IJC Heart & Vasculature 53 (2024) 101433

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

Performance of an artificial intelligence-guided quantitative coronary computed tomography algorithm for predicting myocardial ischemia in real-world practice

Ronald P. Karlsberg [a,*], Nick S. Nurmohamed [b,c,d], Carlos G. Quesada [a], Bruce A. Samuels [a], Suhail Dohad [a], Lauren R. Anderson [a], Tami Crabtree [e], James K. Min [e], Andrew D. Choi [b], James P. Earls [b,e]

[a] Cardiovascular Research Foundation of Southern California – Cedars-Sinai Smidt Heart Institute, Los Angeles, CA, USA
[b] The George Washington University School of Medicine, Washington, DC, USA
[c] Department of Cardiology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands
[d] Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands
[e] Cleerly Inc., Denver, CO, USA

Traditionally, noninvasive stress testing with nuclear perfusion imaging modalities as single-photon emission computed tomography (SPECT) and position emission tomography (PET) has been the gold standard for detection of myocardial ischemia [1]. Up to 50 % of patients suspected of CAD has myocardial ischemia in at least one vascular territory according to [^{15}O]H_2O PET [2]. However, these approaches are associated with a high cost as well as radiation burden, in contrast to coronary CT angiography (CCTA)[3,4]. Therefore, recent efforts have investigated the use of anatomical characteristics from CCTA analyzed by artificial intelligence (Atherosclerosis Imaging-Quantitative Computed Tomopgraphy [AI-QCT], Cleerly Inc, Denver, CO)[5–8] to analyze the probability of vessel-specific coronary ischemia. In two controlled research settings, this novel algorithm (AI-QCT$_{ISCHEMIA}$) showed high accuracy for predicting reduced fractional flow reserve (FFR), at least similar to FFR$_{CT}$, and has shown important value for major adverse cardiovascular events prognostication [9,10]. The present analysis aimed to serve as a novel investigation of the diagnostic accuracy of the recently developed algorithm for prediction of vessel-based ischemia in a real-world setting.

In this single center study, patients suspected of coronary artery disease (CAD) who underwent both CCTA as well as invasive coronary angiography were included. CCTA exams were analyzed using the AI-QCT algorithm including AI-QCT$_{ISCHEMIA}$. As described previously, the AI-QCT$_{ISCHEMIA}$ algorithm utilizes 37 parameters of stenosis, plaque characterization, plaque diffuseness and vascular morphology derived from AI-QCT in a random forest model to predict the presence of myocardial ischemia as defined by a reduced FFR $\leq$ 0.8.[9] AI-QCT$_{ISCHEMIA}$ was previously developed, internally and externally validated in the multicenter Computed Tomographic Evaluation of Atherosclerotic Determinants of Myocardial Ischemia (CREDENCE) and Prospective Comparison of Cardiac PET/CT, SPECT/CT Perfusion Imaging and CT Coronary Angiography With Invasive Coronary Angiography (PACIFIC-1) trials. In the present study, the performance of AI-QCT$_{ISCHEMIA}$ was compared to fractional flow reserve derived from

Table 1
Performance of AI-QCT$_{ISCHEMIA}$ versus FFR$_{CT}$ for predicting of coronary ischemia.

Endpoint	AI-QCT$_{ISCHEMIA}$	FFR$_{CT}$	p-value
Per-vessel			
Sensitivity	82 % (14/17)	94 % (16/17)	0.308
Specificity	76 % (19/25)	44 % (11/25)	0.031
Accuracy	79 % (33/42)	64 % (27/42)	0.133
AUC	0.87	0.85	0.825
Per-patient			
Sensitivity	88 % (14/16)	88 % (14/16)	1.000
Specificity	79 % (15/19)	47 % (9/19)	0.083
Accuracy	83 % (29/35)	66 % (23/35)	0.134
AUC	0.81	0.89	0.406

AUC, area under the curve, AI-QCT, atherosclerosis imaging-quantitative computed tomography; FFR$_{CT}$, fractional flow reserve from CT.

* Corresponding author at: Cardiovascular Research Foundation of Southern California – Cedars-Sinai Smidt Heart Institute, Los Angeles, CA, USA.
E-mail address: karlsberg@cvmg.com (R. P. Karlsberg).

https://doi.org/10.1016/j.ijcha.2024.101433
Received 15 March 2024; Received in revised form 7 May 2024; Accepted 24 May 2024
Available online 31 May 2024

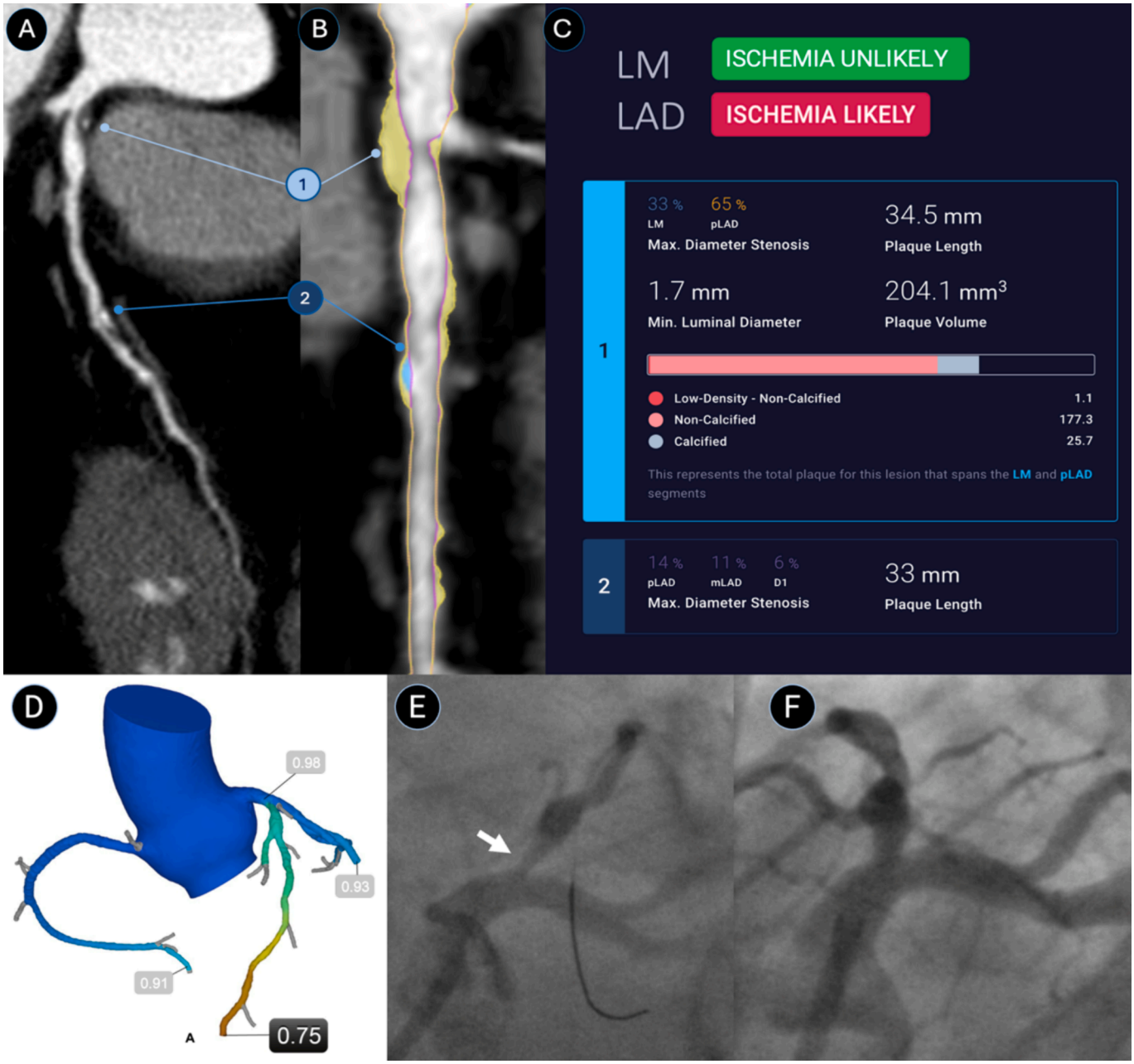

Fig. 1. AI-QCT$_{ISCHEMIA}$ case example. 50-year old male with new-onset stable chest pain. CCTA curved reformat depicts plaque in the LM and LAD (A). AI-QCT depicts predominantly non-calcified plaque (yellow overlay) in the LM/pLAD and mixed plaque (blue overlay) in the mid vessel (B). AI-QCT$_{ISCHEMIA}$ depicts 2 plaques, one extending from the LM (33% stenosis) to the proximal LAD (65% stenosis), the second plaque has a maximal stenosis of 14% (C). AI-QCT$_{ISCHEMIA}$ determined ischemia likely in the LAD, but not in the LM. This was concordant with a reduced FFR$_{CT}$ of 0.75 (D). It was also concordant with invasive angiography where both a 70% stenosis as well as a reduced invasive FFR of 0.67 were found in the pLAD (E). The patient underwent successful placement of a drug-eluting stent with TIMI-3 flow result (F). AI-QCT, atherosclerosis imaging-quantitative coronary computed tomography; CCTA, coronary CT angiography; FFR, fractional flow reserve; FFR$_{CT}$, fractional flow reserve from CT; LM, left main; LAD, left anterior descending; TIMI, Thrombolysis in Myocardial Infarction. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

CCTA (FFR$_{CT}$ Heartflow Inc, Redwood City, CA for the prediction of a reduced invasive FFR (FFR $\leq$ 0.8) or instantaneous wave-free ratio (iFR $\leq$ 0.89) as reference standard for invasive vessel-based ischemia. The analysis was restricted to vessels with an AI-QCT$_{ISCHEMIA}$, FFR$_{CT}$ and invasive measurement available in the main epicardial coronary vessels (left main, anterior descending coronary artery, right coronary artery, and circumflex coronary artery). Predictive performances were assessed using measures of accuracy (sensitivity, specificity and overall accuracy) an area under the receiver operating characteristic curve (AUC) analysis, both on a per-vessel and a per-patient basis. AUCs were compared using a DeLong test. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

A total of 35 patients and 42 vessels were included in the analysis. Mean age was 69.4 $\pm$ 10.0 years, 9 (26 %) patients were female, 22 (63 %) patients had hypertension, 4 (11 %) patients had diabetes, 17 (49 %) patients had a history of smoking and 29 (83 %) patients had dyslipidemia. AI-QCT$_{ISCHEMIA}$ achieved a sensitivity of 82 %, a specificity 76 % and an accuracy of 79 % for predicting vessel-based ischemia. For FFR$_{CT}$, these measures were 94 %, 64 % and 44 %, respectively (Table 1). The AUCs were comparable between the two approaches: AI-QCT$_{ISCHEMIA}$

achieved an AUC of 0.87 and FFR_{CT} achieved an AUC of 0.85 (p = 0.825). Specificity was higher for AI-$QCT_{ISCHEMIA}$ when compared to FFR_{CT} (76 % vs 44 %; p = 0.031). On a per-patient basis, AI-$QCT_{ISCHEMIA}$ achieved a sensitivity of 88 %, a specificity 79 % and an accuracy of 83 % for predicting ischemia. For FFR_{CT}, these measures were 88 %, 47 % and 79 %, respectively. Again, AI-$QCT_{ISCHEMIA}$ and FFR_{CT} achieved a similar AUC (0.81 vs. 0.89; p = 0.406). A case example showing the concordance between AI-$QCT_{ISCHEMIA}$, FFR and FFR_{CT} is shown in Fig. 1.

In this real-world analysis, AI-$QCT_{ISCHEMIA}$ showed high diagnostic accuracy and high specificity for vessel-specific ischemia in this population. These data demonstrate the feasibility of artificial intelligence-guided CCTA for predicting presence of functional myocardial ischemia based on anatomical characteristics, and thus its potential to expand its use as a 3-in-1 approach including assessment of ischemia beyond atherosclerosis and stenosis alone. The current single center study was limited by a small sample size, and lack of a standardized protocol for invasive ischemia assessment (i.e. both FFR and iFR were used), due to the real-world setting. Results may vary in study populations without symptoms, less disease, and a lower incidence of patients with parameters of ischemia. Future larger, multicenter studies are required to further investigate the performance of this novel algorithm.

CRediT authorship contribution statement

Ronald P. Karlsberg: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Data curation, Conceptualization. **Nick S. Nurmohamed:** Writing – review & editing, Writing – original draft. **Carlos G. Quesada:** Writing – review & editing, Data curation. **Bruce A. Samuels:** Writing – review & editing, Data curation. **Suhail Dohad:** Writing – review & editing, Data curation. **Lauren R. Anderson:** Writing – review & editing, Data curation. **Tami Crabtree:** Writing – review & editing, Formal analysis. **James K. Min:** Writing – review & editing. **Andrew D. Choi:** Writing – review & editing, Methodology. **James P. Earls:** Writing – review & editing, Visualization.

Declaration of competing interest

NSN reports grants from the Dutch Heart Foundation (Dekker 03–007-2023–0068), European Atherosclerosis Society (2023), research funding/speaker fees from Cleerly, Daiichi Sankyo and Novartis, and is co-founder of Lipid Tools. ADC reports grant support from GW Heart and Vascular Institute, equity in Cleerly, Inc and consulting with Siemens Healthineers. TC, JKM and JPE are employees of Cleerly Inc. The other authors report no relevant disclosures.

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