Aortic root diameter, main pulmonary artery diameter/aortic root diameter and pericardial fat volume as predictors of occlusive coronary artery disease

Abdulameer A. Al-Mosawi,[1] Hussein Nafakhi,[2] Hadeel K. Hameed[1]

[1]Radiology Department, Medicine College, University of Kufa, Najaf; [2]Internal Medicine Department, Medicine College, University of Kufa, Najaf, Iraq

Correspondence: Hussein Nafakhi, Internal Medicine Department, Medicine College, Kufa University, P.O. 21, Kufa, Najaf, Iraq.
Tel.: +964 78 218 41 16.
Fax: +964 34 09 52.
E-mail: husseinaf.alnaffakh@uokufa.edu.iq

Key words: aortic root, pericardial fat, coronary artery disease, pulmonary artery, multi-detector computed tomography.

Contributions: AM, HN, HKH, data acquisition and interpretation, manuscript critical revision for important intellectual content; HN, HKH, data analysis and manuscript drafting; HN, AM conception and design of the work. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no conflict of interest.

Ethics approval and consent to participate: approval of this study was provided by the IRB of the Medicine College, University of Kufa, Najaf (Iraq) with approval number (MEC-012021). Data were collected and analyzed only by researchers, providing full confidentiality.

Informed consent: verbal informed consent was obtained from all enrolled participants.

Funding: there were no external funding sources for this study.

Availability of data and materials: the datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Received: 24 July 2023.
Accepted: 16 August 2023.
Early view: 13 September 2023.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

©Copyright: the Author(s), 2023
Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2024; 94:2655
doi: 10.4081/monaldi.2023.2655

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

Abstract

The clinical relevance of aortic root diameter (ARD), main pulmonary artery diameter (MPAd), or pericardial fat volume (PFV) in the assessment of coronary artery disease (CAD) is largely unknown. We aimed to assess the relationship of PFV, ARD, MPAd, and MPAd/ARD ratio with occlusive CAD (stenosis >50%).This cross-sectional study included patients who had chest pain suggestive of CAD and underwent a 64-multislice multi-detector computed tomography angiography exam to exclude occlusive CAD presence. A total of 145 patients were enrolled in this study. The mean age was 54±10 years, and 51% were males. The mean PFV, ARD, MPAd, and MPAd/ARD ratio in all patients were 155 cm^3, 29.9 mm, 23.4 mm, and 0.8, respectively. On univariate analysis, PFV [odds ratio (OR) (confidence interval, CI)=1.1 (1.01-1.3), p<0.01], ARD [OR (CI)=1.2 (1.1-1.4), p<0.01], and MPAd/ARD ratio [OR (CI)= 0.2 (0.1-0.5), p=0.02] showed significant association with occlusive CAD presence. After adjusting for cardiac risk factors, only PFV [OR (CI)=1.1 (1.02-1.3), p<0.01], but not ARD [OR (CI)=0.9(0.3-2), p=0.85] or MPAd/ARD ratio [OR (CI)=0.1(0.1-2), p=0.69], was independently associated with occlusive CAD. In conclusion, increased PFV, but not ARD or MPAd/ARD ratio, showed a significant and independent association with occlusive CAD presence in patients with chest pain suggestive of CAD.

Introduction

Overall, the incidence and mortality of coronary artery disease (CAD) are still increasing [1]. Occlusive CAD (>50% stenosis) is more likely to be associated with myocardial ischemia and adverse cardiac outcomes. Thus, early recognition of occlusive CAD by simple and non-invasive imaging markers is essential for better risk stratification [1,2].

The wall of the proximal part of the thoracic aorta functions as a robust biomechanical structure through a complex interplay between vascular wall cells and the extracellular matrix. This robust homeostatic process can be disturbed through a variety of disease processes, including aneurysmal formation, bicuspid aortic valve, or risk factors for CAD [3]. A recent study reported a high prevalence of CAD and narrowing of the proximal part of the ascending aorta in patients with homozygous familial hypercholesterolemia [4].

Anatomical and physiological changes in the proximal segments of large arteries, including the aortic root and main pulmonary artery (MPA), may affect cardiac physiology and performance [2,5]. Progressive changes in aortic root diameter (ARD) and MPA diameter (MPAd) may occur even before cardiac dysfunction,

Non-commercial use only

suggesting a possible link between changes in the proximal segments of these large arteries and several cardiac diseases [5].

ARD, MPAd, and MPAd/ARD ratio, which were previously reported to be clinically relevant to cardiopulmonary disease and prognosis, are simple, reproducible, and easily measured by non-invasive imaging modalities such as computed tomography (CT) of the heart or chest without the need for sophisticated software or advanced expertise [6-8]. The clinical significance of these parameters has been studied in patients with pulmonary hypertension, chronic obstructive pulmonary disease exacerbation, heart failure, and cardiovascular morbidity and mortality [2,6,7]. However, little information is available concerning the association of these parameters with CAD, and their predictive significance remains largely unknown.

Recently, pericardial fat, owing to its anatomical proximity to the heart and coronary arteries and its local and systemic adverse effects, has potential diagnostic and predictive values in assessing cardiovascular risk and CAD risk stratification [9,10]. Local adverse effects of pericardial fat, through its paracrine and endocrine roles, may mediate anatomical and functional changes in coronary arteries, aortic valve, and aortic root, leading to coronary atherosclerosis and increased aortic diameter and stiffness, but the exact pathophysiologic mechanism is still unclear, and there is a paucity of data concerning the association of pericardial fat volume (PFV) and occlusive CAD among different ethnic groups with different risk factors for CAD [1,11].

We aimed to assess the potential relationship of PFV, ARD, MPAd, and MPAd/ARD ratio with occlusive CAD (stenosis severity >50%) in patients with chest pain suggestive of CAD.

Materials and Methods

The present study was a single-center, cross-sectional study conducted at Al-Sader Teaching Hospital in Al-Najaf City, Iraq, between July 2021 and February 2022. Patients who had chest pain suggestive of CAD and underwent a 64-multislice multi-detector CT (MDCT) angiography exam to determine if there was any occlusive CAD were included in this study. A history of cardiac risk factors for CAD was obtained from each patient at the time of MDCT examination, including age, sex, hypertension, diabetes mellitus, smoking, family history of premature CAD, dyslipidemia, and body mass index (BMI), as described in detail in our previous study [10].

Multi-detector computed tomography examination

Coronary angiography CT was performed with a 64-slice scanner (Aquilon 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan), with retrospective electrocardiography gating, as previously described in detail [10]. For the measurement of PFV, the amount of fat within the pericardial sac was quantified in a 3D manner with the help of contrast-enhanced imaging. To create a 3D image of the heart, we manually traced the layer of the pericardium. Then, we calculated the total volume of tissue within the pericardium, whose CT density ranged from -250 to -20 HU, to quantify the PFV. This was done using a dedicated workstation (Vitrea® 2 workstation, Vital Image Inc., Plymouth, MN) for image analysis. Occlusive CAD was defined as a mean lumen diameter reduction of >50% in a single vessel by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections. MPAd was measured at the pulmonary artery bifurcation level (Figure 1). ARD was measured at the level of the sinuses of Valsalva (Figure 2). For a better assessment of ARD, measurements of the axial plane of the aortic root are taken using three lines (one line from each sinus), and an average value is calculated for each case. The largest transverse diameter of both arteries perpendicular to their long axis was measured using oblique multiplanar reconstruction. Two independent radiologists with more than 5 years of experience in coronary MDCT angiography interpretation performed all data analyses, respectively. In the case of disagreement in the measurements between the two readers, the final decision was made by consensus. Verbal informed consent was obtained from all enrolled participants. The study was approved by our Medicine College Board.

Statistical analyses

Continuous data are presented as mean ± standard deviation, and categorical data are presented as numbers with percentages. The correlation between PFV with ARD, MPAd, and MPAd/ARD was performed using the Pearson correlation test. Univariate analysis was employed to assess the effects of PFV, MPAd, and MPAd/ARD ratio in predicting occlusive CAD presence. A multivariate regression analysis was used to assess the associations between MDCT markers and occlusive CAD after adjusting for cardiac risk factors (age, sex,

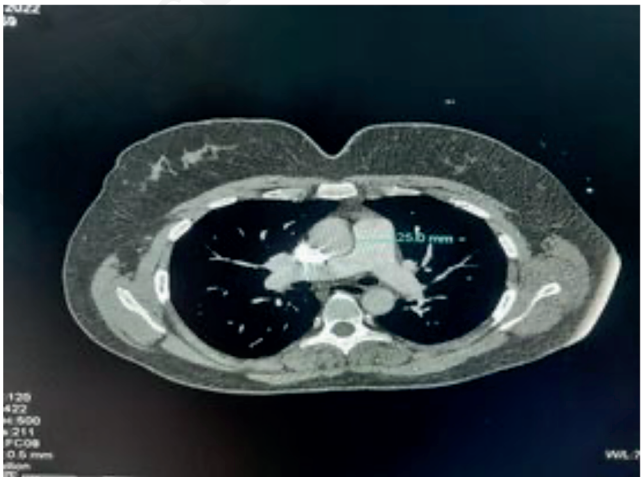

Figure 1. Measurement of main pulmonary artery diameter.

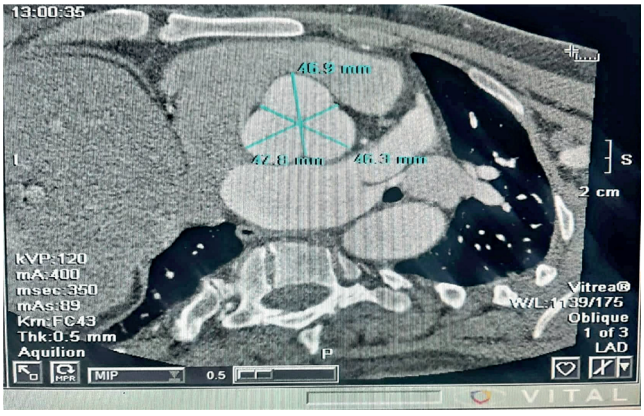

Figure 2. Measurement of aortic root diameter.

OPEN ACCESS

hypertension, diabetes mellitus, smoking, dyslipidemia, family history of premature CAD, and BMI). A p<0.05 was considered statistically significant. All analyses were performed using SPSS for Windows ver. 23.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 145 patients with chest pain suggestive of CAD were enrolled in this study. The mean age was 54±10 years, 51% were males, and nearly half of the patients had a BMI≥30. Baseline comorbidities included diabetes mellitus (30%), hypertension (56%), dyslipidemia (32%), family history of premature CAD (11%), and smoking (20%). Around 30% of patients had occlusive CAD. The mean PFV, ARD, MPAd, and MPAd/ARD ratio in all patients were 155 cm^3, 29.9 mm, 23.4 mm, and 0.8, respectively. The baseline clinical characteristics are shown in Table 1.

As shown in Table 2, PFV showed a significant correlation with ARD (r=0.5, p<0.01) and MPAd/ARD (r=-0.3, p<0.01) while no significant association was noted between PFV and MPAd (r=0.1, p=0.11). On univariate analysis, PFV [odds ratio (OR) (confidence interval, CI)=1.1 (1.01-1.3), p<0.01], ARD [OR (CI)=1.2 (1.1-1.4), p<0.01], and MPAd/ARD ratio [OR (CI)=0.2 (0.1-0.5), p=0.02] showed significant association with occlusive CAD presence, as detailed in Table 3. After adjusting for cardiac risk factors in multivariate regression analysis, only PFV [OR (CI)=1.1 (1.02-1.3), p<0.01], but not ARD [OR (CI)=0.9 (0.3-2), p=0.85] or MPAd/ARD ratio [OR (CI)=0.1(0.1-2), p=0.69], independently associated with occlusive CAD, as shown in Table 4.

Discussion and Conclusions

Our results show that increased PFV, but not ARD or MPAd/ARD ratio, is independently associated with occlusive CAD (stenosis severity >50%) presence. The independent association of PFV with severe CAD is consistent with previous studies that have reported the predictive role of increased cardiac adiposity in CAD progression and development owing to the unique anatomical and functional properties of cardiac adipose tissue. As well as on the development of CAD, PFV assessment could provide helpful data about the cardiovascular prognosis, helping to detect those at risk of adverse outcomes and monitoring patients with metabolic diseases during clinical follow-up [9-12].

A case-cohort study enrolled 998 community-based middle-aged and older adults, who were randomly selected from a 6814 multi-ethnic study of atherosclerosis individuals, and reported that increased PFV assessed by cardiac CT predicts a higher risk of future CAD independent of conventional risk factors, including BMI [13]. The mechanism underlying the relation between pericardial fat and coronary heart disease may be due to its proximity to coronary arteries and the local release of several inflammatory cytokines and mediators. This local inflammatory cytokine release may not be related to the plasma concentrations of circulating cytokines and seems to be independent of other coronary risk factors [14].

A recent comprehensive meta-analysis of 21 studies, involving 846 patients with severe CAD (coronary stenosis ≥50%) and 1762 non-CAD patients, reported that the severe stenosis group had a larger PFV when compared to the coronary stenosis <50% group (p<0.001), supporting the association between increased PFV and the development of CAD [15].

Anatomically, MPA and proximal aorta share a common embryonic origin, and several confounding variables, such as sex,

Table 1. Baseline clinical characteristics.

Variable	n (%) or mean±SD
Age, years	54±10
Obese, BMI≥30	73 (50)
Male	74 (51)
Hypertension	82 (56)
Diabetes mellitus	43 (30)
Dyslipidemia	46 (32)
Family history of premature CAD	16 (11)
Smoking	29 (20)
Occlusive CAD	44 (30)
PFV, cm^3	155±70
ARD, mm	29.9±3
MPAd, mm	23.4±2
MPAd/ARD	0.8±0.09

SD, standard deviation; BMI, body mass index; CAD, coronary artery disease; PFV, pericardial fat volume; ARD, aortic root diameter; MPAd, main pulmonary artery diameter.

Table 2. The correlation of pericardial fat volume with aortic root diameter, main pulmonary artery diameter, and MPAd/ARD ratio.

	PFV	
	r	p
ARD	0.5	<0.01
MPAd	0.1	0.11
MPAd/ARD	-0.3	<0.01

PFV, pericardial fat volume; ARD, aortic root diameter; MPAd, main pulmonary artery diameter.

Table 3. Univariate correlation analysis for the association between occlusive coronary artery disease with pericardial fat volume, aortic root diameter, main pulmonary artery diameter, and MPAd/ARD.

	Occlusive CAD	
Predictors	OR (CI)	p
PFV	1.1 (1.01-1.3)	<0.01
ARD	1.2 (1.1-1.4)	<0.01
MPAd	1 (0.9-1.2)	0.22
MPAd/ARD	0.2 (0.1-0.5)	0.02

CAD, coronary artery disease; OR, odds ratio; CI, confidence interval; PFV, pericardial fat volume; ARD, aortic root diameter; MPAd, main pulmonary artery diameter.

Table 4. Multivariate regression analysis for occlusive coronary artery disease.

	Occlusive CAD	
Predictors	OR (CI)	p
PFV	1.1 (1.02-1.3)	<0.01
ARD	0.9 (0.3-2)	0.85
MPAd	1.2 (0.3-4)	0.76
MPAd/ARD	0.1 (0.1-2)	0.69
Age	1.1 (1-1.4)	<0.01
Male sex	1 (0.9-1.2)	0.70
Diabetes mellitus	4 (1.5-10)	<0.01
Hypertension	1 (0.7-1.1)	0.05
BMI	1 (0.9-1.1)	0.70
Family history of premature CAD	1.4 (0.5-4)	0.71
Dyslipidemia	0.6 (0.2-2)	0.43
Smoking	1.7 (0.4-6)	0.40

CAD, coronary artery disease; OR, odds ratio; CI, confidence interval; PFV, pericardial fat volume; ARD, aortic root diameter; MPAd, main pulmonary artery diameter; BMI, body mass index.

Non-commercial use only

degeneration of the media layer, or body surface area, influence the MPA and ARD equally. Thus, using the MPAd/ARD ratio might provide an internal standardization and show the overall interaction of different risk factors influencing the prognosis of the cardio-respiratory system [16]. Moreover, MPAd and ARD can be measured on just one axial slice at the site of pulmonary artery bifurcation [17]. The common embryonic origin and similarity in the remodeling process involving the arterial wall of MPA and the proximal aorta may explain the clinical use of both arteries as a diagnostic or prognostic tool in pathologic processes related to the cardio-respiratory system [16,18].

Although we observed a significant association between ARD and MPAd/ARD with PFV and between ARD and MPAd/ARD ratio with occlusive CAD in the univariate analysis, the association of ARD and MPAd/ARD with occlusive CAD did not persist after adjusting for cardiac risk factors. Previous clinical studies showed that increased ARD, in the absence of aneurysmatic alterations, was associated with several cardiovascular risk factors and was predictive of a worse cardiovascular prognosis [19-21].

The pathophysiological mechanisms underlying non-aneurysmal dilatation of the proximal aorta are complex and may not be related to atherosclerosis but may be linked to the interplay of other hemodynamic and non-hemodynamic factors, such as wall stress, inflammatory processes, growth factor imbalance, sympathetic nervous system dysfunction, or extracellular matrix disturbances [22].

In the Chin-Shan community cardiovascular cohort study, the predictive role of ARD on cardiovascular morbidity and mortality was assessed in 1851 Chinese participants over a median follow-up period of up to 13 years. Increased ARD was linked to an increased risk of cardiovascular adverse outcomes in univariate analysis. However, this positive association was confounded by age and other conventional cardiovascular risk factors in multivariate regression analysis, suggesting a minor role of atherosclerosis in the dilatation of the proximal aorta [19].

Furthermore, a multicenter, population-based study sponsored by the National Heart, Lung, and Blood Institute found that ARD was positively associated with left ventricular hypertrophy and mass, increased risk for congestive heart failure, stroke, cardiovascular disease mortality, and total mortality, but not with incident myocardial infarction after adjustment for other cardiovascular risk factors [20].

Taken together, these previous findings along with our findings may suggest that increased ARD can be regarded as a marker of later consequences of the impact of several cardiac risk factors, such as older age, diabetes mellitus, or PFV, rather than a mediator of coronary atherosclerosis or acute coronary events [20-22].

The possible strength of the present study is that 3D volumetric measurement of fat deposition in the pericardial sac and MDCT assessment of proximal large arteries and CAD were performed concurrently. In addition, MDCT combined with retrospective electrocardiogram gating provides heart images with high time resolution and reconstructs multiphase images of the whole cardiac cycle for assessing the ARD and MPAd accurately without motion artifacts in comparison to echocardiography measurement [23].

The present study has some limitations. This is a single-center study that included patients with chest pain suggestive of CAD. Therefore, our findings may not be generalizable to other populations. Also, we assessed the association of imaging parameters with occlusive CAD but not acute coronary events. Furthermore, the hemodynamic significance of the functional severity of occlusive coronary lesions was not assessed in this study (using CT-derived coronary fractional flow reserve). ARD and MPA measurements were performed without indexing the body surface area. However, the MPAd/ARD ratio may allow for normalization of the effect of body surface area by accounting for the baseline great vessel size. The causal association between PFV and occlusive CAD cannot be confirmed because of the cross-sectional design of the study, which may not reflect this association over time. Our findings should be prospectively tested for further validation.

In conclusion, increased PFV, but not ARD or MPAd/ARD ratio, showed a significant and independent association with occlusive CAD presence in patients suspected of CAD.

References

1. Yu W, Liu B, Zhang F, et al. Association of epicardial fat volume with increased risk of obstructive coronary artery disease in Chinese patients with suspected coronary artery disease. J Am Heart Assoc 2021;10:e018080.
2. Von Krüchten R, Lorbeer R, Peters A, et al. Association between large arteries diameter and heart function in subjects free of cardiovascular diseases. J Pers Med 2022;12:889.
3. Fletcher AJ, Syed MBJ, Aitman TJ, et al. Inherited thoracic aortic disease: new insights and translational targets. Circulation 2020;141:1570-87.
4. Kholaif N, Mohamed TI, Alharbi IS, et al. Management and clinical outcomes of patients with homozygous familial hypercholesteremia in Saudi Arabia. Monaldi Arch Chest Dis 2023; 93:2503.
5. Chung KS, Kim YS, Kim SK, et al. Functional and prognostic implications of the main pulmonary artery diameter to aorta diameter ratio from chest computed tomography in Korean COPD patients. PLoS One 2016;11:e0154584.
6. Nakanishi R, Rana JS, Shalev A, et al. Mortality risk as a function of the ratio of pulmonary trunk to ascending aorta diameter in patients with suspected coronary artery disease. Am J Cardiol 2013;111:1259-63.
7. Truong QA, Massaro JM, Rogers IS, et al. Reference values for normal pulmonary artery dimensions by noncontrast cardiac computed tomography: the Framingham Heart Study. Circ Cardiovasc Imaging 2012;5:147-54.
8. Karakus G, Kammerlander AA, Aschauer S, et al. Pulmonary artery to aorta ratio for the detection of pulmonary hypertension: cardiovascular magnetic resonance and invasive hemodynamics in heart failure with preserved ejection fraction. J Cardiovasc Magn Reson 2015;17:79.
9. Villasante Fricke AC, Iacobellis G. Epicardial adipose tissue: clinical biomarker of cardio-metabolic risk. Int J Mol Sci 2019; 20:5989.
10. Nafakhi H, Al-Mosawi AA, Mudhafar MM. Pericardial fat versus BMI in the assessment of coronary atherosclerotic burden in patients with diabetes mellitus. Acta Diabetol 2020;57:605-11.
11. Chang SH, Chu PH, Tsai CT, et al. Both epicardial and peri-aortic adipose tissue blunt heart rate recovery beyond body fat mass. Front Cardiovasc Med 2022;9:939515.
12. Tarsitano MG, Pandozzi C, Muscogiuri G, et al. Epicardial adipose tissue: a novel potential imaging marker of comorbidities caused by chronic inflammation. Nutrients 2022;14:2926.
13. Ding J, Hsu FC, Harris TB, et al. The association of pericardial fat with incident coronary heart disease: the multi-ethnic study of atherosclerosis (MESA). Am J Clin Nutr 2009;90:499-504.
14. Mazurek T, Zhang L, Zalewski A, et al. Human epicardial adipose tissue is a source of inflammatory mediators. Circulation 200318;108:2460-6.

Non-commercial use only

OPEN ACCESS

15. Wang Q, Chi J, Wang C, et al. Epicardial adipose tissue in patients with coronary artery disease: a meta-analysis. J Cardiovasc Dev Dis 2022;9:253.
16. Dogan C, Bayram Z, Efe SC, et al. Prognostic value of main pulmonary artery diameter to ascending aorta diameter ratio in patients with advanced heart failure. Acta Cardiol 2021;76: 1108-16.
17. Nguyen-Thu H, Ohyama Y, Taketomi-Takahashi A, et al. Pulmonary artery diameter (PAD) and the pulmonary artery to aorta ratio (PAD/AAD) as assessed by non-contrast cardiac CT: the association with left ventricular (LV) remodeling and the LV function. Intern Med 2022;61:1809-15.
18. Sheikhzadeh S, De Backer J, Gorgan NR, et al. The main pulmonary artery in adults: a controlled multicenter study with assessment of echocardiographic reference values, and the frequency of dilatation and aneurysm in Marfan syndrome. Orphanet J Rare Dis 2014;9:203.
19. Lai CL, Chien KL, Hsu HC, et al. Aortic root dimension as an independent predictor for all-cause death in adults <65 years of age (from the Chin-Shan community cardiovascular cohort study). Echocardiography 2010;27:487-95.
20. Gardin JM, Arnold AM, Polak J, et al. Usefulness of aortic root dimension in persons > or = 65 years of age in predicting heart failure, stroke, cardiovascular mortality, all-cause mortality and acute myocardial infarction (from the cardiovascular health study). Am J Cardiol 2006;97:270-5.
21. Cuspidi C, Facchetti R, Bombelli M, et al. Aortic root diameter and risk of cardiovascular events in a general population: data from the PAMELA study. J Hypertens 2014;32:1879-87.
22. Tadic M, Gherbesi E, Sala C, et al. Is thoracic aortic diameter an independent predictor of cardiovascular disease and mortality? A narrative review. Front Cardiovasc Med 2022;9:867026.
23. Zheng X, Deng YJ, Han FG, et al. Assessment of thoracic aorta in different cardiac phases in patients with non-aorta diseases using cardiac CT. Sci Rep 2021;11:15209.

Non-commercial use only