ESC Congress 2026 **Number : 85581**

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Status : Accepted, submitted on 28/02/2026 15:23

Title : Validation of an aAI-supported vectorcardiography for the detection of coronary artery disease: a comparative study with coronary calcium scoring and CT Angiography (AI-CCC Study)

Topic : 17.3.1 - Noninvasive Diagnostic Methods

Category : Bedside

Option : No Options

Funding Acknowledgements :
Type of funding sources: None
Main funding source(s):
Project Code:
Agreement: 2

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Background/Introduction: Coronary artery disease (CAD) remains a leading cause of global mortality. Although computed tomography angiography (CTA) and calcium scoring (CS) are well-established diagnostic methods, they require specialised equipment and involve radiation and contrast exposure. Vectorcardiography (VCG) is a radiation-free alternative, and recent advances in artificial intelligence (AI) have led to the development of an AI-based 5-lead 3D VCG (5L3DVCG-AI) system that is capable of extracting complex electrophysiological indices to non-invasively characterise myocardial ischaemia.

Purpose: This study evaluates the diagnostic and ordinal staging utility of the 5L3DVCG-AI's CSG-index (a composite measure of cardiac spatial geometry) and p-factor (reflecting repolarisation dispersion) for detecting CAD, using CTA as the reference standard, and compares their performance alongside the Agatston Calcium Score.

Methods: In this observational study, 118 consecutive outpatients (mean age 52.4 years; 47% female) evaluated for suspected CAD underwent 5L3DVCG-AI, non-contrast CT for CS, and CTA. The coronary stenosis was categorised by CTA as follows: Grade 0 (no stenosis, n=71), Grade 1 (<50%, n=26), and Grade 2 (≥50%, n=21). The CSG-index and p-factor were analysed across groups. Diagnostic performance was assessed using receiver operating characteristic (ROC) analysis. Given the non-normal distribution of the predictors, non-parametric tests (Kruskal-Wallis, Wilcoxon) and Tukey HSD post-hoc analyses were utilised. To address data separation, Firth penalised logistic regression and 5-fold cross-validated Ridge regression were applied to assess independent predictive value.

Results: The CSG-index demonstrated a significant stepwise increase across stenosis severity groups ($p<0.001$), with mean values of −0.84 (Grade 0), −0.18 (Grade 1), and +0.07 (Grade 2). Post-hoc analysis showed that the CSG-index significantly differentiated between all three groups, including discrimination between the Grade 1 and Grade 2 ($p=0.029$). While CS was the strongest standalone predictor (AUC 0.971), the CSG-index (AUC 0.817) and p-factor (AUC 0.811) demonstrated strong independent diagnostic discrimination for coronary stenosis. Firth penalised regression confirmed that both the CSG-index ($p=0.002$) and p-factor ($p<0.001$) provided statistically significant additive predictive value beyond the CS. A model integrating CS, CSG-index, and p-factor achieved an AUC of 0.977 (sensitivity 95.7%, specificity 87.1%)

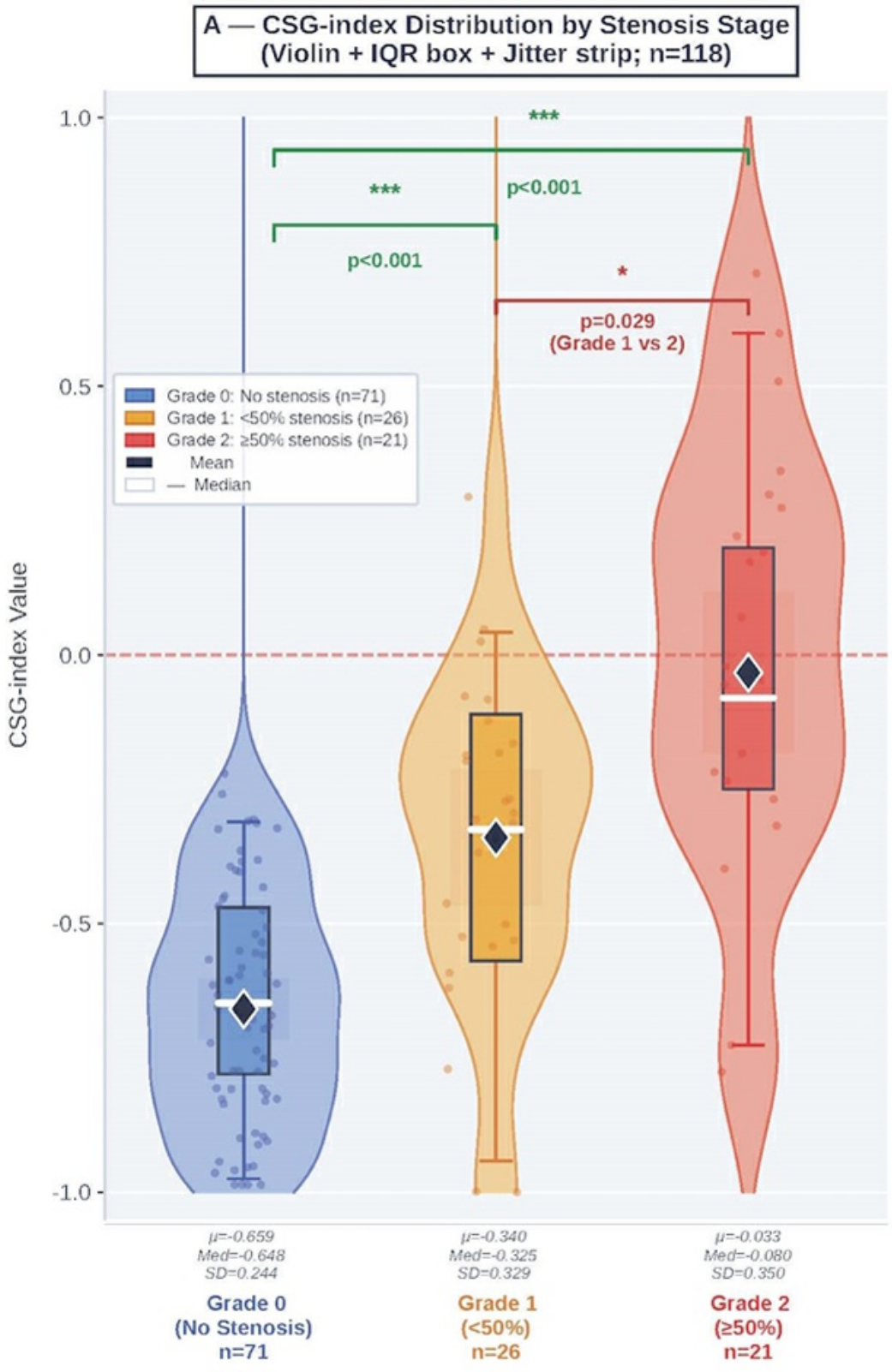
Conclusion(s): The CSG-Index and p-factor demonstrate significant associations with coronary stenosis and offer high diagnostic accuracy. While CS remains the dominant predictor of plaque burden, 5L3DVCG-AI demonstrates strong diagnostic discrimination as a non-invasive, radiation-free modality. Its utilisation may facilitate the optimisation of patient selection for advanced imaging or intervention.

ROC Diagnostic Performance — All Predictors (n=118). DeLong 95%CI and Wilson score 95%CI for proportions.

Predictor	AUC (95%CI)	Threshold (Youden J)	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV
CSG-index	0.817 (0.725–0.897)	> −0.267	76.6% (62.8–86.4%)	87.3% (77.6–93.2%)	80.0%	84.9%
P-FACTOR	0.811 (0.732–0.884)	≥ 0.5	76.6% (62.8–86.4%)	80.3% (69.6–87.9%)	72.0%	83.8%
CS (Calcium Score)	0.971 (0.933–0.999)	> 8.5	93.6% (82.8–97.8%)	98.6% (92.4–99.8%)	97.8%	95.9%
Combined Model (CS+CSG+PF)*	0.982 (0.960–0.997)	Multivariable	93.6%	95.8%	N/A	N/A

PPV = Positive Predictive Value; NPV = Negative Predictive Value. AUC benchmarks: <0.7 inadequate; 0.7–0.8 acceptable; 0.8–0.9 excellent; ≥0.9 outstanding.

- Note: The Combined Model utilizes Ridge regression with 5-fold cross-validation. Confidence intervals and predictive values for the cross-validated model were not extracted in the binary sub-analysis.
- *5-fold CV-AUC for combined model = 0.977 (sensitivity 95.7%, specificity 87.1%)*


A — CSG-index Distribution by Stenosis Stage
(Violin + IQR box + Jitter strip; n=118)
CSG-index Value
1.0
0.5
0.0
-0.5
-1.0
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p<0.001
p<0.001
*
p=0.029
(Grade 1 vs 2)
Grade 0: No stenosis (n=71)
Grade 1: <50% stenosis (n=26)
Grade 2: ≥50% stenosis (n=21)
Mean
Median
μ=-0.659
Med=-0.648
SD=0.244
μ=-0.340
Med=-0.325
SD=0.329
μ=-0.033
Med=-0.080
SD=0.350
Grade 0
(No Stenosis)
n=71
Grade 1
(<50%)
n=26
Grade 2
(≥50%)
n=21