Supplementary

Appendix 1

The explanation about the allocation of the training set and the testing set and determination of the sample size

This study was a diagnostic test, and the sample size was calculated using the area under the receiver operating characteristic (ROC) curve. The smallest area under the ROC curve was set as 0.90 according to the purpose of the study. Then, the type I error α was set as 0.05, and the type II error β was set as 0.1. The ratio of positive [chronic total occlusion (CTO) lesions] to negative (non-CTO lesions) was approximately 1:3. The results of MedCalc (version 18.11.3, MedCalc Software bvba, Ostend, Belgium) showed that the sample size required for clinical test was 19 patients, including 5 patients with CTO lesions and 14 patients with non-CTO lesions.

In order to ensure the robustness of the diagnostic model, we need to increase the amount of data in the training set as much as possible. So we randomly assigned the patients to the training dataset and the testing dataset at a rate of 4:1. According to the proportion of 4:1 (training set:testing set), the minimum required sample size of the training set was 76 patients, of whom 19 with CTO lesions and 57 with non-CTO lesions.

The artificial intelligence (AI) model requires a higher sample size than the conventional prediction model, and it is difficult to develop a robust model with only 95 patients. Therefore, to improve the robustness of our AI model, a total of 537 patients with 1,569 ICA-confirmed atherosclerotic lesions (including 672 lesions with <50% stenosis, 493 lesions with 50–99% stenosis, and 404 CTO lesions) were enrolled in this study.

Appendix 2

Convolutional neural network (CNN) was used to achieve myocardial and coronary artery segmentation and target lesion identification, which are feed-forward neuronal networks, and contain neurons with learnable weights and biases (24).The proposed deep learning framework, which consists of three models: (I) a two-stage 3D U-Net-based myocardium segmentation network to determine the coordinates of the heart contour and segment the myocardium fine structure; (II) a modified 3D U-Net for coronary segmentation, which includes encoding and decoding parts, and a connected growth prediction model (CGPM) to eliminate vascular segmentation errors and then avoid partial or missing vascular segments of CTO lesions effectively; and (III) a vessel-connect algorithm to identify the missing segments of the vessels and connect them with main branches, which in turn localizes and displays the region of CTO lesions (see main text *Figure 2*).

Detailed steps regarding our AI model development are shown as follows: for myocardial segmentation, an automatic segmentation framework was developed, which mainly consisted of two 3D U-Net networks, as shown in *Figure 2B*. The first 3D U-Net is used to determine the coordinates of the heart contour, while the other is used for the segmentation of the myocardium fine structure. For coronary segmentation, a modified 3D U-Net was used, which includes encoding and decoding parts, as shown in *Figure 2C*. The encoding part included four layers of down-sampling, and the decoding part included four layers of the up-sampling. Next, we added the bottleneck connection between down-sampling and up-sampling layers to maintain the multi-scale information in down-sampling process (30). After the 3D U-Net, a CGPM was used to eliminate vascular segmentation errors and then avoid partial or missing vascular segments effectively.

Due to the reduction in the contrast medium at the occlusion site or the distal vessel is prone to cause vessel segmentation errors, following which, the vessel segments were disconnected, and those before and after occlusion were difficult to be demonstrated in curved planar reconstruction (CPR) images. Therefore, we developed a new algorithm, combined with the imaging characteristics, to modify the extraction of the centerline and improve the detection of CTO lesions, as shown in *Figure 2D*.

The model utilized a novel algorithm, which enables automated extraction of the centerlines, to locate the CTO lesions by completing the missing segments. Based on previous myocardial segmentation and coronary segmentation results, the anatomical correlation between the centerline and myocardium location to distinct vessel branches was utilized. Subsequently, each branch of the centerline was labeled, and missing segments of the vessels were identified and connected with main branches, which in turn displayed and detected the CTO lesions. Details are as follows:

(I) On the coronary segmentation, the domain connected to the aorta was selected, the two largest connected domains on the coronary segmentation corresponding to the left and right branches of the coronary artery were identified, and the centerline of the vascular tree was extracted (31,32). The minimum distance between the nearest point

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of the left and right branches to the aorta and myocardium (left atrium, left ventricle, right atrium, and right ventricle) was termed as right coronary artery (RCA) and left main coronary artery (LM), respectively. According to the minimum distance between the bifurcation on the centerline of LM and myocardium and distinct left anterior descending artery (LAD) and left circumflex artery (LCX), the partial points on the centerline corresponding to the three main vessels were determined.

(II) The centerline was also extracted for the free connected domain that was not connected to the aorta in the coronary segmentation results. According to the positional correlation between the points on the centerline and the myocardium (left atrium, left ventricle, right atrium, and right ventricle), it was determined whether the free connected domain was the main vessel or its branch [posterior descending artery (PDA), diagonal branch (D), obtuse marginal (OM), ramus intermedius (RI), right posterior lateral branch (R-PLB)].

(III) If the centerline of connecting domain in step 2 was the main vessel, then based on the centerline in step 1, the nearest two points on the centerline of the free connected domain and the corresponding major branch in (II) are selected as the starting point and the ending point, respectively. Then, the path connecting the free connected domains to the three main vessels were computed by the minimum path algorithm.

(IV) According to the waypoint and centerline in step 3, the missing segments in the occlusion site lost in previous coronary segmentation results was complemented.

(V) Based on the results of the complemented coronary artery, the centerlines of the main vessels and their branches could be extracted such that the missing segments caused by CTO could also be detected on the straightened multiplanar reconstruction (MPR) and CPR.

References

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