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Stenosis Detection and Quantification of Coronary Artery Using Machine Learning and Deep Learning

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Abstract

The aim of this review is to introduce some applications of artificial intelligence (AI) algorithms for the detection and quantification of coronary stenosis using computed tomography angiography (CTA). The realization of automatic/semi-automatic stenosis detection and quantification includes the following steps: vessel central axis extraction, vessel segmentation, stenosis detection, and quantification. Many new AI techniques, such as machine learning and deep learning, have been widely used in medical image segmentation and stenosis detection. This review also summarizes the recent progress regarding coronary stenosis detection and quantification, and discusses the development trends in this field. Through evaluation and comparison, researchers can better understand the research frontier in related fields, compare the advantages and disadvantages of various methods, and better optimize the new technologies. Machine learning and deep learning will promote the process of automatic detection and quantification of coronary artery stenosis. However, the machine learning and the deep learning methods need a large amount of data, so they also face some challenges because of the lack of professional image annotations (manually add labels by experts).

Keywords

stenosis detection, stenosis quantification, machine learning, deep learning, artificial intelligence

Introduction

The detection and quantification of coronary artery stenosis is an important reference for clinical diagnosis of cardiovascular disease. Automatic/semi-automatic detection and quantification of coronary artery stenosis refer to the acquisition of stenosis locations, stenosis sizes and types with minimal manual intervention, which is related to many techniques of image processing and medical imaging.[1]

As a non-invasive imaging method, computed tomography angiography (CTA) is widely used because of its high-quality 3D images, minimal trauma, and complications. However, interpretation of CTA's inspection report usually depends on the expert's diagnostic experience. With the rapid development of the medical imaging and the image processing techniques, automatic/semi-automatic realization of this process has become an important research direction.

The development of coronary artery's stenosis detection has undergone the process from manual to automatic, from two-dimensional to three-dimensional, from the low precision to the high precision. In the recent years, many new artificial intelligence (AI) techniques, such as machine learning and deep learning, have been widely used in the medical image segmentation and the stenosis detection. Machine learning is an approach to achieve AI, which learns from data automatically, and then applies what they have learned to make some informed decisions. Deep learning is a technique for implementing machine learning. Recent research results show that deep learning methods are superior to traditional machine learning methods.[2]

The traditional method is mainly achieved by manual observation and manual measurement to achieve stenosis detection. If automatic or semi-automatic stenosis detection and quantification are to be realized, an AI method should be adopted. These methods include machine learning and deep learning. In fact, FFR-CT (fractional flow reserve-computed tomographic) method can also be regarded as an AI method.[3]

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Machine learning is a field of computer science that uses computer algorithms to identify patterns in large data sets with many variables. Machine learning allows algorithms to learn from experience and improve themselves without the explicit programming by data scientists.[4] Therefore, machine learning technology has become an efficient method for prediction and intelligent decision-making. Compared with conventional statistical methods, the ability of these algorithms to process large data sets and incorporate nonlinear interactions allows more accurate and personalized predictions.[5]

Deep learning is a new research direction in the field of machine learning. It is introduced into machine learning to make it closer to the original goal—AI. Deep learning combines low-level features to form more abstract high-level features to learn the internal laws and representation levels of sample data. The information acquired during deep learning is very helpful in interpreting data. The goal of deep learning is to enable machines to learn analytically like humans and recognize data such as words, images, and sounds.[6] Deep learning is a complex machine learning algorithm that has far surpassed machine learning in speech and image recognition.[7] Machine learning usually requires manual extraction of features, and the process is also known as feature engineering.[8] Deep learning enables automatic learning. It automatically finds features from sample data, so that it can automatically complete sample data classification, identification, and prediction. The difference between machine learning and deep learning is shown in Figure 1. Deep learning has achieved many significant results in many fields, such as search technology, data mining, image processing, machine translation, natural language understanding, multimedia learning, speech processing, and medical auxiliary diagnosis.

There are many types of detection for coronary artery stenosis. For example, binary detection is used to determine whether a coronary artery has stenosis;[9-12] ordinal detection is used to determine the severity of coronary artery stenosis;[13-16] and multinomial detection is used to classify multiple diseases.[17-20]

This paper reviews the recent progresses of coronary stenosis detection and quantification, summarizes the technological procedures, and discusses development trends in this field.

Methodology

Traditional Methods

Accurate vessel segmentation is the prerequisite for accurate detection of stenosis regions and accurate quantification.[21] The stenosis detection and quantification methods discussed in this paper are based on the segmentation results. After the blood vessel is segmented, the diameter of vessel lumen is measured along the central axis, and the expected value of lumen diameter at each position is calculated, then the percentage deviation between the expected diameter and the actual measured diameter is calculated, which is defined as the stenosis ratio. Areas with a stenosis ratio >20% are reported as stenosis samples. Stenosis detection and quantification can be carried out simultaneously.

The images obtained by the angiographic techniques mainly have two characteristics, the blood vessel morphology (tree structure) and the gray scale distribution. The traditional image segmentation algorithm is not ideal for segmentation of coronary CT images; it does not make good use of the morphological characteristics. Currently popular methods are vessel tractography methods, such as the graph segmentation method proposed by Cetin et al.[22] and the robust kernel regression method proposed by Schaap et al.[23] These methods use the vascular morphology, and incorporate the ideas and methods of mathematical morphology, statistics, and pattern recognition. These methods not only overcome the inefficiency of traditional methods, but also enable automatic implementation and provide a reliable basis for subsequent stenosis detection and quantification. Through the determined central axis, a rigorous transformation can generate a corresponding coronary artery tree model, as shown in Figure 2, which provides an intuitive and accurate reference model for vessel segmentation.[24]

The method of vascular tracking can be used for lumen segmentation and many types of coronary stenosis detection. The vascular tracking is inspired by the diffusion tensor imaging (DTI).[25] DTI analyzes the anatomy of nerve cells and a complex neuronal network of the brain. Advanced visualization of DTI data can be obtained via a method commonly referred to as tractography or DTI fiber tracking. Within the Rotterdam Coronary Artery Algorithm Evaluation Framework,[26] the method of ref. 4 ranks the first among the semi-automatic algorithms. In the qualitative expert evaluation and the quantitative validation, this algorithm obtained high visual scores.

Graph cut is a semi-automatic segmentation technique that does not require good initialization.[27] The kernel regression is a non-parametric random conditional expectation prediction technique used in statistics to find the nonlinear relationship of a pair of random variables.[28] Drawing lines on the image, called scribbles, to identify what you want in the foreground and what you want in the background. Then the graph cut method segments the image automatically based on your scribbles. You can refine the segmentation by drawing more scribbles on the image until you are satisfied with the result.[29]

Machine Learning Methods

Commonly used methods of machine learning are mainly divided into supervised and unsupervised learning.[30] Supervised learning uses the existing training samples to train to obtain an optimal model, then use this model to map all inputs to corresponding outputs, and perform simple judgments on the output to achieve the purpose of classification. In this way, it can classify unknown data. Typical examples in supervised

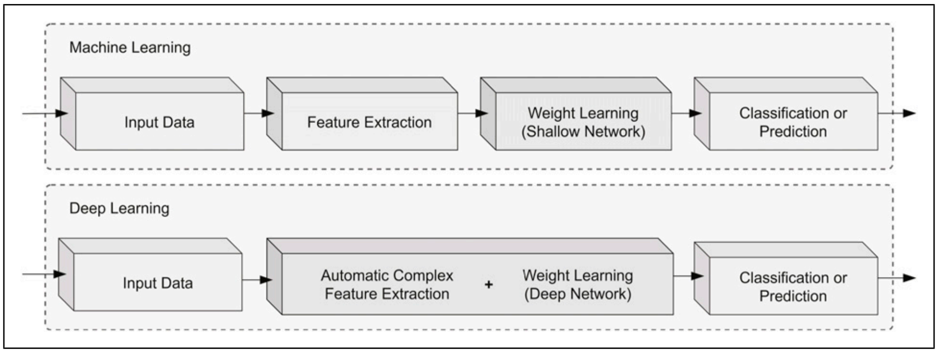

Figure 1. The difference between machine learning and deep learning.

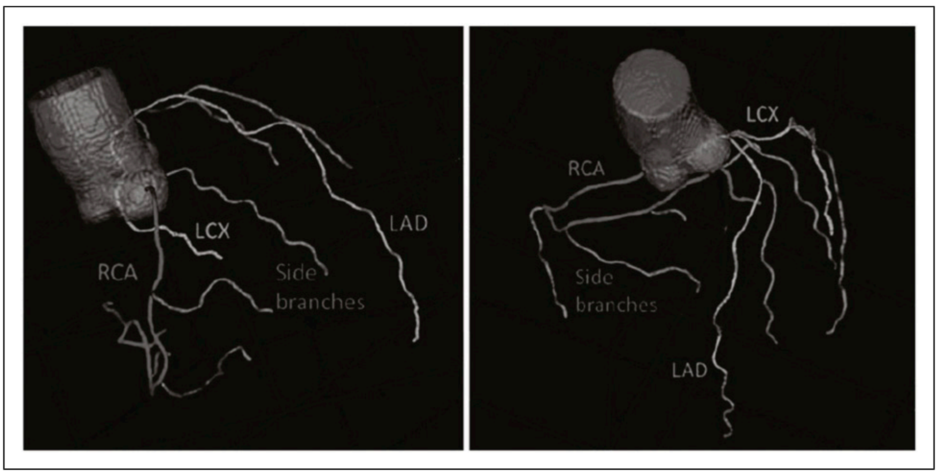

Figure 2. Labeled coronary artery tree. RAO (right anterior oblique projection, RAO left) and LAO (left anterior oblique projection, LAO right).

learning are KNN (K-nearest neighbor) and SVM (support vector machine). The difference between unsupervised and supervised learning is that we do not have any training samples in advance, and we need to directly model the data. A typical example in unsupervised learning is clustering.[31]

The simplest machine learning algorithm includes the k-nearest algorithm (KNN) classifier, which looks for training samples, uses similar eigenvalues as test samples, and allocates test value samples to most classes in these training samples. Linear classifier (LC) models, such as support vector machine (SVM), aim to find out the linear combination of features to separate samples in different classes. The performance of machine learning can usually be improved through combination, such as prediction of decision trees in the average random forest.[32] Artificial neural networks are biologically inspired computational networks designed to simulate the human brain. Their main use in medical science is the convolutional neural network based on deep neural network, which consists of up to hundreds of inner layers and is currently considered to be the most advanced algorithm for outcome prediction using imaging data.[33]

Machine learning has been introduced into cardiovascular imaging treatment decision-making to make reasonable predictions in a more objective and reproducible manner, and to improve diagnostic accuracy. Machine learning can automatically extract image features. Combined with data extracted from medical records, it may make diagnosis and treatment more streamlined and personalized.[34-36] In recent years, the application of machine learning in medical imaging has shown that it can improve the accuracy and prognosis of diagnosis.[37] The research directions of traditional machine learning mainly include research on decision trees, random forests, artificial neural networks, and Bayesian learning.[38]

Deep Learning Methods

Deep learning is basically a neural network algorithm, and it is a representation learning technology that learns hierarchical feature representation from image data.[39-42] One advantage of deep learning is that it can generate high-level feature representations directly from the original image. In addition, with the support of massively parallel architecture GPU (graphics processing unit), deep learning technology has achieved great success in many fields in recent years, that is, effectively solving complex classification, segmentation, and target detection tasks.[43] Deep learning methods automatically extract features that are the most descriptive for the task. Recently, deep learning is widely used in a series of segmentation and detection tasks in medical image analysis.[44]

U-Net (U-network) is a convolutional network structure used to segment images quickly and accurately.[45] So far, it has performed better than the previous best method in the challenge of segmenting the neuron structure in the electron microscope stack at the International Symposium on Biomedical Imaging (ISBI). U-Net combines the location information in the down-sampling path with the context information in the up-sampling path, and finally obtains a general information that combines positioning and context, which is necessary to predict a good segmentation map.[46] Down-sampling is the extraction of some information from a high-resolution image to produce a low-resolution image, that is, the sampling rate of the image is reduced. Up-sampling refers to generating a high-resolution image from a low-resolution image, that is, increasing the sampling rate of the image. The network architecture of U-Net is shown as Figure 3. The role of the first half (left) is feature extraction, and the role of the second half (right) is up-sampling. Each yellow box corresponds to a multi-channel feature map. The number of channels is denoted at the bottom of the box. The blue boxes represent copied feature maps. The arrows denote the different operations.[47]

Convolutional neural network (CNN) is a type of neural network that has been proven to be very effective in the fields of image recognition and classification.[48] Recurrent neural network (RNN) is an extension of the time dimension, which represents the transfer and accumulation of information from the time dimension to the post.[49] The probability of the latter kind of information is based on the former information, and the neural network structure appears as a hidden layer of the neural network. The input is the output of the previous hidden layer of the neural network. Convolutional recurrent neural network (CRNN) is a combination of CNN and RNN network, which realizes end-to-end detection and recognition.[50]

Deep learning can be used to determine the degree of coronary artery stenosis and identify patients with significant coronary artery stenosis. Transfer patients with moderate stenosis to fully automated deep learning left ventricular myocardial (LVM) analysis. Deep learning algorithms characterize LVM, as well as possible encoding information such as shape, texture, and contrast enhancement. Based on these codes, features are extracted and patients are classified as non-significant stenosis or significant stenosis. Deep learning algorithms are more sensitive to subtle changes in LVM caused by significantly narrowed functions. When evaluating the degree of coronary artery stenosis, deep learning analysis of the left ventricular myocardium can improve diagnostic performance and increase the specificity of resting CTA.[51-54]

Clinical Evidence

Stenosis Detection

In the applications of machine learning in the stenosis detection and quantification, machine learning algorithm designed a series of features calculated from the region of interest along the centerline of the artery to describe the local image intensity and artery geometry. Subsequently, they used a supervised classifier to detect and quantify the degree of stenosis. The segmentation algorithm analyzes the local changes and diameter abnormalities of the coronary arteries to describe the coronary lumen, thereby detecting and quantifying the degree of stenosis.[55]

Sankaran et al.[56] developed a machine learning framework to estimate geometric sensitivity in real time. They defined geometric sensitivity as the standard deviation of hemodynamic indicators due to the uncertainty of lumen segmentation. They developed an anisotropic nuclear regression method to evaluate the luminal stenosis score, and proposed a multi-resolution sensitivity algorithm to classify and refine high-sensitivity regions to quantify the sensitivity to the required spatial resolution. They compared the allowable coefficient of variation of the lumen area given the allowable standard deviation in FFR-CT. The results show that when the cavity area coefficient of variation is <6%, the sensitivity of FFR-CT is < .05 and the confidence interval is 95%. Similarly, a coefficient of variation of the lumen area of <11% will translate into a sensitivity of <.10 with 95% confidence. In other words, based on the accuracy of the lumen segmentation algorithm, the error of FFR-CT can be evaluated.

Johnson et al[57] proposed a machine learning model to distinguish patients with and without subsequent death or cardiovascular events. Four types of machine learning models (logistic regression, k-nearest neighbor, bag tree, and classification neural network) are discussed. Some evaluation indicators are applied, such as Coronary Artery Disease Reporting and Data System (CAD-RADS) score,[58] segmental involvement score,[59] segmental plaque score,[60] CT Leaman score,[61] and segmental stenosis score. For prediction of all-cause mortality based on CCTA (coronary computed tomography angiography), the area under the receiver operating characteristic curve (AUC) for a machine learning score was .77, higher than the Coronary Artery Disease Reporting and Data System (CAD-RADS), which was .72. For prediction of coronary artery deaths based on CCTA, the machine learning score also had a higher AUC than the CAD-RADS score (.85 *vs* .79). When deciding whether to start statins, a machine learning score ensures 93% of patients will be administered the drug; if CAD-RADS is used instead, only 69% will be treated. Table 1 shows the discriminatory performance of machine learning model compared with conventional summary scores.

Shi et al[62] proposed a framework for intracranial blood vessel analysis using full convolutional networks (FCNs),

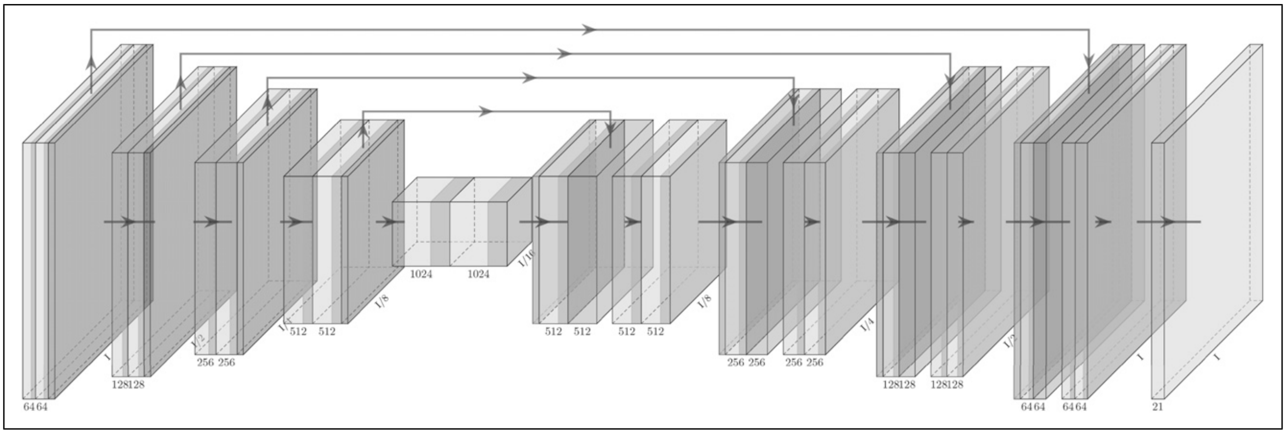

Figure 3. The network architecture of U-Net (U-network). The role of the first half (left) is feature extraction, and the role of the second half (right) is up-sampling. Down-sampling is the extraction of some information from a high-resolution image to produce a low-resolution image. Up-sampling refers to generating a high-resolution image from a low-resolution image.

Table 1. Discriminatory Performance of Machine Learning Model Compared with Conventional Summary Scores.

	All-cause mortality		CHD deaths		CHD death/MI	
Methods	AUC	*P*	AUC	*P*	AUC	*P*
Machine learning score[57]	.77	—	.85	—	.85	—
CAD-RADS CT[58]	.72	<.001	.79	<.001	.80	<.001
SSS (segmental stenosis score)[59]	.72	<.001	.78	<.001	.80	<.001
SIS (segmental involvement score)[59]	.75	<.001	.80	<.001	.83	<.001
SPS (segmental plaque score)[60]	.76	<.001	.83	.005	.84	.37
CT Leaman score[61]	.74	<.001	.82	<.001	.82	<.001

AUC: area under the receiver operating characteristic curve.
CHD: coronary heart disease.
MI: myocardial infarction.
CAD-RADS CT: coronary artery disease reporting and data system computed tomography.

which can extract, straighten, and resample blood vessel segments of interest into two-dimensional slices. The network was trained and verified on 1160 slices and tested on 545 slices. This segmentation method is in good agreement with the manual segmentation results. The dice coefficient of the tube cavity is .89, and the dice coefficient of the tube wall is .77. Dice coefficient is a statistic used to assess the similarity of two samples, which is essentially a measure of the overlap of two samples.

Linares et al[63] proposed a fully automatic method based on deep convolutional neural network (DCNN) for robust and reproducible detection of thrombus regions of interest and subsequent segmentation of thrombus. Their pipeline realizes that the dice coefficient of thrombus segmentation after surgery is >82%, and in most cases, it does not require manual intervention.

Muscogiuri et al[64] developed three Models of deep convolutional neural network to classify CCTA in the correct Coronary Artery Disease Reporting and Data System (CAD-RADS) category. Model A showed a sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of 47%, 74%, 77%, 46%, and 60%, respectively. Model 1 showed a sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of 66%, 91%, 92%, 63%, and 86%, respectively. In the Model 2, the sensitivity, specificity, negative predictive value, positive predictive value, and accuracy are 82%, 58%, 74%, 69%, and 71%, respectively.

Plaque Quantification

Current non-invasive examinations provide data on anatomical narrowing (such as CCTA) or myocardial perfusion defects (such as SPECT (single-photon emission computed tomography). Recent studies have shown that using reconstructed coronary artery blood flow simulations, FFR can be calculated non-invasively by CT scan (FFR-CT method). Dey et al[65] proposed a machine learning integrated ischemia risk core based on CTA quantitative plaque measures, which improves the prediction of ischemia through invasive FFR, over stenosis, plaque measures, and coronary artery disease prediction likelihood. The performance of comprehensive machine learning scores is better than the CTA indicators of visual evaluation and individual quantitative measures.

The traditional CCTA score only includes information about the severity of coronary plaque and plaque composition of the 16-segment coronary tree: modified Duke prognostic index; CCTA-Leaman score; segmental stenosis score (SSS); segmental involvement score (SIS), and traditional CAD classification. Rosendael et al[66] proposed a machine learning model that uses coronary artery stenosis and plaque components derived only from detailed 16-segment CCTA readings to improve the risk of major cardiovascular events compared with the current CCTA risk score stratification. From the multi-center confirmation registration form,[67] patients include complete CCTA risk score information and follow-up for myocardial infarction and death for ≥3 years (primary endpoint). Exclude patients with a history of coronary heart disease. A total of 8844 patients were enrolled. The event discrimination ability expressed in AUC is significantly better than other scores (range from .685 to .701) in the machine learning-based method (.771), $P < .001$.

Zreik et al[68] proposed a recurrent CNN architecture for the automatic detection and classification of coronary plaques and stenosis in CTA. They define the reference standard and identify the type of coronary plaque (no plaque, non-calcified, mixed, calcified), as well as the anatomical significance of the presence and coronary stenosis in the MPR (multi-planar reconstruction) image by identifying the beginning and end points of the artificial annotation. Annotations are to manually add labels to an image by experts. Image annotations are to manually add labels to an image. The effect of arterial plaque is as follows. First, the features of coronary arteries are extracted by using a three-dimensional convolutional neural network. Subsequently, the extracted features are aggregated by a recurrent neural network, which performs two multi-class classification tasks simultaneously. In the first task, the network detects and characterizes the type of coronary plaque. In the second task, the network detects and determines the anatomical significance of coronary artery stenosis. This method uses a three-dimensional convolutional neural network to extract the features of the area near the centerline of the coronary artery. CNN extracts feature from a 25 × 25 × 25 voxel cubes. Subsequently, the recursive CNN network uses GRU to process the entire sequence. The output of the neural network is fed into two classifiers to simultaneously characterize plaque and stenosis.[69]

Hamersvelt et al[70] proposed a deep learning analysis method of LVM in CT angiography of moderate coronary artery stenosis, which can improve the diagnostic accuracy of major stenosis. Figure 4 shows the graphical summary of their deep learning-based method. First, LVM is automatically segmented using a multiscale CNN. The multiscale CNN segmented all CT slices of the entire myocardium, and finally classified a single voxel as myocardium or background. Second, LVM was characterized (encoded) on all CT slices by the algorithm in an unsupervised manner using a convolutional auto-encoder (CAE). Finally, based on the extracted features, the patients were classified into patients with or without significant coronary artery stenosis using support vector machine (SVM).

Radiomics is defined with the aid of computer software, from the vast amounts of medical image in the image mining quantitative image characteristics, using statistical and/or machine learning method, screening the most valuable imaging characteristics of omics, used to analyze the clinical information, the qualitative and grade of tumor staging of the disease, curative effect evaluation and prognosis prediction, etc.[71] The combination of radiomics with machine learning and deep learning is the current research trend.[72,73] Baessler et al[74] found that radiomic texture features are feasible and reproducible on cine MR (magnetic resonance) images and deliver texture parameters, which allow an accurate differentiation between control subjects and patients with both large and small subacute and chronic myocardial scars. Experimental result showed that multiple logistic regression models based on five radiomic texture features allow an accurate discrimination between subacute and chronic myocardial ischemic scarring, with an area under the curve of .92, $P < .001$.

FFR-CT Methods

The fractional flow reserve (FFR) is an important technique of interventional cardiology.[75] FFR technique measures the ratio between the maximum blood flow in a stenosed coronary artery and the theoretical maximum flow in the coronary artery without any stenosis. Compared with angiography imaging, FFR is more reliable in identifying coronary artery disease.

Recently, physics-based flow simulations are used to evaluate the hemodynamic significance of coronary lesions from coronary CT angiography (CCTA) data. This method named as FFR-CT or CT-FFR.[76] FFR-CT combines the advantages of CCTA and FFR. It can evaluate coronary artery stenosis from both structural and functional aspects, and become a new non-invasive detection method to provide anatomical and functional information of coronary lesions. FFR-CT can reduce the false-positive rate of CCTA caused only by the classification of stenosis degree, and it is more helpful for patients with coronary heart disease to select a more appropriate treatment.

If the FFR-CT value is > .80, ischemia is unlikely and no further testing is required. When the FFR-CT value is between .75 and .80, additional parameters such as plaque composition, lesion location, and pressure drop at a specific lesion can guide whether further non-invasive testing can be added. FFR-CT value <.75 indicates that the accuracy of predicting ischemia is moderate, and 1 in 3 patients has a false-positive result. Clinically, this means that when the FFR-CT value is close to the .75 threshold, it should be handled with care and should not directly trigger an invasive examination.

Since 2011, there have been three single-center or multi-center clinical registration trials on FFR-CT. They are

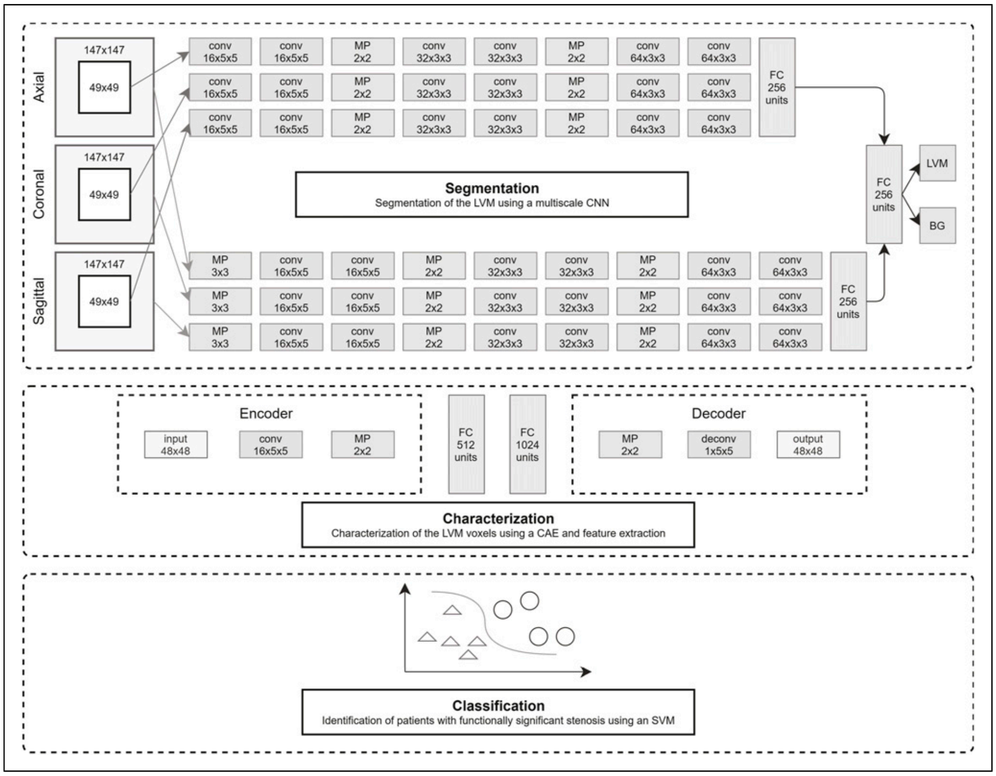

Figure 4. The deep learning-based stenosis detection and quantification method usually consists of three stages: segmentation, characterization, and classification. Conv: convolutional; MP: max-pooling; FC: fully connected layers; deconv: deconvolutional; CNN: convolutional neural network; CAE: convolutional auto-encoder; SVM: support vector machine; US: up-sampling; BG: background.

Discover-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve),[77] DeFACTO (Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography)[78] and NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps).[79] The results of the study have proved that the consistency between FFR-CT and invasive FFR value is high. Supported by the above clinical trial data. Table 2 shows the diagnostic accuracy of FFR-CT compared with invasive FFR. The accuracy of FFR-CT depends on several factors. A major factor is the accurate modeling of the coronary lumen tree. There is still room for improvement in this direction.

Table 2. Diagnostic Accuracy of FFR-CT (Fractional Flow Reserve-Computed Tomographic) Compared with Invasive FFR.

	Discover-Flow	DeFACTO	NXT
Sensitivity	93%	90%	86%
Specificity	82%	54%	79%
PPV	85%	67%	65%
NPV	91%	84%	98%
Processing time	>18 h	>18 h	1~4 h

PPV: positive predictive value.
NPV: negative predictive value.

Discussion

The realization of automatic/semi-automatic stenosis detection and quantification includes following steps: the vessel central axis extraction, the vessel segmentation, the stenosis detection, and quantification. The workflow of coronary artery stenosis detection and quantification is shown in Figure 5. The machine learning methods and the deep learning methods have been used in the vessel segmentation, the stenosis detection and quantification.

The main procedures for the detection and quantification of CTA automatic/semi-automatic stenosis detection include the central axis extraction, the vessel segmentation, and the stenosis detection and quantification as described previously. With the emergence of multiple stenosis detection and quantification algorithms, standardized evaluation of such algorithms is necessary. Through evaluation and comparison, clinicians can compare the advantages and the disadvantages of various technologies, and choose the optimal methods.

The CTA data sets used by the 15th Medical Image Computing and Computer Assisted Intervention Symposium (MICCAI) come from multiple medical centers and several CT scanner vendors. A set of standardized evaluation frameworks is used to compare the more popular algorithms. The CTA scan results of 48 representative cardiovascular patients with different degrees of disease between the ages of

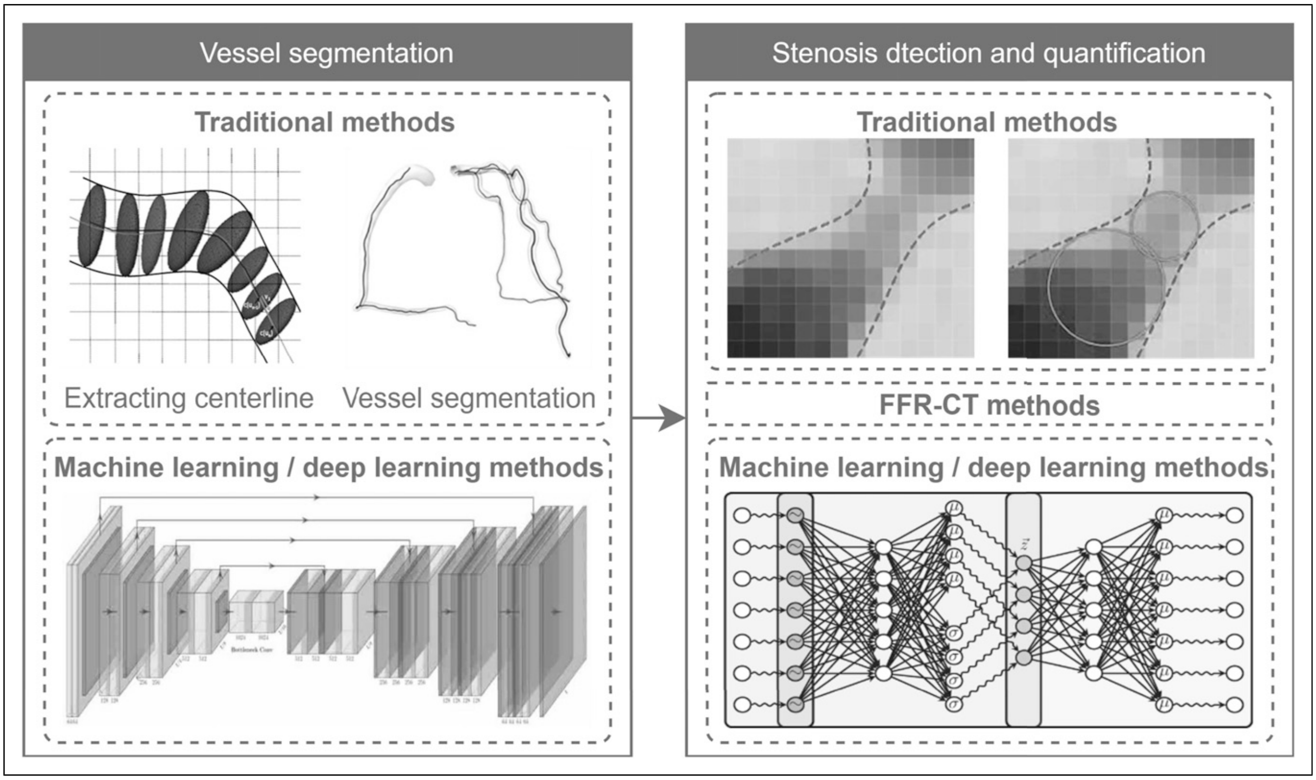

Figure 5. The workflow of coronary artery stenosis detection and quantification. First, the blood vessels are segmented using traditional methods or machine learning/deep learning methods. Then, the stenosis and quantitative detection of coronary artery are achieved by traditional methods, FFR-CT (fractional flow reserve-computed tomographic) methods and machine learning/deep learning methods.

41 and 80 years (mean 58.76 ± 8.71 years) were evaluated. CTA results were obtained from dual-source CT (SOMATOM Definition, Siemens, Munich, Germany), 64-row multi-slice spiral CT (Brilliance 64, Philips, Rotterdam, Netherlands), 320-row dynamic volume CT (Aquilion ONE 320, Toshiba, Tokyo, Japan). At the same time, three experienced experts were invited as observers, and the results of manual extraction of CTA by experts were used as reference standards.

Based on the CTA data set of MICCAI, Shahzad et al first extracted the centerline of the artery, and then segmented the arterial lumen by graph cutting and robust kernel regression.[80] Then, to detect and grade coronary stenosis, the diameter of the segmental lumen is compared with the expected diameter of a healthy lumen. The expected diameter of a healthy lumen is estimated by regression of the lumen diameter of adjacent coronary arteries. The experimental results of the above algorithm are shown in Table 3.

From the evaluation of results, the highest sensitivity of all algorithms is 68%, and the highest accuracy rate is 35%. The best performing algorithm is a deep learning-based algorithm. The highest sensitivity of non-deep learning algorithms is 55%, and the highest accuracy rate is 33%. The mean sensitivity is 41%, and the mean accuracy is 18%. Compared with the mean sensitivity and the accuracy of expert's manual detection (the mean sensitivity is 73%; the mean accuracy is 67%), there is still a certain gap. The semi-automatic algorithm with manual calibration is generally better than the fully automatic implementation algorithm. If the factors such as partial volume effects and motion artifacts are not corrected in time, the execution results will generate numerous false positives, and reduce the performance of algorithm. Therefore, the current stenosis detection and quantification algorithms are only used as the reference of diagnosis, though they have shown some great research value.

Although machine learning and deep learning methods can usually produce accurate predictions, there are still some limitations which are difficult to overcome.

1. The interpretability of the decision results of machine learning and deep learning methods is relatively poor. They are the so-called black box, which often provide some unexpected results, and their decisions cannot be clearly explained.
2. Recent studies have shown that deep neural networks can be forced to make bad decisions using well-designed inputs, and such systems may not be ready to withstand the adversarial example attacks.
3. Machine learning and deep learning methods are data-driven and often be riddled with traditional biases. That may be a big problem in the medical field because they carry a lot of risk. Algorithms are often trained and evaluated in a single center, and this selectivity makes

Table 3. Performance of 3 Experts and 11 Stenosis Detection and Quantification Algorithms.

	Category	Class	Sensitivity (%)	Accuracy (%)
Expert 1	Artificial	—	83	61
Expert 2	Artificial	—	70	81
Expert 3	Artificial	—	66	60
Broersen et al.[81]	Automatic	Unsupervised	27.7	31
Cetin et al.[82]	Semi-automatic	Supervised	53	26
Eslami et al.[83]	Semi-automatic	Unsupervised	51	4
Valencia et al.[84]	Semi-automatic	Unsupervised	15	5
Lor et al.[85]	Semi-automatic	Supervised	32	3
Melki et al.[86]	Automatic	Supervised	43	9
Mohr et al.[87]	Automatic	Unsupervised	51	16
Schaap et al.[88]	Semi-automatic	Supervised	52	27
Wang et al.[89]	Automatic	Supervised	11	33
Hamersvelt et al.[70]	Semi-automatic	Unsupervised	68	36
Naushad et al.[37]	Semi-automatic	Supervised	—	89

the risk of deviation high. In well-structured clinical trials, selection biases are often mitigated, but it is difficult to identify and remedy when using open data sets.

4. The development of AI algorithms requires the analysis of large amounts of data. The privacy aspect of the law is very important. The safety of the use of patient data and the protection of computing storage are issues that must be considered.
5. Machine learning and deep learning methods will reduce costs, improve efficiency, and reduce the burden on clinicians, but will they reduce the labor value of doctors? Who will take responsibility when things go wrong? Machine or doctor?

Conclusion and Future Perspectives

Automatic/semi-automatic stenosis detection and quantification of coronary CT are a kind of computer-aided diagnosis. It is fast and accurate, and it can effectively reduce the instability of human observation, so it has attracted the attention of experts. Many researchers have invested in this field and have made great progress. In the current research status, the technology of vascular central axis extraction is relatively mature, which can get a very accurate coronary artery tree model. Based on this, the diversified development of stenosis detection is directly promoted. But there are still some areas need to be improved and explored. Various stenosis detection algorithms can be used as auxiliary methods for diagnosis and treatment. Machine learning and deep learning will further promote the process of automatic detection and quantification of coronary artery stenosis. Experimental results show that the method based on deep learning can get more accurate and faster results. But they cannot completely replace experts and do not have the ability for large-scale clinical application. Although human interaction is reduced, it does not really achieve a high degree of automation.

Machine learning and deep learning methods need a large amount of data, so they also face some challenges. For example, different modalities data have uncorrelated appearances; data dimensionality is frequently higher than that in 2D computer vision. The main problem at present is the lack of professional image annotations and the lack of sufficient data due to ethical concerns, data accessibility, and security issue.

New developments of automatic/semi-automatic stenosis detection and quantification of CTA are expected in the future: a more complete stenosis detection and quantification system, a more diversified method, a higher detection accuracy and degree of automation. These studies will provide a stronger, more accurate, and quantitative basis for early prediction and diagnosis of cardiovascular disease.

Authors' Note

All authors contributed to (1) conception and design, or acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

Declaration of Conflicting Interests

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