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The Epidemiology of Subclavian Stenosis and its Association with Markers of Subclinical Atherosclerosis: the Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Background—Recent studies indicate that subclavian stenosis (SS), diagnosed by a large systolic blood pressure difference (SBPD) between the right and left brachial arteries, is associated with cardiovascular disease (CVD) risk factors and outcomes. We sought to describe the epidemiology of SS and determine its association with markers of subclinical CVD in the baseline cohort of the Multi-Ethnic Study of Atherosclerosis.

Methods—We defined SS by an absolute SBPD ≥ 15 mmHg. Peripheral artery disease (PAD) was defined by an ankle-brachial index ≤ 0.90 . The coronary artery calcium score (CAC) and the common-carotid artery intima-media thickness (CCA-IMT) were measured by computed tomography and B-mode ultrasound, respectively. Odds ratios for the associations of SS with risk factors and subclinical disease were estimated using logistic regression.

Results—Of 6,743 subjects studied, 307 participants (4.6%) had SS, with a higher prevalence in women (5.1%) than men (3.9%), and in African-Americans (7.4%) and non-Hispanic whites

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(5.1%) than Hispanic (1.9%) or Chinese (1.0%) participants ($p<0.01$). In a model including age, gender, ethnicity, traditional and novel CVD risk factors, significant associations with SS were observed for C-reactive protein (highest vs. three lower quartiles: OR=1.41; 95% CI: 1.06-1.87) and brachial artery pulse pressure (OR=1.12 /10 mmHg; 95% CI: 1.03-1.21). Adjusted for age, gender, ethnicity, traditional and novel CVD risk factors, SS was significantly associated with PAD (OR=2.35; 1.55-3.56), with CCA-IMT (highest vs. the lower three quartiles: OR=1.32; 1.00-1.75), and high CAC (score >100 vs. score=0; OR=1.43; 1.03-2.01).

Conclusions—The subclavian stenosis is positively associated with other markers of subclinical atherosclerosis.

Keywords

subclavian artery; blood pressure; atherosclerosis; epidemiology

Introduction

The term peripheral arterial disease (PAD) is usually associated with the presence of atherosclerotic occlusive lesions affecting the lower limb arteries. It is frequently associated with atherosclerosis in other vascular beds, and predicts subsequent cardiovascular (CVD) events [1-3]. Although ischemic symptoms are much less frequent in the upper compared to the lower limbs, atherosclerosis also affects the upper limbs, especially the subclavian (and innominate) arteries, and may likewise be a marker of diffuse atherosclerosis and increased risk for cardiovascular events [4,5]. The simplest method to detect subclavian stenosis (SS) is to compare the systolic blood pressures in the left and right brachial arteries [4,5]. Using angiography [4], a threshold difference of at least 15 mmHg between both arms appears to be an optimal cut-point for defining SS, and has been found to be associated with CVD risk factors and other cardiovascular comorbidities [5].

Data on the epidemiology of SS in the general population are scarce [5-7]. Moreover, to our knowledge no data on ethnic-specific prevalence of SS has previously been reported. The Multi-Ethnic Study of Atherosclerosis (MESA) provides a unique opportunity to describe the epidemiology of SS in an ethnically diverse cohort and to investigate its relationships with both CVD risk factors and subclinical CVD. We hypothesized that SS is positively associated with risk factors for CVD while also being significantly associated with a higher prevalence of subclinical CVD in other major vascular beds.

Methods

Subjects

MESA investigates the prevalence, correlates, and progression of subclinical CVD in a multi-ethnic, population-based sample of 6814 men and women aged 45–84 years, free of clinical cardiovascular diagnoses at baseline [8]. Participants were enrolled and initially examined from 2000-2002 at six U.S. field centers: Baltimore City and Baltimore County, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan and the Bronx, NY; and St. Paul, MN. The study included 53% women and four ethnic groups: 38% non-Hispanic white, 28% African American, 22% Hispanic, 12% Chinese American. The Institutional Review Boards at all centers approved the study and participants gave informed consent.

The baseline examination, on which this report is based, included ascertainment of medical history and demographic information. Information was collected on anthropometry, blood pressure, ankle-brachial index (ABI), carotid ultrasound, and cardiac computed tomography

for presence of coronary artery calcium (CAC). Medication use (anti-hypertensive drugs, statins, oral hypoglycemic agents, and insulin) was ascertained by self-report and medication inventory.

Laboratory methods

Fasting serum samples were collected from all participants, frozen, and shipped to the the University of Vermont, where they were stored at -80°C prior to being assayed. A detailed description of the laboratory methods has been published [8].

Definition of CVD risk factors

Smoking habits were assessed by quantifying the number of pack-years of cigarettes smoked during lifetime. Diabetes was defined by fasting blood glucose ≥ 126 mg/dl or use of oral hypoglycemic agents or insulin. Systolic and diastolic blood pressures (SBP, DBP) were measured 3 times in the right arm of seated participants with a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL). The average of the last 2 measurements was used in the analyses. The satisfying validity and reproducibility of the blood pressure measurement in MESA are published elsewhere. [9] Hypertension was defined as self-reported history with use of anti-hypertensive medications, or SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg. We also analyzed the respective contributions of the steady and pulsatile components of blood pressure [10], expressed as mean blood pressure (MBP = $2/3\text{DBP} + 1/3\text{SBP}$) and pulse pressure (PP = SBP - DBP). Body mass index (BMI) was calculated by dividing weight by the square of height and expressed in units of kg/m^2 . Dyslipidemia was defined by a total/HDL-cholesterol ratio > 5 or use of lipid-lowering agents [11]. We estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation, as suggested by recent published guidelines and defined chronic kidney disease (CKD) as eGFR < 60 mL/min/1.73m² [12].

Subclinical Disease Measures

The ABI was computed separately for each leg, using the highest of either the posterior tibial artery or dorsalis pedis artery systolic pressures as the numerator and the highest of either the right or left brachial systolic pressures as the denominator [2,3,8,13]. The index ABI was the lower of either the right or left ABI. An ABI ≤ 0.90 was considered abnormal and indicative of PAD.

The protocols for computed tomography of coronary arteries to assess calcification, and measurement of the intima-media thickness by carotid ultrasound were previously described [8,14-16].

Subclavian stenosis screening

The systolic blood pressures of the right and left arms were used to calculate the brachial systolic blood pressure difference (SBPD = systolic pressure in the right arm minus systolic pressure in the left arm). An absolute SBPD ≥ 15 mmHg was used to define subclavian stenosis.

Statistical Methods

Analyses were performed using Stata 10.0 (College Station, Texas). The prevalence of SS by gender (overall and within ethnic groups) was compared using chi-square tests. Logistic regression was used to evaluate the associations of SS with traditional cardiovascular risk factors, as well as pulse pressure, BMI, CKD, C-reactive protein (CRP), interleukin-6 (IL-6), homocysteine and factor-VIIIc. We evaluated the unadjusted association between subclavian stenosis and each risk factor individually, followed by age-, gender-, and

ethnicity-adjusted analyses. In subsequent models we additionally adjusted for smoking, diabetes, hypertension, BMI, dyslipidemia, and pulse pressure. In the final multivariable model we also added non-traditional risk factors (CKD, CRP, IL-6, Factor-VIIIc and homocysteine). Next we evaluated the association of SS with 1) an abnormal ABI, 2) the presence of coronary artery calcification (CAC) and 3) Common carotid artery intima-media thickness (CCA-IMT), using the same model-building strategy as the previous risk factor analysis.

Results

We excluded 71 (1%) study participants who had missing data on brachial systolic blood pressure, leaving 6743 subjects for the analysis. The distribution is presented in Figure 1. The mean SBPD of the study population was -0.63 ± 7.17 mmHg. In 48.1% of participants, the left arm SBP was higher than the right one; the opposite occurred in 38.7%. Both arms' SBPs were exactly equal in 13.2%. Overall, 307 participants (4.5%) had SS (left side, 41.7%; right side, 58.3%). Total SS prevalence was higher in women ($p < 0.05$) than men in all ethnic groups (Table 1). Overall, SS was significantly ($p < 0.01$) more frequent in African Americans (7.4%) and Non-Hispanic Whites (5.1%) than in Hispanics (1.9%) or Chinese Americans (1.0%). The prevalence of SS increased with age in both genders (Figure 2), up to 6.9% among African American women older than 74 years of age.

Adjusted for age, gender and ethnicity (Table 2, model 1), we found diabetes, hypertension, pulse pressure, BMI, and CRP significantly associated with the presence of SS. With full adjustment (Table 2, model 3), only pulse pressure and CRP were positively and significantly associated with SS ($p < 0.05$). However, associations with smoking pack-years, diabetes, hypertension, BMI, dyslipidemia and homocysteine were all in the expected direction (but not statistically significant).

Among subjects with SS, 11.4% also had an ABI ≤ 0.90 (vs. 3.6% in those without SS, $p < 0.001$). In turn, 13.1% of those with PAD had SS, compared to 4.2% in those without PAD ($p < 0.001$). Significantly unadjusted lower value of ABI and higher value of CCA-IMT were seen in participants with SS, compared to those without SS (Table 3). No significant differences were found for CAC scores.

The associations of SS with PAD (ABI ≤ 0.90), elevated CCA-IMT (top quartile, > 0.97 mm) and elevated (> 100) CAC score are shown in table 4. Adjusted for age, gender and ethnicity, a significant positive association was found between SS and PAD, which was observed in both genders, and which was only slightly attenuated, albeit still statistically significant, in the final model. A significant association between SS and elevated CCA-IMT was also found in the fully adjusted model, although it was only statistically significant in men. No heterogeneity was found according to sex. Associations between SS and CAC score > 100 were also seen (Table 4) but without statistical significance with stratification by gender. In an additional series of analyses, the associations between SS and the three markers of subclinical disease (ABI ≤ 0.90 , top quartile CCA-IMT, and CAC > 100) were reassessed by using a lower SBPD threshold to define SS (i.e. 10 mmHg), and none were significant (data not shown).

Discussion

The results of this study support the hypothesis that subclavian stenosis is independently associated with PAD (ABI ≤ 0.90), carotid intima-media thickness (highest vs. other quartiles) and coronary artery calcium score (> 100). Additionally, SS was found to be significantly more frequent among women than men, and in non-Hispanic whites and

African Americans than in Hispanics and Chinese Americans. Significant fully-adjusted risk factor associations were limited to pulse pressure and C-reactive protein, although associations in the expected direction were also seen for other cardiovascular risk factors (e.g., smoking and BMI).

Current research aims at improving risk prediction in the intermediate and low risk Framingham scores by addition, for example, of data on subclinical atherosclerosis markers [17,18]. There is strong evidence that presence and amount of CAC, elevated CCA-IMT and low ABI are able to detect high-risk patients for future CVD events. However, only ABI can be used in the primary care setting, although several reasons (technical aspects, time constraints) limit its extensive use as recommended. [19] Yet, the gap between current risk scores and high-technology (and expensive) methods could be filled by some clinical and easy-access methods. Accordingly, use of the upper limb blood pressure difference could be considered a viable and easy method for determining those at higher risk. [20] It is important to stress that, as a marker of atherosclerosis, we do not consider the upper limb blood pressure difference as a substitute for the ABI. In our cohort, 86.9% of those with PAD (ABI ≤ 0.90) did not have SS, while 88.6% with SS did not have PAD. Yet, we consider these 2 easy-access markers as complementary. Besides, in clinical practice, every patient should have blood pressure measured in both arms, in order to avoid the underestimation of a high blood pressure.

The analysis of longitudinal data from one community-dwelling and two vascular laboratories patients cohorts showed poorer prognosis in those with a SS [6]. During a follow-up of almost 10 years, a SBPD ≥ 15 mmHg was independently associated with an excess risk of overall mortality (OR=1.40, $p<0.01$), and of fatal and non-fatal CVD events (OR=1.57, $p<0.05$) [6]. While SS is mostly (>95%) due to atherosclerosis [21], it may also result from other chronic conditions such as vasculitis, congenital malformations, extrinsic compressions and radiation therapy. Yet, in order to validate SS as a subclinical marker of atherosclerosis, we assessed its association with other markers of atherosclerosis in a large and multi-ethnic population cohort who were free of clinical CVD.

In agreement with two previous reports, the SBPD distribution in MESA showed higher systolic blood pressure in the left arm (fig. 1) and, accordingly, SS was more frequent on the right side [7,22]. However, more studies found the right arm SBP slightly higher than then left one [5,23-25]. We do not have any plausible explanation for the reason why SS has been predominantly found on the right side in our cohort. Notably, the mean SBPD reported in previous studies as well as the one reported in our study are trivial, and the SBPD >15 mmHg retained here as the diagnostic criteria is far beyond differences related to anatomical particularities or random variation [24]. In an angiographic study, a SBPD >15 mmHg was highly specific for SS (at 90%) and of moderate sensitivity (only at 50%).⁴ While severe bilateral SS is exceptional [21], the low sensitivity of SBPD >15 mmHg might in part be due to a concomitant diffusion of severe atherosclerosis in both subclavian arteries [26]. Some authors proposed a SBPD >10 mmHg to define SS [7,27,28]. As expected, this lower threshold is more sensitive (65%) but less specific (85%) of angiographically-determined SS of $>50\%$ [29]. We did not find any association between SBPD >10 mmHg and subclinical CVD, and an earlier report did not reveal any significant relationship between SBPD >10 mmHg and mortality [6]. These findings strongly support the choice of the 15 mmHg threshold for SS as a marker of CVD.

Past clinical studies have already reported an association between SS and other atherosclerosis locations. In a series of patients at high risk for CAD [30], those with SS (7% of their study population) had significantly higher rates of ischemic heart disease detected by stress myocardial single-photon emission computed tomography; a greater extent and

severity of myocardial ischemia in those with SS was also found. In this same study, higher rates of PAD history among those with SS were observed [30]. Among 94 patients in primary care, Clark et al. [28] found a negative correlation between systolic and diastolic magnitudes of inter-arm pressure differences with ABI. In a series of 134 patients referred to vascular surgery, Frank et al. studied different thresholds of SBPD but did not find a significant association between SS and CAD [22]. Conversely, a significant association was found between PAD and systolic inter-arm pressure differences of ≥ 10 mm Hg, ≥ 15 mm Hg, ≥ 20 mm Hg, or ≥ 45 mm Hg [22]. Finally, pooling data from two vascular laboratory and two community-dwelling cohorts, Shadman et al. [5] reported a strong association between SS and PAD (OR=5.11, $p<0.001$) independently of age, gender, ethnicity and traditional risk factors. Conversely, they found a negative association between SS and clinical CAD (OR=0.66, $p=0.05$).

To our knowledge, our study is the first large-scale study in a general population free of clinical CVD to report significant associations of SS with PAD and coronary and carotid markers of atherosclerosis. The association with PAD may be underestimated in our study, because patients with SS could have lower arms' systolic blood pressures overall than those without SS, due to obstructive lesions in both arms. In this case, the ABI calculation could be overestimated, thus resulting in some borderline cases of PAD being categorized as normal (>0.90) ABI.

The reason why higher prevalence of SS in women, already reported in other studies [5], is unclear. This could be related to a different distribution of atherosclerosis in both genders, but this hypothesis requires confirmation. However, the higher prevalence of SS in women can make this condition even more useful to detect subclinical CVD in this gender group. Further analyses in MESA are needed to assess the prognostic value of this condition for CVD events and mortality.

Our study has several limitations. We cannot exclude the possibility that some cases of bilateral SS may be misclassified, resulting in a SBPD of <15 mmHg. This bias, however, would underestimate the associations observed in our study. Also, due to the low rates of SS in at least two ethnic groups (Hispanics and Chinese Americans), we were unable to provide ethnic-specific data regarding risk factors and the association with subclinical CVD. Finally, our data are cross-sectional, and temporality could not be established.

Conclusion

Subclavian stenosis was common in our cohort, especially in non-Hispanic whites and African Americans. In our study, an elevated pulse pressure and C-reactive protein were found to be positively and significantly associated with SS, independently of other risk factors. Other cardiovascular risk factors were shown to be related to SS, although not significantly so, including smoking, diabetes, hypertension, BMI, and dyslipidemia. Subclavian stenosis appears to be associated with subclinical CVD in other vascular beds, and physicians should be alerted by the presence of a significant (≥ 15 mmHg) systolic blood pressure difference in the arms.

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References

1. Criqui MH, Langer RD, Fronek A, Fiegelson HS, Klauber MR, McCann TJ, Browner D. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992;326:381–6. [PubMed: 1729621]
2. Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B. American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006 Mar 21;113(11):e463–654. [PubMed: 16549646]
3. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR. on behalf of the TASC II working group. Inter-society consensus for the management of peripheral arterial disease (TASC II). *Eur J Vasc Endovasc Surg* 2007;33:S1–S75. [PubMed: 17140820]
4. Osborn LA, Vernon SM, Reynolds B, Timm C, Allen K. Screening for subclavian stenosis in patients who are candidates for coronary bypass surgery. *Cathet Cardiovasc Intervent* 2002;56:162–5.
5. Shadman R, Criqui MH, Bundens WP, Fronek A, Denenberg JO, Gamst AC, McDermott MM. Subclavian stenosis: the prevalence, risk factors and association with other cardiovascular diseases. *J Am Coll Cardiol* 2004;44:618–23. [PubMed: 15358030]
6. Aboyans V, Criqui MH, McDermott MM, Allison MA, Denenberg JO, Shadman R, Fronek A. The vital prognosis of subclavian stenosis. *J Am Coll Cardiol* 2007;10(49):1540–5. [PubMed: 17418292]
7. Kimura A, Hashimoto J, Watabe D, Takahashi H, Ohkubo T, Kikuya M, Imai Y. Patient characteristics and factors associated with inter-arm difference of blood pressure measurements in a general population in Ohasama, Japan. *J Hypertens* 2004;22:2277–83. [PubMed: 15614021]
8. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, et al. Multi-ethnic study of atherosclerosis: objectives and design. *Am J Epidemiol* 2002;156:871–81. [PubMed: 12397006]
9. Ni H, Wu Colin, Prineas R, Shea S, Liu K, Kronmal R, Bild D. Comparison of Dinamap Pro-100 and mercury sphygmomanometer blood pressure measurements in a population study. *Am J Hypertens* 2006;19:353–60. [PubMed: 16580569]
10. Safar, ME.; London, GM. The arterial system in human hypertension. In: Swales, JD., editor. *Textbook of Hypertension*. London, UK: Blackwell Scientific; 1994. p. 85-102.
11. Natarajan S, Glick H, Criqui M, Horowitz D, Lipsitz SR, Kinossian B. Cholesterol measures to identify and treat individuals at risk of coronary heart disease. *Am J Prev Med* 2003;25:50–7. [PubMed: 12818310]
12. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. *Am J Kidney Dis* 2002;39(Suppl 1):S1–S266. [PubMed: 11904577]

13. Aboyans V, Criqui MH, McClelland RL, Allison MA, McDermott MM, Goff DC, Manolio TA. Intrinsic contribution of gender and ethnicity to normal anklebrachial index values: The Multi-Ethnic Study of Atherosclerosis (MESA). *J Vasc Surg* 2007;45:319–27. [PubMed: 17264011]
14. Carr JJ, Crouse JR, Goff DC, D'Agostino RB, Peterson NP, Burke GL. Evaluation of sub-second gated helical CT for quantification of coronary artery calcium and comparison with electron beam CT. *Am J Radiol* 2000;174:915–21.
15. Carr JJ, Nelson JC, Wong ND, McNitt-Gray M, Arad Y, Jacobs DR, et al. Calcified coronary artery plaque measurement with cardiac CT in population-based studies: standardized protocol of Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Radiology* 2005;234:35–43. [PubMed: 15618373]
16. McDermott MM, Liu K, Criqui MH, Ruth K, Goff D, Saad M, et al. Ankle-brachial index and subclinical cardiac and carotid disease. The Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol* 2005;162:33–41. [PubMed: 15961584]
17. Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations. A statement of healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 1999;100:1481–92. [PubMed: 10500053]
18. Greenland P, Abrams J, Aurigemma GP, Bond MG, Clark LT, Criqui MH, Crouse JR, Friedman L, Fuster V, Herrington DM, Kuller LH, Ridker PM, Roberts WC, Stanford W, Stone N, Swan J, Taubert KA, Wexler L. Prevention Conference V. Beyond secondary prevention: Identifying the High-Risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing group III. *Circulation* 2000;101:e16–e22. [PubMed: 10618318]
19. Mohler ER III, Treat-Jacobson D, Reilly MP, Cunningham KE, Miani M, Criqui MH, Hiatt WR, Hirsch AT. Utility and barriers to performance of the ankle-brachial index in primary care practice. *Vasc Med* 2004;9:253–60. [PubMed: 15678616]
20. Aboyans V, Criqui MH. Can we improve the cardiovascular risk prediction beyond risk equations in the physician's office? *J Clin Epidemiol* 2006;59:547–558. [PubMed: 16713516]
21. Ackerman H, Diener HC, Dichgans J. Stenosis and occlusion of the subclavian artery: ultrasonographic and clinical findings. *J Neurol* 1987;234:396–400. [PubMed: 3309193]
22. Frank SM, Norris EJ, Christopherson R, Beattie C. Right- and left-arm blood pressure discrepancies in vascular surgery patients. *Anesthesiology* 1991;75:457–63. [PubMed: 1888053]
23. Cassidy P, Jones K. A study of inter-arm blood pressure differences in primary care. *J Hum Hypertens* 2001;15:519–22. [PubMed: 11494088]
24. Eguchi K, Yacoub M, Jhalani J, Gerin W, Schwartz JE, Pickering TG. Consistency of blood pressure differences between the left and right arms. *Arch Intern Med* 2007;167:388–393. [PubMed: 17325301]
25. Lane D, Beevers M, Barnes N, Bourne J, John A, Malins S, Beevers DG. Inter-arm differences in blood pressure: when are they clinically significant? *J Hypertension* 2002;20:1089–95.
26. Kadwa AM, Robbs JV, Abdool-Carrim ATO. Aortic arch angiography prior to carotid endarterectomy. Is its continued use justified? *Eur J Vasc Endovasc Surg* 1997;13:527–30. [PubMed: 9236704]
27. Clark CE, Campbell JL, Evans PH, Millward A. Prevalence and clinical implications of the inter-arm blood pressure difference: a systematic review. *Journal of Human Hypertension* 2006;20:923–931. [PubMed: 17036043]
28. Clark CE, Campbell JL, Powell RJ, Thompson JF. The inter-arm blood pressure difference and peripheral vascular disease: cross-sectional study. *Fam Pract* 2007;24:420–6. [PubMed: 17670807]
29. English JL, Carell ES, Guidera SA, Tripp HF. Angiographic prevalence and clinical predictors of left subclavian stenosis in patients undergoing diagnostic cardiac catheterization. *Cathet Cardiovasc Intervent* 2001;54:8–11.
30. Igarashi Y, Chikamori T, Tomiyama H, Usui Y, Hida S, Tanaka H, Nagao T, Yamashina A. Clinical significance of inter-arm pressure difference and anklebrachial pressure index in patients with suspected coronary artery disease. *J Cardiology* 2007;50:281–9.

Figure 1.
Distribution of SBPD (right SBP – left SBPD) in the MESA cohort, 2000-2002.

Figure 2.
Prevalence of subclavian stenosis in age- and gender groups. MESA cohort, 2000-2002.

Table 1

Baseline prevalence of subclavian stenosis in the MESA cohort (2000–2002).

	Total		Non-Hispanic Whites		African Americans		Hispanics		Chinese Americans	
	men	women	men	women	men	women	men	women	men	women
	N (%)		N (%)		N (%)		N (%)		N (%)	
Subclavian Stenosis	125 (3.9)	182 (5.1)*	58 (4.6)	75 (5.6)	53 (6.3)	85 (8.3)	11 (1.5)	17 (2.2)	3 (0.8)	5 (1.2)

* P<.05 versus men.

Table 2

Associations between cardiovascular disease risk factors and subclavian stenosis in the MESA cohort, 2000-2002.

Factors	OddsRatio (95% CI)			
	Unadjusted	Model 1 ^a	Model 2 ^b	Model 3 ^c
≥ 10 pack-years of smoking	1.38 (1.09 – 1.75)	1.19 (0.93 – 1.52)	1.18 (0.92 – 1.51)	1.18 (0.92 – 1.52)
Diabetes	1.53 (1.13 – 2.07)	1.53 (1.12 – 2.10)	1.27 (0.92 – 1.77)	1.29 (0.92 – 1.80)
Hypertension	2.11 (1.66 – 2.67)	1.72 (1.34 – 2.22)	1.34 (1.00 – 1.79)	1.28 (0.95 – 1.73)
Pulse Pressure (per 10 mmHg)	1.22 (1.15 – 1.29)	1.17 (1.09 – 1.26)	1.11 (1.02 – 1.20)	1.12 (1.03 – 1.21)
BMI (per 5.5 kg/m²)	1.33 (1.20 – 1.47)	1.25 (1.12 – 1.40)	1.17 (1.04 – 1.32)	1.13 (0.99 – 1.28)
Dyslipidemia	1.14 (0.90 – 1.44)	1.22 (0.96– 1.56)	1.08 (0.84 – 1.39)	1.12 (0.87 – 1.45)
C-Reactive Protein^d	1.86 (1.47 – 2.37)	1.64 (1.28 – 2.11)	1.44 (1.11 – 1.88)	1.40 (1.05 – 1.86)
Interleukin-6^d	1.42 (1.10 – 1.83)	1.28 (0.99 – 1.65)	1.09 (0.83 – 1.43)	1.00 (0.74 – 1.34)
Homocysteine^d	1.39 (1.08 – 1.78)	1.24 (0.95 – 1.61)	1.15 (0.88 – 1.51)	1.08 (0.81 – 1.45)
Factor VIII^{c,d}	1.34 (1.04 – 1.72)	1.12 (0.86 – 1.45)	1.06 (0.81 – 1.38)	0.99 (0.76 – 1.31)
CKD	1.10 (0.76 – 1.59)	0.92 (0.63 – 1.36)	0.83 (0.56 – 1.23)	0.74 (0.49 – 1.12)

^a Adjusted for age, gender and ethnicity

^b Adjusted for covariates in Model 1 and pack-years, diabetes, hypertension, pulse pressure, bmi and dyslipidemia.

^c Adjusted for covariates in Model 2 and CRP, IL-6, homocysteine, factor VIIIc, and eGFR.

^d Comparison is between highest and lower three (reference) quartiles.

Table 3

Mean values of subclinical CVD markers according to the presence of subclavian stenosis (SS) in the MESA baseline cohort (2000-2002).

	no-SS	SS	p Value
ABI	1.10 (0.11)	1.02 (0.14)	<0.0001
CCA-IMT (mm)	0.87 (0.19)	0.92 (0.19)	<0.0001
CAC score (Agatston's Unit)	144 (414)	179 (495)	0.1592

Abbreviations: ABI: ankle-brachial index. CAC: coronary artery calcium. CCA-IMT: common carotid artery intima-media thickness. SS: subclavian stenosis.

Table 4

Association of subclavian stenosis with markers of subclinical CVD in the MESA, 2000-2002. Multivariate analysis.

	Odds Ratio (95% CI)		
	Model 1 ^a	Model 2 ^b	Model 3 ^c
ABI $\leq$ 0.90^d			
Total	2.49 (1.68 – 3.69)	2.33 (1.55 – 3.49)	2.33 (1.54 – 3.52)
Men	2.11 (1.10 – 4.04)	2.02 (1.04 – 3.94)	2.25 (1.14 – 4.42)
Women	2.77 (1.68 – 4.56)	2.49 (1.49 – 4.1724)	2.36 (1.39 – 4.02)
CCA-IMT^e			
Total	1.57 (1.20 – 2.05)	1.36 (1.03 – 1.79)	1.34 (1.01 – 1.77)
Men	1.82 (1.22 – 2.723)	1.60 (1.06 – 2.43)	1.63 (1.07 – 2.49)
Women	1.41 (0.98 – 2.01)	1.21 (0.84 – 1.75)	1.17 (0.81 – 1.70)
CAC^f			
total 1-100	1.06 (0.78 – 1.44)	0.95 (0.70 – 1.31)	1.00 (0.72 – 1.37)
>100	1.56 (1.14 – 2.14)	1.33 (0.96 – 1.84)	1.43 (1.02 – 2.00)
men 1-100	0.96 (0.59 – 1.57)	0.88 (0.53 – 1.45)	0.94 (0.56 – 1.57)
>100	1.39 (0.86 – 2.25)	1.23 (0.74 – 2.02)	1.31 (0.78 – 2.19)
women 1-100	1.10 (0.74 – 1.63)	0.97 (0.65 – 1.46)	1.01 (0.67 – 1.53)
>100	1.69 (1.11 – 2.57)	1.40 (0.91 – 2.16)	1.54 (0.99 – 2.40)

^a Adjusted for age, sex and ethnicity

^b Adjusted for covariates in Model 1 and pack-years, diabetes, hypertension, pulse pressure, BMI and dyslipidemia.

^c Adjusted for covariates in Model 2 and CRP, IL-6, homocysteine, factor VIIc, and eGFR.

^d Excludes persons with ABI >1.40.

^e Comparison is between highest (>0.97 mm) and lower three quartiles (0.97 mm) taken as reference.

^f Comparison is to zero CAC (reference).

Abbreviations: see table.