Clinical Evaluation of Automatic Coronary Artery Disease Reporting and Data System (CAD-RADS TM) in Coronary CT Angiography Using Convolutional Neural Networks

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Research Article

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Abstract

Background: The coronary artery disease reporting and data system (CAD-RADS^{TM}) was recently introduced for standard reporting. We aimed to evaluate the utility of an automatic post-processing and reporting system based on CAD-RADS in suspected CAD patients.

Methods: The clinical evaluation was encompassed 346 patients who underwent coronary computed tomography angiography (CCTA). We compared deep learning (DL)-based CCTA with Readers for classification of CAD-RADS with commercially-available automated segmentation and manual post-processing in a prospective validation cohort.

Results: Compared with invasive coronary angiography (ICA), the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of DL model for diagnosis of CAD were 79.02%, 86.52%, 89.50%, 73.94% and 82.08%, respectively. There was no significant difference between the DL-based and Readers-based CAD-RADS grading in CCTA. The consistency test showed that the *Kappa* value between the model and Readers was 0.775 (*95% CI*: 0.728-0.823, $P < 0.001$), 0.802 (*95% CI*: 0.756-0.847, $P<0.001$), and 0.796 (*95% CI*: 0.750-0.843, $P < 0.001$), respectively. This system reduces the time consumed from 14.97 ± 1.80 min to 5.02 ± 0.8 min ($P < 0.001$).

Conclusion: The standardized report of DL-based CAD-RADS in CCTA can accurately evaluate suspected CAD patients with time-saving, and has good consistency with the radiologists.

Background

Coronary artery disease (CAD) is a global medical problem and a leading cause of morbidity and mortality [1]. Patients with CAD are at risk for ischemic stroke, myocardial infarction, and cardiovascular death [2]. Coronary computed tomography angiography (CCTA) is increasing being used as a noninvasive evaluation to assess patients with chest pain because it has high sensitivity and specificity for the detection of CAD [3, 4]. Moreover, unlike functional stress testing, CCTA provides an anatomical assessment of the coronary arteries, allowing for the detection and quantification of obstructive and non-obstructive atherosclerotic plaque [5].

The coronary artery disease reporting and data system (CAD-RADS™) was introduced for standard reporting and decision making since 2016 [6]. Unlike prior classifications of CAD that were based on the number of affected vessels, CAD-RADS classify patients based on the highest grade of coronary artery stenosis. Xie *et al.* recently reported that CAD-RADS effectively identified patients at risk for myocardial infarctions and all-cause mortality to a similar degree as the CAD extent classification and Duke CAD Index [7].

Computer-aided diagnosis has been rapidly growing and active in radiological assessment [8, 9]. Deep convolutional neural networks (CNN) are a newly emerging form of computer-aided diagnosis analysis that allow the automatic extraction of features and supervised learning of large amounts of data to form quantitative decisions [10]. Accumulated evidence suggests that deep learning analysis might be a potential alternative to conventional hand-crafted methodologies for solving pattern recognition and imaging classification problems [11, 12]. Currently, no data focused on combining CNN and CCTA to solve lesion detection and classification based on CAD-RADS.

Thus, we aimed to assess the utility of an automatic post-processing and reporting system based on CAD-RADS™ in suspected CAD or CAD patients. We also sought to investigate the performance of DL-based CCTA for assist radiologists in their daily work and establish a time-saving work process.

Methods

The present study was approved by the institutional review board of the Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology and was conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

Patients

We retrospectively searched database of CCTA that were performed from July 2017 to December 2019. The study population consisted of 346 consecutive patients who were suspected of CAD or CAD was included (Figure 1). General exclusion criteria were poor quality images could not be diagnosis, images couldn't be recognized or analyzed by DL, patients with incomplete records or previously underwent percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) or other cardio surgery.

CCTA images acquisition and analysis

Multidetector row CT imaging was performed with dual-source CT scanner (Somatom Definition, Siemens Medical Solutions, Forchheim, Germany) and 256-slice CT scanner (Brilliance iCT; Philips Healthcare, Cleveland, OH). Heart rate control (HR≥65 beats/min) was performed with beta-blockers before the scan. Scanning parameters were as following: Detector collimation 128×2×6mm, tube voltage 120kV, tube current 280 mAs. For contrast enhancement, 60-80mL of iopromide (370mgI/mL, Bayer Schering Pharma Germany) followed by 30-40 mL of pure saline with a flow rate of 4-5 mL/sec. The iodine contrast agent was automatically triggered into descending aorta of 100 HU threshold units. Then the scanning was performed during an inspiratory breath hold of 8 to 14 s after delay of 2s. The reconstruction images were automatic send to a workstation (CoronaryDoc, Shukun technology, Beijing, China) equipped with coronary analysis software tool (Computer Aided Diagnosis of Coronary Artery, Version 1.8, Shukun technology, Beijing, China).

Deep Learning

The patients in the test set were under ICA examination with an interval of less than 30 days after CCTA procedure. We have previously reported the validation of our deep learning system [13, 14]. Before training, the aorta, coronary artery and plaques were labeled on each image by a multi-layer manually annotation system consisting of multiple layers of trained graders. The first layer of graders is comprised of radiologists who had knowledge of medical imaging and coronary anatomy. The second layer of graders is comprised of radiologists with more than three years of work experience in radiology, which is a preliminary inspection of the accuracy of the label. The third and final layer of graders was consistence of experienced experts with over five years of work experience who verify the correctness of label of each image. In this study, we adopted an improved 3-dimensional (3-D) U-Net architecture added a Bottle-Neck model for segmentation coronary arteries and aorta, then a Growing Iterative Prediction Network (GIPN) model was developed to solve the problem of vascular segmentation fracture, final the full coronary tree segmentation was obtained [15]. Based

on coronary tree segmentation, multiple planar reformat (MPR), curve planar reformat (CPR), maximum intensity projection (MIP) and volume rendering (VR) images were reconstructed. To detect stenosis, we developed a 3D segmentation neural network and a one-dimensional sequence checking hybrid technique [16]. Firstly, a 3D segmentation neural network was applied to MRP and CPR images to detect stenosis, and then a one-dimensional sequence checking algorithm was used to reduce false positive results (Figure 2).

Three readers with 5 years of experience in cardiac CT imaging diagnosis recorded the CAD-RADS classification based on the degree of coronary stenosis (CAD-RADS 0: 0%, CAD-RADS 1: 1-24%, CAD-RADS 2: 25-49%, CAD-RADS 3: 50-69%, CAD-RADS 4A: 70-99%, CAD-RADS 4B: Left main > 50% or 3-vessel disease, 70-99%, CAD-RADS 5: 100%) according to the CAD-RADS consensus document [6]. Structured report including CAD-RADS category was showed based on the model independently. 100 patients were randomly selected for time consumption (including post-processing, report-writing, typesetting and print) analysis. CAD was defined as stenosis > 50% in coronary artery segment ≥ 2mm in diameter.

Statistical Analysis

Continuous variables were presented as mean ± SD. Categorical variables were presented as percentages or absolute values. We used either the chi-square test, or Fisher's exact test as appropriate for categorical variables. The diagnostic performance of CAD with DL-based CCTA was determined as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy by comparison with ICA as the standard of reference. The agreement of the CAD-RADS categories was compared between Readers and the model using the linear weighted kappa identity test. P 0.05 was considered as statistical significance. All statistical analysis was performed using SPSS version 18 (SPSS, Inc., Chicago, IL) and MedCalc Statistical Software version16.8.4.0 (Ostend, Belgium).

Results

Table 1 showed baseline characteristics of the 346 study participants (mean age: 62.9 years; range from 33 to 85 years).

Table 1
Basic Characteristics of the included patients

Characteristics	Total (N = 346)
Age	62.9 ± 9.1
Male, No. (%)	191 (55)
BMI (Kg/m^2)	25.2 ± 7.3
Hypertension	210 (60.7)
DM	93 (26.9)
CKD	37 (10.7)
TG	2.0 ± 1.7
TC	4.7 ± 1.1
HDL-C	1.2 ± 0.3
LDL-C	2.8 ± 0.9
SCR	71.4 ± 38
BUN	5.6 ± 1.9
EF (%)	59.6 ± 5.8

BMI = body mass index, DM = diabetes mellitus, CKD = chronic kidney disease, TG = triglyceride, TC = total cholesterol, HDL-C = high density lipoprotein-C, LDL-C = low density lipoprotein-C, SCR = serum creatinine, BUN = blood urea nitrogen, EF = ejection fraction

Of the 346 patients, 181 (52.3%), 181 (52.3%), 180 (52.0%), 180 (52.0%) were diagnosed CAD by DL model, Reader 1, Reader 2, and Reader 3, respectively. There were no statistical differences between readers and DL model for detecting CAD. The positive predictive value, negative predictive value, sensitivity, specificity and accuracy of the DL model for diagnosis of CAD were 79.02%, 86.52%, 89.50%, 73.94% and 82.08%, respectively when using ICA as the reference standard (Table 2).

Table 2. Diagnostic performance of DL for detecting CAD compared with Readers

Variable	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
DL	162	122	19	43	79.02 (72.68-84.25)	86.52 (79.51-91.49)	89.50 (83.87-93.40)	73.94 (66.43-80.31)	82.08 (77.62-86.54)	0.83 (0.78-0.87)
Reader 1	164	124	17	41	80.00 (73.73-85.12)	87.94 (81.13-92.61)	90.61 (85.15-94.27)	75.15 (67.71-81.39)	83.24 (78.92-87.55)	0.84 (0.80-0.88)
Reader 2	160	121	20	45	78.05 (71.63-83.39)	85.82 (78.70-90.91)	88.89 (83.14-92.91)	72.89 (65.35-79.35)	81.21 (76.64-85.78)	0.82 (0.78-0.86)
Reader 3	163	124	17	42	79.51 (73.21-84.69)	87.94 (81.13-92.61)	90.56 (85.07-94.23)	74.70 (67.26-80.97)	83.95 (78.60-87.30)	0.84 (0.80-0.88)

DL = Deep Learning, CAD = coronary artery disease, TP = true positive, TN = true negative, FP = false positive, FN = false negative, PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve.

The distribution classification of CAD-RADS by DL model assessed of 38 CAD-RADS 0, 19 as CAD-RADS 1, 108 as CAD-RADS 2, 90 as CAD-RADS 3, 58 as CAD-RADS 4A, 24 as CAD-RADS 4B and 9 as CAD-RADS 5 (Fig. 3). As shown in Table 3, agreement between the DL model and reader 1 for CAD-RADS classification was good (*Kappa* = 0.775; *95% CI*: 0.782–0.823). In addition, agreement between the DL model and reader 2 working in consensus was excellent (*Kappa* = 0.802; *95% CI*: 0.756–0.847). Agreement between the DL model and reader 3 was also good (*Kappa* = 0.796; *95% CI*: 0.750–0.843).

Table 3
Agreement between the DL model and Readers for CAD-RADS classification

Comparison	Linear Weighted Kappa Value	*P* Value
DL vs. Reader 1	0.775 (0.728–0.823)	< 0.001
DL vs. Reader 2	0.802 (0.756–0.847)	< 0.001
DL vs. Reader 3	0.796 (0.750–0.843)	< 0.001
DL = Deep Learning, CAD-RADS = Coronary Artery Disease-Reporting and Data System		

Consumed time (including post-processing, report-writing, typesetting and print) of three readers was 14.51 ± 1.92 min, 15.28 ± 1.64 min and 15.11 ± 1.83 min, respectively. Compared with DL, the average time consumed was reduced from 14.97 ± 1.80 min to 5.02 ± 0.8 min ($P < 0.001$, Fig. 4). We also found that the consumed

time was different in CAD patients and non-CAD patients by manually recognized, while there was no significant different in DL.

Discussion

In this study, we first developed a novel CNN model with CCTA images and evaluated its performance for categorized coronary artery stenosis based on CAD-RADS. Then, the utilization of automatic post-processing and reporting system based on CAD-RADS™ was assessed in suspected CAD patients.

As a standardized reporting system of CCTA, the primary aim of CAD-RADS is to facilitate the consistent fashion among physicians, including recommendations for further investigations and management [6, 17]. Moreover, the common language of coronary artery stenosis provided by this reporting system increase the clarity between radiologists and clinicians in diagnosis and treatment planning of suspected CAD patients. In addition, the achieved standardization of reporting will be of benefit in education, research, peer review, and quality assurance and may ultimately result in improved quality of care [18].

Cancer imaging standardized reporting systems such as Lung-RADS and BI-RADS have been widely accepted by offering reliable and consistent assessment categories to radiologists and physicians who will supply appropriate management recommendations for specific patients. Structured reporting tools have applied in cardiac imaging for improving imaging data integrity and then establishing standard databases with education, patient care and research purposes [19]. Structured reporting platforms based on automated CAD-RADS calculations have been proposed by Dewey *et al.* [20] and Szilveszter *et al.* has revealed good agreement between manual and automated CAD-RADS classification using a structured reporting platform [21]. Through previous methods for automated CAD or CAD-RADS assessment showed strong agreement and inter-observer reproducibility [22, 23]. However, no machine learning or DL models have been used in these studies.

Recently, promising applications of machine learning or artificial intelligence (AI) have been used in cardiovascular image and cardiology for processing several algorithms that are already in routine clinical use [24, 25]. These algorithms are likely to provide a process to improve quality and speed of acquisition, reduce manual post processing, measurement and manual report writing time, and allow prompt diagnoses, which in turn would improve workflow and patient care. Moreover, these could facilitate screening programs and promote to establish more effective referral mechanism in medicine, particularly in remote or low-resource areas, leading to a broad clinical and public health impact [26]. In addition, they encourage researchers to improve the performance of future models and help drive the field forward.

Machine learning algorithms have been extensively used for optimization of information extraction from CCTA. A two-step support vector machine (SVM) based learning with CCTA was established by Kang *et al.* [27] for detecting non-obstructive and obstructive CAD and resulted in an accuracy of 94% and an AUC of 0.94 which had a higher accuracy than the present study. However, only two classifications were used in the study and obstructive CAD was defined as lesion with stenosis ≥ 25%. CAD-RADS classification system was applied and we used the widely accepted definition of CAD (lesion with stenosis ≥ 50%) in our study. Moreover, a small CCTA datasets with 42 patients were included in the study. While our study has a relatively larger

sample size as 346 patients was selected in the analyiss. In addition, our DL platform was trained and validated using the Digital Imaging and Communications in Medicine (DICOM) standards make the CCTA images from different manufactures (dual-source CT and Philips ICT) reasonably consistent. Finally, our study developed a DL model which was able to automatically extract coronary arteries and detect stenosis.

Accumulate researches revealed automatic detection and quantification with CCTA images. Schuhbaeck *et al.* evaluated an interscan reproducibility of quantitative measurements of coronary plaque volumes using a standardized automated method [28]. A recent study showed that CCTA-derived plaque markers combined with a DL based CT-FFR portended predictive value to identify lesion-specific ischemia when compared to CCTA stenosis grading alone [29]. Quantification of coronary artery calcium score (CACS) derived from CCTA with DL algorithm has also been validated accurately measured [30, 31]. A previous study demonstrated that a machine learning algorithm based CT-FFR value was able to assess the functional significance of CAD and make the therapeutic decision. They showed excellent performance (sensitivity of 97%, specificity of 100%, PPV 100%, NPV of 97%, and accuracy of 99%) of ML based CT-FFR with CCTA in determining the appropriate treatment strategy [32]. However, few studies focus on DL based CCTA using CAD-RADS for stratifying the risk of suspected CAD patients. The present study constitutes to evaluate the feasibility of CAD-RADS classifications by using the DL based on CCTA images (Fig. 5).

Some limitations in the study should be addressed. First, this was a retrospective analysis of a relatively small sample size from a signal center. Prospective multicenter studies of large samples will enhance the application of CAD-RADS among cardiologists and radiologists. Second, in order to restrict our analysis, we did not include CAD-RADS modifiers to describe patients with stents (modifier S), vulnerable plaque features (modifier V), or grafts (modifier G). Further studies should include more patients into training set and test of DL to improve CAD-RADS classification scheme.

Conclusion

The standardized report of DL-based CAD-RADS in CCTA images can accurately evaluate suspected CAD patients with time-saving, and has excellent consistency with the radiologists.

Abbreviations

CAD-RADS: coronary artery disease reporting and data system; CCTA: coronary computed tomography angiography; DL: deep learning; ICA: invasive coronary angiography; CAD: coronary artery disease; CNN: convolutional neural networks; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; GIPN: Growing Iterative Prediction Network; MPR: multiple planar reformat; CPR: curve planar reformat; MIP: maximum intensity projection; VR: volume rendering; PPV: positive predictive value; NPV: negative predictive value.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jianwei Xiao, Yun Hu, Zuoqin Li and Ning Guo. The first draft of the manuscript was written by Zengfa Huang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research was approved by the Institutional Review Board of the Clinical Research Institute at The Central Hospital of Wuhan.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

References

1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C *et al*: **Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association**. *Circulation* 2017, **135**(10):e146-e603.
2. Connolly SJ, Eikelboom JW, Bosch J, Dagenais G, Dyal L, Lanas F, Metsarinne K, O'Donnell M, Dans AL, Ha JW *et al*: **Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial**. *Lancet* 2018, **391**(10117):205–218.
3. Investigators S-H, Newby DE, Adamson PD, Berry C, Boon NA, Dweck MR, Flather M, Forbes J, Hunter A, Lewis S *et al*: **Coronary CT Angiography and 5-Year Risk of Myocardial Infarction**. *N Engl J Med* 2018, **379**(10):924–933.
4. Adamson PD, Williams MC, Dweck MR, Mills NL, Boon NA, Daghem M, Bing R, Moss AJ, Mangion K, Flather M *et al*: **Guiding Therapy by Coronary CT Angiography Improves Outcomes in Patients With Stable Chest Pain**. *J Am Coll Cardiol* 2019, **74**(16):2058–2070.

5. Bittencourt MS, Hulten EA, Veeranna V, Blankstein R: **Coronary Computed Tomography Angiography in the Evaluation of Chest Pain of Suspected Cardiac Origin**. *Circulation* 2016, **133**(20):1963–1968.
6. Cury RC, Abbara S, Achenbach S, Agatston A, Berman DS, Budoff MJ, Dill KE, Jacobs JE, Maroules CD, Rubin GD *et al*: **CAD-RADS(TM) Coronary Artery Disease - Reporting and Data System. An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NASCI). Endorsed by the American College of Cardiology**. *J Cardiovasc Comput Tomogr* 2016, **10**(4):269–281.
7. Xie JX, Cury RC, Leipsic J, Crim MT, Berman DS, Gransar H, Budoff MJ, Achenbach S, B OH, Callister TQ *et al*: **The Coronary Artery Disease-Reporting and Data System (CAD-RADS): Prognostic and Clinical Implications Associated With Standardized Coronary Computed Tomography Angiography Reporting**. *JACC Cardiovascular imaging* 2018, **11**(1):78–89.
8. Lynch CJ, Liston C: **New machine-learning technologies for computer-aided diagnosis**. *Nat Med* 2018, **24**(9):1304–1305.
9. Ebigbo A, Mendel R, Probst A, Manzeneder J, Souza LA, Jr., Papa JP, Palm C, Messmann H: **Computer-aided diagnosis using deep learning in the evaluation of early oesophageal adenocarcinoma**. *Gut* 2019, **68**(7):1143–1145.
10. Song Y, Zhang YD, Yan X, Liu H, Zhou M, Hu B, Yang G: **Computer-aided diagnosis of prostate cancer using a deep convolutional neural network from multiparametric MRI**. *J Magn Reson Imaging* 2018, **48**(6):1570–1577.
11. Schmidhuber J: **Deep learning in neural networks: an overview**. *Neural Netw* 2015, **61**:85–117.
12. Alipanahi B, Delong A, Weirauch MT, Frey BJ: **Predicting the sequence specificities of DNA- and RNA-binding proteins by deep learning**. *Nat Biotechnol* 2015, **33**(8):831–838.
13. Chen M, Wang X, Hao G, Cheng X, Ma C, Guo N, Hu S, Tao Q, Yao F, Hu C: **Diagnostic performance of deep learning-based vascular extraction and stenosis detection technique for coronary artery disease**. *Br J Radiol* 2020, **93**(1113):20191028.
14. Huang Z, Xiao J, Xie Y, Hu Y, Zhang S, Li X, Wang Z, Li Z, Wang X: **The correlation of deep learning-based CAD-RADS evaluated by coronary computed tomography angiography with breast arterial calcification on mammography**. *Sci Rep* 2020, **10**(1):11532.
15. Yang G, Kitslaar P, Frenay M, Broersen A, Boogers MJ, Bax JJ, Reiber JH, Dijkstra J: **Automatic centerline extraction of coronary arteries in coronary computed tomographic angiography**. *Int J Cardiovasc Imaging* 2012, **28**(4):921–933.
16. Ronneberger O FP, Brox T.: **U-Net: convolutional networks for biomedical image segmentation**. **arXiv:1505.04597**. **https://arxiv.org/abs/1505.04597**. **Published May 18**, 2015. **Accessed March 12, 2018**.
17. Chandrashekhar Y, Min JK, Hecht H, Narula J: **CAD-RADS: A Giant First Step Toward a Common Lexicon?** *JACC Cardiovasc Imaging* 2016, **9**(9):1125–1129.
18. Nieman K, Hoffmann U: **Cardiac computed tomography in patients with acute chest pain**. *Eur Heart J* 2015, **36**(15):906–914.

19. Faggioni L, Coppola F, Ferrari R, Neri E, Regge D: **Usage of structured reporting in radiological practice: results from an Italian online survey**. *Eur Radiol* 2017, **27**(5):1934–1943.
20. Dewey M: **Structure or entropy in reporting cardiac CT findings**. *Int J Cardiovasc Imaging* 2016, **32**(11):1657–1658.
21. Szilveszter B, Kolossvary M, Karady J, Jermendy AL, Karolyi M, Panajotu A, Bagyura Z, Vecsey-Nagy M, Cury RC, Leipsic JA *et al*: **Structured reporting platform improves CAD-RADS assessment**. *J Cardiovasc Comput Tomogr* 2017, **11**(6):449–454.
22. Maroules CD, Hamilton-Craig C, Branch K, Lee J, Cury RC, Maurovich-Horvat P, Rubinshtein R, Thomas D, Williams M, Guo Y *et al*: **Coronary artery disease reporting and data system (CAD-RADS(TM)): Inter-observer agreement for assessment categories and modifiers**. *J Cardiovasc Comput Tomogr* 2018, **12**(2):125–130.
23. Abdel Razek AAK, Elrakhawy MM, Yossof MM, Nageb HM: **Inter-observer agreement of the Coronary Artery Disease Reporting and Data System (CAD-RADS(TM)) in patients with stable chest pain**. *Pol J Radiol* 2018, **83**:e151-e159.
24. Henglin M, Stein G, Hushcha PV, Snoek J, Wiltschko AB, Cheng S: **Machine Learning Approaches in Cardiovascular Imaging**. *Circ Cardiovasc Imaging* 2017, **10**(10).
25. Dey D, Slomka PJ, Leeson P, Comaniciu D, Shrestha S, Sengupta PP, Marwick TH: **Artificial Intelligence in Cardiovascular Imaging: JACC State-of-the-Art Review**. *J Am Coll Cardiol* 2019, **73**(11):1317–1335.
26. Kermany DS, Goldbaum M, Cai W, Valentim CCS, Liang H, Baxter SL, McKeown A, Yang G, Wu X, Yan F *et al*: **Identifying Medical Diagnoses and Treatable Diseases by Image-Based Deep Learning**. *Cell* 2018, **172**(5):1122–1131 e1129.
27. Kang D, Dey D, Slomka PJ, Arsanjani R, Nakazato R, Ko H, Berman DS, Li D, Kuo CC: **Structured learning algorithm for detection of nonobstructive and obstructive coronary plaque lesions from computed tomography angiography**. *J Med Imaging (Bellingham)* 2015, **2**(1):014003.
28. Schuhbaeck A, Dey D, Otaki Y, Slomka P, Kral BG, Achenbach S, Berman DS, Fishman EK, Lai S, Lai H: **Interscan reproducibility of quantitative coronary plaque volume and composition from CT coronary angiography using an automated method**. *Eur Radiol* 2014, **24**(9):2300–2308.
29. von Knebel Doeberitz PL, De Cecco CN, Schoepf UJ, Duguay TM, Albrecht MH, van Assen M, Bauer MJ, Savage RH, Pannell JT, De Santis D *et al*: **Coronary CT angiography-derived plaque quantification with artificial intelligence CT fractional flow reserve for the identification of lesion-specific ischemia**. *Eur Radiol* 2019, **29**(5):2378–2387.
30. Schuhbaeck A, Otaki Y, Achenbach S, Schneider C, Slomka P, Berman DS, Dey D: **Coronary calcium scoring from contrast coronary CT angiography using a semiautomated standardized method**. *J Cardiovasc Comput Tomogr* 2015, **9**(5):446–453.
31. Wang W, Wang H, Chen Q, Zhou Z, Wang R, Wang H, Zhang N, Chen Y, Sun Z, Xu L: **Coronary artery calcium score quantification using a deep-learning algorithm**. *Clin Radiol* 2019.
32. Tesche C, Vliegenthart R, Duguay TM, De Cecco CN, Albrecht MH, De Santis D, Langenbach MC, Varga-Szemes A, Jacobs BE, Jochheim D *et al*: **Coronary Computed Tomographic Angiography-Derived Fractional Flow Reserve for Therapeutic Decision Making**. *Am J Cardiol* 2017, **120**(12):2121–2127.

Figures

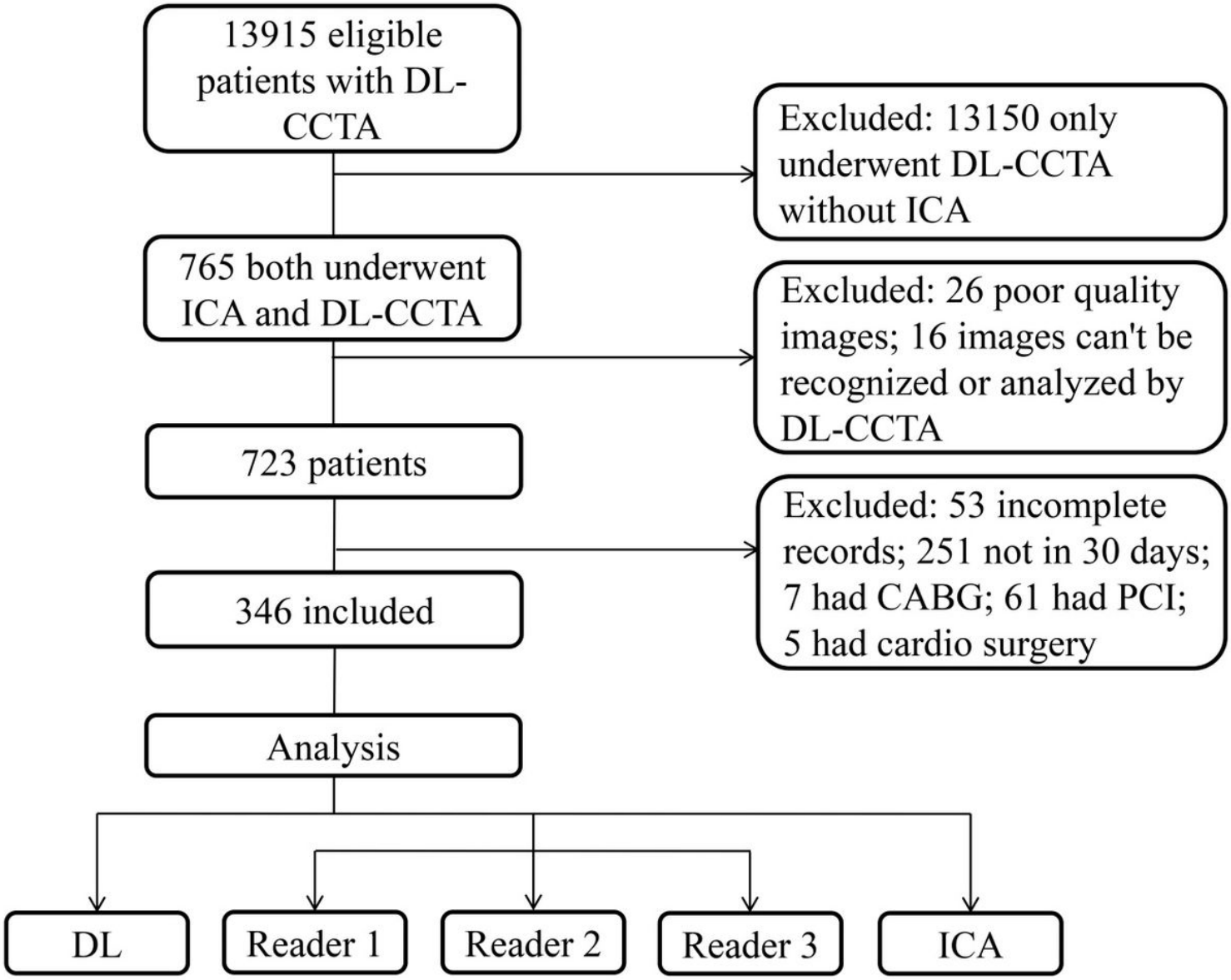

Figure 1

Flowchart illustrates exclusion criteria and final study population.

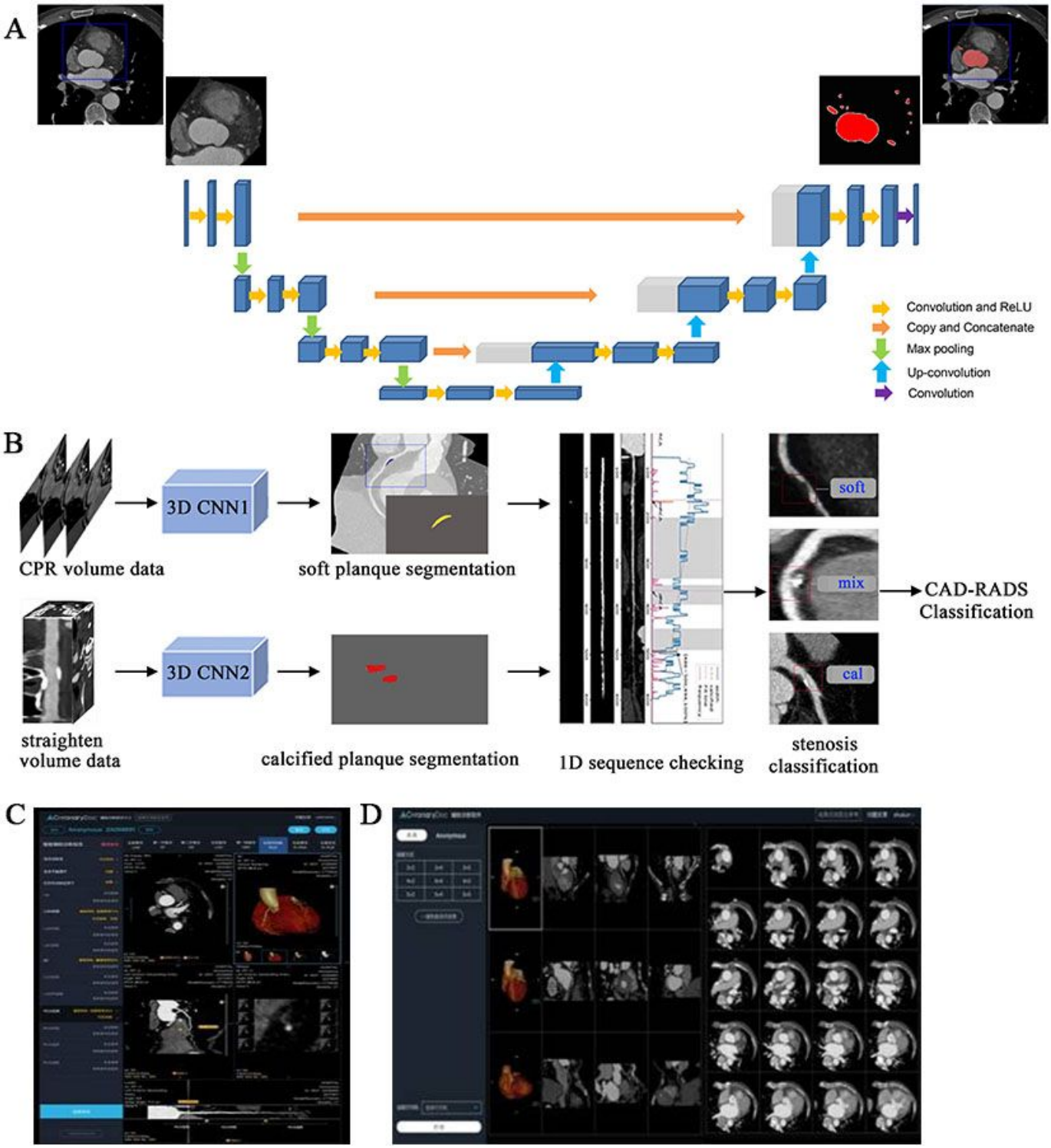

Figure 2

The flowchart of the process of the model; CNN Networks and DL based CCTA assistant diagnosis system. A, Diagram shows complete workflow of aorta, coronary artery and plaque labeling and segmentation network. Each blue box corresponds to a convolutional layer, with matrix size and depth indicated at each layer. Colored arrows indicate different operations: yellow = convolution and rectified linear unit (ReLU), orange = copy and concatenate from down-sampling path to up-sampling path, green = maximum pooling, blue = up-convolution and purple = convolution. The input is images from CCTA acquisition, whereas the output is the

aorta, coronary artery and plaque contours if these are detected on the image. B, CNN Networks for CAD-RADS classification. Plaques segmentation was used by a 3D UNET network on CPR image and straightened image respectively, and then the output results are modified and classified by a one-dimensional back-detection model, finally, CAD-RADS classification output according to the degree of stenosis. C&D, DL based CCTA assistant diagnosis system.

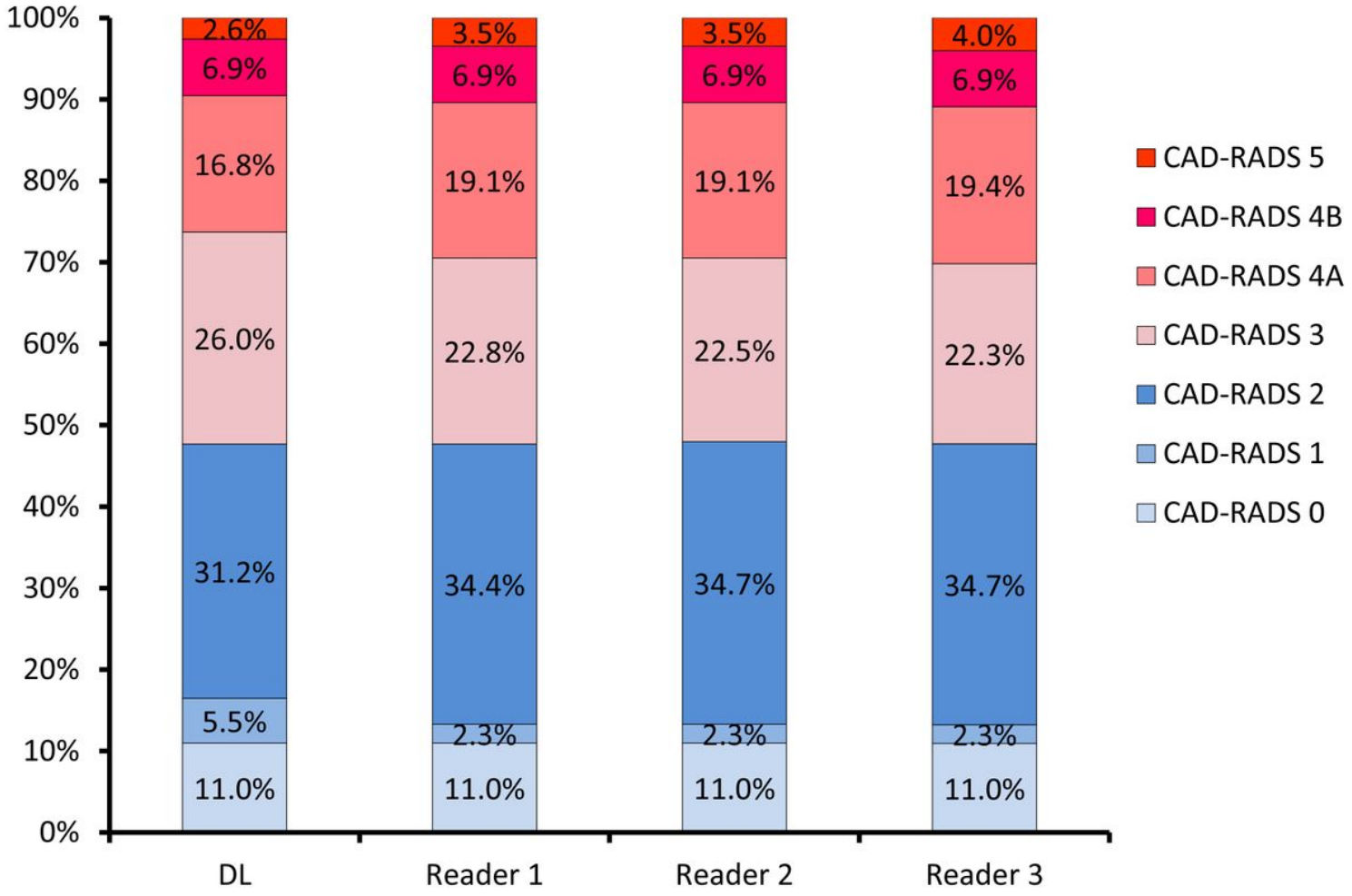

Figure 3

The distribution classification of CAD-RADS by DL and Readers.

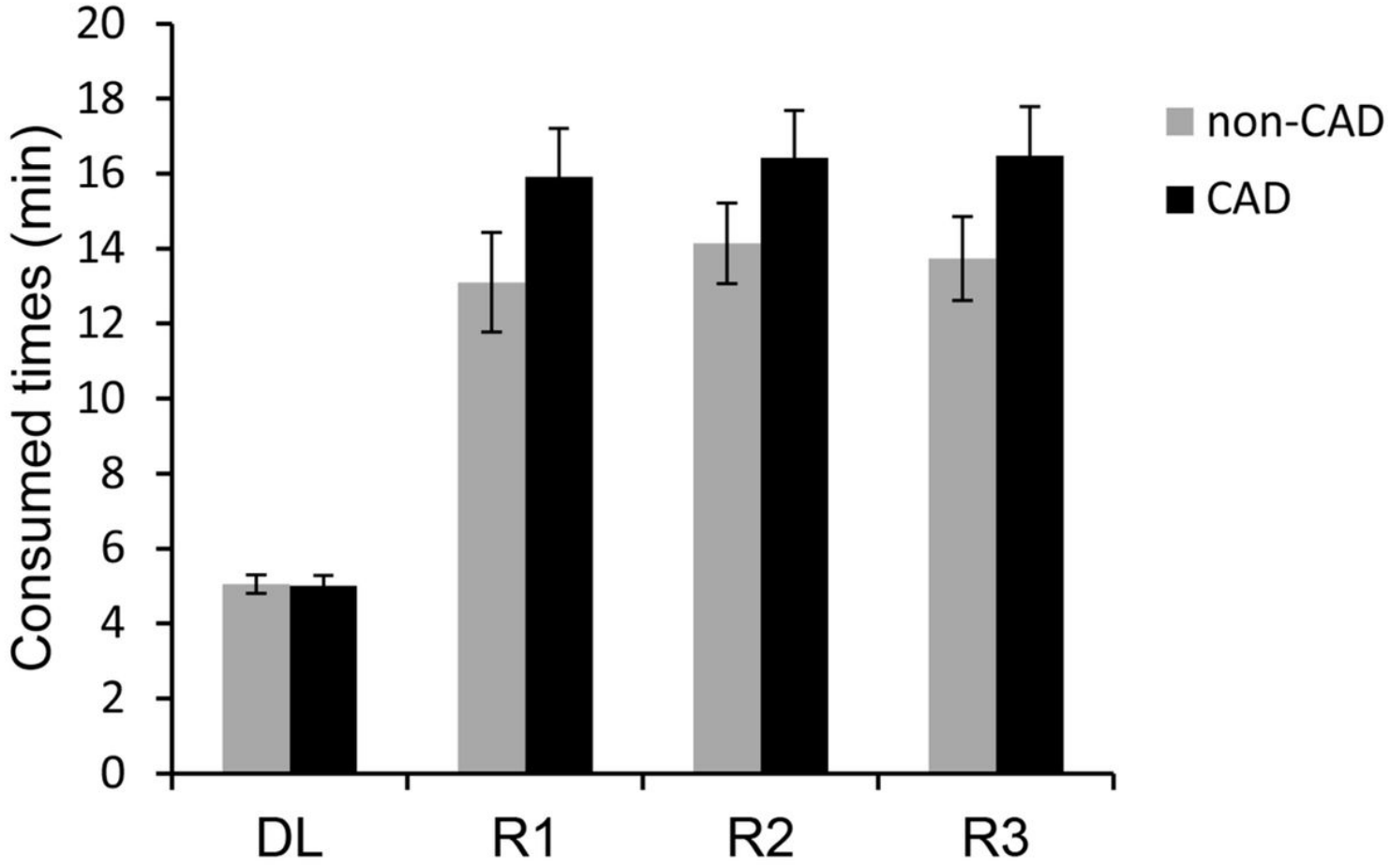

Figure 4

The comparison of consumed time between the DL and Readers.

Figure 5

DL-based CAD-RADS classification.