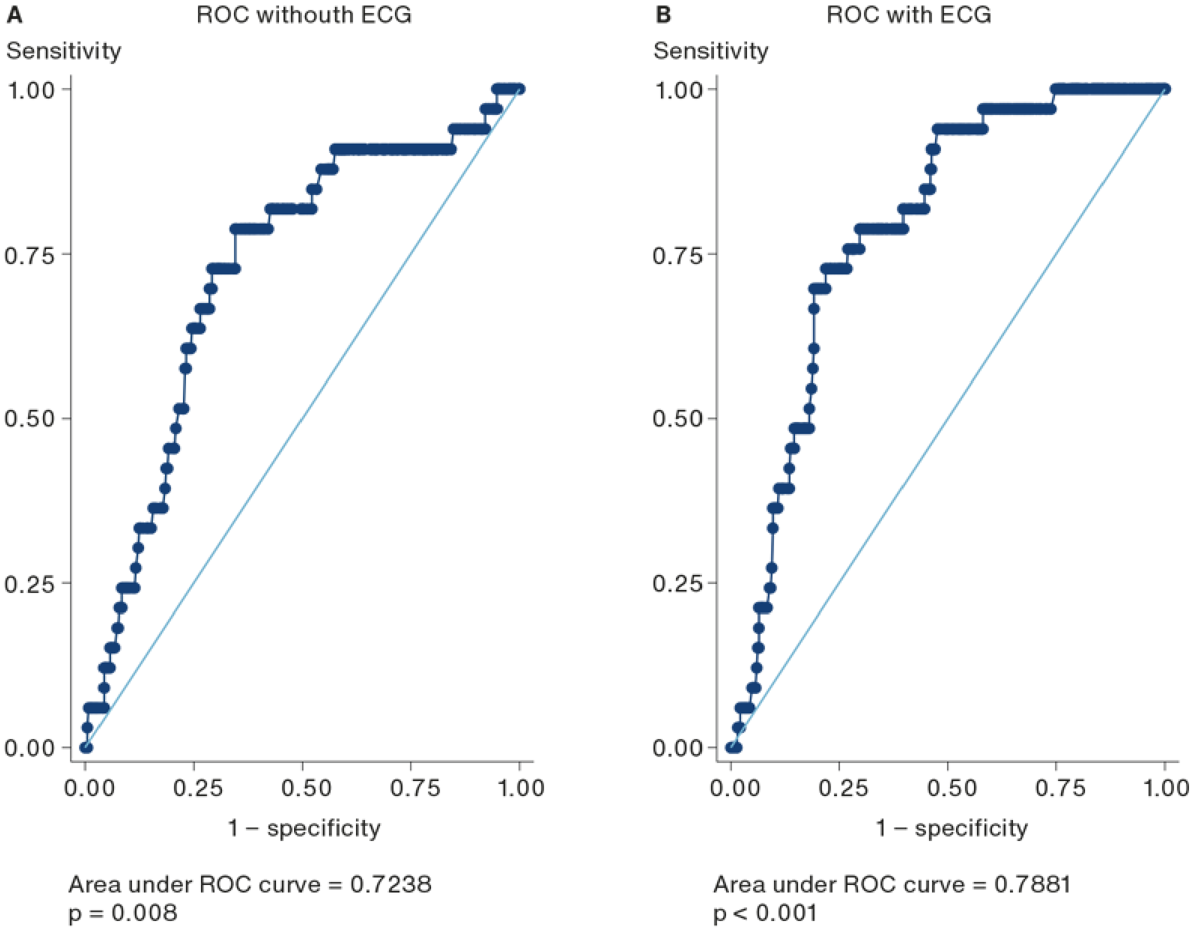
Comparing ECG abnormalities in the three LVEF groups, we found a significant association between ECG abnormalities and reduced LVEF ($p \leq 0.001$).

Among the 248 patients with abnormal ECG findings, 217 patients (87.5%) presented with LVEF 50-60%. The LVEF 41-49% group consisted of 14 patients, of whom 12 (85.7%) presented with an abnormal ECG. All of the 19 patients in the LVEF ≤ 40% group had abnormal ECG findings.

Prediction of reduced left ventricular ejection fraction through the abnormal electrocardiogram

To assess the strength of a prediction model for LVEF < 50%, our logistic regression model was applied to a ROC curve. The result was an AUC of 0.72 for traditional risk factors alone. Adding the ECG to the model, the AUC increased significantly to 0.79. See **Figure 1** for ROC curves and risk factors of the two models.

FIGURE 1 A. Receiver operated curve (ROC) for a multivariable logistic regression model with six risk factors (age, sex, hypertension, hypercholesterolaemia, diabetes and coronary heart disease). **B.** Model in which the electrocardiogram (ECG) was added to the six risk factors.



The electrocardiogram as a diagnostic tool

The cardiologist classified 31 patients (93.9%) with LVEF < 50% with abnormal ECG findings. Two patients were found to have normal ECGs despite subsequent echocardiographic findings of LVEF < 50%. In the LVEF ≥ 50%

group, the cardiologist found 217 patients (58.4%) with abnormal ECG findings. See **Table 3** for estimated sensitivity, specificity, PPV, NPV, LR+ and LR–.

TABLE 3 Estimated sensitivity, specificity, predictive values and likelihood ratio for the electrocardiogram in the diagnosis of heart failure with left ventricle ejection fraction < 50%.

Evaluation of ECG	Characteristics	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	LR+	LR–
Cardiologist	LVEF < 50% + abnormal ECG	94.0 (80.0-99.3)	41.4 (36.3-47.0)	12.5 (11.2-14.0)	98.7 (95.2-100)	1.6	0.15
Automated	LVEF < 50% + abnormal ECG	97.0 (84.2-100)	40.5 (35.5-45.7)	12.7 (11.6-13.9)	99.3 (95.6-100)	1.6	0.07

CI = confidence interval; ECG = electrocardiogram; LR+ = positive likelihood ratio; LR– = negative likelihood ratio; LVEF = left ventricle ejection fraction; NPV = negative predictive value; PPV = positive predictive value.

The automated electrocardiogram interpretation

According to the automated interpretation, 32 patients (97%) with LVEF < 50% presented with abnormal ECGs. Thus, one patient presented with a normal ECG, despite LVEF < 50%. For the LVEF ≥ 50% group, the automated interpretation found 220 patients (59.5%) with abnormal ECG findings.

Sensitivity was 97.0%, specificity 40.5%, PPV 12.7%, NPV 99.3%, LR+ 1.6 and LR– 0.07. See Table 3 for a comparison with the ECG as interpreted by the cardiologist.

DISCUSSION

The present study shows that a normal ECG has a high diagnostic NPV of 98.7% for excluding heart failure with reduced LVEF. The normal ECG seems reliable and safe in its ability to identify patients with LVEF ≥ 50% and may be used as a gatekeeping tool for prioritising primary care patients referred on suspicion of heart failure.

Concerning ECG interpretation, the automated interpretation seems equal to the cardiologist's interpretation with a high sensitivity (97.0%) and NPV (99.3%) and a low specificity (40.5%). Therefore, the automatic interpretation may assist the physician in clinical decision-making in relation to suspicion of heart failure with reduced LVEF.

Predicting heart failure with LVEF < 50% through established risk factors, we estimated an AUC of 0.72. Adding the ECG to the model significantly increased the AUC to 0.79, which emphasises the importance of ECG when assessing risk of heart failure.

Comparing findings with previous studies

Previous studies have assessed the power of the ECG as a diagnostic tool for heart failure, and these findings illustrate similar trends with a high sensitivity (73-94%) and a low specificity (20-61%) [7, 11-16]. Supporting our findings, one study [14] found that NPV was so high that it was possible to effectively exclude heart failure in a cohort from primary care on the basis of ECG. Another study [7] evaluated specific ECG findings and also found the ECG in itself to have a high sensitivity and NPV for heart failure.

Assessing our multivariable logistic regression model, a recent study [8] examining patients with type II diabetes for risk of heart failure found an increase in AUC if the ECG was added to traditional risk factors for heart failure, supporting our findings of an increased AUC.

For the automatic interpretation, it was not possible to identify studies assessing the usefulness of this interpretation without utilising deep learning in finding patients with heart failure. To the best of our knowledge, the present study is the first to compare the automatic interpretation and the cardiologist's interpretation of ECG.

Strengths and limitations

We identified 33 patients with LVEF < 50% in a population of 403 patients referred for echocardiography from primary care on suspicion of heart failure. The prevalence of heart failure with LVEF < 50% was 8.1% in the study population. Comparing our population with a populations of the same mean age, we found a similar prevalence of heart failure (7.5-7.6%) [1, 11]. Thus, our study population does not differ from populations investigated in the past with respect to age, prevalence of ECG changes or when assessing comorbidities [7, 11, 17, 18]. This highlights the significance of exploring novel screening methods for heart failure. One potential avenue is the use of ECG as the selection of a random sample of patients similar to our cohort would yield equivalent prevalence rates.

Regarding ECG, it should be noted that the same model ECG machine was not used to examine patients in all primary care clinics. For patients who were unable to have their ECG performed in primary care, all had their ECG made with a single model of ECG machine used at the hospital.

We would also like to address that current standards of measuring LVEF are only estimates of LVEF as they are based on echocardiographic estimation [9, 10]. This source of error could have been eliminated by 3D measurement of LVEF. Furthermore, in the planning of our study, we did not make a standardised echocardiography protocol specifying which measurements were required. Thus, we did not explore whether structural abnormalities or diastolic dysfunction may explain the symptoms of patients in the group with preserved LVEF (LVEF ≥ 50%). NT-pro-BNP could also have excluded heart failure if the patient did not have elevated levels of NT-pro-BNP.

Lastly, a layer of inter-observer variability may exist as the ECG assessments were handled by five cardiologists. Inter-observer variability might also be present in the performance of echocardiography. A previous systematic review [19] evaluated multiple studies of the Simpson biplane method for LVEF estimation and found inter-observer variation ranging from ± 15.4% to ± 18% and an intra-class correlation coefficient (ICC) of 0.79-0.94. Furthermore, intra-observer variation ranged from ± 3.95% to ± 12% and ICC from 0.92 to 0.97, suggesting reduced variability when a single investigator performs echocardiography. This study also suggested using 3D LVEF estimation as this seemed to reduce inter- and intra-observer variation alike [19].

Another study compared formal quantitative LVEF estimation methods, including the Simpson biplane method, with the visually estimated LVEF, the so-called "eyeballing" method, and found no statistically significant difference between formal methods and visual estimation [20].

CONCLUSION

The ECG is a satisfactory screening tool when it comes to ruling out heart failure with LVEF <50% and may be a gatekeeping tool in patients referred to the cardiac outpatient clinic on suspicion of heart failure. Thus, an ECG may be used to prioritise between patients at referral, and it seems reasonable and safe to examine patients with an abnormal ECG before patients with a normal ECG.

To correctly identify patients with LVEF < 50% by ECG, the cardiologist and the automated interpretation seem equal. Therefore, the automated interpretation may assist both the physician in a busy clinic and the physician without experience in interpreting ECGs. This study thus provides the physician with an extra screening tool to find the relevant patients once a suspicion of heart failure has been raised.

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Conflicts of interest Potential conflicts of interest have been declared. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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