Distal aortic diameter and peripheral arterial occlusive disease

Maurice A. A. J. van den Bosch, MSc,^{a,b} Yolanda van der Graaf, MD, PhD,^a Bert C. Eikelboom, MD, PhD,^c Ale Algra, MD, PhD,^{a,d} and Willem P. Th. M. Mali, MD, PhD,^c for the SMART Study Group,* Utrecht, The Netherlands

Objective: Several studies have reported an association between abdominal aortic dilatation and peripheral arterial occlusive disease. Narrowing of aortic diameter, also called abdominal aortic hypoplasia, and peripheral arterial occlusive disease have received insufficient attention. Precise estimates of the relationship between aortic hypoplasia and peripheral arterial occlusive disease are lacking. In this study, we assessed the relationship between abdominal aortic diameter and peripheral arterial occlusive disease.

Methods: In this cross-sectional study, we analyzed 1572 patients 18 to 79 years of age, newly referred to the vascular center of our hospital with clinically manifest atherosclerotic arterial disease or for treatment of cardiovascular risk factors. Diameter measurements were used to subdivide patients according to tertiles of abdominal aortic diameter. Peripheral arterial occlusive disease was assessed by adjusted Rose questionnaire, ankle-brachial pressure index, and the presence of gangrene or leg ulcers.

Results: Compared with patients with normal aortic diameter, peripheral arterial occlusive disease was twice as prevalent in patients at both ends of the aortic diameter spectrum. When the lowest tertile was compared with the middle tertile in male patients, the adjusted odds ratio was 1.7 (95% CI, 1.0-3.1). When the highest tertile was compared with the middle tertile, the adjusted odds ratio was 2.1 (95% CI, 1.2-3.4). Similar results were found in female patients. The adjusted odds ratio of lowest versus middle tertile was 2.4 (95% CI, 1.1-5.0) and 1.8 (95% CI, 0.8-4.0) when the highest tertile was compared with the middle tertile.

Conclusion: The risk of peripheral arterial occlusive disease was increased in the lower and upper distribution of aortic diameter. Apparently, both patients with an aortic diameter too large and patients with an aortic diameter too small are prone to peripheral arterial occlusive disease. This is the first large study that shows that small aortic diameter is associated with peripheral arterial occlusive disease. (J Vasc Surg 2001;34:1085-9.)

Results of previous studies suggest that distal aortic diameter plays a role in the development of peripheral arterial occlusive disease. It has been shown that as much as 40% of patients with abdominal aortic aneurysms have peripheral arterial occlusive disease.¹⁻³ Studies that focused on hypoplasia of the distal aorta, as found in the small aortic syndrome, also reported an association with peripheral arterial occlusive disease.⁴⁻⁷

As opposed to studies on aortic aneurysms, the studies on aortic hypoplasia are scarce and there is no generally accepted definition of aortic hypoplasia. Furthermore, studies investigating the relationship between hypoplasia of the

- From the Julius Center for General Practice and Patient Oriented Research,^a and the Departments of Radiology,^b Vascular Surgery,^c and Neurology,^d University Medical Center Utrecht.
- Competition of interest: nil.
- Supported by a grant from the Health Research and Development Council of The Netherlands (grant no. 21000020) and from the University Medical Center Utrecht (Vaatvlag).
- *Members of the Second Manifestations of ARTerial Disease (SMART) Study Group are listed in the acknowledgments.
- Reprint requests: Professor Y van der Graaf, MD, Julius Center for General Practice and Patient Oriented Research, University Medical Center Utrecht, D.01.335, PO Box 85500, 3508 GA Utrecht, The Netherlands (e-mail: y.vandergraaf@jc.azu.nl).

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 $0741-5214/2001/\$35.00 + 0 \quad 24/1/118809$

doi:10.1067/mva.2001.118809

distal aorta and peripheral arterial occlusive disease have frequently selected patients who already had signs of peripheral arterial occlusive disease and so were prone to selection bias. Precise estimates of the relationship between aortic hypoplasia and peripheral arterial occlusive disease are lacking.

To answer the question of whether aortic diameter is associated with peripheral arterial occlusive disease, we conducted a cross-sectional study to assess the association between distal aortic diameter and peripheral arterial occlusive disease in patients with clinically manifest vascular disease and patients treated for cardiovascular risk factors.

METHODS

Patients and study design. Patients included in the Second Manifestations of ARTerial Disease (SMART) Study were included in the present analyses. The SMART study is an ongoing prospective cohort study, started at the Vascular Center of the University Medical Center Utrecht in September 1996. All eligible patients, aged 18 to 79 years, were newly referred to the hospital with atherosclerotic cardiovascular disease, including transient ischemic attack, minor stroke, peripheral arterial occlusive disease, diabetic foot, abdominal aortic aneurysm, angina pectoris, myocardial infarction, and renal artery stenosis, or for treatment of cardiovascular risk factors, including hyperlipidemia, diabetes mellitus, hypertension, and renal insufficiency. Definitions of the diseases qualifying for enrollment are reported elsewhere.⁸ Excluded were

Published online Oct 12, 2001.

Table I. Adjusted Rose questionnaire

Questions	Answer
1. Do you get pain in one or both legs when walking?	Yes*/No
2a. Pain includes calf/calves?	Yes*/No
2b. Pain includes upper leg?	Yes/No
2c. Pain includes buttock?	Yes/No
2d. Pain located elsewhere in leg?	Yes/No
3. Do you get pain when you walk uphill or hurry?	Yes*/No
4. Do you get pain when you walk level at an ordinary pace?	Yes/No
5. Does the pain ever disappear while you continue walking?	Yes/No*
6. What do you do if you get pain when you are walking?	Stop*/Continue
7. What happens to the pain if you stop walking?	Relieved*/Not relieved
8. How soon?	≤10 min*/>10 min
9. Does the pain ever begin when you are at rest?	Yes/No*

*If questions 1, 2a, 3, and 5 through 9 are answered in the manner designated by the asterisk, the adjusted algorithm is positive and the symptoms of the patient are classified as intermittent claudication.

Table II. Characteristics of the study population*

Total	1572
Referral diagnosis (%)	
Transient ischemic attack or minor ischemic stroke	22
Coronary ischemia	21
Peripheral arterial occlusive disease	20
Renal artery stenosis	1
Diabetes mellitus type 1 or 2	11
Diabetic foot	2
Hyperlipidemia	12
Hypertension	11
Age (y)	56 (18-79)
Male sex (%)	66
Body mass index (kg/m ²)	26 (16-55)
Smoking past or current (%)	75
Hypertension (%)†	48
Hypercholesterolemia (%)‡	86
Diabetes mellitus (%)§	27

*Values are percentages or medians with range in parentheses.

†Systolic pressure ≥160 mmHg, diastolic pressure ≥95 mm Hg, or taking antihypertensive drugs.

 \pm Total cholesterol \geq 6.5 mmol/L, triglycerides \geq 2.3 mmol/L, high-density–lipoprotein cholesterol \leq 1.0 mmol/L, or taking lipid-lowering drugs. \$Fasting serum glucose \geq 7.0 mmol/L, nonfasting serum glucose \geq 11.1 mmol/L, or taking insulin therapy/oral blood sugar–lowering drugs.

patients with terminal malignancy and patients not sufficiently fluent in Dutch. The study was approved by the ethics committee of the hospital, and all patients gave written informed consent. The first objectives of the SMART study were to determine the prevalence of concomitant arterial disease at other sites and risk factors in all patients and to study the incidence of future cardiovascular events and their predictors. We used the baseline data of SMART patients and conducted a cross-sectional study to assess the relationship between distal aortic diameter and lower-extremity ischemia in this population.

Data collection. We used data from the first 1768 patients who were enrolled in the SMART study. One hundred seventy-four patients referred for abdominal aortic

aneurysm were excluded because they were a priori selected on aortic diameter. Subsequently, 22 patients were excluded because the abdominal aorta was heavily calcified and ultrasound scan measurement of the aortic diameter could not be performed. A total of 1572 patients, aged 18 to 79 years, was finally included for analysis. Patients underwent baseline examinations, including a questionnaire on cardiovascular disease, height, weight, and blood pressure measurements, blood tests, ultrasound scanning of the abdominal aorta and carotid arteries, and a treadmill test to assess atherosclerosis of the leg arteries.⁸

We categorized smokers as current, past, or never. Body mass index was calculated as body weight divided by height squared (kg/m²). Hypertension was defined by a systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 95 mm Hg or use of an antihypertensive medication. Hypercholesterolemia was defined by a serum total cholesterol ≥ 6.5 mmol/L or use of cholesterol-lowering medication. Diabetes mellitus was defined by fasting serum glucose ≥ 7.0 mmol/L or nonfasting serum glucose ≥ 11.1 mmol/L, or use of glucose-lowering medication.

Measurement of the aortic diameter. Ultrasound scanning was carried out using an HDI 3000 scanner (ATL, Bothell, Wash) equipped with transducers of 2-MHz and 5-MHz, respectively. The ultrasound scan assessment of the aortic diameters was performed by trained examiners. Luminal size of the abdominal aorta was measured 10 mm above the bifurcation. All diameter measurements were performed anteroposteriorly. The echo-free lumen of the vessels was measured between the inner trailing edge of the anterior wall and the inner edge of the posterior wall. The measurements were performed in both transverse and longitudinal sections, taking special care to perform all diameter measurements perpendicular to the long axis of the vessel. To reduce machine variability, all measurements were performed with the same scanner.

Indicators and definition of peripheral arterial occlusive disease. In this cross-sectional study we used the following indicators of peripheral arterial occlusive disease⁹:

	Lowest tertile	Middle tertile	Highest tertile
Men	n = 314	n = 325	n = 400
Tertile range (mm)	8.0-15.9 mm	16.0-17.9 mm	18.0-63.0 mm‡
Mean age (y) (range)	53 (19-78)	55 (18-79)	61 (24-79)
Intermittent claudication [†]	32 (10)	18 (6)	55 (14)
Resting ABPI ≤0.90	86 (27)	57 (18)	119 (30)
Gangrene/ulcers	24 (8)	21 (6)	24 (6)
At least one of above	105 (33)	75 (23)	141 (35)
Women	n = 178	n = 199	n = 156
Tertile range (mm)	8.0-13.0 mm	13.1-15.0 mm	15.1-50.0 mm§
Mean age (y) (range)	51 (18-77)	54 (19-79)	59 (27-79)
Intermittent claudication [†]	19 (11)	10 (5)	16 (10)
Resting ABPI ≤ 0.90	49 (28)	48 (24)	49 (31)
Gangrene/ulcers	16 (9)	10 (5)	9 (6)
At least one of the above	61 (34)	56 (28)	57 (37)

Table III.	Indicators of periphera	l arterial occlusiv	e disease acco	ording to tertile	of abdominal	aortic diameter in
patients*						

*Percentages are given in parentheses except where otherwise indicated.

†Positive adjusted Rose algorithm.

 \pm Aortic diameter > 55.0 mm, n = 30. Aortic diameter > 55.0 mm, n = 3.

\$Aortic diameter 30.0-55.0 mm, n = 1.

- 1. Intermittent claudication was present if the algorithm of the adjusted Rose questionnaire was positively answered, such as the following: patient gets pain in one or both legs on walking, the pain includes calf/calves, pain when walking uphill or in a hurry, the pain does not disappear while walking, pain disappears within 10 minutes after termination of walking, and there is no pain at rest (Table I).¹⁰
- Presence of atherosclerosis in the leg arteries was evaluated by measuring the ankle-brachial pressure index (ABPI) at rest. The systolic blood pressure in the posterior tibial and dorsal pedal arteries (left and right) was measured with an 8-MHz continuous-wave Doppler probe connected to an IMEXLAB 9000 Vascular Diagnostic System (Imex Medical Systems, Golden, Colo) and in both brachial arteries with a semiautomatic oscillometric device (Omega 1400, In Vivo Research Laboratories, Broken Arrow, Okla). For analysis, the lowest resting ABPI of both legs of each patient was calculated and dichotomized as abnormal ABPI (≤0.90) and normal ABPI (>0.90).
- 3. Presence of gangrene or arterial ulcers in one or both legs, reported by the patient in the questionnaire at time of referral to the vascular center, was a third indicator.

In this study, peripheral arterial occlusive disease was defined as presence of intermittent claudication, gangrene, or arterial ulcers, or a resting ankle-brachial pressure of 0.90 or less in one or both legs.

Statistical analysis. Aortic diameter was assessed as a continuous variable and expressed in millimeters. To assess the prevalence of peripheral arterial occlusive disease according to aortic size, aortic diameters were subsequently subdivided into tertiles. Because aortic diameter is influenced by gender, with men having larger diameters than women, tertiles were separately calculated for male and female patients.¹¹ To evaluate the association between peripheral arterial occlusive disease and abdominal aortic diameter, multiple logistic regression models were used. Odds ratios and 95% confidence intervals (CI) were calculated for the lowest and highest tertile and compared with the reference, the middle tertile. Adjustment was made for factors related to both aortic diameter and risk of peripheral arterial occlusive disease. Increased age and increased body mass index are related to increased aortic diameter and increased risk of peripheral arterial occlusive disease. For this reason, adjustment for these two factors was made. In addition, odds ratios were adjusted for putative confounders, ie, smoking, hypercholesterolemia, diabetes, and hypertension.

RESULTS

Table I presents the adjusted Rose questionnaire. Intermittent claudication was present if questions 1, 2a, 3, and 5 through 9 were positively answered. Based on the questionnaire, 150 patients (10%) were classified as having intermittent claudication, 105 men (10%) and 45 women (9%).

Referral diagnosis and characteristics of the participants are shown in Table II. Age of the 1572 patients varied between 18 and 79 years (median, 56 years), and 66% of the patients were men. The prevalence of traditional cardiovascular risk factors was high in the study population; 75% of the patients were current or past smokers, 48% were hypertensive, 86% had hypercholesterolemia, and 27% had diabetes mellitus.

Table III shows the indicators of peripheral arterial occlusive disease according to tertile of the abdominal aortic diameter in 1039 male and 533 female patients. Compared with their incidence in patients of the middle tertile, intermittent claudication, a resting ABPI ≤ 0.90 , and presence of gangrene or leg ulcers were all more prevalent

Table IV. Odds ratios (95% CI) for peripheral arterial occlusive disease in relation to tertiles of the aortic diameter*

	Crude OR	Adjusted OR†
Male patients		
First vs second tertile	1.8(1.0-3.2)	1.7(1.0-3.1)
Third vs second tertile	2.2 (1.3-3.7)	2.1(1.2-3.4)
Female patients	· · · · ·	· · · · ·
First vs second tertile	2.2(1.1-4.6)	2.4(1.1-5.0)
Third vs second tertile	2.0 (1.0-4.2)	1.8 (0.8-4.0)

*Peripheral arterial occlusive disease was defined as presence of lifestylelimiting intermittent claudication, gangrene, or ulcers, or a resting ABPI of less than 0.90 in one or both legs.

†Adjusted for age and body mass index.

OR, Odds ratio.

in patients of the lowest tertile. A similar association was found when the highest tertile was compared with the middle tertile; male and female patients of the highest tertile presented signs of lower-extremity ischemia more often.

Table IV presents the adjusted odds ratios reflecting the strength of the association between peripheral arterial occlusive disease and aortic diameter in male and female patients. Peripheral arterial occlusive disease in male patients was more prevalent in the lowest tertile. Compared with that of the middle tertile, the adjusted odds ratio was 1.7 (95% CI, 1.0-3.1). When the highest tertile was compared with the middle tertile, peripheral arterial occlusive disease was more prevalent in the highest tertile; the adjusted odds ratio was 2.1 (95% CI, 1.2-3.4).

Similar results were found in female patients. When the lowest tertile was compared with the middle tertile, the adjusted odds ratio was 2.4 (95% CI, 1.1-5.0). Compared with that of the middle tertile, peripheral arterial occlusive disease was also more prevalent in the highest tertile; the adjusted odds ratio was 1.8 (95% CI, 0.8-4.0). The results did not change after additional adjustment for atherosclerotic risk factors, ie, smoking, hypercholesterolemia, diabetes, and hypertension.

DISCUSSION

The abdominal aortic diameter is normally distributed and represents a continuum of sizes in which patients with a small diameter and patients with a large diameter represent the ends of this continuum.¹¹⁻¹³ Compared with patients with a normal aortic diameter, peripheral arterial occlusive disease was twice as prevalent in patients at both ends of this aortic diameter spectrum and was equally distributed in men and women. Apparently, both patients with an aortic diameter too large and patients with an aortic diameter too small are prone to peripheral arterial occlusive disease. It is possible that in these patients, abnormal aortic diameters induce hemodynamic changes that could result in vessel-wall damage and so cause peripheral arterial occlusive disease.

In this study, peripheral arterial occlusive disease was defined as the presence of intermittent claudication, gangrene, or arterial ulcers, or a resting ABPI of 0.90 or less in one or both legs. In each tertile, there was a significant difference between the number of patients with a resting ABPI ≤ 0.90 and the number that actually had intermittent claudication. This discrepancy indicates that there is a portion of patients with low ABPI without symptoms. However, results of previous studies have already pointed out that low ABPI is not automatically related to symptoms of intermittent claudication.⁹

The relationship between aortic diameter and peripheral arterial occlusive disease may have considerable implications for the risk management of these patients. Control of conventional risk factors (smoking, hypertension, diabetes, and hypercholesterolemia) may be particularly important in these patients. We believe that determination of abdominal aortic diameter by ultrasound scan should be considered as a part of total risk profile assessment. In this way patients at high risk could be identified.

The association between abdominal aortic aneurysm and peripheral arterial occlusive disease is well known and is found in about 20% to 40% of patients with abdominal aortic aneurysms.¹⁻³ In 1988, Allerdice et al² screened the abdominal aorta in 100 patients with peripheral arterial occlusive disease and in 100 controls. The incidence of abdominal aortic aneurysm in the patient group was 20%, as compared with 2% in the control group.² More recently, Kanagasabay et al¹⁴ compared patients with abdominal aortic aneurysm with patients with a normal aortic diameter and concluded that patients with aortic aneurysm presented symptoms of lower-extremity ischemia more often. Our results are consistent with these findings.

The association between aortic hypoplasia and peripheral arterial occlusive disease was also reported in several studies.⁴⁻⁷ However, most of these studies were hampered by methodologic problems such as lack of a good definition of hypoplasia and selection bias. Hypoplasia of the abdominal aorta is known in the literature under many different names, such as small aortic syndrome, atresia of the aorta, and hypoplastic aorta iliac syndrome, frequently meaning slightly different, not well-defined disease entities. There is not a single definition of hypoplasia of the abdominal aorta, nor is it known how it should be measured.¹⁵⁻²⁴ Clemetson et al⁶ defined aortic hypoplasia as a corrected internal diameter of 12.5 mm or less measured on angiogram but did not indicate where the measurement had to be done. Shin et al²⁴ defined hypoplasia as an aortic diameter of 10 to 12 mm measured by computed tomography 1 cm below the orifice of the superior mesenteric artery.²⁴ None of these studies took into account the normal distribution of aortic diameter, nor did they differentiate between men and women. Only Cronenwett et al¹³ recognized this and defined a small aorta by using the aortic diameter minus one standard deviation below overall mean measured on angiogram in a population of women with atherosclerotic disease.

Another methodologic problem is selection bias. Most studies on aortic hypoplasia were done in a selected population with peripheral arterial occlusive disease, because angiograms on which the measurements to assess hypoplasia were done were nearly always made because of peripheral arterial occlusive disease. This means that an association between hypoplasia and peripheral arterial occlusive disease is always found. Only recently have noninvasive diagnostic tests such as ultrasound scan made it possible to investigate aortic diameter in larger populations that are not a priori selected on peripheral arterial occlusive disease.

In our study, we used ultrasound scan to investigate a population with severe atherosclerotic disease that was not selected on peripheral arterial occlusive disease. To avoid definition problems, we divided the patient group into tertiles and compared the highest and lowest tertiles with the middle tertile. Furthermore, we could differentiate between the diameters of men and women. In this way, our study showed that the association between aortic hypoplasia and peripheral arterial occlusive disease did not differ between men and women, although much literature has suggested this. Because overall aortic diameter in women is smaller than in men, women tend to be over-represented when single absolute cutoff values are taken to define hypoplasia.

In conclusion, both small and large aortic diameters are associated with peripheral arterial occlusive disease. The results regarding small aortic diameter are new. This is the first large study that shows that small aortic diameter is associated with peripheral arterial occlusive disease in a population of patients with risk factors or clinically manifest vascular disease. Because aortic diameter is influenced by age, sex, and body mass index, it is difficult to define precise criteria for aortic hypoplasia. We concluded that the entity hypoplasia is one extreme of a continuous spectrum, as is the entity aneurysm at the other extreme.

The SMART Study Group consists of:

A. Algra, MD, PhD, Julius Center for General Practice and Patient Oriented Research and Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands.

J. D. Banga, MD, PhD, Department of Internal Medicine, University Medical Center Utrecht, Utrecht, The Netherlands.

B. C. Eikelboom, MD, PhD, Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands.

Y. van der Graaf, MD, PhD, Julius Center for General Practice and Patient Oriented Research, University Medical Center Utrecht, Utrecht, The Netherlands.

D. E. Grobbee, MD, PhD, Julius Center for General Practice and Patient Oriented Research, University Medical Center Utrecht, Utrecht, The Netherlands.

P. P. Th. de Jaegere, MD, PhD, Department of Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands.

L. J. Kappelle, MD, PhD, Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands.

H. A. Koomans, MD, PhD, Department of Nephrology, University Medical Center Utrecht, Utrecht, The Netherlands.

W. P. Th. M. Mali, MD, PhD, Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands.

A. J. Rabelink, MD, PhD, Department of Internal Medicine, University Medical Center Utrecht, Utrecht, The Netherlands.

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Submitted Mar 9, 2001; accepted May 25, 2001.