Predicting coronary artery calcified plaques using perivascular fat CT radiomics features and clinical risk factors

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Research Article

Keywords: Coronary artery, Plaque, Radiomics, Perivascular fat attenuation

Posted Date: February 21st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1263374/v1>

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Abstract

Background: This study was performed to investigate the value of the radiomics features of perivascular fat in predicting the texture of coronary artery plaques.

Methods: The data of 200 patients with coronary plaques were retrospectively reviewed. In total, 828 radiomics features were extracted for each lesion, and 12 features obtained after filtering screening were used to build a machine learning model. Clinical risk factors for hypertension, diabetes, and hyperlipidemia were collected, and a combined model was established. Decision curve analysis was used to evaluate the clinical utility of the model.

Results: The radiomics features of perivascular fat could significantly differentiate whether a plaque was calcified or not, and a correlation was found between age and plaque calcification among clinical risk factors. The discrimination of the combined model improved slightly after the addition of the age factor, and the areas under the receiver operating characteristic curves were 0.98 (95% confidence interval, 0.95–1.00) and 0.97 (95% confidence interval, 0.92–1.00) for the combined model training and testing groups, respectively. The sensitivity was 0.92 and 0.86 and the specificity was 0.99 and 1, respectively. Through decision curve analysis, the clinical usefulness of the combined model was demonstrated to be optimal in the four-group model.

Conclusions: The combined model established and validated based on enhanced computed tomography radiomics features and clinical risk factors has high value in predicting coronary artery calcified plaque.

Background

Coronary artery disease is a common cardiovascular disease that seriously endangers human health, and the most important pathological basis for the occurrence of this disease is atherosclerosis. When unstable atherosclerotic plaques rupture, become dislodged, or induce thrombosis, acute coronary syndrome is likely to occur and may even lead to death [1]. Coronary atherosclerotic plaques may be either calcified or non-calcified, and the latter easily become dislodged. Therefore, the analysis of plaque components is of great clinical value for prevention of plaque instability. Coronary computed tomography angiography (CCTA) has high-density resolution, and it can effectively detect and determine the composition of coronary plaques; however, its accuracy is limited [2, 3]. Perivascular adipose tissue (PVAT) is the adipose tissue that surrounds the outer membrane of blood vessels, and it is involved in the development of atherosclerosis [4]. Clinical studies have shown that coronary PVAT is correlated with the degree of coronary stenosis and the plaque stage [5–9]. CCTA facilitates visualization of the coronary PVAT. Radiomics, an emerging post-processing method, can be used for disease prediction and early diagnosis by extracting and quantifying useful features in medical imaging data [10]. This study was performed to investigate the value of predicting the nature of plaques by examining the computed tomography (CT) radiomics features of coronary PVAT in lesioned segments with plaques and patients' clinical risk factors.

Methods

Patients' information

We retrospectively reviewed images of patients diagnosed with vascular plaque lesions by CCTA at our hospital from June 2019 to May 2020. The patients were divided into a calcified plaque group and soft plaque group according to the imaging diagnosis. When a patient's image had multiple plaque lesions, the lesion with the clearest imaging features was selected for analysis. The inclusion criteria were the acquisition of complete CT-enhanced images strictly according to a fixed scan and no history of interventional therapy. The exclusion criteria were significant imaging noise or other quality problems in the image and soft plaques and calcified plaques within a single lesion. Data regarding age, sex, diseased blood vessels, hypertension, diabetes, and hyperlipidemia were collected from the medical records.

Image acquisition

Each patient underwent cardiac coronary plain and enhanced CT scans (Discovery CT750 or GE Optima CT680; GE Healthcare, Chicago, IL, USA). A total dose of 84 mL of iohexol contrast agent with 60 mL of saline was injected into the elbow vein through a high-pressure syringe at an injection rate of 4.5 mL/s. The acquisition parameters were as follows: tube voltage, 120 KVp; tube current, 450 to 480 mA; layer thickness, 0.625 mm; and layer spacing, 0.625 mm. Images were acquired in Digital Imaging and Communications in Medicine format from the workstation.

Medical image segmentation and feature extraction

According to the ITK-SNAP software application (www.itksnap.org), PVAT has a radial distance equal to the diameter of a blood vessel [10]. First, the plaque lesion was identified perpendicular to the vessel, and the PVAT was outlined layer by layer until the plaque completely disappeared. Feature extraction was further performed by Z-score normalization of the original image as well as determination of the region of interest by Artificial Intelligence Kit software (A.K. Software, version 3.3.0.R; GE Healthcare). The feature types included the first order, shape, gray-level co-occurrence matrix (GLCM), gray-level size zone matrix (GLSZM), and gray-level run-length matrix (GLRLM), as well as log and wavelet transformed features. The extracted features comprised 198 first order features, 14 shape features, 264 GLCM features, 176 GLSZM features, and 176 GLRLM features. The specific feature classification is shown in Table 1.

Table 1 All extracted features and classifications											
	original	log-sigma		wavelet							
		2.0	3.0	HHH	HHL	HLH	HLL	LHH	LHL	LLH	LLL
Shape	14										
First Order	18	18	18	18	18	18	18	18	18	18	18
GLCM	24	24	24	24	24	24	24	24	24	24	24
GLSZM	16	16	16	16	16	16	16	16	16	16	16
GLRLM	16	16	16	16	16	16	16	16	16	16	16

Feature selection and model building

The data were divided into a training set and validation set at a ratio of 7:3. The features were first screened in the training set using the minimum redundancy maximum relevance (mRMR) method. They were then further screened using the least absolute shrinkage and selection operator (LASSO) 10-fold cross-validation method to find the lambda value when the minimum binomial deviation was 0, and the features with coefficients that were not 0 at this point were retained. The final retained features were modeled with different machine learning models (logistics, K-nearest neighbor, support vector machine with radial basis function kernel [svmRadial], random forest, and neural network) and validated in the validation set. For clinical features, continuous variables such as age were analyzed using independent-samples t-tests or rank-sum tests. For categorical variables, the chi-square test or Fisher's exact test was used. Clinical risk factors were analyzed by one-way logistic regression; features with a p value of <0.05 were screened to construct a clinical risk factor model by logistic regression (p < 0.05 was an independent predictor), whereas features with a variance inflation factor of >10 were excluded and combined with the best radiomics model to construct a combined model. All statistical analyses were performed using R software version 3.5.0 (<https://www.r-project.org>), and p values of <0.05 were considered statistically significant with a two-tailed test.

Using the proposed combined model, columnar line plots were developed in the form of graphical representations. Calibration curves were created using the Hosmer–Lemeshow test [11, 12] to identify the agreement between the probabilities predicted by the columnar line plots and the actual rates of calcified plaques in the training and validation cohorts (Figure 1).

Results

Clinical characteristics

In total, 200 patients were included in this study; 105 (52.5%) had calcified plaques, and 95 (47.5%) had non-calcified plaques. The patients' basic clinicopathological characteristics were compared between the calcified and non-calcified plaque groups in the training and validation groups using univariate logistic regression analysis (Table 2). Univariate analysis showed no significant correlation of sex, hypertension, diabetes mellitus, or hyperlipidemia with the nature of the plaques (p > 0.05). Age (odds ratio, 0.953; 95% confidence interval [CI], 0.917–0.988; p < 0.01) was an independent predictor in the training group. The final univariate clinical model yielded an area under the curve (AUC) of 0.63 (95% CI, 0.54–0.72) in the training cohort and 0.60 (95% CI, 0.45–0.74) in the validation cohort.

Table 2
Comparison of patient and clinical risk factors in training and validation cohorts

	Training dataset (n = 141)			Validation dataset (n = 59)		
	Hard (n = 74)	Soft (n = 67)	<i>p</i>	Hard (n = 31)	Soft (n = 28)	<i>p</i>
Age (years)	61.95±10.15	57.76±10.04	0.007	63.58±9.02	59.93±9.92	0.212
Gender	0.234			0.470		
Male	38 (51.4%)	46(68.7%)		18(58.1%)	14(50.0%)	
Female	36(48.6%)	21(31.3%)		13(41.9%)	14(50.0%)	
Hypertension	0.538			0.090		
Yes	32(43.2%)	37(55.2%)		18(58.1%)	18(64.3%)	
No	42(56.8%)	30(44.8%)		13(41.9%)	10(35.7%)	
Diabetes	0.229			0.597		
Yes	10(13.5%)	6(9.0%)		6(19.4%)	5(17.9%)	
No	64(84.5%)	61(91.0%)		25(80.6%)	23(82.1%)	
Hyperlipidemia	0.248			0.066		
Yes	5(6.8%)	6(9.0%)		5(16.1%)	2(7.1%)	
No	69(93.2%)	61(91.0%)		26(83.9%)	26(92.9%)	
Diseased blood vessel	0.808			0.226		
LM	4(5.4%)	4(6.0%)		3(9.7%)	1(3.5%)	
LAD	43(58.1%)	40(59.7%)		18(58.1%)	16(57.1%)	
D	1(1.4%)	3(4.5%)		0(0)	2(7.1%)	
LCx	10(13.5%)	4(6.0%)		3(9.7%)	1(3.6%)	
RCA	14(18.9%)	15(22.3%)		7(22.5%)	8(28.6%)	
PDA	2(2.7%)	1(1.5%)		0(0)	0(0)	

Qualitative variables are expressed as n (%) and were analyzed using the chi-square test or Fisher's exact test, and quantitative variables are expressed as mean ± standard deviation and were analyzed using the t-test. A p value of <0.05 was considered statistically significant [11].

After extracting the features, two feature selection methods (mRMR and LASSO) were used to select features. First, mRMR was performed to eliminate redundant and irrelevant features, and 30 features were retained. Next, LASSO was performed to select an optimized subset of features to construct the final model, taking into account the imbalance of the data. Considering the imbalance of the data, a small number of features was oversampled, and 12 features were finally retained (Figure 2).

Machine learning models were built using different classifiers, including logistics, K-nearest neighbor, svmRadial, random forest, and neural network, and each classifier was cross-validated 100 times in the process of model building (Figure 3) and prediction performance (Figure 4). The relative standard deviation (RSD) was calculated as follows:

$$\text{RSD\%} = \sigma_{\text{AUC}} / \mu_{\text{AUC}} \times 100\%$$

Moreover, the performance of each model was verified in the validation set data.

Nomogram development and verification

Using a random forest model combined with clinical features to establish a prediction model nomogram, the receiver operating characteristic curve (Figure 5) showed that the radiomics features in both the non-calcified and calcified plaque groups had satisfactory prediction performance. The AUC in the training group was 0.97 (95% CI, 0.95–1.00), and that in the verification group was 0.97 (95% CI, 0.92–1.00). After combining clinical risk factors, the combined model predicted performance in the training group (AUC, 0.98 vs. 0.97;

95% CI, 0.95–1.00) and validation group (AUC, 0.97 vs. 0.97; 95% CI, 0.92–1.00). The accuracy and specificity were slightly improved (Table 3).

Table 3
Results of radiomics model, clinical model, and combined model

		Accuracy	AccuracyLower	AccuracyUpper	Sensitivity	Specificity	Pos.Pred.Value	Neg.Pred.Value
Radiomics	Train	0.929	0.873	0.965	1.000	0.865	0.870	1.000
	Test	0.898	0.792	0.962	0.857	0.935	0.923	0.879
Clinics	Train	0.603	0.517	0.684	0.634	0.590	0.388	0.797
	Test	0.627	0.491	0.750	0.650	0.615	0.464	0.774
Combined	Train	0.950	0.900	0.980	0.917	0.986	0.985	0.919
	Test	0.932	0.835	0.981	0.875	1.000	1.000	0.871

The best radiological classification model was combined with the predicted clinical characteristics to establish a nomogram (Figure 6a) [13, 14]. This nomogram was used to evaluate the consistency between the predicted probability and the actual observed value. The Hosmer–Lemeshow test was used to test the difference between these values. The training set $p = 0.535$, the validation set $p = 0.383$, and $p > 0.05$ indicated good agreement between the predicted probability and the actual observed value (Figure 6b). Using the decision analysis curve to evaluate the clinical utility of the model, the combined model also showed better results than the clinical model. These results indicate that the combination of radiomics features and clinical features provides more effective information for assessing whether a plaque is calcified and therefore has higher clinical application value (Figure 7) [15].

The x-axis represents the patient’s personal threshold probability (for example, $x = 0.6$ means that the probability of calcification is 60%), and the y-axis represents the net benefit. The green line represents the clinical factor model. The red line represents the combined model. The blue line represents the hypothesis that all patients have calcified plaques. The thin black line indicates the assumption that no patient has plaques. The net benefit is calculated by subtracting the proportion of all false-positive patients from the proportion of true positives, and then weighted according to the relative harm of previous treatment and the negative consequences of unnecessary treatment. The decision curve shows that the performance of the combined model is much higher than the remaining three items. This indicates that the radiographic images were used to predict plaque calcification in almost all patients in the current study. This was more accurate than the clinical factors, all of which were either calcified plaques or no calcification.

Discussion

Both invasive and noninvasive methods are available for detecting cardiovascular risk. Invasive methods, such as fractional blood flow reserve, are effective; however, they are also expensive and require surgery [16]. Noninvasive methods include CCTA, measurement of the circulating levels of proinflammatory mediators (e.g., high-sensitivity C-reactive protein, interleukin 6, interleukin 1b, and others), detection of high-risk plaque characteristics, and calculation of the perivascular fat attenuation index [17]. Detection of high-risk plaque characteristics has low sensitivity but high specificity for cardiovascular risk [18]. The perivascular fat attenuation index is significantly different between patients with obstructive coronary artery disease and non-atherosclerotic blood vessels, and it is positively correlated with the total coronary plaque burden [7, 19]. The combination model based on CCTA (perivascular fat attenuation index, risk factors, degree of atherosclerotic disease, and high-risk plaques) performed well in predicting cardiovascular mortality in the present study (AUC, 0.962; 95% CI, 0.940–0.983) [10].

Studies have revealed an interaction between the coronary artery wall and its surrounding fatty tissue (the PVAT). In the presence of vascular inflammation, the release of proinflammatory molecules from the diseased blood vessel wall will inhibit the differentiation and lipid accumulation of pre-PVAT adipocytes, resulting in lipolysis, reduced adipogenesis, and water accumulation within the PVAT [20]. The plaque composition is closely related to obstructive coronary stenosis and acute coronary syndrome [21]. The plaque configuration and composition are significantly different between non-calcified and calcified plaques [22]. Non-calcified plaques mainly contain lipids, old blood, and inflammatory cells; are relatively unstable; and may fall off with the impact of blood flow. Calcified plaques mainly contain fibrous tissue hyperplasia and calcification, and they have a hard texture. The chance of shedding is low, but local necrosis and embolism may occur.

In this study, we proposed a model that combines clinical risk factors and radiological characteristics of PVAT to predict plaque calcification. First, PVAT radiomics analysis can significantly distinguish between non-calcified and calcified plaques. The AUC in the training group was 0.97, and that in the validation group was 0.97. Second, our statistical analysis showed that age was the clinical factor most closely related to distinguishing calcified plaques. However, the performance of establishing clinical models is limited. Therefore, we developed a comprehensive model to test whether radiomics features and clinical factors are complementary. The nomogram based on the integrated model exhibited the most ideal performance in the training and verification cohorts, with an AUC of 0.98 and 0.97, respectively.

With respect to important predictors in clinical models, only age in the training group was relevant in this study. Hypertension, diabetes, and dyslipidemia, as clinical factors associated with cardiovascular risk, were not relevant for identifying calcified plaques in this experiment. The improvement of the combined model by clinical risk factors was not substantially great. This may have been caused by the limited sample size, and a sufficiently large sample may produce better statistics.

This study had several limitations. First, the sample size was small. A larger sample would have produced higher statistical value. Second, our results only support the detection of PVAT characteristics in symptomatic patients; the clinical value of our findings in asymptomatic patients remains unclear. Third, we did not conduct a detailed classification of non-calcified plaques nor an analysis of their components. Finally, the plaques in this study were not confirmed by pathologic examination.

Conclusion

We verified that age and radiomics features had good predictive ability for calcified plaques. We propose a noninvasive method that can assist the clinical diagnosis and decision-making for patients with plaques.

Abbreviations

AUC: area under curve

CCTA: coronary CT angiography

CI: confidence interval

CT: Computed tomography

D: diagonals

GLCM: Gray Level Cooccurrence Matrix

GLSZM: Gray Level Size Zone Matrix

GLSZM: Gray Level Run Length Matrix

LAD: left artery descending

LCx: left circumflex

LM: left main

OM: obtuse marginal

OR: odd ratio

PDA: posterior descending branch

PVAT: perivascular adipose tissue

RCA: right coronary artery

ROC: receiver operating characteristic curve

SD: Standard deviation

VIF: variance inflation factor

Declarations

Ethics approval and consent to participate:

This retrospective study was approved by The Medical Research Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China. The Medical Research Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China waived the requirement for written informed consent to participate in this retrospective study, as no personal patient privacy was involved (Committee's reference number: 2021-RE-144). The method used in this study was in accordance with the medical Research Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Committee's reference number: 2021-RE-144). The study protocol conforms to the ethical guidelines of the 2002 Declaration of Helsinki.

Consent for publication:

Not applicable.

Availability of data and materials:

The data that support the findings of this study are available from the corresponding author but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the corresponding author.

Competing interests:

All authors have completed the ICMJE uniform disclosure form. The authors declare that they have no commercial or associative interest that represents a conflict of interest in connection with the work submitted.

Funding:

This work was supported by the Special Funds for Basic Research Operations of Central Universities (WK9110000002) and the National Natural Science Foundation of China (81501468).

Authors' contributions:

Guo-qing Hu: Conception and design, collection and assembly of data, validation, writing—original draft. Ya-qiong Ge: Data analysis and interpretation. Xiao-kun Hu: Methodology. Wei-Wei: Administrative support, provision of study materials or patients, supervision.

Acknowledgment:

We thank Angela Morben, DVM, ELS, from Liwen Bianji (Edanz) (www.liwenbianji.cn/) for editing the English text of a draft of this manuscript.

References

1. M. Goeller, S. Achenbach, S. Cadet, A.C. Kwan, F. Commandeur, P.J. Slomka, H. Gransar, M.H. Albrecht, B.K. Tamarappoo, D.S. Berman, M. Marwan, D. Dey, Pericoronary Adipose Tissue Computed Tomography Attenuation and High-Risk Plaque characteristics in Acute Coronary Syndrome Compared With Stable Coronary Artery Disease, *Jama Cardiology* 3(9) (2018) 858-863.

2. M. Hoshino, H. Kawai, M. Sarai, A. Sadato, M. Hayakawa, S. Motoyama, Y. Nagahara, K. Miyajima, H. Takahashi, J. Ishii, I. Nakahara, Y. Hirose, Y. Ozaki, Noninvasive Assessment of Stenotic Severity and Plaque Characteristics by Coronary CT Angiography in Patients Scheduled for Carotid Artery Revascularization, *Journal of Atherosclerosis and Thrombosis* 25(10) (2018) 1022-1031.
3. G.R. Small, B.J.W. Chow, CT Imaging of the Vulnerable Plaque, *Current treatment options in cardiovascular medicine* 19(12) (2017) 92.
4. R.J. Gillies, P.E. Kinahan, H. Hricak, Radiomics: Images Are More than Pictures, They Are Data, *Radiology* 278(2) (2016) 563-577.
5. C. Antoniades, C.P. Kotanidis, D.S. Berman, State-of-the-art review article. Atherosclerosis affecting fat: What can we learn by imaging perivascular adipose tissue?, *Journal of Cardiovascular Computed Tomography* 13(5) (2019) 288-296.
6. A.S. Antonopoulos, M. Margaritis, P. Coutinho, J. Digby, R. Patel, C. Psarros, N. Ntusi, T.D. Karamitsos, R. Lee, R. De Silva, M. Petrou, R. Sayeed, M. Demosthenous, C. Bakogiannis, P.B. Wordsworth, D. Tousoulis, S. Neubauer, K.M. Channon, C. Antoniades, Reciprocal Effects of Systemic Inflammation and Brain Natriuretic Peptide on Adiponectin Biosynthesis in Adipose Tissue of Patients With Ischemic Heart Disease, *Arterioscler. Thromb. Vasc. Biol.* 34(9) (2014) 2151-2159.
7. A.S. Antonopoulos, F. Sanna, N. Sabharwal, S. Thomas, E.K. Oikonomou, L. Herdman, M. Margaritis, C. Shirodaria, A.-M. Kampoli, I. Akoumianakis, M. Petrou, R. Sayeed, G. Krasopoulos, C. Psarros, P. Ciccone, C.M. Brophy, J. Digby, A. Kelion, R. Uberoi, S. Anthony, N. Alexopoulos, D. Tousoulis, S. Achenbach, S. Neubauer, K.M. Channon, C. Antoniades, Detecting human coronary inflammation by imaging perivascular fat, *Science Translational Medicine* 9(398) (2017).
8. X. Dai, J. Deng, M. Yu, Z. Lu, C. Shen, J. Zhang, Perivascular fat attenuation index and high-risk plaque features evaluated by coronary CT angiography: relationship with serum inflammatory marker level, *International Journal of Cardiovascular Imaging* 36(4) (2020) 723-730.
9. M. Yu, X. Dai, J. Deng, Z. Lu, C. Shen, J. Zhang, Diagnostic performance of perivascular fat attenuation index to predict hemodynamic significance of coronary stenosis: a preliminary coronary computed tomography angiography study, *European Radiology* 30(2) (2020) 673-681.
10. E.K. Oikonomou, M. Marwan, M.Y. Desai, J. Mancio, A. Alashi, E.H. Centeno, S. Thomas, L. Herdman, C.P. Kotanidis, K.E. Thomas, B.P. Griffin, S.D. Flamm, A.S. Antonopoulos, C. Shirodaria, N. Sabharwal, J. Deanfield, S. Neubauer, J.C. Hopewell, K.M. Channon, S. Achenbach, C. Antoniades, Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome, *Lancet* 392(10151) (2018) 929-939.
11. D. Gu, Y. Hu, H. Ding, J. Wei, K. Chen, H. Liu, M. Zeng, J. Tian, CT radiomics may predict the grade of pancreatic neuroendocrine tumors: a multicenter study, *European Radiology* 29(12) (2019) 6880-6890.
12. A.A. Kramer, J.E. Zimmerman, Assessing the calibration of mortality benchmarks in critical care: The Hosmer-Lemeshow test revisited, *Critical Care Medicine* 35(9) (2007) 2052-2056.
13. J. Peng, J. Zhang, Q. Zhang, Y. Xu, J. Zhou, L. Liu, A radiomics nomogram for preoperative prediction of microvascular invasion risk in hepatitis B virus-related hepatocellular carcinoma, *Diagnostic and Interventional Radiology* 24(3) (2018) 121-+.
14. M.W. Kattan, J.A. Eastham, A.M.F. Stapleton, T.M. Wheeler, P.T. Scardino, A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer, *Jnci-Journal of the National Cancer Institute* 90(10) (1998) 766-771.
15. A.J. Vickers, A.M. Cronin, E.B. Elkin, M. Gonen, Extensions to decision curve analysis, a novel method for evaluating diagnostic tests, prediction models and molecular markers, *Bmc Medical Informatics and Decision Making* 8 (2008).
16. W.C. Hu, X.J. Wu, D. Dong, L.B. Cui, M. Jiang, J.B. Zhang, Y.B. Wang, X.J. Wang, L. Gao, J. Tian, F. Cao, Novel radiomics features from CCTA images for the functional evaluation of significant ischaemic lesions based on the coronary fractional flow reserve score, *International Journal of Cardiovascular Imaging* 12.
17. C. Antoniades, A.S. Antonopoulos, J. Deanfield, Imaging residual inflammatory cardiovascular risk, *European Heart Journal* 41(6) (2020) 748-+.
18. K. Otsuka, S. Fukuda, A. Tanaka, K. Nakanishi, H. Taguchi, M. Yoshiyama, K. Shimada, J. Yoshikawa, Prognosis of vulnerable plaque on computed tomographic coronary angiography with normal myocardial perfusion image, *European Heart Journal-Cardiovascular Imaging* 15(3) (2014) 332-340.
19. Y.A. Elnabawi, E.K. Oikonomou, A.K. Dey, J. Mancio, J.A. Rodante, M. Aksentijevich, H. Choi, A. Keel, J. Erb-Alvarez, H.L. Teague, A.A. Joshi, M.P. Playford, B. Lockshin, A.D. Choi, J.M. Gelfand, M.Y. Chen, D.A. Bluemke, C. Shirodaria, C. Antoniades, N.N. Mehta, Association of Biologic Therapy With Coronary Inflammation in Patients With Psoriasis as Assessed by Perivascular Fat Attenuation Index, *Jama Cardiology* 4(9) (2019) 885-891.

20. E.K. Oikonomou, M.C. Williams, C.P. Kotanidis, M.Y. Desai, M. Marwan, A.S. Antonopoulos, K.E. Thomas, S. Thomas, I. Akoumianakis, L.M. Fan, S. Kesavan, L. Herdman, A. Alashi, E.H. Centeno, M. Lyasheva, B.P. Griffin, S.D. Flamm, C. Shirodaria, N. Sabharwal, A. Kelion, M.R. Dweck, E.J.R. Van Beek, J. Deanfield, J.C. Hopewell, S. Neubauer, K.M. Channon, S. Achenbach, D.E. Newby, C. Antoniades, A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography, *European Heart Journal* 40(43) (2019) 3529-3543.

21. M.J. Park, J.I. Jung, Y.S. Choi, S.H. Ann, H.J. Youn, G.N. Jeon, H.C. Choi, Coronary CT angiography in patients with high calcium score: evaluation of plaque characteristics and diagnostic accuracy, *International Journal of Cardiovascular Imaging* 27 (2011) 43-51.

22. J.K. Min, M. Edwardes, F.Y. Lin, T. Labounty, J.W. Weinsaft, J.H. Choi, A. Delago, L.J. Shaw, D.S. Berman, M.J. Budoff, Relationship of coronary artery plaque composition to coronary artery stenosis severity: Results from the prospective multicenter ACCURACY trial, *Atherosclerosis* 219(2) (2011) 573-578.

Figures

Figure 1

Workflow of the radiomics analysis

Figure 2

Twelve features obtained after screening and their regression coefficients

Figure 3

Stability of different models

The ordinate is the average of 100 cross-validations of the AUC and accuracy for each classifier, and the abscissa is the RSD. AUC, area under the curve; RSD, relative standard deviation

Figure 4

Predictive performance of different models

(a) One hundred cross-validations of the ACC, AUC, NPV, PPV, sensitivity, and specificity of different models. (b) The validation set was used to verify the performance of each model. ACC, accuracy; AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value

Figure 5

Receiver operating characteristic curves

Comparison of receiver operating characteristic curves to predict calcified plaques. The figure includes (a) training and (b) validation clinical models (green), an imaging omics model (blue), and a comprehensive model (red) that combines clinical risk factors and imaging omics features. AUC, area under the curve

Figure 6

Nomogram of combined model and consistency curve

(a) Nomogram developed for the main population using a combination of radiographic scores and age factors. The calibration curve was plotted for the (b) training group and (c) verification group. The y-axis represents the actual calcified plaque probability, and the x-axis represents the predicted risk of a calcified plaque. The diagonal line represents the ideal prediction of the ideal model. The pink dotted line indicates the performance of the nomogram; better prediction is achieved as it approaches the diagonal.

Figure 7

Decision curves of comprehensive model