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ORIGINAL ARTICLE

Artificial intelligence calculated global longitudinal strain and left ventricular ejection fraction predicts cardiac events and all-cause mortality in patients with chest pain

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Abstract

Background: Assessment of left ventricular ejection fraction (LVEF) and myocardial deformation with global longitudinal strain (GLS) has shown promise in predicting adverse cardiovascular events. The aim of this study was to evaluate whether artificial intelligence (AI) calculated LVEF and GLS is associated with major adverse cardiac events (MACE) and all-cause mortality in patients presenting with chest pain.

Methods: We studied 296 patients presenting with chest pain, who underwent transthoracic echocardiography (TTE). Clinical data, downstream clinical investigations and patient outcomes were collected. Resting TTE images underwent AI contouring for automated calculation of LVEF and GLS with Ultromics EchoGo Core 2.0. Regression analysis was performed to identify clinical and AI calculated parameters associated with MACE and all-cause mortality.

Results: During a median follow-up period of 7.8 years (IQR 6.4, 8.8), MACE occurred in 34 (11.5%) patients and all-cause mortality in 60 (20%) patients. AI calculated LVEF (Odds Ratio [OR] .96; 95% CI .93–.99 and .96; 95% CI .93–.99) and GLS (1.11; 95% CI 1.01–1.21 and 1.08; 95% CI 1.00–1.16) were independently associated with MACE and all-cause mortality, respectively. According to Cox proportional hazards, a LVEF $< 50\%$ was associated with a 3.7 times MACE and 2.8 times all-cause mortality hazard rate compared to those with a LVEF $\geq 50\%$. Those with a GLS $\geq 15\%$ was associated with a 2.5 times MACE and 2.3 times all-cause mortality hazard rate compared to those with a GLS ≤ 15.

Conclusion: AI calculated resting LVEF and GLS is independently associated with MACE and all-cause mortality in high CVD risk patients. These results may have significant clinical implications through improved risk stratification of patients with chest pain, accelerated workflow of labour-intensive technical measures, and reduced healthcare costs.

KEYWORDS
artificial intelligence, cardiac events, echocardiography, ejection fraction, global longitudinal strain

1 | INTRODUCTION

The ability to detect and provide early intervention for patients with suspected coronary artery disease (CAD) is critical for the prevention of adverse cardiovascular events. Non-invasive identification of CAD remains a clinical challenge despite the widespread utilisation of imaging and provocative testing. Stress echocardiography is widely used for the assessment of CAD and selecting patients for coronary angiography. Despite this, improved strategies are required to increase the diagnostic yield in routine clinical practice, since fewer than 40% of patients undergoing elective cardiac catheterisation have significant CAD.[1]

Severe CAD leads to left ventricular (LV) dysfunction; however, in the early stages, LV function is preserved. Global longitudinal strain (GLS) is a valuable tool for the quantitative assessment of myocardial deformation beyond LVEF and regional wall motion abnormalities.[2] Studies indicate that significant CAD is associated with impaired longitudinal function, which can be detected using GLS, even in the presence of a visually normal LVEF.[3–5] This could be because GLS is largely determined by the contraction of longitudinal fibres that reside in the subendocardium,[6] which itself is the myocardial layer most sensitive to myocardial ischaemia.[7] Indeed, several studies have shown the value of GLS throughout the entire cascade of ischaemic heart disease, ranging from healthy individuals with cardiovascular disease risk factors to stable angina, acute myocardial infarction, and heart failure.[8–11]

In current practice, quantitative LV assessment using LVEF and GLS is operator dependent and requires off-line analysis with manual identification and correction of image contours, which can introduce variability. Artificial intelligence (AI) algorithms can reduce observer variability, as well as be deployed at scale for accelerated analysis of variables that normally require specialist training.[12] Recently, AI image processing of echocardiograms for the automated calculation of LVEF and GLS has been developed.[13] This approach has been shown to improve precision for identification of LV changes in COVID-19 infection.[14] However, investigating the clinical usefulness of AI-calculated LVEF and GLS in patients presenting with chest pain is warranted, especially considering the increased risk of cardiovascular events in this population.[15] We hypothesise that automated AI-calculated LVEF and GLS extracted from a large number of resting echocardiograms is independently associated with major adverse cardiac events and all-cause mortality in patients presenting with chest pain.

2 | METHOD

2.1 | Study design

The study population consisted of 296 (24 studies of a total 320 were excluded due to poor image quality and inability for the AI software to fully assess LV boarder delineation) patients (age 65.2 ± 11.4 years) presenting with cardiac chest pain at Parma University Hospital, Italy between From January 1, 2008 to December 31, 2012. All patients underwent a resting transthoracic echocardiogram (TTE) followed by functional dipyridamole stress testing for evaluation of myocardial ischaemia. Clinical characteristics were recorded at the time of the patients TTE (Table S1). The inclusion criteria were: age > 18 years; referral for known or suspected CAD; no severe primary valvular, cardiomyopathies or congenital heart disease, or presence of prognosis-limiting comorbidities, such as advanced cancer, reducing life expectancy to <1 year; echocardiography of acceptable quality at rest to allow resting GLS; willingness to give their written informed consent allowing scientific utilization of observational data.

This study conformed to the Declaration of Helsinki, apart from prior registration in a database. All patients provided informed consent before testing and the local research ethics committee gave ethical approval.

2.2 | Transthoracic image analysis

All patients underwent a resting transthoracic echocardiogram according to local guidelines. Image analysis of the LV was performed locally using commercially available AI algorithms created by machine learning (Ultromics, EchoGo Core 2.0), which automatically calculated LVEF and GLS (no manual correction). In brief, the AI algorithm was used for automated contouring of the endocardial border of every frame from the apical 4-, 3- and 2-chamber (A4C, A3C and A2C respectively) views, automated identification of the end-diastolic and the end-systolic frames based upon the size of the enclosed area, and automated selection of the cardiac cycle (Figure 1). The automated LV contours and selection of frames were verified and approved by at least one accredited echocardiographer who was blinded to all clinical and study information. The criteria for operator verification of AI includes the correct end diastolic and end systolic frame selection, accurate delineation and tracking of the LV endocardial boarder and tracking of all apical images. Between three blinded operators, the agreement for AI image verification on 214 studies was 96.4%. All LV volumes and LVEF were obtained by performing endocardial tracings and using the biplane method of disks (modified Simpson's rule). Only cases with acceptable-quality LV views were included, which was defined as lack of apical foreshortening with adequate visualization of all segments and delineation of the entire LV endocardial border by the AI from all views as previously described.[16,17] Longitudinal strain was calculated as the average Legrangian strain from the A4C, A3C, and A2C views. Cut-offs for mild, moderately, and severely reduced LVEF were determined by the 2015 American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) guidelines for cardiac chamber quantification.[18] Abnormal GLS was defined as ≥15%.[19]

2.3 | Dipyridamole stress echo

All patients underwent a dipyridamole stress echocardiogram (DSE), either with or without ultrasound contrast. Dipyridamole was infused at a total dose of .84 mg/kg over 6 min. Two-dimensional

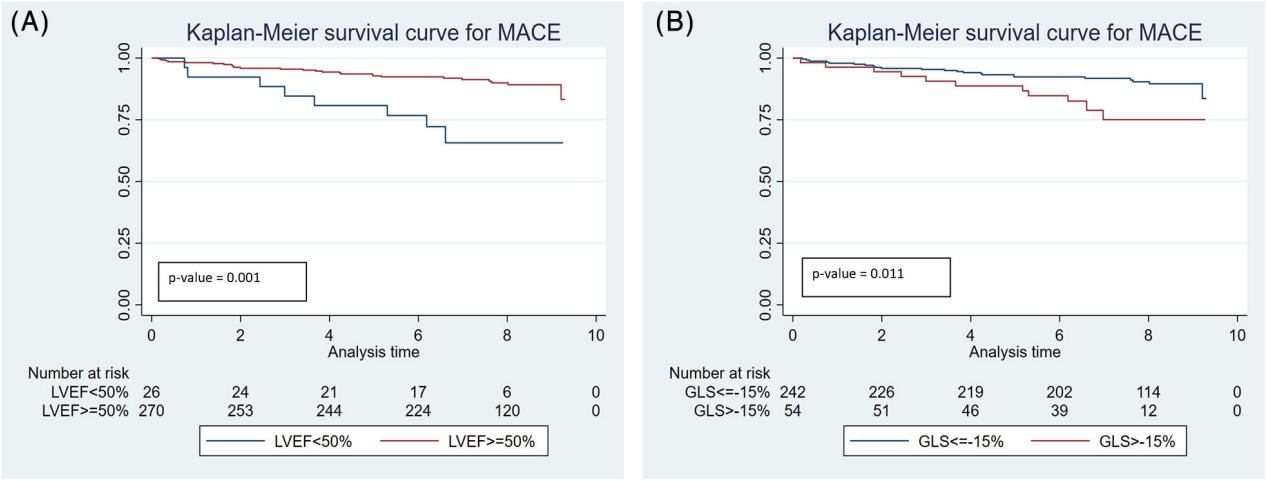

FIGURE 1 EchoGo core is an automated, cloud-based software medical device for processing of echocardiographic images. Echocardiographic images are uploaded to the cloud-based environment in DICOM format whereby an automated pipeline identifies the apical 2, 3, and 4 chamber images available for analysis. Trained and accredited cardiac physiologists (operators) review the identified images and ensure image selection is appropriate. Apical images are then passed to convolutional neural networks which delineate the left ventricular (LV) endocardium, predict the position of endocardial segments using the 18-segment model and then contour the endocardial border. Operators conduct a quality control check of all contours produced by the software by either accepting or rejecting them. Operators are unable to manually edit or adjust contours but they are able to select available alternative images for auto-contouring. LV global longitudinal strain is calculated as the average Lagrangian strain from contours of the apical 2, 3, and 4 chamber images. LV volumes and ejection fraction are calculated using the apical 2 and 4 chamber contours using the Simpson's biplane method.

echocardiography, 12-lead electrocardiograms and blood pressure monitoring were performed in accordance with standard protocols. Aminophylline was routinely used to reverse the effect of dipyridamole. All images were acquired in the A4C, A3C, and A2 views using an S5 broadband transducer (Philips, Eindhoven, Netherlands). Wall motion was evaluated at baseline and peak stress and a semi quantitative wall motion score was calculated (normal, hypokinesia and akinesia) using a 17-segment model of the left ventricle. Myocardial ischeamia was defined as the occurrence of stress-induced new dyssynergy or worsening of rest hypokinesia in ≥1 myocardial segment.

2.4 | Participant follow-up and outcomes

Follow-up was obtained by review of the patient's hospital chart, electronic records, and national health status database. The principle end-point of interest for this analysis was major adverse cardiac events (MACE) and, secondarily, all-cause mortality, with patients censored at the time of event or at the last follow-up. A MACE was defined as cardiac death (due to myocardial infarction, cardiac arrhythmias, or congestive heart failure) or non-fatal myocardial infarction (NFMI). A NFMI was defined by the standard criteria of ischaemic chest pain associated with an elevation of cardiac enzymes with or without electrocardiographic changes (only the first event was counted between cardiac death and NFMI). The diagnosis of cardiac death required documented life-threatening arrhythmias, cardiac arrest, and death attributable to congestive heart failure or myocardial infarction in the absence of any other precipitating factor. Sudden unexpected death was classified as a cardiac death when an obvious non-cardiac explanation was excluded. In patients who underwent coronary angiography within 90-days of their TTE, significant CAD was defined according to ≥50% left main disease and/or ≥70% luminal narrowing in the left anterior descending, circumflex, or right coronary artery by visual assessment.

2.5 | Statistical analysis

Unless otherwise specified, data are presented as mean ± SD or *n* (%). Group comparisons were performed using the Student's *t*-test or a Mann–Whitney *U* test for continuous data and categorical data were compared with chi-squared (χ^2) test.

To analyse the time-to-event where the event is taken as MACE or all-cause mortality, separately, according to time since the patient's echocardiogram, Cox proportional hazards regression and Kaplan–Meier cumulative event curves were constructed and compared using the log-rank test with a p value $< .05$ considered statistically significant. Dichotomization of the continuous variables was performed using their clinical cut-off and data were stratified according to (A) LVEF ≥50% and <50% and (B) GLS ≤15% and ≥15%.

Univariate logistic regression was conducted to establish associations, independent of time, between the outcomes (MACE or all-cause mortality) and clinical information (including baseline clinical characteristics, echocardiography results, and clinical outcomes). Finally, multivariable logistic regression analysis was performed using

clinically prognostic variables (Model 1) and then adding AI calculated GLS (Model 2) and AI calculated LVEF (Model 3). Odds ratios (OR) and corresponding 95% CIs are reported. All analyses were conducted using RStudio Version 1.1.456 and Strata/SE 17.0 for Windows (65-bit x86-64).

3 | RESULTS

3.1 | Study population, procedures and outcomes

All 296 patients underwent TTE and DSE. A greater proportion of the population were male (63.9%) and 93 (31.4%) patients had known CAD, of which 67 (22.6%) had a prior myocardial infarction. Following DSE, 81 (27.4%) patients had evidence of myocardial ischaemia. The AI calculated resting LVEF and GLS was 63.6 ± 9.9% and −18.8 ± 4.5%, respectively (Table S1). In total, 39 patients underwent coronary angiography within 90-days of their TTE and MPI. Of these, three had left main disease with or without other vessel disease, seven had significant triple vessel disease, seven double vessel disease, 20 single vessel disease, and five had no significant CAD on angiography. During a median follow-up period of 7.8 years (IQR 6.4, 8.8), MACE occurred in 34 (11.5%) patients and all-cause mortality in 60 (20.3%) patients.

3.2 | AI-quantification of LVEF and GLS: MACE

Patients who experienced a MACE during the follow-up period were significantly older, more likely to have previous CAD events, hypercholesterolaemia, and prescribed cardiovascular protective medication. In addition, a larger proportion of MACE patients had inducible ischaemia and underwent coronary revascularisation. All-cause mortality was also significantly higher in MACE patients. Importantly, AI calculated LVEF (58.6 ± 13.1% vs. 64.2 ± 9.2%; $p = .002$) and GLS (−16.5 ± 5.2% vs. −19.1 ± 4.4%; $p = .001$) were significantly lower in MACE patients (Table 1). In univariate logistic regression analysis, older age, previous MI, previous revascularisation, hypercholesterolaemia, cardiovascular medication, lower LVEF, lower GLS, follow-up revascularisation, and all-cause mortality were significantly associated with MACE's (Table S2). Following multivariate analysis using clinic information and backwards stepwise model selection (Model 1), older age, previous PCI, and follow-up revascularisation were independently associated with a MACE. AI calculated GLS (OR 1.11; 95% CI 1.01–1.21) was independently associated with a MACE (Model 2) and the addition of GLS significantly improved MACE discrimination (Table 2). AI calculated LVEF (OR .96; 95% CI.93–.99) was independently associated with a MACE (Model 3) and the addition of LVEF significantly improved MACE discrimination (Table 2). The Kaplan-Meier curves for the cumulative survival and freedom from MACE are presented in Figure 2, dichotomised according to (A) LVEF ≥ 50% and <50% and (B) GLS ≤ 15% and ≥15%. An LVEF < 50% and GLS ≥ 15% was associated with a 3.7 and 2.5 times increased risk of MACE, respectively, during the follow-up period.

3.3 | AI-quantification of LVEF and GLS: All-cause mortality

Patients who died during the follow-up period were significantly older, more likely to have had a previous myocardial infarction, undergone previous revascularisation, and prescribed cardiovascular protective medication. In addition, a greater proportion of patients who died had myocardial ischaemia, follow-up revascularisation and experienced a MACE. Importantly, AI calculated LVEF (59.6 ± 13.5% vs. 64.6 ± 8.5%; $p < .001$) and GLS (−17.1 ± 5.3% vs. −19.3 ± 4.2%; $p = .001$) was significantly lower in patients who died during the follow up period (Table 3). In unadjusted analysis, older age, previous MI, previous revascularisation, cardiovascular medication use, lower AI LVEF and GLS, myocardial ischaemia, follow-up revascularisation, and MACE were significantly associated with all-cause mortality (Table S2). Following multivariate analysis using clinic information and backwards stepwise model selection (Model 1), older age and previous MI were independently associated with all-cause mortality. AI calculated GLS (OR 1.08; 95% CI 1.00–1.16) was independently associated with all-cause mortality (Model 2) and the addition of GLS significantly improved discrimination for all-cause mortality (Table 4). AI calculated LVEF (OR .96; 95% CI .93–.99) was independently associated with all-cause mortality (Model 3) and the addition of LVEF significantly improved discrimination for all-cause mortality (Table 4). The Kaplan-Meier curves for the cumulative survival and freedom from all-cause mortality are presented in Figure 3, dichotomised according to (A) LVEF ≥50% and <50% and (B) GLS ≤15% and ≥15%. An LVEF < 50% and GLS ≥ 15% was associated with a 2.8 and 2.3 times increased risk of all-cause mortality, respectively, during the follow-up period.

4 | DISCUSSION

This study has demonstrated that AI-calculated LVEF and GLS in resting TTE images provides independent prognostic value for MACE and all-cause mortality in patients with chest pain. In our study, using clinical cut-off values, a LVEF < 50% was associated with a MACE hazard rate of 3.7 times the hazard rate of those with a LVEF ≥ 50%. Those with a GLS ≥ 15% was associated with a MACE hazard rate 2.5 times the hazard rate in those with a GLS ≤ 15. These findings were similar for all-cause mortality. Importantly, these results are despite significantly greater prescription of cardioprotective pharmacotherapy in those that had adverse events, and the utilisation of downstream investigation including DSE (assessment of myocardial ischaemia) and coronary intervention during the follow-up period. This data supports the increasing benefit of incorporating LVEF and GLS into standard routine TTE assessment in patients with chest pain. A reduced GLS should prompt healthcare providers to consider prospective surveillance TTE imaging to reduce the risk of deteriorating cardiac function and resultant heart failure.

The non-invasive risk stratification of patients reporting chest pain and suspected as having CAD remains challenging in clinical

TABLE 1 Characteristics of patients according to no MACE and MACE.

Characteristic	No MACE ($N = 262$)	MACE ($N = 34$)	p-Value
Demographics			
Age (years)	64.3 (11.4)	72.3 (8.9)	<.001
Female sex (%)	98 (37.4%)	9 (26.5%)	.212
Cardiovascular disease risk factors			
Previous MI	48 (18.3%)	19 (55.9%)	<.001
Previous PCI	53 (20.2%)	19 (55.9%)	<.001
Previous CABG	14 (5.3%)	5 (14.7%)	.036
Family history of CAD	80 (30.5%)	11 (32.4%)	.829
Smoke	58 (22.1%)	5 (14.7%)	.319
Hypercholesterolemia	141 (53.8%)	25 (73.5%)	.029
Diabetes	49 (18.7%)	11 (32.4%)	.062
Hypertension	158 (60.3%)	26 (76.5%)	.067
Obesity	15 (5.7%)	4 (11.8%)	.176
Cardiac medication			
Aspirin	151 (57.6%)	32 (94.1%)	<.001
Other antiplatelet	46 (17.6%)	18 (52.9%)	<.001
Beta-blockers	147 (56.1%)	29 (85.3%)	.001
Anti-hypertensives	160 (61.1%)	29 (85.3%)	.006
Statins	137 (52.3%)	30 (88.2%)	<.001
AI quantification			
LVEF (%)	64.2 (9.2)	58.6 (13.1)	.002
GLS (%)	−19.1 (4.4)	−16.5 (5.2)	.001
Heart rate (b min^{-1})	69.8 (12.3)	67.0 (10.0)	.226
Functional assessment			
Baseline WMSI	1 (1, 1.06)	1 (1, 1.12)	.153
Peak WMSI	1 (1, 1.06)	1 (1, 1.19)	.138
Myocardial ischaemia	65 (24.8%)	16 (47.1%)	.006
Adverse events			
Revascularisation	40 (15.3%)	21 (61.8%)	<.001
All-cause mortality	41 (15.7)	19 (55.9)	<.001

Note: MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; WMSI = wall motion score index.

TABLE 2 Multivariate predictors of major adverse cardiac events.

	Model 1	Model 2	Model 3
Characteristic	OR (95% CI) [p-value]	OR (95% CI) [p-value]	OR (95% CI) [p-value]
Age (years)	1.07 (1.02, 1.12) [.006]	1.06 (1.01, 1.11) [.014]	1.06 (1.01, 1.11) [.014]
Previous PCI	3.16 (1.39, 7.15) [.006]	3.14 (1.38, 7.17) [.007]	3.40 (1.48, 7.84) [.004]
Revascularisation	6.75 (3.00, 15.20) [.000]	6.79 (2.98, 15.47) [.000]	7.09 (3.10, 16.23) [.000]
GLS (%)	–	1.11 (1.01, 1.21) [.025]	–
LVEF (%)	–	–	.96 (.93, .99) [.013]
R^2 statistic	.243	.267[a]	.272[b]

Note: PCI = percutaneous coronary intervention; GLS = global longitudinal strain; LVEF = left ventricular ejection fraction.

[a]A likelihood ratio test shows that Model 2 explains the data significantly better than Model 1. LR chi-squared = 5.15; p-value .023.

[b]A likelihood ratio test shows that Model 3 explains the data significantly better than Model 1. LR chi-squared = 6.13; p-value .013.

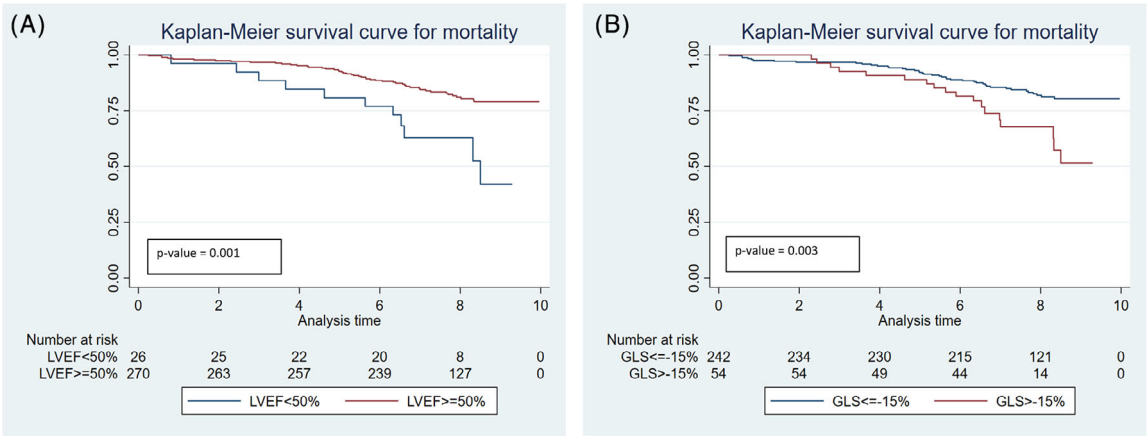

FIGURE 2 Kaplan-Meier curves for the cumulative survival and freedom from major adverse cardiac events, dichotomised according to (A) LVEF ≥50% and < 50% and (B) GLS ≤−15% and > −15%.

TABLE 3 Characteristics of patients according to alive or all-cause mortality.

Characteristic	Alive (*N* = 236)	All-cause mortality (*N* = 60)	*p*-Value
Demographics			
Age (years)	62.9 (10.8)	74.2 (8.9)	<.001
Female sex (%)	90 (38.1%)	17 (28.3%)	.158
Cardiovascular disease risk factors			
Previous MI	41 (17.4%)	26 (43.3%)	<.001
Previous PCI	51 (21.6%)	21 (35.0%)	.031
Previous CABG	11 (4.7%)	8 (13.3%)	.014
Family history of CAD	78 (33.1%)	13 (21.7%)	.088
Smoke	52 (22.0%)	11 (18.3%)	.532
Hypercholesterolemia	127 (53.8%)	39 (65.0%)	.119
Diabetes	47 (19.9%)	13 (21.7%)	.763
Hypertension	146 (61.9%)	38 (63.3%)	.834
Obesity	17 (7.2%)	2 (3.3%)	.275
Cardiac medication			
Aspirin	137 (58.1%)	46 (76.7%)	.008
Other antiplatelet	42 (17.8%)	22 (36.7%)	.002
Beta-blockers	135 (57.2%)	41 (68.3%)	.117
Anti-hypertensives	144 (61.0%)	45 (75.0%)	.044
Statins	124 (52.5%)	43 (71.7%)	.008
AI quantification			
LVEF (%)	64.6 (8.5)	59.6 (13.5)	<.001
GLS (%)	-19.2 (4.2)	-17.1 (5.3)	.001
Heart rate (b min^{-1})	69.8 (12.2)	68.4 (11.4)	.465
Functional assessment			
Baseline WMSI	1 (1, 1.06)	1 (1, 1.13)	.115
Peak WMSI	1 (1, 1.06)	1 (1, 1.19)	.054
Myocardial ischaemia	55 (23.3%)	26 (43.3%)	.002
Adverse events			
Revascularisation	43 (18.2%)	18 (30.0%)	.044
MACE	15 (6.3%)	19 (31.7%)	<.001

Note: MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; GLS = global longitudinal strain; WMSI = wall motion score index; MACE = major adverse cardiac event.

TABLE 4 Multivariate predictors of all-cause mortality.

	Model 1	Model 2	Model 3
Characteristic	OR (95% CI) [*p*-value]	OR (95% CI) [*p*-value]	OR (95% CI) [*p*-value]
Age (years)	1.13 (1.08, 1.18) [.000]	1.13 (1.08, 1.17) [.000]	1.13 (1.08, 1.17) [.000]
Previous MI	2.65 (1.33, 5.28) [.006]	2.40 (1.19, 4.82) [.014]	2.45 (1.22, 4.94) [.012]
GLS (%)	–	1.08 (1.00, 1.16) [.043]	–
LVEF (%)	–	–	.96 (.93, .99) [.020]
R^2 *statistic*	.223	.237[a]	.243[b]

Note: MI = myocardial infarction; GLS = global longitudinal strain; LVEF = left ventricular ejection fraction.
[a]A likelihood ratio test shows that Model 2 explains the data significantly better than Model 1. LR chi-squared = 4.27; *p*-value .039.
[b]A likelihood ratio test shows that Model 3 explains the data significantly better than Model 1. LR chi-squared = 5.77; *p*-value .016.

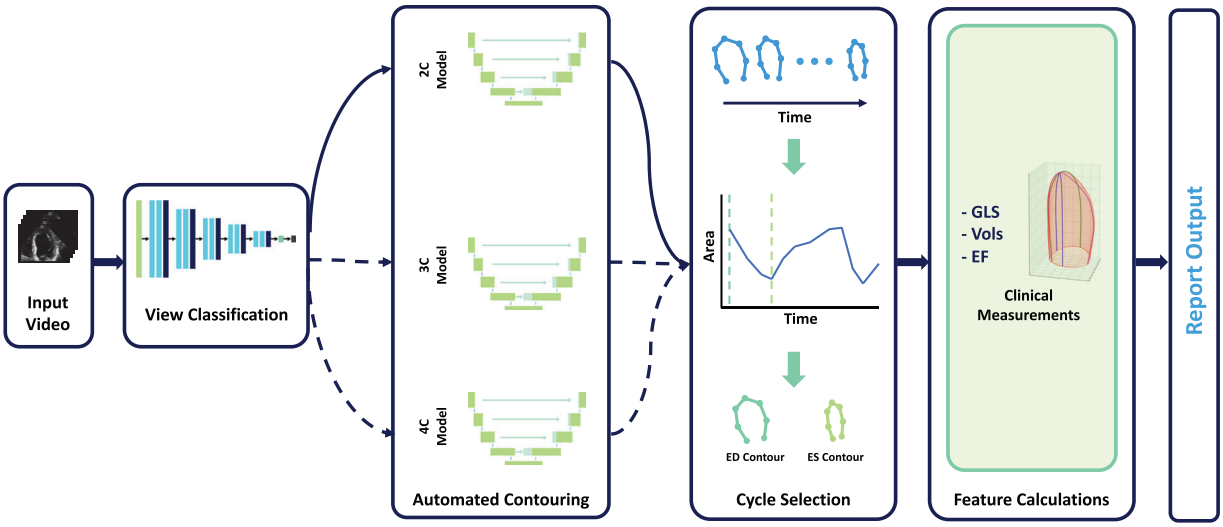

FIGURE 3 Kaplan–Meier curves for the cumulative survival and freedom from all-cause mortality, dichotomised according to (A) LVEF ≥50% and <50% and (B) GLS ≤15% and ≥15%.

practice, since many patients referred for coronary angiography report non-obstructive CAD.[1] Previous research has demonstrated the value of GLS for the prediction of CAD in patients reporting no chest pain at the time of investigation,[20] inpatients hospitalised with chest pain[21] and those with severe CAD with normal LVEF and no regional wall motion abnormalities.[4] In addition, previous research[22,23] has reported greater accuracy for the identification of CAD from endocardial compared to epicardial strain in patients presenting with non-ST segment elevation acute coronary syndrome. This is likely due to the endocardial layer being the most sensitive to myocardial ischaemia[7] as well as undergoing the greatest deformation change during systole.[24] However, prior research has demonstrated greater reproducibility for the acquisition of epicardial GLS compared to endocardial GLS,[25,26] as well as reporting that the epicardium is easier to manually trace.[27] Importantly, the AI image processing pipeline utilised in this study automatically calculates GLS from the endocardium, removing operator dependence and manual identification and correction of image contours, which with greater utilisation may prove clinically important for the risk stratification of high cardiovascular disease patients. If deployed at scale, this technology has potential to provide accurate and accelerated quantitative analysis of variables that normally require specialist training,[12] which combined with prognostic capabilities may culminate in improved clinical workflow, patient care and reduced healthcare costs.

AI calculated resting LVEF and GLS also independently predicted all-cause mortality. It is well known that a reduced LVEF is associated with an increased mortality.[28] However, LVEF measures were within the normal range for both MACE and all-cause mortality patients at baseline. Importantly, recent research demonstrated that the potential value of GLS measures was greatest in patients considered to have preserved systolic function using conventional TTE measures.[29] In addition, these findings demonstrate the value of resting AI calculated LVEF and GLS over myocardial ischaemia and ischaemic burden on stress for the long-term prediction of MACE and all-cause mortality. Indeed, recent research demonstrated that resting GLS was an independent predictor of all-cause mortality in patients with and without CAD, those with a LVEF > 50%, as well as patients who experienced a MACE, with ischaemia on stress providing no independent predictive

value.[30] These findings demonstrate that AI calculated GLS and LVEF is independently associated with long-term adverse outcomes and these variables should be routinely reported in resting TTE examinations. Furthermore, a reduced GLS in the presence of a preserved LVEF should prompt follow-up assessment to optimise medical therapy and reduce cardiovascular complications.

5 | LIMITATIONS

Our study has limitations. This was a retrospective, single centre study, which may be subject to case selection bias. In addition, the sample size was small to moderate. However, despite the sample size, there was statistical power to predict adverse outcomes in a typical cardiology patient. As such, future clinical trials may require smaller sample sizes with the implementation of AI technology.

6 | CONCLUSION

AI calculated LVEF and GLS is independently associated with major adverse cardiac events and all-cause mortality in high CVD risk patients. Wide deployment of AI technology has potential to significantly impact clinical outcomes and workflow, through improved risk stratification of patients with chest pain, accelerated quantification of labour-intensive technical measures, and reduce healthcare costs.

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DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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