# Integrating AI-ECG and point-of-care cardiac ultrasound for screening structural heart disease: A proof-of-concept study

**Francisco B. Alexandrino, MD**[a,#], **Reid Schlesinger, MD**[b,#], **Jared Bird, MD**[a], **Eunjung Lee, PhD**[a], **Abhishek J. Deshmukh, MBBS**[a], **Vuyisile T. Nkomo, MD, MPH**[a], **Jae K. Oh**[a], **Peter A. Noseworthy, MD**[a], **Patricia A. Pellikka, MD**[a], **Zachi Attia, PhD**[a], **Francisco Lopez-Jimenez, MD**[a], **Paul A. Friedman**[a], **Garvan C. Kane, MD, PhD**[a], **Sorin V. Pislaru, MD, PhD**[a], **and Gal Tsaban, MD, PhD**[a]

## ABSTRACT

**Background** Early structural heart disease (SHD) detection is crucial for improving prognostic outcomes, but widely accessible screening methods are lacking. The advent of artificial intelligence-enabled electrocardiograms (AI-ECG) and point-of-care cardiac-ultrasonography (POCCUS) offers promising new approaches for patient screening. We explored the feasibility and potential of integrating these innovative technologies into a practical SHD screening framework.

**Methods** Outpatients undergoing ECG at the Mayo Clinic ECG laboratory between November 2023 and February 2024 were pragmatically offered POCCUS, performed by novice operators and reviewed by expert echocardiographers. AI-ECG and POCCUS findings were integrated to assess SHD, including reduced left ventricular systolic function (ejection-fraction<50%), aortic stenosis, and increased left ventricular wall thickness suggestive of cardiac amyloidosis or hypertrophic cardiomyopathy. Operators were blinded to patients' comorbidities and formal echocardiogram results.

**Results** Of 486 patients (median-age 64 years; 49% women), 286 had available formal echocardiography, with 17.5% having SHD. AI-ECG had a 32% positive predictive value (PPV) and a 94% negative predictive value (NPV) to detect any SHD. Adding POCCUS increased the overall PPV to 64% with an NPV of 93%, with an increase in diagnostic accuracy from 67% to 88%. Notably, 89.5% (17/19) of the "false positives" by AI-ECG + POCCUS had less-than-moderate-SHD. Applying the AI-ECG + POCCUS screening workflow on the entire cohort resulted in a number-needed-to-screen of 8 to identify 1 patient requiring formal echocardiography.

**Conclusions** The integration of AI-ECG and POCCUS holds promise as a potentially effective screening method for SHD, facilitating improved patient selection for formal echocardiography. (Am Heart J 2026;294:107337.)

## Background

Structural heart diseases (SHD), including left ventricular systolic dysfunction (LVSD), aortic stenosis (AS), cardiac amyloidosis (CA), and hypertrophic cardiomyopathy (HCM), pose significant risks of heart failure and mortality, often evading detection until advanced stages or fatal outcomes manifest.[1-4] Advances in medicine have introduced treatments that alter the course of SHD, emphasizing the critical need for early diagnosis and proactive clinical and imaging follow-up to identify candidates for beneficial interventions.[5,6] Thus, standardized, easy-to-implement, and cost-effective screening measures for SHD are needed.

Artificial intelligence-enabled electrocardiogram (AI-ECG) algorithms have proven effective in detecting SHD in the general population, boasting high accuracy with areas under the curve ranging from 0.85 to 0.96 and an impressive negative predictive value (NPV) nearing 99%.[7-10] However, their low positive predictive value (PPV; 11%-34%) limits their utility as standalone screening tools, potentially leading to frequent unnecessary and costly transthoracic echocardiograms (TTEs). This issue is compounded by the overuse of expensive diagnostics and the constrained capacity of echocardiography laboratories to manage screening TTEs for patients flagged by

---

*From the [a]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, [b]Department of Internal Medicine, Mayo Clinic, Rochester, MN*

*[#]Equal contribution*

*Submitted October 21, 2025; accepted December 29, 2025*

*Reprint requests: Gal Tsaban, MD, PhD, Department of Cardiovascular Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905.*

*E-mail address: tsaban.gal@mayo.edu.*

*0002-8703*

*https://doi.org/10.1016/j.ahj.2025.107337*

positive AI-ECG results, necessitating an innovative approach.

Recent advances in medical technology have facilitated the development of compact, high-quality portable ultrasound devices. The emergence of small, handheld ultrasound machines capable of acquiring high-resolution 2D echocardiography images has transformed point-of-care assessment. Portable, cost-effective, and increasingly deployed across various clinical settings, point-of-care cardiac-ultrasonography (POCCUS) enables straightforward qualitative evaluation of cardiac function and structure through simple 2-dimensional imaging.[11]

Considering these developments, integrating POCCUS screening with current AI-ECG models presents a promising and underexplored opportunity to identify patients with SHD. Outpatient ECG labs, bustling with activity, are ideal settings where AI-driven ECG analyses are routinely conducted. This environment offers a practical, real-world context for combining ECG and POCCUS for screening purposes. The current study aims to assess the feasibility and predictive implications of integrating AI-ECG and POCCUS screening for SHD within a diverse outpatient population.

## Methods

### Study design

We conducted a proof-of-concept quality-of-care project at the ECG Laboratory of Mayo Clinic in Rochester, Minnesota, USA. This analysis aimed to assess the feasibility and diagnostic yield of a unique screening framework employing a 2-layer screening process integrating AI-ECG and POCCUS classifications.

To explore the feasibility of integrating POCCUS scanning into the ECG lab, the Mayo Clinic Echocardiography and ECG laboratories initiated an in-house real-world project (Supplementary Figure 1). Novice internal medicine residents' operators with no echocardiography experience (FBA, RS), trained in-house to acquire POCCUS imaging, were present in the ECG lab between November 1, 2023, and February 28, 2024. In total, handheld POCCUS was available on 27 days across the study period, corresponding to approximately 6.5 days per month. Since the study was not designed to maximize patient recruitment, operators were instructed to obtain verbal patient consent before initiating scans. Patient enrollment ranged from 9 to 35 patients per scan day. A target enrollment of 500 patients was predefined to ensure adequate feasibility and precision of proportion estimates, and recruitment stopped once this goal was reached. Adult patients (≥18 years) undergoing ambulatory ECG on days when POCCUS operators were available were offered POCCUS after their ECG, regardless of AI-ECG results, using a pragmatic convenience sampling approach. Interested patients were briefed by the ECG technician and the POCCUS operator and provided oral consent before scanning. In summary, inclusion required 3 criteria: (1) patient availability and willingness to participate, (2) verbal consent, and (3) presence of a trained novice operator to perform the scan. POCCUS studies were uploaded and stored on an encrypted online patient-care platform after acquisition and subsequently reviewed by a trained cardiologist with 8 years of experience (GT) to assess the likelihood of structural heart disease (SHD). Any abnormal findings not previously documented were communicated to the patient's primary provider. Patients with poor-quality POCCUS images were excluded. No further exclusion criteria were applied. The Mayo clinic institutional review board approved the project.

### AI-ECG

The Mayo Clinic ECG Laboratory performs an average of 250 ECGs daily. All ECGs are acquired by a technician in the supine position at a sampling rate of 500 Hz using a GE-Marquette ECG machine (Marquette, WI). The data are stored using the MUSE data management system (GE Healthcare, Chicago, IL) for review and immediate clinical interpretation. AI-ECG data, generated through validated algorithms, becomes accessible upon confirmation of the ECG clinical interpretation report. This data provides probabilities and categorizations for aortic stenosis, decreased left ventricular ejection fraction (LVEF), HCM, and CA using specific thresholds: 40.6%, 25.6%, 11%, and 48.5%, respectively.[7-9,12] These data are available for healthcare providers to review on a separate platform linked to the patient's electronic medical record. Of note, the cut-off for LVSD in the AI-ECG algorithm used in the current study was validated for detecting LVEF <35%. However, its application in the general population also demonstrated an AUC of 0.880 for identifying LVEF <50%.[13]

### POCCUS

Novice POCCUS operators, first-year postgraduate physicians with no prior cardiac ultrasound training, participated in a structured, 2-day training program led by an expert advanced cardiac sonographer. The 2-day POCCUS training program followed a standardized curriculum designed for novice physician trainees. Day 1 included self-directed, video-based modules on cardiac anatomy, ultrasound principles, and handheld device operation. Day 2 consisted of hands-on scanning sessions supervised by an expert cardiac sonographer, during which trainees practiced acquiring parasternal, apical, and subcostal views on healthy volunteers (Supplementary Table 1). While implemented with physician trainees, this model is intended to be scalable to non-physician personnel for broader adoption (Supplementary Table 1). POCCUS was conducted using a portable Lumify S4-1 handheld ultrasound device (Phillips Healthcare). Lumify S4-1, as most hand-held devices, doesn't have quantitative Doppler. Although patients were imaged in the supine position due to the ECG lab setting, operators were instructed to request a left lateral decubitus position when feasible, particularly to optimize parasternal and apical views. POCCUS was obtained regardless of the AI-ECG result. Clips were acquired in 10-second loops from parasternal (long and short axes), apical (4 chambers), and subcostal acoustic windows. The studies were saved with patient-identifier numbers, uploaded, and stored on a dedicated, secured POCCUS review platform (Qpath, Telexy, Canada). Subsequently, a trained cardiologist reviewed the studies to assess the likely presence of SHD. Interpretation relied on visual assessment of the 2-dimensional POCCUS studies. Suspected LVSD was defined as LVEF less than 50%, possible AS was defined by significant calcification or restricted excursion of the aortic valve leaflets, and increased left ventricular wall thickness (ILVWT) was determined by offline assessment of LV walls. Patients with ILVWT were grouped under a single category, without formal distinction between HCM and CA; however, features such as asymmetrical septal thickening or cavity obliteration suggested HCM, whereas concentric thickening, myocardial speckling, and pericardial effusion raised suspicion for CA. The physician operators conducting POCCUS and the interpreting cardiologists were blinded to patients' medical records and AI-ECG results.

## Image interpretation and quality assessment

A 4-point scoring system was used to evaluate the image quality of 2D POCCUS. This scale was developed specifically for the purposes of this feasibility study, with criteria based on the visibility of key cardiac structures, appropriate optimization of imaging parameters (including orientation, gain, depth, and focus), and the overall interpretability of each scan. While novel to this study, the scoring system is conceptually similar to image quality grading frameworks used in standard transthoracic echocardiography and aligns with protocols previously described in the literature.[14]

Although most patients were imaged in the supine position due to the spatial constraints of the ECG laboratory, novice operators were instructed to request a left lateral decubitus position whenever feasible, particularly to optimize parasternal and apical views. While apical windows were occasionally limited, parasternal views frequently provided sufficient visualization of the target anatomy to allow diagnostic screening for structural heart disease. This highlights the feasibility of handheld POCCUS for use in pragmatic screening settings. All POCCUS images were interpreted by a single cardiologist with expertise in echocardiography. To assess intraobserver reproducibility, a subset of 40 patient scans was randomly selected from the study cohort for each of the 3 diagnostic targets: (1) low EF, (2) AS, and (3) increased LV wall thickness suggestive of hypertrophic cardiomyopathy or cardiac amyloidosis. Care was taken to ensure that each subset included a balanced mix of positive and negative findings to represent the full spectrum of image interpretations encountered in the study. Each scan was re-evaluated in a blinded fashion several months after the initial interpretation by the same cardiologist with echocardiographic expertise. Diagnostic findings were recorded as binary outcomes (0 = negative, 1 = positive), focusing on 3 predefined screening targets: LVSD, AS, and increased LV wall thickness suggestive of HCM or cardiac amyloidosis. Intraobserver agreement was assessed using Cohen's $\kappa$ coefficient, which accounts for chance agreement.

The scoring system for POCCUS image quality is summarized in Supplementary Table 2, ranging from 1 (non-diagnostic) to 4 (good) based on visualization of key cardiac structures and overall interpretability.

## Data collection

All baseline characteristics, encompassing demographics, medical comorbidities, cardiovascular history, and results of formal echocardiography studies, were extracted and validated through meticulous manual chart review. After enrollment and based on the availability of a formal echocardiogram, gold-standard for diagnostic comparison, in the electronic medical record, patients were retrospectively stratified.

Valvular heart disease was categorized as any degree (mild, moderate, or severe) of stenosis or regurgitation affecting any of the 4 cardiac valves. For the purposes of diagnostic performance analysis, only patients with AS meeting criteria for AI-ECG detection were included in the SHD-positive group, while other valvular abnormalities were excluded as they fall outside the scope of current AI-ECG algorithms.

## Statistical analysis

The main aim of the current analysis was to examine the feasibility and diagnostic yield of incorporating AI-ECG and POCCUS to screen for SHD in a nonselective patient population. Since operators were blinded to the patient's medical history and diagnostic workup, the study population comprised patients with and without recently available formal TTE evaluation.

The analysis was conducted in 2 stages. The first stage focused on evaluating diagnostic performance among patients with a previously available formal TTE, which served as the reference standard. The NPV and PPV of the AI-ECG alone and of the combined AI-ECG + POCCUS approach were assessed for detecting SHD (Supplementary Table 3). These metrics were calculated both overall and by SHD subtype, including LVSD, AS, ILVWT. Patients with prior AVR were excluded from the AS analysis but included in the LVSD and ILVWT analyses, consistent with the validation cohorts for these algorithms.

Given the relatively high prevalence of cardiac amyloidosis among patients with AS and low EF, and the risk of underdiagnosing HCM in this population, we retained these patients in the screening workflow for non-AS outcomes. Additionally, no data currently supports that post-surgical changes impair AI-ECG precision, highlighting the added value of the POCCUS layer in these cases. The second stage involved a screening simulation conducted in the full study cohort, regardless of TTE availability. A 2-step model was applied: first, AI-ECG was used to screen all patients. Those flagged as "positive" were subsequently further classified using POCCUS. The goal was to simulate a stepwise screening algorithm that leverages the high NPV of AI-ECG while accounting for the potential logistical complexity and cost associated with widespread POCCUS use. Patients classified as "positive" by both methods were considered likely to have SHD and were identified as candidates for formal TTE referral. The NNS was calculated as the number of patients who would need to undergo the AI-ECG plus POCCUS workflow for 1 patient to be triaged to formal TTE, reflecting eligibility for referral rather than confirmed disease and depending on the characteristics of the screened population and disease prevalence.

Data are presented as means and standard deviations or median and interquartile range (IQR) for continuous variables, per the variable's distribution, and as frequencies and percentages for categorical variables. Comparisons between groups were performed using chi-square tests for categorical variables and independent *t*-tests or Mann–Whitney U test for continuous variables, according to the variable's distribution.

A 2-sided *P*-value of less than 0.05 was considered statistically significant for all analyses. Statistical analysis was performed using the JMP software version 17.0.0.

## Results

During the days of available POCCUS imaging in the ECG lab, an average of 250 ± 32 ECGs were performed in the ECG lab every day. A daily average of 25 (9-37) POCCUS studies were performed, corresponding to 10% to 15% of all daily ECGs. The average duration of the POCCUS studies was 6 ± 2 minute from when the ECG was done until the POCCUS operator left the room.

A total of 500 patients were included in the study. A total of 14 patients were excluded because of unavailable POCCUS studies: eleven due to upload and storage failures and 3 due to uninterpretable imaging. This resulted in a final study population of 486 patients, 286 of which with a previous formal echocardiogram (Figure 1). One-hundred and twenty-one (42%) of TTEs were done on the same day as the POCCUS and only 39 (13%) were done $\geq$ 1 year before and the remaining 45% were done within this intermediate time frame. Agreement was excellent across all diagnostic categories, with $\kappa$ values of 1.00 for LVSD, 0.95 for AS, and 0.92 for increased LV wall thickness. These results demonstrate high reproducibility and support the reliability of focused POCCUS interpretation in a handheld screening context under real-world conditions.

### Baseline characteristics

Patients had a median age of 64 years (IQR: 53.2-71.4) and 49% were female. Baseline characteristics of the study population across formal echocardiographic assessment availability status are provided in Table 1. Patients with available TTEs had higher rates of hypertension, diabetes, atrial fibrillation, and clinical heart failure but lower rates of coronary artery disease and chronic kidney disease. A total of 28 patients had previous aortic valve replacement, all of whom had TTE evaluation. LVSD, HCM, and CA were diagnosed in 10%, 2%, and 2%, respectively. Of the patients with available formal TTE assessment, 50 (17.5%) had documented confirmed SHD. Among the 51 patients identified with valvular heart disease in Table 1, several had conditions not currently detectable by AI-ECG algorithms, including MR, MS, TR, AR, or less-than-severe AS. These patients were not included in the SHD-positive group used for PPV/NPV calculations, which focused exclusively on AI-detectable conditions: LVSD, AS, HCM, and CA.

### AI-ECG SHD classification

The median AI-ECG probability averages were 11.2% (IQR: 2.5-35.5) for AS, 0.96% (IQR: 0.41-3.1) for LVSD, 0.08% (IQR: 0.01-0.58) for (HCM), and 11.0% (IQR: 3.4-29.0) for CA. Most participants (67%) were negative for SHD by AI-ECG. Among those identified as "positive" for SHD, 21%, 8%, 3%, and 1% were positive for 1, 2, 3, or 4 SHDs, respectively (Table 2).

Screening performance parameters using AI-ECG only are provided in Figure 2. Among the 286 patients with formal echocardiographic assessment, the NPV and PPV to detect any SHD by AI-ECG were 94% and 32%, respectively. The respective NPVs and PPVs for screening individual SHDs were 97% and 49% for LVSD, 89% and 38% for AS, and 99% and 15% for ILVWT (consistent with CA or HCM).

### POCCUS SHD classification

The predictive correlates utilizing the stepwise screening approach of AI-ECG followed by POCCUS are shown in Figure 2. Incorporating POCCUS as a second layer of screening for SHD in patients with formal TTE evaluation resulted in an increase in PPV to 64% and a slightly insignificant decrease in NPV to 93% to detect the existence of any SHD. The increase in PPV was consistent across all individual SHDs and was more prominent in less prevalent SHDs (AS). The NPVs were either un-

**Figure 1.** Study's flowchart.

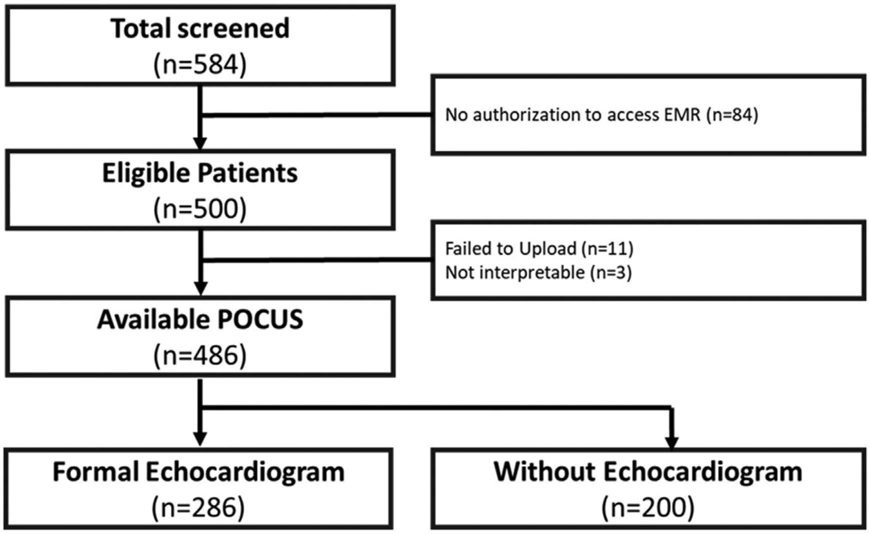


**Table 1.** Baseline characteristics of the study population across formal TTE status.

| | Without TTE (*n* = 200) | With TTE (*n* = 286) | Total (*n* = 486) | *P*-value |
|---|---|---|---|---|
| Age (median, IQR) | 61.0 (49.7, 68.7) | 56.0 (57.0, 73.9) | 64.0 (53.2, 72) 71.4) | <.01 |
| Female (%) | 112 (56) | 127 (44) | 239 (49) | .01 |
| Hypertension (%) | 50 (25) | 106 (37) | 156 (32) | <.01 |
| Diabetes (%) | 17 (9) | 43 (15) | 60 (12) | .02 |
| Chronic Kidney Disease (%) | 14 (7) | 52 (18) | 66 (14) | <.01 |
| Coronary artery disease (%) | 36 (18) | 97 (34) | 133 (27) | <.01 |
| Heart failure (%) | 3 (1) | 75 (26) | 78 (16) | <.01 |
| Valvular heart disease (%) | NA | 51 (18) | 51 (10) | <.01 |
| AVR (%) | 0 (0) | 28 (10) | 28 (5) | <.01 |
| Atrial fibrillation (%) | 9 (5) | 94 (33) | 103 (21) | <.01 |
| HCM (%) | NA | 6 (2) | 6 (1) | <.01 |
| CA (%) | NA | 5 (2) | 5 (1) | <.01 |

CA, cardiac amyloidosis; HCM, hypertrophic cardiomyopathy; S/P AVR, status post aortic valve replacement; TTE, transthoracic echocardiogram.

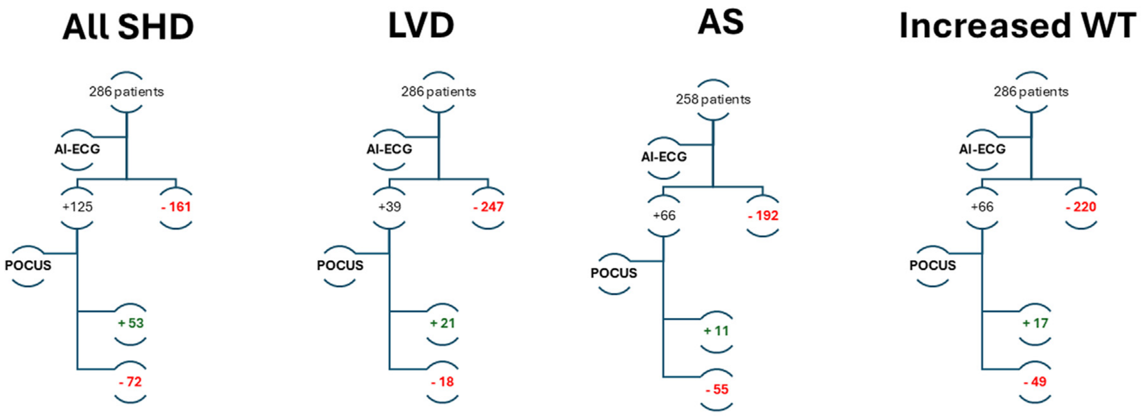
**Table 2.** AI-ECG SHD classification across the entire study population.

AI ECG probability average (%)

| Algorithm | Without TTE (*n* = 200) | With TTE (*n* = 286) | Total (*n* = 486) | *P*-value |
|---|---|---|---|---|
| AS | 6.0 (0.84-17.8) | 18.6 (0.8-17.8) | 11.2 (2.5-35.5) | <.01 |
| LVSD | 0.62 (0.28-1.38) | 1.3 (0.51-5.8) | 0.96 (0.41-3.1) | <.01 |
| HCM | 0.06 (0.01-0.25) | 0.12 (0.01-0.25) | 0.08 (0.01-0.58) | <.01 |
| CA | 7.7 (1.9-17.6) | 14.7 (4.8-17.6) | 11.0 (3.4-29.0) | <.01 |
| AI-ECG positive variables | | | | |
| 0 (%) | 163 (82) | 161 (56) | 324 (67) | <.01 |
| 1 (%) | 31 (15) | 72 (25) | 103 (21) | |
| 2 (%) | 5 (2) | 34 (12) | 39 (8) | |
| 3 (%) | 1 (1) | 16 (6) | 17 (3) | |
| 4 (%) | 0 (0) | 3 (1) | 3 (1) | |

AI-ECG, artificial intelligence-enabled electrocardiogram; AS, aortic stenosis; CA, cardiac amyloidosis; HCM, hypertrophic cardiomyopathy; LVSD, left ventricular systolic dysfunction; TTE, transthoracic echocardiogram.
Previously validated AI-ECG cutoffs are 40.6%, 25.6%, 11%, and 48.5% for AS, LVSD, HCM and CA, respectively.

**Figure 2.** Predictive value of screening using a POCCUS-integrated AI-ECG approach AS, aortic stenosis; ILVWT, increased left ventricle wall thickness; LVSD, left ventricular systolic dysfunction; SHD, structural heart disease.


All SHD

LVD

AS

Increased WT

| | AI | AI and POCUS |
|---|---|---|
| NPV (%) | 94 | 93 |
| PPV (%) | 32 | 64 |
| Sens (%) | 80 | 68 |
| Spec (%) | 64 | 92 |
| Accuracy (%) | 67 | 88 |

| | AI | AI and POCUS |
|---|---|---|
| NPV (%) | 97 | 96 |
| PPV (%) | 49 | 81 |
| Sens (%) | 61 | 55 |
| Spec (%) | 92 | 98 |
| Accuracy (%) | 89 | 94 |

| | AI | AI and POCUS |
|---|---|---|
| NPV (%) | 89 | 84 |
| PPV (%) | 38 | 64 |
| Sens (%) | 64 | 64 |
| Spec (%) | 77 | 98 |
| Accuracy (%) | 76 | 97 |

| | AI | AI and POCUS |
|---|---|---|
| NPV (%) | 99 | 99 |
| PPV (%) | 15 | 47 |
| Sens (%) | 64 | 64 |
| Spec (%) | 80 | 97 |
| Accuracy (%) | 80 | 96 |

changed or slightly, insignificantly, reduced across all examined SHDs. The respective NPVs and PPVs for screening individual SHDs were 96% and 81% for LVSD, 84% and 64% for AS, and 99% and 47% for ILVWT, consistent with CA or HCM.

Of the nineteen patients classified as "false-positives" by the integrated AI-ECG and POCCUS pathway, seventeen exhibited less than moderate structural heart disease (Graphical abstract): 8 had aortic valve sclerosis or mild aortic stenosis, 6 showed ILVWT but without HCM or CA, 2 had normal ejection fraction with regional wall motion abnormalities, and 1 had severe right ventricular failure.

### Application of a 2-layer screening method on a nonselective patient population

The application of a hypothetical screening method for SHD, first applying AI-ECG, followed by the application of POCCUS among AI-ECG “SHD-positive” patients (Supplementary Figure 2). The number needed to screen, reflecting the number of patients necessary to undergo screening to identify 1 patient suspected of SHD eligible for formal TTE screening, was also calculated. When applying the hypothetical screening workflow on the entire patient population (n = 486), the NNS to detect 1 patient with suspected SHD was 8. The NNS for individual SHDs was 22, 31, and 26 to detect 1 patient suspected to have LVSD, AS, or ILVWT consistent with CA or HCM.

## Discussion

This study, conducted among 486 pragmatically enrolled outpatients referred for clinically indicated ECG at the Mayo Clinic ECG laboratory, demonstrates the potential of AI-ECG combined with POCCUS for screening patients at risk of SHD. The study was built around a feasibility question: whether POCCUS could be used in real time and how a 2-step AI-ECG + POCCUS workflow would triage patients to formal echocardiography in an unselected outpatient population. Although this operational modeling was the main focus, more than half of the cohort had a recent TTE, which allowed us to report performance metrics for this approach for the first time. These early data indicate that incorporating POCCUS can help offset the limited positive predictive value of AI-ECG alone and support the practicality of a stepped screening strategy that keeps downstream echocardiography volume at a manageable level.

Among 286 patients who underwent formal echocardiograms, this pathway demonstrated a 93% NPV and a 64% PPV, with higher values observed for specific SHD types such as LVSD and AS. The second stage, screening simulation, used the entire study cohort, 486 patients, to model the practical application of the workflow in an unselected population, providing insight into how POCCUS can help rule out patients flagged as positive by AI-ECG and estimate the operational impact on downstream TTE referrals. The NNS was 8 to identify 1 patient requiring formal echocardiographic evaluation. Importantly, among the nineteen patients classified as "false positives," seventeen exhibited less-than-moderate or other coexisting SHD in their formal echocardiograms.

SHD is often asymptomatic or subclinical before leading to morbidity or mortality. The 4 SHD types detected by current AI-ECG models carry substantial risk, including increased mortality even in asymptomatic stages. Screening must balance disease prevalence, cost, feasibility, and patient benefit. While LVSD is more common, conditions such as AS increase with age, and rare diseases like CA and HCM pose specific challenges. Effective screening may target patients aged ≥50 years[15]; our study population (mean age 64, balanced sex distribution) represents this target group. Observed prevalence differed from prior community-based studies (e.g., EAGLE)[12] due to the outpatient hospital setting. The primary goal here was feasibility, not large-scale effectiveness; a 2-stage AI-ECG triggering POCCUS strategy is now being tested in a prospective trial (NCT06891222). This approach aims to optimize resources, focusing advanced imaging on higher-risk patients, with AI-assisted POCCUS potentially enhancing scalability.

Previous studies show AI-ECG improves LVSD detection,[12] and echocardiographic screening in asymptomatic populations reveals substantial valvular heard disease prevalence (28.2% any valvular heart disease; 2.4% moderate/severe),[13] consistent with real-world findings (2.5%).[14] However, TTE is costly, time-intensive, often low-yield in primary care, and limited by resource constraints.[16,17] Many asymptomatic community-dwelling patients are never referred until clinically evident disease develops. Given the low prevalence of SHD in the general population (6.4%-7.6%),[18,19] universal TTE screening is neither feasible nor cost-effective. AI-ECG offers a scalable first-line screening tool with high NPV, but its modest PPV limits utility as a stand-alone triage method.[10,20]

We propose a 2-step, augmented screening strategy: AI-ECG as a broad initial screen, followed by POCCUS for patients flagged as AI-ECG positive. This approach enriches the screened population, improves positive predictive value, and maintains sensitivity, providing a practical pathway for outpatient SHD detection. POCCUS, performed by minimally trained operators using 10-second loops, efficiently captures diagnostic cardiac cycles, and limiting scans to AI-ECG-positive patients enhances scalability. Although real-time triage was not feasible due to AI-ECG processing delays, future workflow integration may enable rapid bedside decision-making. Compared with conventional TTE (30-45 minutes), POCCUS requires <5 minutes per patient, supporting high-throughput implementation. Ongoing advances in AI-assisted POCCUS may further streamline interpretation, allowing automated classification from limited cardiac cycles.[21,22]

Our findings support POCCUS-augmented AI-ECG as an efficient 2-tiered screening strategy, in which POCCUS refines assessment in AI-ECG-positive patients, improving specificity and maintaining sensitivity while enabling scalable detection of SHD. POCCUS can be effectively performed by novice operators after brief training, achieving acceptable sensitivity and specificity.[23,24] In our 2-step approach, AI-ECG serves as a broad "screen-out" layer, while POCCUS refines selection among positives, improving specificity and overall diagnostic accuracy from 67% with AI-ECG alone to 88% with the combined strategy.

This study has several limitations. POCCUS, particularly when performed by less experienced operators, may yield variable image quality, a limitation accentuated by the ECG laboratory environment, which is not optimized for echocardiographic acquisition and may compromise apical views. Nevertheless, parasternal views were generally sufficient to support structural heart disease (SHD) screening. Technical constraints of the POCCUS review platform, including slow image transfer and limited measurement functionality, further underscore the need for improved technological infrastructure. Despite these limitations, interpretation by experienced echocardiographers demonstrates the feasibility of this approach and provides a foundation for future integration of POCCUS-specific AI algorithms. Although patients were pragmatically enrolled in outpatient ECG settings, the cohort may represent a higher-risk population, as reflected by the observed disease prevalence, heterogeneous ECG indications, and variable availability of formal transthoracic echocardiography. In addition, the analysis was restricted to 4 SHDs with validated AI-ECG algorithms derived from Mayo Clinic data, which may limit external generalizability. Expansion of AI-ECG models to additional conditions, including mitral regurgitation, tricuspid regurgitation, and constrictive pericarditis, could enhance the clinical utility of this workflow. Recently described AI-ECG algorithms that identify a shared SHD-related ECG phenotype may further augment screening when POCCUS image quality is inadequate, although disease-specific performance requires validation in dedicated prospective studies. Overall, this work should be interpreted as a proof-of-concept platform.

In conclusion, our study confirms the feasibility and accuracy of integrating POCCUS and AI-ECG for detecting SHD. This approach addresses current screening challenges and sets a precedent for future innovations in cardiovascular care. Looking forward, the incorporation of AI into POCCUS has the potential to revolutionize global SHD screening, offering scalable solutions comparable to recent advancements in large-scale echocardiogram analysis. Harnessing AI's potential could reduce reliance on expert cardiologist reviews, expedite diagnostic timelines, and improve patient outcomes.

## Conflict of interest

P.A.F., Z.I.A., E.L., F.L.-J., and J.K.O. have invented algorithms licensed to ANUMANA and may benefit from algorithm commercialization via Mayo Clinic. P.A.F., Z.I.A., and F.L.-J. are members of the scientific advisory board to ANUMANA. Other authors declare no competing interests.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2025.107337.

## CRediT authorship contribution statement

**Francisco B. Alexandrino:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Reid Schlesinger:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Jared Bird:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Eunjung Lee:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Abhishek J. Deshmukh:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Vuyisile T. Nkomo:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Jae K. Oh:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Peter A. Noseworthy:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Patricia A. Pellikka:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Zachi Attia:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Francisco Lopez-Jimenez:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Paul A. Friedman:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Garvan C. Kane:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Sorin V. Pislaru:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Gal Tsaban:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

## References

1. Wang TJ, Levy D, Benjamin EJ, Vasan RS. The epidemiology of "asymptomatic" left ventricular systolic dysfunction: implications for screening. Ann Intern Med 2003;138:907–16.
2. Généreux P, Stone GW, O'Gara PT, et al. Natural history, diagnostic approaches, and therapeutic strategies for patients with asymptomatic severe aortic stenosis. J Am Coll Cardiol 2016;67:2263–88.
3. Castaño A, Narotsky DL, Hamid N, et al. Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. Eur Heart J 2017;38:2879–87.
4. Maron BJ, Desai MY, Nishimura RA, et al. Diagnosis and evaluation of hypertrophic cardiomyopathy. J Am Coll Cardiol 2022;79:372–89.
5. Maurer Mathew S, Kale Parag, Fontana Marianna, et al. Patisiran treatment in patients with transthyretin cardiac amyloidosis. N Engl J Med 2023;389:1553–65.
6. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Rev Esp Cardiol Engl Ed 2022;75:524.
7. Cohen-Shelly M, Attia ZI, Friedman PA, et al. Electrocardiogram screening for aortic valve stenosis using artificial intelligence. Eur Heart J 2021;42:2885–96.
8. Grogan M, Lopez-Jimenez F, Cohen-Shelly M, et al. Artificial intelligence–enhanced electrocardiogram for the early detection of cardiac amyloidosis. Mayo Clin Proc 2021;96:2768–78.
9. Ko WY, Siontis KC, Attia ZI, et al. Detection of hypertrophic cardiomyopathy using a convolutional neural network-enabled electrocardiogram. J Am Coll Cardiol 2020;75:722–33.
10. Attia ZI, Kapa S, Lopez-Jimenez F, McKie PM, Ladewig DJ, Satam G, et al. Screening for cardiac contractile dysfunction using an artificial intelligence-enabled electrocardiogram. Nat Med 2019;25:70–4.
11. Díaz-Gómez JL, Mayo PH, Koenig SJIngelfinger JR, editor. Point-of-care ultrasonography. editor. N Engl J Med 2021;385:1593–602.
12. Yao X, Rushlow DR, Inselman JW, et al. Artificial intelligence-enabled electrocardiograms for identification of patients with low ejection fraction: a pragmatic, randomized clinical trial. Nat Med 2021;27:815–19.
13. Kashou AH, Medina-Inojosa JR, Noseworthy PA, et al. Artificial intelligence-augmented electrocardiogram detection of left ventricular systolic dysfunction in the general population. Mayo Clin Proc 2021;96:2576–86.
14. Gaspari R, Teran F, Kamilaris A, Gleeson T. Development and validation of a novel image quality rating scale for echocardiography during cardiac arrest. Resusc Plus 2021;6:100097.
15. d'Arcy JL, Coffey S, Loudon MA, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study†. Eur Heart J 2016;37:3515–22.
16. Thoenes M, Bramlage P, Zamorano P, et al. Patient screening for early detection of aortic stenosis (AS)—review of current practice and future perspectives. J Thorac Dis 2018;10:5584–94.
17. Moore M, Chen J, Mallow PJ, Rizzo JA. The direct health-care burden of valvular heart disease: evidence from US national survey data. Clin Outcomes Res CEOR 2016;8:613–27.
18. d'Arcy JL, Coffey S, Loudon MA, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. Eur Heart J 2016;37:3515–22.
19. Lindekleiv H, Løchen ML, Mathiesen EB, et al. Echocardiographic screening of the general population and long-term survival: a randomized clinical study. JAMA Intern Med 2013;173:1592–8.

20. Poterucha TJ, Jing L, Ricart RP, et al. Detecting structural heart disease from electrocardiograms using AI. Nature 2025;644:221–30.
21. Zhang J, Gajjala S, Agrawal P, et al. Fully automated echocardiogram interpretation in clinical practice. Circulation 2018;138:1623–35.
22. Hu H, Huang H, Li M, et al. A wearable cardiac ultrasound imager. Nature 2023;613:667–75.
23. Kobal SL, Trento L, Baharami S, et al. Comparison of Effectiveness of Hand-Carried Ultrasound to Bedside Cardiovascular Physical Examination. Am J Cardiol 2005;96:1002–6.
24. Martin LD, Howell EE, Ziegelstein RC, et al. Hand-carried Ultrasound Performed by Hospitalists: Does It Improve the Cardiac Physical Examination? Am J Med 2009;122:35–41.