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Predictors Associated With Increased Prevalence of Abdominal Aortic Aneurysm in Chinese Patients with Atherosclerotic Risk Factors

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WHAT THIS PAPER ADDS

This study determined the prevalence and predictors of abdominal aortic aneurysm (AAA) in Chinese patients with atherosclerotic risk factors. Although epidemiological screening studies have demonstrated that the prevalence of AAA of Asian origin appeared to be lower, this is the first study to focus on AAA prevalence in Chinese patients with atherosclerotic risk factors. The results from the present study demonstrate that the recent screening strategies for AAA may not be applicable to the Chinese population, and a high risk group that may be suitable for AAA screening is identified.

Objective/Background: Epidemiological screening studies have demonstrated that the prevalence of abdominal aortic aneurysm (AAA) of Asian origin appears to be low and so increases uncertainty about the cost effectiveness of screening for AAAs in Chinese people. Some studies have demonstrated a higher prevalence of AAA in patients with atherosclerotic risk factors. The purpose of the study was to determine the prevalence of AAA and to explore the high risk group of AAA in Chinese patients with atherosclerotic risk factors.
Methods: From November 2014 to July 2015, a prospective observational study was conducted in Guangdong General Hospital. In total, 1582 consecutive patients with atherosclerotic risk factors and undergoing coronary angiography for suspected or known coronary artery disease were enrolled to be screened for AAA by abdominal aortic ultrasound. Because of inadequate ultrasound image quality, the analysis was based on the 1541 (97.4%) patients whose abdominal aortic ultrasound images were adequate.
Results: The prevalence of AAA was 1.6% in the whole study population and 2.9% in male patients aged over 65 years. In multivariate analysis, age $\geq$ 65 years ($p = .029$), smoking ($p = .037$), hypertension ($p = .026$), and aortic root diameter > 30 mm ($p = .003$) were independent predictors of AAA. The prevalence of AAA was 0% (0/153) in patients without any independent predictor, 0.6% (3/502) in patients with one predictor, 1.0% (6/597) in patients with two predictors, 4.8% (12/249) in patients with three predictors, and up to 10% (4/40) in patients with four predictors ($p < .001$; p value for trend $< .001$).
Conclusion: Age $\geq$ 65 years, smoking, hypertension, and aortic root diameter > 30 mm emerged as independent predictors of AAA in Chinese patients. Stepwise increases in the prevalence of AAA were found to depend on the number of independent predictors. Ultrasound screening for AAA could be considered in these high risk patients, especially those with three or four predictors.

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INTRODUCTION

Abdominal aortic aneurysm (AAA) is an important cause of preventable death in the elderly. In spite of the development of further understanding and better treatment of AAA over the last few decades, it continues to be a major cause of death, with 80% overall mortality in the event of rupture.[1,2]

Four large randomised controlled trials (RCTs),[3–6] with AAA prevalence rates of 4—7.2%, demonstrated that screening for AAA in elderly men would reduce AAA specific mortality by 40% during the 3—5 year follow-up period.[7] Owing to the benefit of AAA screening, the 2014

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European Society of Cardiology (ESC) guidelines on the diagnosis and treatment of aortic diseases recommended that population screening for AAA with ultrasound should be performed in all men > 65 years of age (Class I, Level A) and may be considered in women > 65 years of age with a history of current/past smoking (Class IIb, Level C).[8]

However, some studies have demonstrated that the prevalence of AAA of Asian origin may be low.[9–11] The cost effectiveness of screening AAA in these populations with low prevalence was uncertain. As the cost effectiveness of screening AAA is affected by disease prevalence, the present study sought to evaluate a specific population with the potential for higher detection rates of AAA.[12]

Epidemiological screening studies have demonstrated a higher prevalence of AAA in patients with atherosclerotic risk factors than in the normal population.[13–15] AAA and atherosclerosis may share some risk factors, such as age, smoking, hypertension, and hyperlipidaemia.[16] A meta-analysis demonstrated that the prevalence of AAA is approximately 2.4 times higher among patients with a history of coronary artery disease (CAD) compared with the general population without CAD.[17] It was assumed that screening for AAA in these higher risk populations may be more effective.

The purpose of the study was to determine the prevalence of AAA and to explore the high risk group of AAA in Chinese patients with atherosclerotic risk factors.

MATERIALS AND METHODS

Study patients

From November 2014 to July 2015, a prospective observational study was conducted at the Department of Cardiology, Guangdong General Hospital, Guangzhou, People's Republic of China. The study was approved by the ethics committees of Guangdong General Hospital and written informed consent was obtained from all the patients in the study. Screening for AAA by abdominal aortic ultrasound was performed in 1582 consecutive patients with atherosclerotic risk factors undergoing coronary angiography for suspected or known CAD. Atherosclerotic risk factors in the study included smoking history, hypertension, diabetes mellitus, and hyperlipidaemia. Patients with known AAA or with a previous replacement or endovascular aortic surgery for aneurysmal disease were also included. Excluded were patients with abdominal aortic ultrasound images of inadequate quality, autoimmune diseases, or neoplasia. Because of obesity or intestinal gas leading to inadequate quality of the abdominal aortic ultrasound images, 41 (2.6%) patients were excluded from the study. The analysis was based on the 1541 (97.4%) patients whose abdominal aortic ultrasound images were adequate. Demographic data and risk factors were collected prospectively.

Coronary angiography

The study population included patients with atherosclerotic risk factors undergoing coronary angiography for suspected or known CAD. Therefore, coronary angiography was performed in all the patients. CAD was defined by coronary angiography as the existence of a stenosis > 50% of the lumen diameter of at least one major coronary vessel. The severity of CAD referred to the number of identified stenosed vessels (lumen diameter < 50%; one, two, or three vessel disease) and was evaluated by two experienced cardiologists who were blinded to patient demographics and ultrasound evaluation of the abdominal aorta. A third cardiologist was advised in case of disagreement, and the majority view was adopted.

Echocardiography and ultrasound screening of the abdominal aorta

Transthoracic echocardiography was routinely performed in patients with atherosclerotic risk factors. Routine transthoracic echocardiography, including two dimensional, M-mode, and Doppler techniques was performed and measurements were made according to the guidelines of the American Society of Echocardiography.[18] The aortic root diameter was measured at the level of the sinus of Valsalva from the parasternal long axis view at the onset of the QRS complex.

AAA was diagnosed by ultrasound scanning with a Philips iE 33 imager equipped with a 2.0–5.0-MHz multiplane probe. All studies were reviewed by two experienced echocardiographers who were blinded to patient demographics and coronary profile. A third echocardiographer was advised in case of disagreement, and the majority view was adopted.

Following the 2014 ESC guidelines on the diagnosis and treatment of aortic diseases,[8] ultrasound scanning of the abdominal aorta was performed with the patient in the supine position. Scanning the abdominal aorta consisted of longitudinal and transverse images, from the diaphragm to the aortic bifurcation. The maximum infrarenal anterior–posterior aortic diameter was measured from outer edge to outer edge. Final diagnosis of AAA was based on the maximum abdominal aortic diameter measurement of > 30 mm.

Evaluation of atherosclerotic risk factors

The atherosclerotic risk factors evaluated in the present study included age, sex, smoking history, hypertension, diabetes mellitus, hyperlipidaemia, and coronary artery disease.

Hypertension was defined as present if the blood pressure measured twice in the hospital exceeded 140 mmHg (systolic) or 90 mmHg (diastolic), or if the patient had a history of hypertension or current usage of antihypertensive medications.

Diabetes mellitus was defined as present if the fasting plasma glucose exceeded 7.0 mmol/L or 11.1 mmol/L 2 h after a meal, or if the patient had a history of diabetes or current usage of diabetic medications.

Hyperlipidaemia was defined as a low density lipoprotein cholesterol level > 4.1 mmol/L, or total cholesterol level > 5.7 mmol/L, or triglyceride level > 1.7 mmol/L, or current usage of medication to treat hyperlipidaemia.

Fasting blood samples were taken on the morning of the second day in hospital. Serum lipid levels were measured by standard laboratory methods in the clinical laboratory of Guangdong General Hospital.

Statistics

Quantitative data are presented as mean ± SD, and qualitative data as frequencies. Differences between groups were evaluated by the unpaired *t* test for parametric variables, and by the chi-square test for categorical variables. Receiver—operating characteristic (ROC) curve analysis was used to determine the discriminating cutoff value of aortic root diameter for predicting AAA. A multiple logistic regression analysis was used to elucidate the independent predictors of AAA. A p value of $< .05$ was considered statistically significant. All the statistical analyses were done with SPSS for Windows, version 20.0 (IBM, Armonk, NY, USA).

RESULTS

Clinical characteristics of the study population

Of the 1541 study patients (male 70.7%; mean age, 64 ± 10 years) undergoing coronary angiography and abdominal aortic ultrasound, 25 had AAA and 1240 had CAD. In the entire study, the prevalence of AAA was 1.6% (25/1541). Prevalence of AAA was 2.0% (22/1089) in men and 0.7% (3/452) in women. The prevalence of AAA was 1.9% (24/1240) in patients with CAD and 0.3% (1/301) in patients without CAD (statistically non-significant: $p = .085$).The clinical characteristics of patients with and without AAA are given in Table 1.

Aortic root diameter was significantly larger in patients with AAA than in those without (30.56 ± 4.03 vs. 28.26 ± 3.21 mm; $p = .001$). As the normal value of aortic root diameter for Chinese has not yet been determined, ROC curve analysis was used to determine the discriminating cutoff value for predicting AAA. Aortic root diameter > 30 mm was the predictive cutoff value for AAA (area under the curve = .68, sensitivity 56%, specificity 78%; $p = .002$).

Table 1. Clinical characteristics of patients with and without abdominal aortic aneurysm (AAA).

Characteristics	AAA ($n = 25$)	Non-AAA ($n = 1516$)	p
Age (y)	70.12 ± 8.08	63.61 ± 10.11	.001
Age ≥ 65 y	17 (68)	726 (47.9)	.046
Sex (male)	22 (88)	1067 (70.4)	.055
Smoking	15 (60)	534 (35.2)	.010
Hypertension	21 (84)	940 (62.0)	.024
Diabetes mellitus	3 (12)	416 (27.4)	.085
Hyperlipidaemia	12 (48)	628 (41.4)	.508
CAD	24 (96)	1216 (80.2)	.085
Coronary profile			.057
No significant lesion	1 (4)	299 (19.7)	
One vessel disease	9 (36)	353 (23.3)	
Two vessel disease	3 (12)	293 (19.3)	
Three vessel disease	12 (48)	571 (37.7)	
Aortic root diameter (mm)	30.56 ± 4.03	28.26 ± 3.21	.001
Aortic root diameter > 30 mm	14 (56)	336 (22.2)	.001
Abdominal aortic diameter (mm)	43.52 ± 18.16	18.61 ± 2.68	.001

Data are presented as mean ± SD or *n* (%).
Note. CAD = coronary artery disease.

Factors associated with the presence of AAA

To identify independent factors associated with the presence of AAA, clinical variables (age ≥ 65 years, sex, smoking, hypertension, diabetes mellitus, hyperlipidaemia, CAD and aortic root diameter > 30 mm) were entered into a multivariate logistic regression model. On multivariate analysis, age ≥ 65 years (odds ratio [OR] 2.69, 95% confidence interval [CI] 1.11—6.54; $p = .029$), smoking (OR 2.63, 95% CI 1.06—6.49; $p = .037$), hypertension (OR 3.47, 95% CI 1.16—10.38; $p = .026$), and aortic root diameter > 30 mm (OR 3.54, 95% CI 1.56—8.06; $p = .003$) were independent predictors of AAA. However, CAD was not an independent factor associated with the presence of AAA. The factors associated with the presence of AAA are shown in Fig. 1.

Prevalence of AAA in patients with different risk factors

According to the 2014 ESC guidelines on AAA screening,[8] the prevalence of AAA was 2.9% (14/478) in male patients over 65 years of age. As age ≥ 65 years, smoking, hypertension, and aortic root diameter > 30 mm were independent predictors of AAA, stepwise increases in the prevalence of AAA were found to depend on the number of independent predictors ($p < .001$; p value for trend $< .001$). Prevalence of AAA was 0% (0/153) in patients without any independent predictors, 0.6% (3/502) in patients with one predictor, 1.0% (6/597) in patients with two predictors, 4.8% (12/249) in patients with three predictors, and up to 10% (4/40) in patients with four predictors. The prevalence of AAA in patients with different predictors is shown in Fig. 2.

DISCUSSION

In the present study it was found that the prevalence of AAA was 1.6%. The prevalence of AAA was 2.9% in male patients aged over 65 years of age, according to the 2014 ESC guidelines on AAA screening.[8] To the best of the authors' knowledge, this is the first study to focus on the prevalence of AAA in Chinese patients with atherosclerotic risk factors. The prevalence of AAA in the present study appeared to be lower than in older population studies but not so different from modern data.

Several screening programs in northern Europe during the 1990s reported that the prevalence of AAA in men aged > 65 years ranges between 4.0% and 7.7%.[13] A meta-analysis that included 10 studies reported the prevalence of AAA among male patients with angiography verified CAD or undergoing coronary artery bypass grafting to be 9.5%.[17] However, a study from Sweden in 2011 reported a prevalence of 1.7% of screening detected AAAs in a general population of 65 year old men.[19] Preliminary results from the ongoing English screening program have also revealed a low prevalence of AAA.

The results of the four large RCTs on AAA screening consisted of multiple reports demonstrating a decrease in mortality from ruptured AAA during the last few

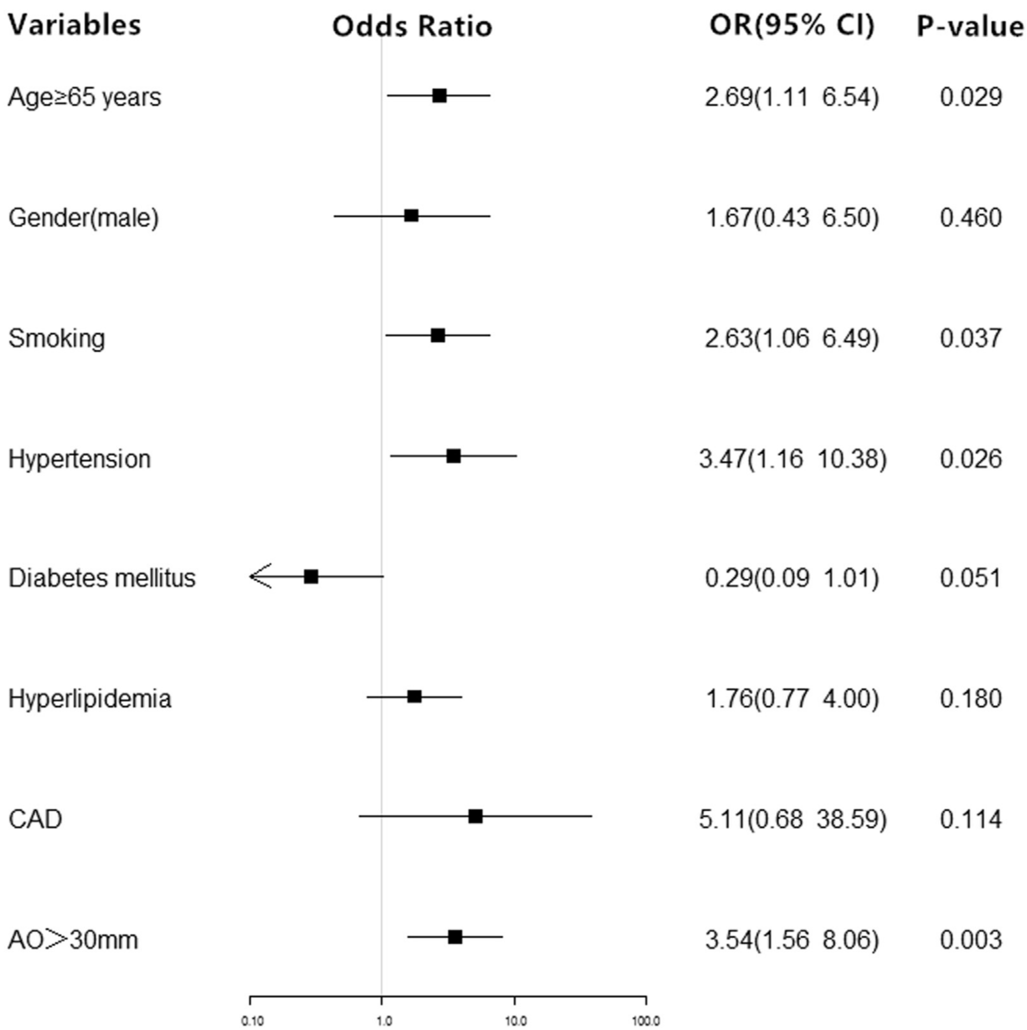

Figure 1. Factors associated with the presence of abdominal aortic aneurysm. *Note.* The dependent variables were the presence of abdominal aortic aneurysm (AAA). The factors analysed included age $\geq$ 65 years, gender, smoking, hypertension, diabetes mellitus, hyperlipidaemia, coronary artery disease (CAD), and aortic (AO) root diameter > 30 mm. OR = odds ratio; CI = confidence interval.

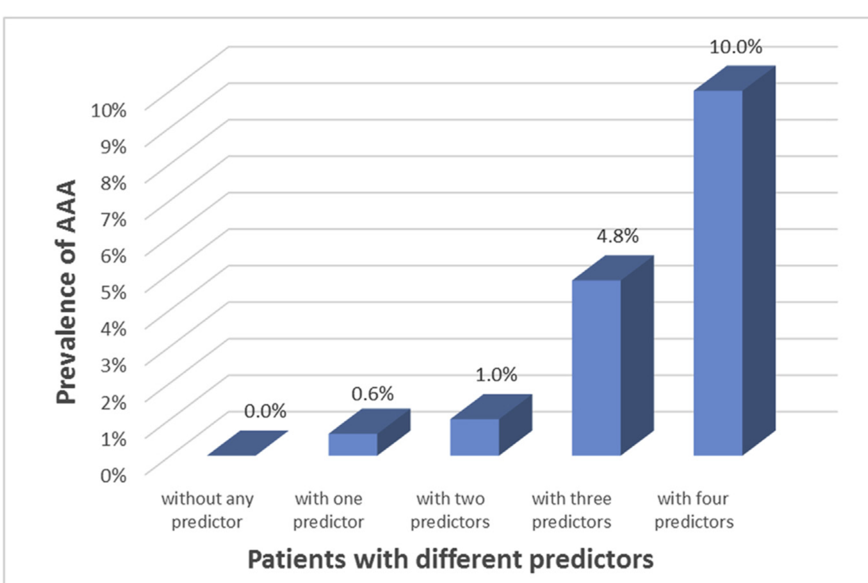

Figure 2. Prevalence of abdominal aortic aneurysm (AAA) in patients with different predictors.

decades.[7,20] It is recommended by the 2014 U.S. Preventive Services Task Force that one time ultrasound screening for AAA should be performed in men aged 65–75 years who have ever smoked, which was consistent with the 2014 ESC guidelines.[8,21] However, the majority of evidence for the guidelines was based on the Caucasian population. Therefore, these screening strategies may not be applicable to ethnically diverse populations.

Furthermore, some studies demonstrated that the prevalence of AAA of Asian origin may be low.[9,11,22] A previous study carried out in England reported that the prevalence of AAA was 4.69% and 0.45% in Caucasians and Asians, respectively.[11] A study from Hong Kong showed that the annual prevalence of AAA was estimated to be 1.05% for those aged 65 years or older. When considering patients with severe CAD, the prevalence of AAA was only 1.8%.[2]

The results of the present study support the hypothesis that the prevalence of AAA in Chinese may be low. The reasons for the low prevalence rate may be as follows. Firstly, Chinese may have smaller abdominal aortic size than other ethnic groups, such as Caucasians, in consideration of obvious body size difference. Recently, a Chinese cohort study found that the average maximum diameter of the infrarenal abdominal aorta was 14.6 ± 2.2 mm (range 7.3–51.3 mm), which is much smaller than in Caucasians.[23] The use of the 30 mm definition for AAA may not be appropriate for the Chinese.[2] Several authors have proposed using an alternative definition of a 50% increased of the normal abdominal aortic diameter. However, when the limit between the aneurysmal and disease free zones is not well delineated, this cannot always be determined.[8] Secondly, besides body size, as well as novel and traditional cardiovascular disease risk factors, either ethnicity related or unmeasured genetic factors may play an independent role in the prevalence of AAA in different ethnic groups.[23] Thirdly, until the late 1990s and early 2000s, prevalence rates of 4–9% among elderly men were reported. During the past decade, however, multiple studies report prevalence rates $< 2\%$ in 65 year old men.[7] The result of the present study is consistent with several recent studies that indicate a low prevalence of AAA in the general population.

As the cost effectiveness of screening AAA is affected by disease prevalence, evaluation of a specific population with the potential for higher AAA detection rates was sought.[12] Therefore, the recent screening strategies for AAA may not be applicable to Chinese populations. In the current study, age ≥ 65 years, smoking, hypertension, and aortic root diameter > 30 mm emerged as independent predictors of AAA. Stepwise increases in the prevalence of AAA were found to depend on the number of independent predictors. Considering the patients with all four of the independent predictors, the prevalence of AAA was up to 10%. Therefore, screening for AAA could be considered in these high risk patients, especially those with multiple risk factors.

The association between AAA and CAD has been mentioned in several studies and explained by the fact that the two diseases share several risk factors.[15,24] In the present study, the prevalence of AAA was 1.9% (24/1240) in patients with CAD and 0.3% (1/301) in patients without CAD, non-significant differences ($p = .085$). In multivariate analysis, some atherosclerotic risk factors such as advanced age, smoking, and hypertension emerged as independent risk factors for the presence of AAA. However, CAD was not associated with the presence of AAA independently. Likewise, some previous observational studies reported no association between AAA and the severity of CAD.[25] These results indicated that AAA and atherosclerosis may share several risk factors, but atherosclerosis alone cannot causally explain AAA.

Atherosclerosis was traditionally thought to be a cause of AAA. However, some recent studies challenged the atherosclerosis theory on the development and progression of AAA based on epidemiological, genetic, and biochemical information. The association between atherosclerosis and AAA formation was also not strong in animal models. Animal models developing atherosclerosis by means of gene modification or diet rarely developed AAA.[25,26] The pathogenesis of AAA and atherosclerotic diseases such as CAD share some similar processes but not all. Macrophage infiltration, inflammation, thrombus formation, and increased vascular smooth muscle cell (VSMC) turnover are involved in the pathogenesis of both AAA and atherosclerosis. However, the density of VSMCs is low in the media and adventitia of aneurysmal wall because of cell apoptosis, while atherosclerosis affects the media and intima of the vessel wall by means of the proliferation of VSMCs. Atherosclerosis will lead to increased intima media thickness and endothelial dysfunction of vessels by macrophage and VSMC migration, lipid deposition, and foam cell formation.[27] In the present study, some of the risk factors for CAD, such as advanced age, smoking, and hypertension, did emerge as being independently associated with the presence of AAA. However, according to recent studies, it is now not possible to determine whether these risk factors increase the risk of AAA by means of promoting atherosclerosis, or if they promoted AAA further leading to CAD development.

Transthoracic echocardiography is routinely performed in patients with atherosclerotic risk factors to evaluate left ventricular (LV) systolic function, detect regional LV wall motion abnormalities and complications, and assess prognosis in Guangdong General Hospital. In the present study, the aortic root diameter was significantly larger in patients with AAA than in those without. Previous studies have reported that the ascending aorta was larger in patients with AAA than in those without, and screening for AAA during transthoracic echocardiography was useful.[28,29] Moreover, evaluation of the abdominal aortic size during transthoracic echocardiography is not time consuming or laborious, nor is there additional cost.[30] However, the discriminating cutoff value of ascending aortic diameter for predicting AAA in the Chinese was not determined. In the present study, it was found that aortic root diameter > 30 mm was predictive of AAA by ROC curve analysis. After adjusting for age, sex, and some atherosclerotic risk factors, aortic root diameter $>$ 30 mm was independently associated with the presence of AAA. The results of the present study suggest that screening for AAA during transthoracic echocardiography may be effective in patients with atherosclerotic risk factors and a large (> 30 mm) aortic root size.

There were several limitations to this study. Firstly, as the study population was composed of patients with atherosclerotic risk factors in hospital, the prevalence of AAA may not be applicable to the general populations because of this selection bias. Therefore AAA screening in a larger population is necessary to elucidate the prevalence of AAA clearly. Secondly, although the results from the study demonstrate that the recent screening strategies for AAA may not be applicable to the Chinese population, and a high risk group that may be suitable for AAA screening has been identified, more RCTs are required to evaluate the cost effectiveness of screening for AAA in Chinese people. Thirdly, although the study found that AAA and atherosclerosis may share several risk factors, the association between AAA and atherosclerosis has not yet been clarified. It needs more carefully designed, hypothesis driven human and animal studies to clarify the association between AAA and atherosclerosis.

In, conclusion, the prevalence of AAA in Chinese patients with atherosclerotic risk factors appeared to be low. The recent screening strategies for AAA may not be applicable to Chinese populations. Age $\geq$ 65 years, smoking, hypertension, and aortic root diameter > 30 mm emerged as independent predictors of AAA. Stepwise increases in the prevalence of AAA were found to depend on the number of independent predictors. Ultrasound screening for AAA could be considered in these high risk patients, especially those with three or four predictors.

CONFLICT OF INTEREST

None.

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COUP D'OEIL

Bilateral Common Femoral Vein Aneurysms Responsible for Massive Pulmonary Embolism

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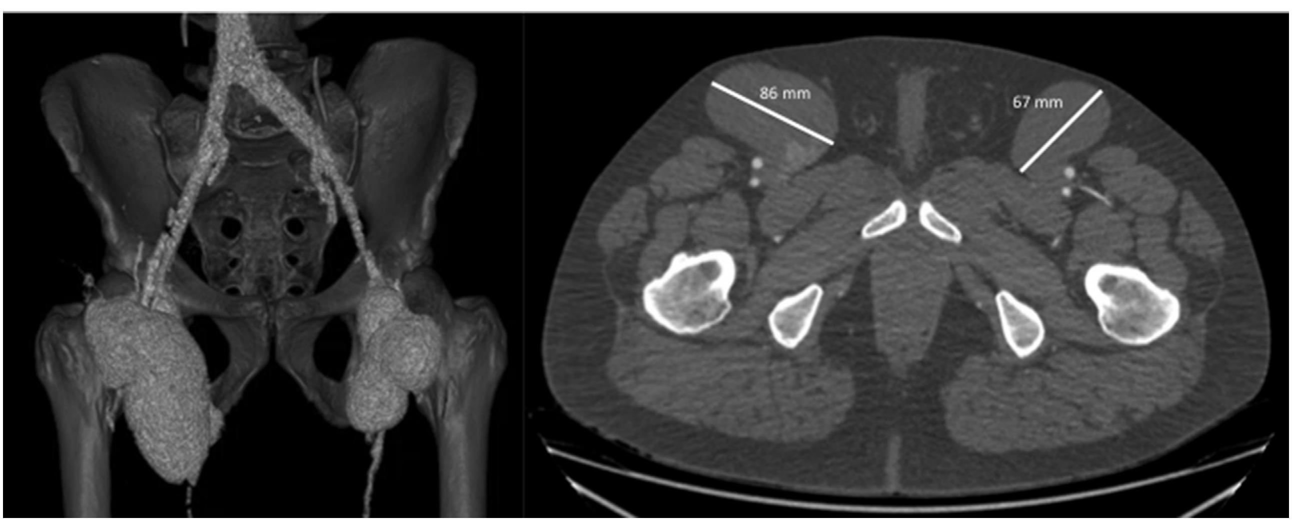

A 55 year old man presented with bilateral groin masses observed when standing, but which disappeared when lying down. Computed tomography angiography, confirmed by Duplex ultrasound, demonstrated two large common femoral vein aneurysms (CFVA) without great saphenous vein varicosities. The right CFVA was treated first by open tangential resection and lateral venorrhaphy. The next day, the patient developed massive pulmonary embolism despite therapeutic anticoagulation. Caval filter placement and left CFVA venorrhaphy were performed with open pulmonary embolectomy under extracorporeal circulatory bypass. Residual thrombus was found in left CFVA that might account for pulmonary embolism. The post-operative course was uneventful afterwards.

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