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Clinical Research

Opportunistic Screening for Asymptomatic Left Ventricular Dysfunction With the Use of Electrocardiographic Artificial Intelligence: A Cost-Effectiveness Approach

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ABSTRACT

Background: The burden of asymptomatic left ventricular dysfunction (LVD) is greater than that of heart failure; however, a cost-effective tool for asymptomatic LVD screening has not been well validated. We aimed to prospectively validate an artificial intelligence (AI)–enabled electrocardiography (ECG) algorithm for asymptomatic LVD detection and evaluate its cost-effectiveness for opportunistic screening.

Methods: In this prospective observational study, patients undergoing ECG at outpatient clinics or health check-ups were enrolled in 2 hospitals in Taiwan. Patients were stratified into LVD (left ventricular ejection fraction $\leq$ 40%) risk groups according to a previously devel-

RÉSUMÉ

Contexte : Le fardeau de la dysfonction ventriculaire gauche (DVG) asymptomatique est plus important que celui de l'insuffisance cardiaque; cependant, un outil profitable pour le dépistage de la DVG asymptomatique n'a jamais été correctement validé. Notre objectif était de valider de manière prospective un algorithme d'électrocardiographie (ECG) activé par l'intelligence artificielle (IA) pour la détection de la DVG asymptomatique et d'évaluer son rapport coût-efficacité dans le cadre d'un dépistage opportuniste.

Méthodes : Dans cette étude observationnelle prospective, des patients subissant un ECG dans des cliniques externes ou lors de bilans

Heart failure (HF) affects more than 23 million people worldwide and has a high rate of morbidity and mortality, leading to a serious global public health problem.[1] The detection of HF mainly relies on clinical presentations such as dyspnoea on exertion, orthopnoea, and peripheral edema. However, some patients may have decreased left ventricular (LV) function before the appearance of obvious HF symptoms. This results in a prevalence of asymptomatic left ventricular dysfunction (LVD) in the general population of approximately 3%-6%, which is 3 to 4 times higher than that in clinical HF patients.[2,3] In Taiwan, the prevalence of LVD varies from 1.4% (left ventricular ejection fraction [LVEF] < 40%) and 6.1% (LVEF < 50%).[4] Patients with asymptomatic LVD have an 8.4% risk of progression to clinical HF every year, and the risk of mortality is 1.6 times higher in patients with asymptomatic LVD than in those with normal LVEF.[3,5] Early detection of asymptomatic LVD and follow-up with adequate treatment can effectively reduce the risk of incident HF and mortality.[5] B-Type natriuretic peptide (BNP) has been suggested as a cost-effective marker for asymptomatic LVD screening; however, its routine clinical use is limited by the possibility of false positives in various conditions.[6] Furthermore, echocardiography, which is an accurate assessment tool for LVD, requires specialised technical skills and is unsuitable for widespread screening.

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oped ECG algorithm. The performance of AI-ECG was used to conduct a cost-effectiveness analysis of LVD screening compared with no screening. Incremental cost-effectiveness ratio (ICER) and sensitivity analyses were used to examine the cost-effectiveness and robustness of the results.

Results: Among the 29,137 patients, the algorithm demonstrated areas under the receiver operating characteristic curves of 0.984 and 0.945 for detecting LVD within 28 days in the 2 hospital cohorts. For patients not initially scheduled for ECG, the algorithm predicted future echocardiograms (high-risk, 46.2%; medium-risk, 31.4%; low-risk, 14.6%) and LVD (high-risk, 26.2%; medium-risk, 3.4%; low-risk, 0.1%) at 12 months. Opportunistic screening with AI-ECG could result in a negative ICER of −$7,439 for patients aged 65 years, with consistent cost-savings across age groups and particularly in men. Approximately 91.5% of the cases were found to be cost-effective at the willingness-to-pay threshold of $30,000 in the probabilistic analysis.

Conclusions: The use of AI-ECG for asymptomatic LVD risk stratification is promising, and opportunistic screening in outpatient clinics has the potential to reduce costs.

de santé ont été recrutés dans 2 hôpitaux de Taïwan. Les patients ont été stratifiés en groupes de risque de DVG (fraction d'éjection ventriculaire gauche ≤ 40 %) selon un algorithme d'ECG précédemment développé. La performance de l'ECG-IA a été utilisée pour réaliser une analyse coût-efficacité du dépistage de la DVG par rapport à l'absence de dépistage. Le ratio coût-efficacité incrémental (RCEI) et des analyses de sensibilité ont été utilisés pour examiner le rapport coût-efficacité et la robustesse des résultats.

Résultats : Parmi les 29 137 patients, l'algorithme a démontré des aires sous la courbe de la fonction d'efficacité du récepteur de 0,984 et 0,945 pour détecter la DVG dans les 28 jours dans les deux cohortes hospitalières. Pour les patients chez lesquels un ECG n'avait pas été initialement planifié, l'algorithme a prédit de futurs échocardiogrammes (haut risque, 46,2 %; risque moyen, 31,4 %; faible risque, 14,6 %) et une DVG (haut risque, 26,2 %; risque moyen, 3,4 %; faible risque, 0,1 %) à 12 mois. Un dépistage opportun avec l'ECG-IA pourrait se traduire par un RCEI négatif de -7 439 $ pour les patients âgés de 65 ans, avec des économies de coûts constantes à travers les groupes d'âge et particulièrement chez les hommes. L'analyse probabiliste a montré qu'environ 91,5 % des cas étaient financièrement avantageux au seuil de consentement à payer de 30 000 $.

Conclusions : L'utilisation de l'ECG-IA pour la stratification du risque de DVG asymptomatique est prometteuse, et un dépistage opportun dans les cliniques externes a le potentiel de réduire les coûts.

Therefore, a precise and accessible screening test is required to identify individuals at risk of asymptomatic LVD.

Deep learning techniques, an extensive field of artificial intelligence (AI), have been used to identify cardiovascular diseases with the use of electrocardiograms (ECGs) with cardiologist-level precision.[7] Studies have shown that deep learning algorithms can identify LVD with area under the receiver operating characteristic curve (AUC) values exceeding 0.90.[8,9] Screening for asymptomatic LVD with the use of an AI-enabled ECG is promising. A study conducted by Tseng et al. in the United States found that screening for asymptomatic LVD using AI-ECG at ages 55 and 65 was cost-effective, but not at age 75, at a willingness-to-pay (WTP)[10] threshold of $50,000.[11] Because of advanced age, the limited improvement in effectiveness resulting from screening and subsequent treatment leads to a higher incremental cost-effectiveness ratio (ICER) at age 75 years compared with age of 65 years. However, the cost of screening, subsequent examinations, and treatment varies greatly owing to differences in economic and health insurance systems between regions, which play a crucial role in determining cost-effectiveness.

In the present study, we aimed to validate the performance of AI-enabled ECG in detecting asymptomatic LVD at outpatient clinics in a prospective cohort. Furthermore, we conducted an economic evaluation to assess the cost-effectiveness of screening for asymptomatic LVD using AI-enabled ECG compared with no screening under a social insurance system.

Methods

Study design and participants

In this prospective observational study, patients who underwent an ECG examination at either the Tri-Service General Hospital (TSGH), a tertiary centre hospital, or the Tingzhou branch of TSGH, a district hospital in Taiwan, were recruited from March 2020 to February 2022. Patients who were 18 years of age or older and had undergone ECG in outpatient departments or during health check-ups were eligible to participate in the screening program. Patients who underwent ECG examinations in the emergency department or during hospitalisation were excluded to avoid the inclusion of patients with obvious heart failure. Patients with a history of heart failure or previous echocardiography were also excluded. The recruited patients might subsequently undergo transthoracic echocardiography arranged by clinicians owing to various indications, such as breathlessness, peripheral edema, chest pain, arrhythmia, or suspected valvular heart disease. The timing and results of transthoracic echocardiography of the recruited patients after the index ECGs were analysed. The study was reviewed and approved by the Institutional Ethics Committee of TSGH (C202105049).

Procedures

The use of an AI-based alarm system (AI-S) is described in this study. AI-S is designed to predict the LVEF automatically by analysing ECGs uploaded in real time. The system uses a convolutional neural network trained on 58,431 independent pairings of 12-lead ECGs and echocardiograms from the TSGH.[8] The training process was published in our previous work[8] and is described in the Supplemental Appendix S1. AI-S automatically calculates LVEF, with LVEF ≤ 40% defined as LVD. AI-S uses the maximum Youden index of AUC to establish a medium-risk LVD cutoff value and the area under the precision-recall curve (PRAUC) to establish a high-risk LVD cutoff value.[12] Every ECG was given an AI-predicted LVEF value, which was stored in electronic medical records.

When AI-S detected LVD, a warning message was immediately sent to the frontline physician in charge of the patient and the on-duty cardiologist. A notification appeared on the recipients' smartphone message systems to prompt attention during the shift. The short message was triggered only once for the earliest triggering rule and was not triggered by negative samples after multiple background calculations by AI-S. The study cohort was then categorised based on the risk of LVD predicted by AI-S, and physicians determined whether the patient required a cardiac ultrasound examination.

Study outcomes

The primary analysis aimed to evaluate the performance of AI-S for LVD detection with the use of the F-measure, precision, and recall, and the secondary analysis assessed the risk of future adverse events (such as all-cause mortality, hospitalisation, and emergency department visits) in patients with and without echocardiography. In addition, cardiovascular events, including HF, atrial fibrillation, coronary artery disease, stroke, and acute myocardial infarction, were calculated.

Cost-effectiveness analysis and assumptions

To evaluate the cost-effectiveness of AI-enabled ECG (AI-ECG) screening for asymptomatic LVD compared with no screening, we used a decision-analytic model incorporating Markov processes to simulate a cohort of 65-year-old patients followed over the rest of their projected remaining lifetime horizon. Owing to disease prevalence and health check-up policies in Taiwan, we focused our analysis on individuals aged 65 as the base-case scenario. The structure of the cost-effectiveness analysis used in this study was adopted from the literature.[11] The health care payer's perspective was chosen. The decision-analytic model consists of a decision tree and a Markov model, taking into consideration the prevalence of asymptomatic LVD, AI-ECG screening performance, costs, and outcomes related to early intervention. This includes the associated costs and effects of LVD and HF on long-term mortality and quality of life. The short-term decision tree model is illustrated in the left part of Figure 1. Positive AI screening would lead to transthoracic echocardiography to confirm true-positive cases or rule out false-positive cases of asymptomatic LVD. After the confirmation of LVD with echocardiography, a thallium myocardial perfusion scan was conducted as a post-confirmatory test to evaluate the presence of coronary artery disease. The hypothetical cohort entered the Markov model in one of 3 health states after screening: 1) treated with asymptomatic LVD if positively screened using AI algorithm and TTE (true positive); 2) untreated with asymptomatic LVD if AI algorithm failed to detect existing condition (false negative); or 3) untreated without asymptomatic LVD if the condition was absent.

As shown in the right side of Figure 1, those treated and untreated for asymptomatic LVD could progress to symptomatic heart failure, leading all individuals to be treated upon disease advancement. In addition, transitions to a dead state can occur annually from any of the predefined health conditions, following specified transition probabilities.

Health outcomes, costs and discounting

Table 1 summarises estimated values of the AI-ECG performance, health outcomes, costs, utilities, and other factors in the model. The AI-ECG performance in detecting medium- and high-risk groups in the internal validation cohort was applied to the model. The sensitivity of AI-ECG for detecting medium risk of asymptomatic LVD was 0.926 (standard error [SE] 0.042), with a specificity of 0.927 (SE 0.003). The sensitivity and specificity for the detection of high-risk patients were 0.630 (SE 0.154) and 0.987 (SE 0.002), respectively. In this analysis, the prevalence of asymptomatic LVD was set at 1.6% among the 65-year-old cohort in Taiwan, according to the published literature.[13] Individuals were simulated to receive treatment for asymptomatic LVD using a combination of angiotensin-converting enzyme inhibitors (ACEis) and beta-blockers. Annual transition probabilities to symptomatic HF from treated and untreated patients and their utility scores were built mainly on data used in previous studies and their calculations.[11] The transition of patients without LVD on initial screening to death accounted for the age- and sex-specific survival of general population, according to Taiwan life tables.[14]

The cost of the AI-ECG was assumed to be the same as that of an electrocardiogram (US$4.96) in the base case and increased to 5 times higher in the sensitivity analysis, because it is still unclear how to set the price of AI-ECG. The costs of health resources were calculated based on Taiwan National Health Insurance, as presented in Table 1. Cost and effectiveness were both discounted at 1.5%. Discounting accounts for time preference, with higher costs being valued or effectiveness gains being realized now rather than later.

Analytical methods

One-way deterministic sensitivity analyses were performed to evaluate the robustness of the model with respect to the starting ages of cohort, costs of AI-ECG screening, diagnosis, outpatient attendance, hospitalisation, treatment, the performance of AI-ECG, and discounting rates. To better assess the covariate uncertainty, a probabilistic sensitivity analysis was conducted. Probability distributions were assigned to each of the input variables: the estimated mean values, estimated SEs, and types of distribution for each variable. Probabilities and utilities were modelled with the use of beta distributions, because these take on values between 0 and 1. In contrast, costs were modelled as gamma distributions, which are nonnegative right-tailed distributions that are well suited to modelling costs. Point estimates for ICER were calculated with a Monte Carlo simulation of 5000 iterations of parameters from their estimated probability distributions. The model was constructed and analysed with the use of TreeAge Pro version 2022. Costs were converted to U.S. dollars according to the currency rate obtained from the Bank of Taiwan on January 16, 2023. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist and Canadian Agency for Drugs and Technologies in Health (CADTH) recommendations were used to serve as evidence of our adherence to the reporting elements outlined in the CHEERS guidelines[15] and to ensure the generalisability to Canadian standard (Supplemental Tables S1 and S2).

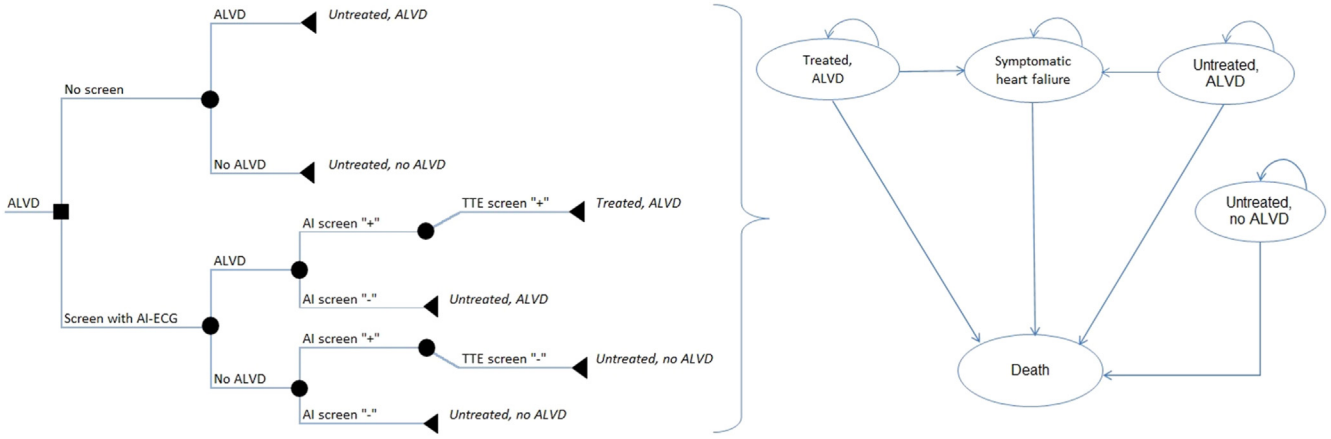


Figure 1. The structure of the decision-analytic model. The first part (left) follows a decision tree that represents the screening outcome. The second part (right) consists of a Markov structure where patients' costs and effects are simulated for the analyzed horizon. The model was adopted from Tseng et al.[11] AI, artificial intelligence; ALVD, asymptomatic left ventricular dysfunction; TTE, transthoracic echocardiography.

Statistical analysis

Patient characteristics are presented as means with standard deviations, numbers of patients, or percentages, as appropriate. Comparisons between groups were made using either the Student *t* test or the chi-square test, depending on the type of data being analysed. Cox proportional hazard models adjusted for sex and age were used, presenting standardised hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs). A normality distribution test was conducted using the "nortest" package. Statistical analysis was carried out using R software version 3.4.4, and a significance level of $P < 0.05$ was used throughout the analysis.

Results

AI-S prediction and future echocardiography

In this study, 29,137 patients were recruited and categorised based on their risk levels for LVD predicted by AI-S. Of these patients, 244 (0.84%) were classified as high-risk, 974 (3.34%) as medium-risk, and 27,919 (95.82%) as low-risk. The number of echocardiographic examinations in each risk group was calculated, as shown in Figure 2. The patients recruited in the academic centre were considered as the internal validation cohort, and those in the district hospital were considered as the external validation cohort. The high-risk group had a higher proportion of men, older age, and comorbidities than did the low- and medium-risk groups, as presented in Supplemental Table S3. Moreover, in the internal validation set, the high- and medium-risk groups had a higher proportion of patients who underwent echocardiography within 28 days (42.7% and 40.4%, respectively) than the low-risk group (24.5%) (Fig. 3). The adjusted HRs for undergoing echocardiography within 28 days were 1.93 (95% CI 1.54-2.41) and 1.77 (95% CI 1.57-2.00) for the high-and medium-risk groups, respectively. The internal and external validation sets showed similar results. Furthermore, among patients who were not initially scheduled to undergo echocardiography within 28 days, the high- and medium-risk groups underwent more echocardiograms (high-risk, 46.2%; medium-risk, 31.4%) within 12 months than the low-risk group (low-risk, 14.6%) (Fig. 3).

The performance of AI-S for LVD detection

In the medium-risk group, AI-S was able to predict LVEF $\leq$ 40% by 12-lead ECG with an AUC of 0.984, a sensitivity of 92.6%, a specificity of 93.8%, a positive predictive value (PPV) of 6.9%, and a negative predictive value of 100% in the internal validation cohort. In the high-risk group, AI-S achieved an F-score of 0.321, sensitivity of 63.0%, specificity of 98.9%, and PPV of 21.5% for identifying LVD. AI-S also demonstrated robust performance, with an AUC of 0.945 in the external validation cohort, as shown in Figure 4. In addition, the proportion of patients being diagnosed with LVEF $\leq$ 40% within 12 months was significantly higher in the high-risk (26.2% and 17.9%) and medium-risk (3.4% and 2.5%) groups compared to the low-risk group (0.1% and 0.2%), in the internal and external validation sets, respectively. The adjusted HR for the diagnosis of LVD in the high-risk group was 65,397.04 and 82.92 in the internal and external validation sets, respectively (Fig. 5). Moreover, significant abnormal findings on echocardiography, such as moderate to severe valvular heart disease or pulmonary artery systolic pressure $>$ 50 mm Hg, were more likely to be found in the medium- and high-risk groups than in the low-risk group (Supplemental Fig. S1). Although the presented AI algorithm's performance was limited to patients who underwent echocardiography within 28 days, as the follow-up period extended to 12 months, the performance of the AI algorithm to detect LVD in this subgroup remained consistent (Supplemental Figs. S2-S4).

We also assessed the prognostic capability of AI-S in predicting future adverse events, including all-cause mortality, hospitalisation, emergency department visits, and cardiovascular events, in patients who underwent an echocardiographic exam as well as in those who did not, as depicted in Supplemental Figures S5- S8. AI-S exhibited promising diagnostic and prognostic performance in screening for LVD and predicting future adverse events in patients undergoing ECG at outpatient clinics or during health check-ups.

Table 1. Summary of model and parameter estimates

Factor	Estimate (SE)	Distribution modelled	Source
Prevalence of asymptomatic LVD		Uniform	Wang et al.[13]
Age 40-59, M/F	0.0084/0.0020		
Age 60-69, M/F	0.0288/0.0032		
Age 70-79, M/F	0.0452/0.0040		
Age 80-99, M/F	0.0572/0.0076		
Probabilities and outcomes			
Sensitivity of AI (medium and high risk)	0.926 (0.042)	Beta	
Specificity of AI (medium and high risk)	0.938 (0.003)	Beta	
Sensitivity of AI (high risk)	0.630 (0.154)	Beta	
Specificity of AI (high risk)	0.989 (0.002)	Beta	
Annual transition from asymptomatic LVD to HF without treatment	0.098 (0.026)	Beta	SOLVD Investigators[20]
Annual transition from asymptomatic LVD to HF with treatment	0.065 (0.011)	Beta	SOLVD Investigators[20]
Annual probability of HF hospitalisation	0.33 (0.13)	Beta	SOLVD Investigators[20,21]
Annual subsequent HF hospitalisation	0.11 (0.05)	Beta	SOLVD Investigators[20,21]
Utility score for asymptomatic LVD without treatment	0.855 (0.005)	Beta	Göhler et al.[22]
Utility score for asymptomatic LVD with treatment	0.855 (0.005)	Beta	Göhler et al.[22]
Utility score for HF	0.771 (0.005)	Beta	Göhler et al.[22]
Additional mortality risk of asymptomatic LVD compared with no asymptomatic LVD (without treatment)	3.3 (1-4)	Uniform	SOLVD Investigators[20]
Additional mortality risk of asymptomatic LVD compared with no asymptomatic LVD (with treatment)	2.9 (1-4)	Uniform	SOLVD Investigators[20]
Additional mortality risk of HF compared with no asymptomatic LVD	4.9 (3-9)	Uniform	Heidenreich et al.[23]
Age-specific mortality			Taiwan Life Tables[14]
Costs (2022 U.S. dollars)			
Screening with AI algorithm	4.96	Uniform	NHIRD
Screening with TTE	62.50	Uniform	NHIRD
Asymptomatic LVD evaluation (post-confirmatory testing)	209.26	Uniform	NHIRD
Annual costs of ACEi and BB treatment	172.82	Uniform	NHIRD
Cost of HF hospitalisation	2,887 (1,444)	Gamma	Liao et al.[24]
Annual cost of outpatient HF management	5,400 (2,700)	Gamma	Liao et al.[24]
Discounting			
Costs	1.5%	Uniform	Assumption
Outcomes	1.5%	Uniform	Assumption

ACEi, angiotensin-converting enzyme inhibitor; AI, artificial intelligence; LVD, left ventricular dysfunction; BB, beta-blocker; HF, heart failure; NHIRD, National Health Insurance Research Database of Taiwan; SE, standard error; SOLVD, Studies of Left Ventricular Dysfunction; TTE, transthoracic echocardiography.

Cost-effectiveness analysis

In the base-case scenario, AI-ECG screening of 5000 individuals resulted in 56 HF cases (33.5%) and 52 deaths (31.1%) cumulatively within the first 4 years among the 167 LVD individuals. In contrast, among those who were not screened for LVD, there were 70 HF cases (41.0%) and 51 deaths (30.1%) in the first 4 years among 170 individuals with LVD.

Regarding cost-effectiveness (Table 2), AI-ECG screening showed dominance, with lower average costs for the entire simulated AI-ECG group compared with nonscreened patients. This pattern held true for both medium-risk and high-risk groups. In the medium-risk category, AI-ECG resulted in an average cost reduction of $44 per patient, alongside a slight increase in quality-adjusted life years (QALY) expectancy (0.006 QALY gained per patient), yielding a negative ICER of −$7,439. This cost-saving effect was notably pronounced

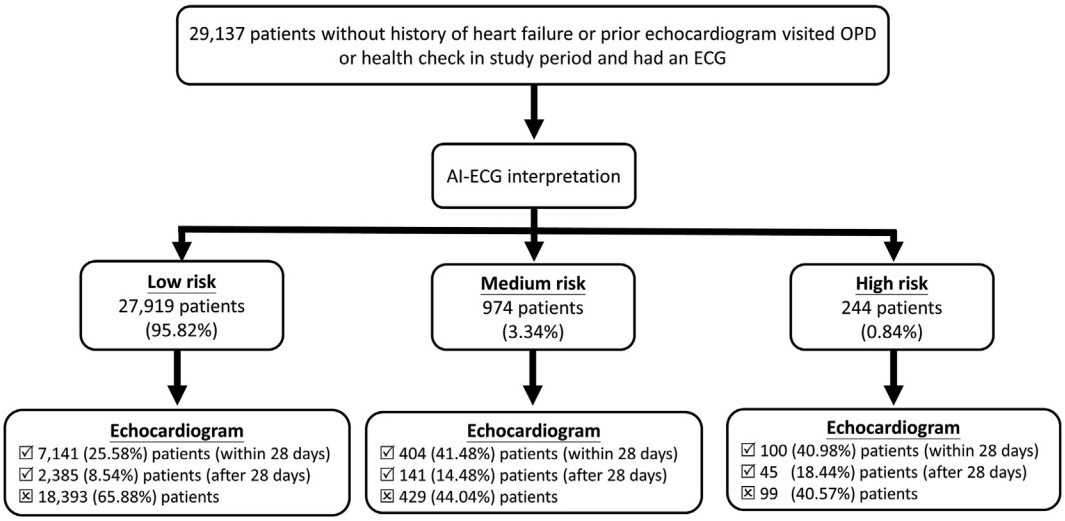


Figure 2. Flowchart depicting the enrollment process of patients who underwent artificial intelligence–enabled electrocardiography (AI-ECG) risk stratification followed by echocardiography. OPD, outpatient department.

in men. Although AI-ECG screening cost slightly more for women compared with no screening ($111 vs $104) and had marginal QALY gains, the resulting ICER of $6,262 indicates continued cost-effectiveness.

One-way sensitivity analysis (Supplemental Fig. S9) revealed that the costs of outpatient attendance, treatment (ACEis and beta-blockers), hospitalisation, asymptomatic LVD evaluation (post-confirmatory testing), and the specificity of AI-ECG had a significant effect on cost-effectiveness. Higher costs of outpatient attendance and hospitalisation due to HF increased cost-effectiveness (ie, screening for asymptomatic LVD avoids more subsequent HF than no screening), whereas higher costs of treatment and asymptomatic LVD evaluation decreased cost-effectiveness. Of note, even when the cost of AI-ECG screening was raised to 500% of the current cost, AI-ECG screening for asymptomatic LVD was still dominant over no screening.

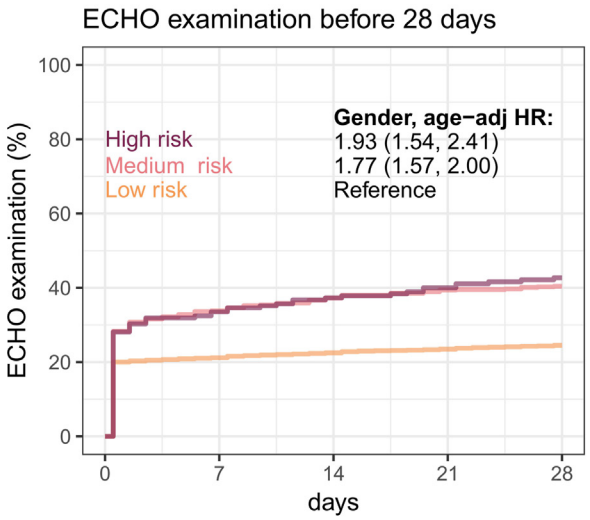
In the probabilistic sensitivity analysis, Figure 6 graphically illustrates that 62.8% of the 5000 simulations resulted in estimates for AI-ECG screening that were both more effective and less costly compared with no screening. Furthermore, for a WTP threshold of $30,000, most simulations (91.5%) yielded ICERs below the threshold. The cost-effectiveness increased even more for payers with any WTP threshold exceeding 0 (Fig. 6B). Analysis of AI-ECG screening for asymptomatic LVD across various age groups consistently revealed cost-effective outcomes from age 45 onward, regardless of sex and risk-stratification strategies (Table 2). Optimal cost-effectiveness was observed with screening at age 65. These findings underscore the efficacy of widespread AI-ECG screening for detecting asymptomatic LVD.

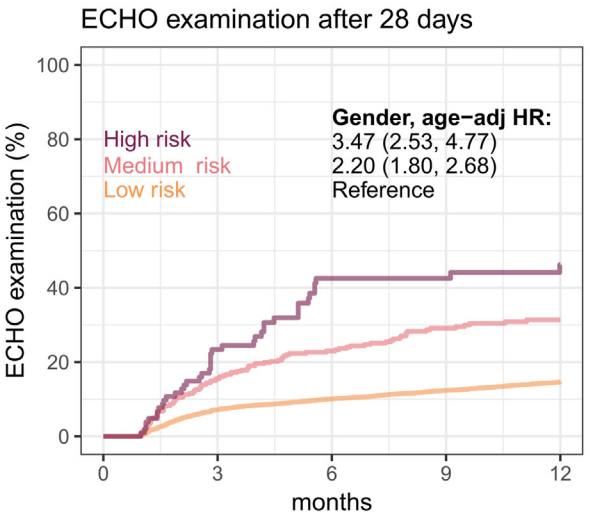
Discussion

In this study, we conducted a prospective assessment of an AI-ECG to screen for LVEF $\leq$ 40% in patients at outpatient clinics or during health check-ups. The algorithm demonstrated high accuracy in detecting LVD, with AUCs of 0.984 and 0.945 for the internal and external validation sets, respectively. By stratifying patients into high-, medium-, and low-risk categories, the algorithm could detect those susceptible to LVD early. In addition, among patients who were not initially scheduled to undergo echocardiographic examination, the algorithm accurately predicted the need for future echocardiography as well as the risk of LVD and cardiovascular adverse events within 1 year. Using this powerful AI screening tool, we analysed the cost-effectiveness of AI-enabled ECG screening for asymptomatic LVD compared with no screening in different age groups. The results showed that screening for asymptomatic LVD with the algorithm can lead to an improvement in QALYs and a reduction in medical costs by preventing future incident HF and associated costs, particularly in patients over the age of 65. To the best of our knowledge, this is the first study to evaluate the cost-effectiveness of asymptomatic LVD screening using AI-enabled ECG in a country with social insurance, indicating comprehensive insurance coverage and relatively low health care costs. These findings suggest that AI-ECG could be widely applied in clinical practice for the detection of asymptomatic LVD, resulting in improved patient outcomes and cost savings.

AI algorithms used in ECG for LVD detection have been widely proposed in recent years. Yao et al. conducted a randomised controlled trial involving 22,641 patients to compare the diagnostic rate of LVEF $\leq$ 50% within 90 days of ECG between an AI-assisted group and a usual care group.[16] Compared with usual care, physicians with additional information from AI-ECG predictions could identify 32% more patients with LVEF $\leq$ 50% with the use of similar echocardiography utilisation rates between the 2 groups (18.2% in usual care and 19.2% in the AI-assisted group; $P =$ 0.17).[16] Similarly, another study prospectively enrolled 16,056 patients and used AI-enabled ECG to detect EF $\leq$ 35%.[17] The algorithm detected patients with LVEF $\leq$ 35% with an AUC of 0.918, and 39.8% of the false-positive results had an LVEF of 36% to 50%.[17] Compared with previous

Internal validation set





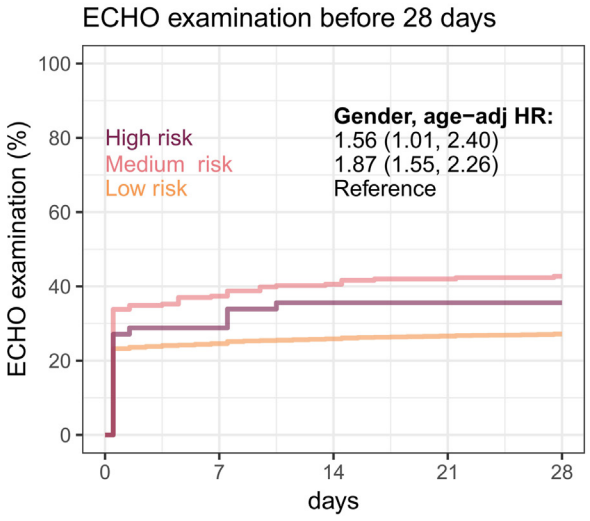
Number at risk/event rate (%)

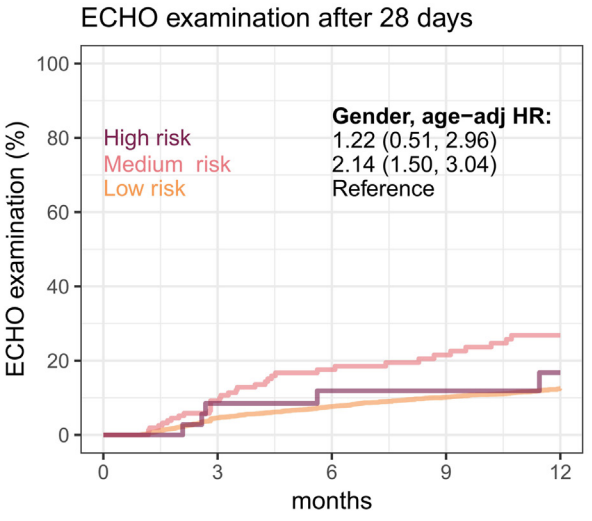
185	121	115	109	106
(0.0%)	(35.1%)	(38.4%)	(41.6%)	(42.7%)
693	453	430	419	413
(0.0%)	(35.2%)	(38.5%)	(39.7%)	(40.4%)
20591	16152	15894	15705	15546
(0.0%)	(21.7%)	(23.0%)	(23.9%)	(24.5%)

Number at risk/event rate (%)

106	60	40	34	26
(0.0%)	(28.1%)	(42.5%)	(44.1%)	(46.2%)
410	271	204	154	124
(0.0%)	(19.6%)	(25.1%)	(30.4%)	(31.4%)
15462	11592	9473	7850	6438
(0.0%)	(8.4%)	(10.8%)	(13.1%)	(14.6%)

External validation set





Number at risk/event rate (%)

59	39	38	38	38
(0.0%)	(35.6%)	(35.6%)	(35.6%)	(35.6%)
281	172	164	162	161
(0.0%)	(39.9%)	(42.0%)	(42.7%)	(42.7%)
7328	5485	5415	5367	5337
(0.0%)	(25.3%)	(26.2%)	(26.8%)	(27.2%)

Number at risk/event rate (%)

38	27	24	19	16
(0.0%)	(11.9%)	(11.9%)	(11.9%)	(16.8%)
160	118	84	72	60
(0.0%)	(13.6%)	(18.5%)	(24.7%)	(26.8%)
5316	4369	3670	3155	2694
(0.0%)	(5.7%)	(8.7%)	(10.9%)	(12.5%)

Figure 3. Timing, number, and hazard ratio (HR) of patients who underwent echocardiography (echo) after the index electrocardiogram in each risk group. Left: the proportions of patients who underwent echocardiography in the internal and external validation sets, respectively. Right: the proportions of patients who did not undergo echocardiography within 28 days but later had subsequent echocardiography. adj, adjusted.

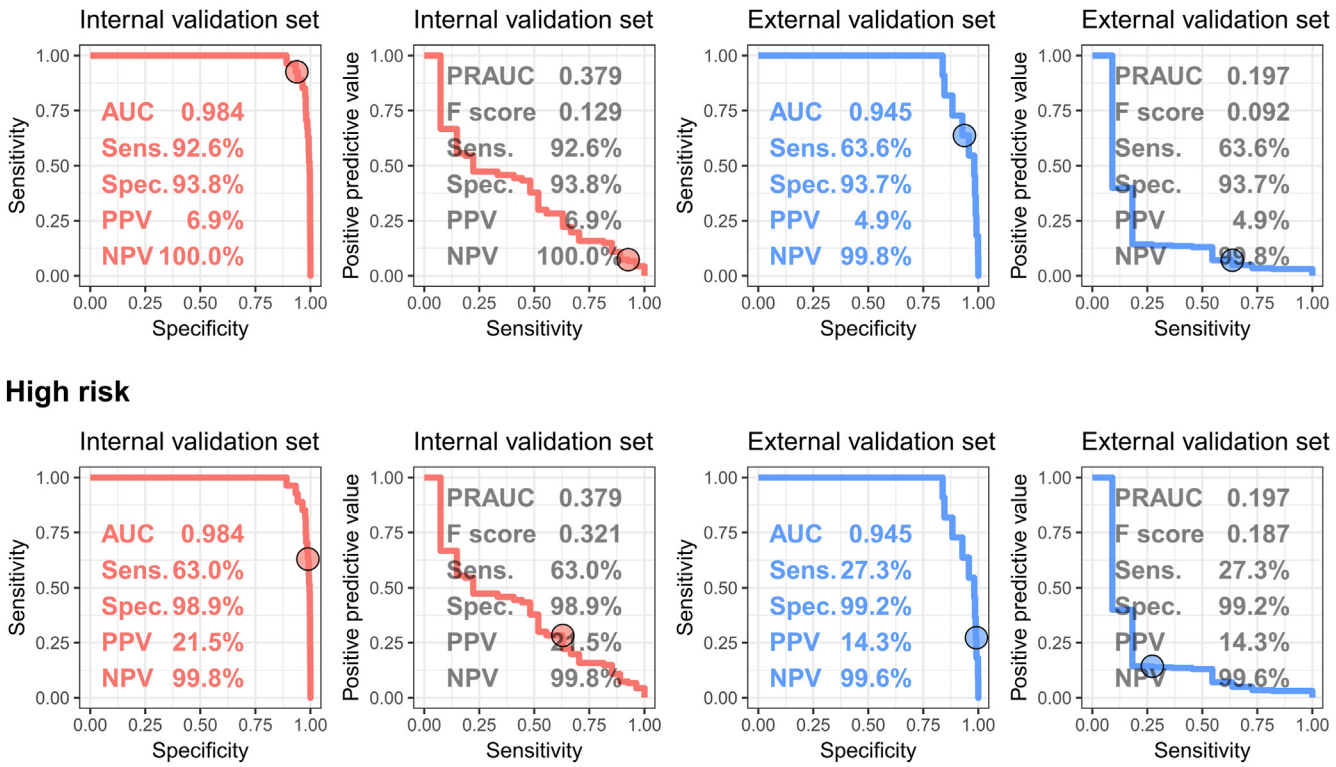


Figure 4. The areas under the receiver operating characteristic (AUC) and the precision-recall (PRAUC) curves of deep-learning model (DLM) predictions based on an AI-based alarm system (AI-S) to detect left ventricular ejection fraction $\leq$ 40%. The operating point for medium risk was selected using the maximum of Youden index of AUC (the sum of sensitivity [Sens.] and specificity [Spec.]), and for high risk it was selected using the maximum of Youden index of PRAUC (the sum of positive predictive value [PPV] and Sens.) within the tuning set. The corresponding operating points are marked by circles, and associated metrics such as AUC, PRAUC, Sens., Spec., PPV, and negative predictive value (NPV) are calculated accordingly.

studies, our study prospectively included 29,137 patients without previous cardiac evaluation, of whom 7645 (26%) underwent echocardiographic examination within 28 days. The algorithm accurately identified in advance patients who required echocardiography in both the internal and the external validation cohorts. Among patients who were not initially scheduled for echocardiography, the high-risk group identified by AI underwent more echocardiographic examinations during the follow-up period. Moreover, patients with normal LVEF but a high risk predicted by AI had more structural abnormalities on echocardiography. In clinical practice, physicians may encounter asymptomatic patients without traditional risk factors for LVD but with a positive AI alarm. With the risk stratification provided by our AI model, physicians can comprehensively evaluate the possibility of LVD and arrange subsequent examinations and treatments precisely.

The performance of the AI models in screening for various cardiovascular diseases was similar to that of cardiologists. Moreover, the cost-effectiveness of opportunistic screening using these algorithms is promising. For example, Pickhardt et al. conducted a cost-effectiveness analysis of an AI-based cardiovascular disease screening using abdominal computed tomography (CT).[18] The algorithm was able to automatically quantify abdominal aortic calcium, and based on the results, moderate- to high-intensity statin treatment was recommended. Compared with the no screening group, opportunistic screening using an AI-assisted CT scan was found to be a clinically effective and cost-saving strategy.[18]

In the case of diagnosing asymptomatic LVD, AI-enabled ECG has demonstrated excellent diagnostic ability compared with previous risk-prediction scoring models.[19] Because AI-ECG provides significant diagnostic improvements compared with usual care, the cost-effectiveness of AI in detecting asymptomatic LVD should be remarkable. In our model, early identification of asymptomatic LVD and subsequent intervention resulted in the avoidance of more cases of HF compared with the control group. Consequently, AI-ECG screening demonstrated dominance, with lower average costs and higher QALY gained for the entire simulated AI-ECG group compared with nonscreened patients. Even with uncertainty in AI-ECG costs and potential variations in interventions, AI-ECG screening for asymptomatic LVD remained dominant compared with no screening, even when AI screening and health care costs increased 5-fold from the base-case costs. Furthermore, it is noteworthy that increased costs associated with outpatient attendance and hospitalisation resulting from HF contribute to improved cost-effectiveness. Conversely, escalated costs related to treatment and asymptomatic LVD evaluation have the opposite effect, diminishing

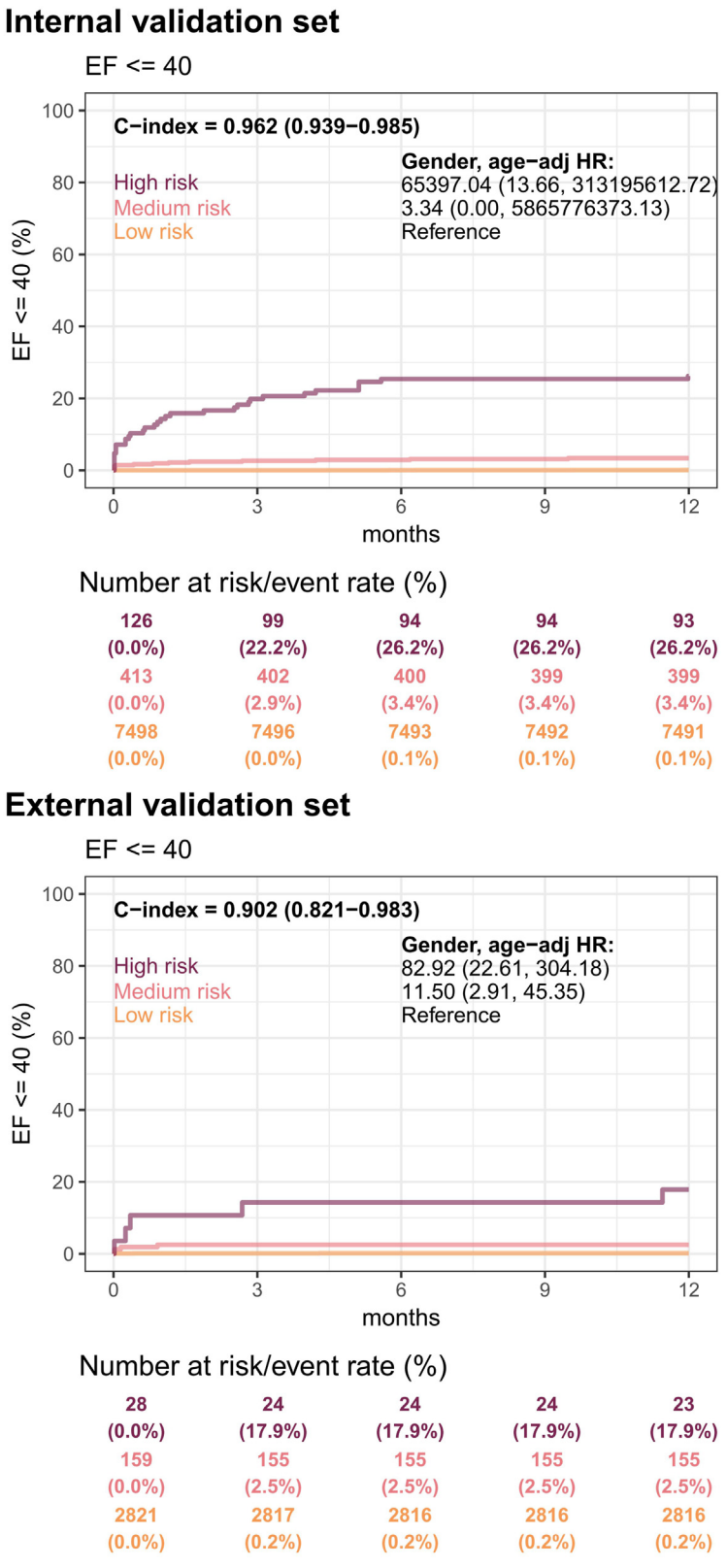


Figure 5. The timing, number, and hazard ratio (HR) of patients diagnosed with left ventricular ejection fraction (EF) $\leq$ 40% after the index electrocardiogram in each risk group. adj, adjusted; C-index, concordance index.

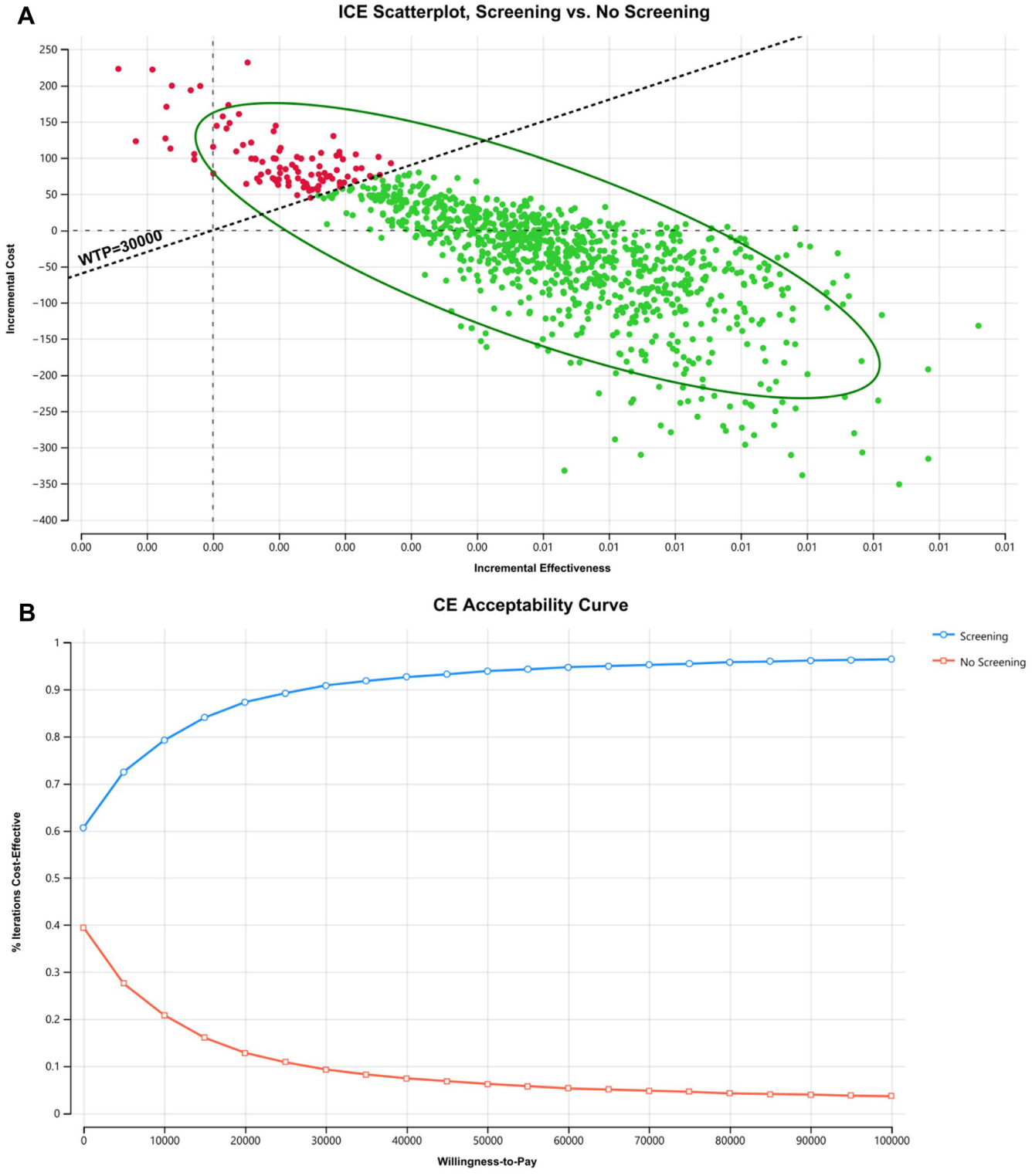


Figure 6. Cost-effectiveness of artificial intelligence—enabled electrocardiographic (AI-ECG) screening vs no screening for asymptomatic left ventricular dysfunction (LVD). (**A**) The incremental cost-effectiveness (ICE) scatterplot depicts the distribution of 5000 simulations, with **red dots** indicating non—cost-effective and **green dots** indicating cost-effective. AI-ECG screening for LVD was found to be cost-effective if willingness-to-pay (WTP) is set to $30,000 in 90.9% of the simulations. AI-ECG screening for LVD was dominant (quality-adjusted life-years gained and cost saved) in 62.4% of the simulations. (**B**) The cost-effectiveness (CE) acceptability curve depicts the probability of AI-ECG screening being acceptable in terms of the cost-effectiveness depending on the willingness-to-pay threshold of a payer. The range of willingness-to-pay was expanded from 0 to USD 10,000 and did not considerably change beyond this threshold.

Table 2. Cost, effect, and incremental cost-effectiveness ratio of screening with artificial intelligence (AI) algorithm vs no screen for age of 65 and other age groups

Strategy	Cost (USD)	Effect (QALY)	ICER (USD)
No screening (base-case: age 65)			
All	487	14.636	reference
Men	826	13.844	reference
Women	104	15.500	reference
Screening with AI-ECG (base-case: age 65, strategy 1)			
All	443	14.642	−7,439, dominant
Men	735	13.854	−9,062, dominant
Women	111	15.501	6,262
Screening with AI-ECG (base-case: age 65, strategy 2)			
All	455	14.640	−8,081, dominant
Men	765	13.851	−9,000, dominant
Women	103	15.500	−688, dominant
No screening (age 45)			
All	275	26.463	reference
Men	427	25.243	reference
Women	111	27.806	reference
Screening with AI-ECG (age 45, strategy 1)			
All	275	26.466	−1,051, dominant
Men	408	25.249	−3,317, dominant
Women	122	27.808	77,738
Screening with AI-ECG (age 45, strategy 2)			
All	268	26.465	−2,806, dominant
Men	411	25.247	−4,120, dominant
Women	113	27.807	2,007
No screening (age 55)			
All	227	20.796	reference
Men	348	19.733	reference
Women	92	21.963	reference
Screening with AI-ECG (age 55, strategy 1)			
All	223	20.796	−1,263, dominant
Men	330	19.737	−3,392, dominant
Women	104	21.965	9,592
Screening with AI-ECG (age 55, strategy 2)			
All	220	20.798	−3,697, dominant
Men	332	19.736	−5,247, dominant
Women	94	21.964	2,209
No screening (age 75)			
All	345	8.206	reference
Men	602	7.837	reference
Women	59	8.604	reference
Screening with AI-ECG (age 75, strategy 1)			
All	345	7.664	−7,149, dominant
Men	538	7.844	−9,579, dominant
Women	73	8.605	20,104
Screening with AI-ECG (age 75, strategy 2)			
All	323	8.209	−8,571, dominant
Men	557	7.841	−9,877, dominant
Women	62	8.605	6,039

Strategy 1: patients with medium risk or high risk of left ventricular dysfunction as stratified by AI-ECG undergo echocardiography. Strategy 2: patients with high risk of left ventricular dysfunction as stratified by AI-ECG undergo echocardiography.

ECG, electrocardiography; ICER, incremental cost-effectiveness ratio; USD, United States dollar; QALY, quality-adjusted life years.

cost-effectiveness. The probabilistic sensitivity analysis revealed that in 62.8% of the 5000 simulations, the estimates for AI-ECG screening indicated both greater effectiveness and lower costs compared with no screening. Although the WTP threshold can vary in different countries and may not be a critical criterion for decision making, the results suggest that cost-effectiveness improved even further for payers with any WTP exceeding 0. Moreover, the probability of AI-ECG screening being considered acceptable was higher than 91.5% under a threshold of $30,000 and did not change significantly beyond this threshold.

Limitations

Our study has several limitations. First, the lack of a control group posed challenges in assessing AI-ECG screening's effectiveness. Therefore, we used economic modelling to compare its cost-effectiveness against no screening. Although our focus was asymptomatic LVD detection, inclusion of mildly symptomatic patients might have affected algorithm accuracy. In addition, the extra cost of implementing the AI algorithm was not counted in the economic modelling. Despite AI-ECG pricing uncertainty, AI-ECG screening remained dominant over no screening even when assuming an ECG cost increase of up to 500% in the sensitivity analysis. Finally, transition and treatment data relied on a 30-year-old study, because recent relevant trials are absent. Because of the limitations of available data, our economic model is not exhaustive. Robust post−AI implementation studies are needed to assess real-world cost-effectiveness comprehensively.

Conclusion

The algorithm using ECG demonstrated high accuracy in detecting LVEF $\leq$ 40%, and the risk stratification predicted by AI suggested the probability of being diagnosed with LVD in both the short term and the long term. Applying AI-ECG for systemic asymptomatic LVD screening could be cost-saving, especially in men, in a social insurance country.

Ethics Statement

The research has adhered to relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This research received approval from the Institutional Review Board of Tri-Service General Hospital, Taipei, Taiwan (IRB no. C202105049). Because we used encrypted and de-identified data from the hospital, a waiver for informed consent was granted by the data controller for this study.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2023.11.044.