Journal of the American College of Cardiology
Vol. 50, No. 16, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.07.015
© 2007 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Renal Artery Calcium Is Independently Associated With Hypertension

Matthew A. Allison, MD, MPH,*† Elizabeth O. Lillie, PhD,† Dominic DiTomasso, BS,‡
C. Michael Wright, MD,† Michael H. Criqui, MD, MPH*†

San Diego, California

Objectives We tested the hypothesis that renal artery calcium (RAC), a marker of atherosclerotic plaque burden, is also significantly associated with higher blood pressure levels and a diagnosis of hypertension.

Background In the nonrenal systemic vasculature, atherosclerotic plaque burden has been shown to be significantly associated with hypertension.

Methods A total of 1,435 consecutive patients were evaluated at a university-affiliated disease prevention center for the extent of calcified atherosclerosis in the systemic vasculature.

Results The overall prevalence of calcium in either renal artery was 17.1%, with men having a significantly higher prevalence (19.0%, 153 of 804) than women (14.7%, 93 of 631) ($p = 0.03$). After adjustment for age and gender, subjects with a RAC score >0 had a significantly higher prevalence of hypertension (41.2 vs. 29.5, $p < 0.01$). In a logistic model that adjusted for age, gender, body mass index, percent body fat, diabetes, smoking, dyslipidemia, and the extent of calcified atherosclerosis in the nonrenal vasculature, those with any RAC had a significantly higher odds ratio (1.61, $p = 0.01$) for hypertension than those with no RAC.

Conclusions The results of this study suggest that the presence of RAC is associated with higher odds for prevalent hypertension, independent of CVD risk factors and the extent of calcified atherosclerosis in the nonrenal vasculature.
(J Am Coll Cardiol 2007;50:1578–83) © 2007 by the American College of Cardiology Foundation

Although the pathophysiology of blood pressure elevation is multifactorial, renal mechanisms appear to play a primary role (1). It has been proposed that renal microvascular disease is the central and unifying pathophysiologic mechanism of hypertension (HTN) (2). A key component of this hypothesis is that several factors, such as obesity, sympathetic nervous system stimulation, increased uric acid, and endothelial dysfunction, result in preglomerular arteriosclerosis and tubulointerstitial disease. As the arteriosclerosis develops, persistent local renal vasoconstriction, ischemia, and inflammation occur, with subsequent release of renin from juxtaglomerular cells around the afferent arteriole (3). Consequently, the renin-angiotensin system is up-regulated, and blood pressure is increased (3,4).

Atherosclerosis is a chronic reparative inflammatory process that proceeds through a sequence of pathophysiologic steps and is the result of injurious stimuli to the endothelium of the arterial wall (5,6). Risk factors for atherosclerosis are similar to those for preglomerular arteriosclerosis and include high levels of low-density lipoprotein (LDL) cholesterol, high blood pressure, cigarette smoking, diabetes/obesity, and a family history of premature coronary heart disease (CHD) (7). Furthermore, studies indicate that atherosclerosis affects not only the larger conduit vessels, but also smaller arterioles (8–10).

Classic histologic studies have demonstrated that calcium is deposited during the process of atherosclerosis (5,11,12). Oxidized LDL cholesterol in the intima of the arterial wall results in inflammation and recruitment of activated macrophages to the endothelium, which propagates the inflammatory process (5,6). This includes morphologic and physiologic changes in medial smooth-muscle vascular cells that participate in vascular calcification. Once the lipid core is formed, calcium granules appear (type IV lesion). With progression to type V atherosclerotic lesions, lumps or plates of calcium are formed and, eventually, calcium is the predominant component of advanced lesions (11,12). These calcified plaques can be detected in many vascular beds and quantified by computed tomography (CT) (13). The extent of calcified atheromatous plaque found on CT is a valid and reproducible measure of the total atherosclerotic plaque

From the Departments of *Family and Preventive Medicine, †Medicine, and ‡Bioengineering, University of California at San Diego, San Diego, California. This work was supported by a grant (to Dr. Allison) and a summer research fellowship (to Dr. DiTomasso) from the American Heart Association. Franz Messerli, MD, served as Guest Editor for this article.

Manuscript received April 2, 2007; revised manuscript received July 13, 2007, accepted July 16, 2007.

burden in a vascular bed, although the burden of calcium in a given vascular bed is only modestly correlated with the degree of luminal stenosis (14,15). Importantly, previous studies have demonstrated calcium in the coronary arteries to be a significant and independent predictor of future cardiovascular disease (CVD) events (16–20).

We hypothesized that the presence and extent of calcified atherosclerosis in the renal arteries is a surrogate marker for preglomerular atherosclerosis and would be significantly associated with HTN. Accordingly, in a population free of clinical CVD, the aim of the present study was to determine the magnitude and significance of any association between renal artery calcium (RAC) and both blood pressure levels and a diagnosis of HTN.

Because the majority of cases of HTN are classified as "essential" or idiopathic (4), detection of calcium in the renal arteries may provide clinical information on the specific etiology for an individual patient. The presence of RAC may also be clinically important for detection of those at increased risk for concomitant CVD in other vascular areas. In support of this hypothesis, we have recently found strong and significant correlations between RAC and calcium in the coronaries, carotids, thoracic aorta, abdominal aorta, and iliac arteries, as well as the aortic and mitral annuli (21).

Materials and Methods

Subjects. From February 1, 2001, to June 29, 2001, 1,461 consecutive patients were evaluated by electron beam computed tomography (EBCT) at a university-affiliated disease prevention center in San Diego, California, for the extent of calcified atherosclerosis in 5 different vascular beds: the carotid, coronary, thoracic aorta, abdominal aorta, and iliac vessels. This is a clinical population where subjects either self-referred or were referred on the recommendation of their personal physician as an adjunct to their preventive health care. Previous results from this cohort have been published (22–27). For the current study, we excluded individuals with a history of clinical CVD (myocardial infarction, stroke, transient ischemic attack, angina, coronary revascularization [coronary artery bypass grafting, angioplasty, or stenting]), or carotid artery surgery.

All study data were collected at the same patient visit. Participants completed a detailed health history questionnaire that collected information on history of HTN, diabetes, high cholesterol, smoking, family history of CHD, medications, diet, exercise, and prior surgeries. After the patient had rested for 5 min in the seated position, and using a standardized protocol, trained technicians obtained systolic and diastolic blood pressures in the right upper extremity by automated oscillometry. Casual serum total, high-density lipoprotein (HDL) and LDL cholesterol, and glucose measurements were obtained by fingerstick using the Cholestech LDX system (Cholestech, Hayward, California). Body mass index (BMI) was calculated with the patient lightly clothed (without shoes). Body fat measurement was conducted using bioimpedence (Omron HBF-300, Omron, Schaumburg, Illinois).

Hypertension was defined as a systolic blood pressure (SBP) or diastolic blood pressure (DBP) ≥140 or ≥90 mm Hg respectively, or self-report of physician-diagnosed HTN and current use of an antihypertensive medication (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, alpha- and beta-blockers, calcium channel blockers, diuretics, or combination agents). Mean arterial pressure (MAP) was calculated using the following equation: MAP = DBP + 1/3(SBP − DBP). Pulse pressure (PP) was the difference between systolic and diastolic blood pressures. Smoking status was defined as current, former or never. Diabetes was defined by current use of physician-prescribed antiglycemic medications or a glucose >200 mg/dl (28). Individuals with a total-to-HDL cholesterol ratio >5 or who reported using a medication for high cholesterol were classified as dyslipidemic (29–32). The study protocol was approved by the Human Research Protection Program at the University of California at San Diego, which granted a waiver of informed consent.

Abbreviations and Acronyms

- **CT** = computed tomography
- **CVD** = cardiovascular disease
- **DBP** = diastolic blood pressure
- **HDL** = high-density lipoprotein
- **HTN** = hypertension
- **LDL** = low-density lipoprotein
- **MAP** = mean arterial pressure
- **PP** = pulse pressure
- **RAC** = renal artery calcium
- **SBP** = systolic blood pressure

Imaging. Imaging was conducted using an Imatron C-150 scanner (General Electric, San Francisco, California). Images for each vascular bed were obtained from a single scan using 100-ms scan time and proceeding caudally from the base of the skull to the symphysis pubis. Each bed was obtained by a distinct scan of the segment in question employing the following slice thicknesses: 3 mm for the coronary bed; 5 mm for the thorax; and 6 mm through the neck, abdomen, and pelvis. Cardiac tomographic imaging was electrocardiographically triggered at 40% or 65% of the R-R interval, depending on the subject's heart rate. Imaging of the heart, thorax, and abdomen was conducted during separate breath holds at one-half–maximal inspiration.

Atherosclerotic calcium was defined as a plaque area ≥1 mm^2 with a density of ≥130 Hounsfield units (HU). Quantitative calcium scores were determined according to the method described by Agatston et al. (13). In brief, the calcium score per lesion was calculated by multiplying the area of the contiguous pixels by the corresponding density number using the following scale for density (1 = 130 to 199 HU, 2 = 200 to 299 HU, 3 = 300 to 399 HU, 4 = ≥400 HU). The total calcium score was then determined by summing the lesion scores from all of the slices for that segment. Agatston calcium scores for vascular beds other than the coronaries were adjusted for

JACC Vol. 50, No. 16, 2007
October 16, 2007:1578–83

Table 1 Cohort Characteristics Stratified by the Presence of RAC

Variable	RAC >0 (n = 246)	RAC = 0 (n = 1,189)	p Value
Age (yrs), mean (SD)*	72.5 (8.8)	58.6 (10.0)	<0.01
Female, n (%)†	90 (34.3)	552 (46.0)	<0.01
BMI (kg/m^2), mean (SD)‡	25.1 (4.4)	25.9 (4.6)	0.13
Total body fat (%), mean (SD)‡	28.6 (8.9)	29.1 (8.4)	0.44
Ever smoker, n (%)‡	125 (50.8)	537 (45.2)	0.15
Diabetes mellitus, n (%)‡	9 (3.8)	26 (2.2)	0.18
Total cholesterol‡	178.8 (75.4)	178.8 (72.3)	0.99
LDL cholesterol‡	97.2 (55.1)	96.7 (53.5)	0.90
HDL cholesterol‡	44.5 (23.8)	46.5 (23.9)	0.26
Dyslipidemia, n (%)‡	78 (31.8)	326 (27.4)	0.20
Hypertension, n (%)‡	101 (41.2)	351 (29.5)	<0.01
Family history of CHD, n (%)‡	75 (30.6)	286 (24.1)	0.06
Carotid calcium score, median (interquartile range)	89 (0–372)	0 (0–0)	<0.01
Coronary calcium score, median (interquartile range)	222 (31–769)	1.6 (0–47)	<0.01
Thoracic aorta calcium score, median (interquartile range)	510 (134–1,496)	0 (0–39)	<0.01
Abdominal aorta calcium score, median (interquartile range)	1,484 (490–3,505)	0 (0–187)	<0.01
Iliac calcium score, median (interquartile range)	1,103 (150–3,013)	2 (0–199)	<0.01

*Adjusted for gender. †Adjusted for age. ‡Adjusted for age and gender.
BMI = body mass index; CHD = coronary heart disease; HDL = high-density lipoprotein; LDL = low-density lipoprotein; RAC = renal artery calcium.

slice thickness using the following formula: adjusted score = original score × slice thickness/3.0. Volume averaging was avoided by scoring each homogeneous slice thickness segment separately.

Using the Agatston method for calcium scoring and the same software used for scoring the vascular beds, image files of the abdomen were retrospectively interrogated for the presence and extent of calcium in both renal arteries (33). During scoring, calcium in these arteries was categorized as arising from the ostia or arterial segment proper. Calcium in the wall of the abdominal aorta was not included in the assessment for RAC by excluding any visible calcium in the extrapolated plane of the aorta at the renal artery origin. The total amount of calcium in the renal arteries was calculated as the sum of the ostial and arterial segments. The reader for RAC viewed only images that contained the renal arteries, and this individual was blinded to the scores for the other beds.

Statistical analysis. The level of significance for this study was 0.05 (2-tailed). Tests for group differences for those with and without any renal calcium were conducted using analysis of variance or the Kruskal-Wallis test (as appropriate) for continuous variables and the chi-square test for categorical variables. Mean risk factor values by RAC group were adjusted for age and gender using analysis of covariance. The potential association between the presence of RAC and HTN was explored by multivariable logistic regression (34). These models were conducted unadjusted and then adjusted for the traditional CVD risk factors and the extent of nonrenal vascular calcium.

Results

After exclusions for prevalent CVD, the total number of subjects available for analysis was 1,435. The overall prevalence of calcium in either renal artery was 17.1%, with men having a significantly higher prevalence (19.0%, 153 of 804) than women (14.7%, 93 of 631, $p = 0.03$). Because of the high number of subjects with no RAC, the distributions of these variables were highly right-skewed. Accordingly, the median RAC score was 0, with a minimum of 0 and a maximum of 779. The overall prevalence of HTN in this cohort was 25.6%.

The characteristics of the cohort stratified by the presence and absence of RAC are provided in Table 1. Those with any RAC were significantly older (72.5 vs. 58.6, $p < 0.01$), with a significantly higher proportion of men (65.7 vs. 54.0%, $p < 0.01$). Those with a RAC score >0 had significantly higher median calcium scores in the carotid, coronary, thoracic and abdominal aorta, and the iliac arteries. After adjustment for age and gender, subjects with a RAC score >0 had a significantly higher prevalence of HTN but not diabetes, dyslipidemia, or smoking; a family history of CHD was of borderline significance. Although not collected specifically for this study, subsequent assessment of the ethnic distribution of patients presenting at the clinic showed that nearly all (~90%) were non-Hispanic white.

In the RAC >0 group, the mean SBP was 127.8 mm Hg, compared with 125.6 mm Hg in the RAC = 0 group. Although this difference was small and not statistically significant ($p = 0.12$), it underestimated the SBP-RAC association, as there were essentially 3 times as many blood pressure medication users in the RAC >0 group as in the RAC = 0 group (25.1% vs. 8.6%, $p < 0.01$). Furthermore, after adjustment for age and gender, the mean systolic and diastolic blood pressures were significantly higher in those hypertensive patients receiving medications compared with those who were not hypertensive (systolic: 131.9 vs. 119.8 mm Hg; diastolic: 82.0 vs. 76.5 mm Hg; $p < 0.01$ for both).

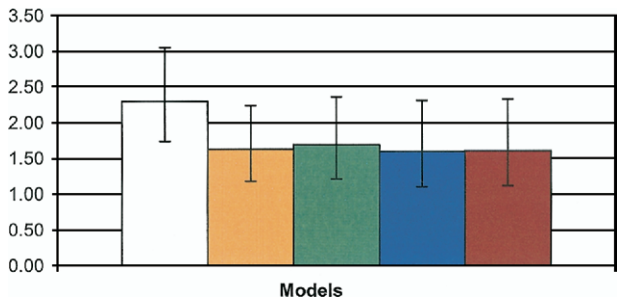

Figure 1 **Magnitude of Association Between Prevalent Renal Artery Calcium and Hypertension**

White bar = unadjusted; **orange bar** = age and gender; **green bar** = age, gender, and cardiovascular disease (CVD) risk factors (RFs); **blue bar** = age, gender, CVD RFs, and abdominal aortic calcium score; **maroon bar** = age, gender, CVD RFs, and total extrarenal calcium score. **Vertical bars** = 95% confidence interval; $p < 0.05$ for all models.

We further explored the association between RAC and HTN by examining whether there were differences in both the number and types of blood pressure medications between the RAC groups. Compared to the RAC = 0 group, there were higher prevalences of single (16.7% vs. 6.3%) and multiple (8.4% vs. 2.3%) medication use in the RAC >0 group ($p < 0.01$ for both). These differences remained significant after adjustment for age and gender. There was also a significantly higher prevalence of angiotensin-converting enzyme inhibitor (11.0% vs. 2.9%), angiotensin receptor blocker (3.4% vs. 0.9%), beta-blocker (8.7% vs. 3.0%), and diuretic (3.8 vs. 1.2%) use in the RAC >0 group compared to the RAC = 0 group ($p < 0.05$ for all). With adjustment for age and gender, all of these differences remained statistically significant except for diuretics, which was of borderline significance ($p = 0.06$).

The results of logistic regression analyses assessing the magnitude of association between prevalent RAC and being classified with HTN are shown in Figure 1. There was no significant interaction between gender and RAC for HTN. After adjustment for age and gender, the odds ratio (OR) for HTN was 1.63 times higher in those with any RAC compared to those with none ($p < 0.01$). Additional adjustment for BMI and percent body fat, as well as these variables plus smoking, diabetes, dyslipidemia, and family history of premature CHD, did not reduce the magnitude of this association (OR = 1.74 and 1.70, respectively; $p < 0.01$ for both). With further adjustment for the extent of calcium in the abdominal aorta, the association was only slightly attenuated and remained significant (OR = 1.60, $p = 0.01$). When abdominal aortic calcium was replaced by the total amount of calcium in all of the nonrenal vascular beds, the OR was essentially unchanged (OR = 1.61, $p = 0.01$).

To further characterize the relationship between calcium of the renal arteries and HTN, we compared the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in predicting the presence of HTN by the presence/absence of calcium in the nonrenal vascular beds versus the presence/absence of RAC (Table 2). Compared to the presence of calcium in the carotids, coronaries, thoracic aorta, abdominal aorta, or iliacs, any RAC was associated with the highest specificity (86.2%), positive predictive value (40.2%), and, most importantly, overall accuracy (71.2%) for the presence of HTN, despite having the lowest sensitivity.

Discussion

In this large cross-sectional study of individuals free of clinical CVD, and after adjustment for the traditional CHD risk factors and the extent of calcium in the systemic vasculature, the presence of any RAC was significantly associated with more than 60% higher odds of having HTN. Furthermore, compared with the presence of calcium in other vascular beds, the presence of any RAC provided the highest overall accuracy for correctly distinguishing those who had HTN at the time of their EBCT scan. To our knowledge, this is the first report of a significant association between calcium of the renal arteries determined by CT and HTN.

After adjustment for age, gender, and blood pressure medication status, there were no significant differences in the levels of SBP, DBP, PP, or MAP between those who did and did not have any RAC. Notably, among those receiving a blood pressure medication, the levels of these parameters were nearly identical for those with any RAC and those with no RAC (133.1 vs. 133.0, $p = 0.96$; 81.1 vs. 81.9, $p = 0.83$; 51.7 vs. 51.1, $p = 0.83$; 98.6 vs. 98.9, $p = 0.90$; respectively). Conversely, the levels among those not receiving a blood pressure medication were consistently higher (126.9 vs. 124.7, $p = 0.13$; 80.4 vs. 79.2, $p = 0.27$; 46.5 vs. 45.4, $p = 0.35$; 95.9 vs. 94.4, $p = 0.16$; respectively). These results demonstrate control of blood pressure to a similar level by blood pressure medication regardless of RAC status while, at the same time, the consistently higher values, as well as larger differences among those not receiving a blood pressure medication, suggest that RAC may be associated with higher blood pressure levels and that the

Table 2 **Relationships Between Calcium in Different Vascular Beds and HTN**

Disease: HTN (Yes vs. No)
"Exposure": Calcium in a Vascular Bed (Any vs. None)

Vascular Bed	Sensitivity	Specificity	PPV	NPV	Accuracy
Renals	27.0	86.2	40.2	77.5	71.2
Carotids	43.7	71.9	34.8	78.9	64.7
Coronaries	75.7	45.3	32.1	84.5	53.0
Thoracic aorta	52.7	60.2	31.2	78.8	58.3
Abdominal aorta	71.6	47.1	31.7	82.9	53.4
Iliacs	68.9	47.7	28.8	81.7	53.1

Accuracy = (true positives + true negatives)/(true positives + false positives + true negatives + false positives); HTN = hypertension; NPV = negative predictive value; PPV = positive predictive value.

significant association between RAC and prevalent HTN is largely driven by those receiving blood pressure medications.

Approximately 90% of renal artery stenosis cases are due to atherosclerosis (35). This condition results in an increase in preglomerular arterial resistance that is proportional to the degree of the stenosis and causes a decrease in renal blood flow. This may cause a secondary increase in systemic arterial pressure attributable to either increased renin secretion and angiotension formation or activation of afferent renal sympathetic nerves because of the renal baroreceptor response. However, the association between HTN and atherosclerotic renal artery stenosis is complex because renovascular HTN is not a necessary consequence of this disease (35). Furthermore, split renal function studies show that in patients with impaired renal function and unilateral nonocclusive renal artery stenosis, the kidney with the nonstenosed artery is just as likely to have impaired function as the one with renal artery stenosis (36). These results suggest that factors other than the degree of luminal stenosis may be influencing blood pressure regulation.

Because RAC is very modestly related to the degree of stenosis in these arteries (14) and other studies have shown that calcium attributable to atherosclerosis is more highly correlated with total plaque burden than the severity of stenosis (37), the results of our study suggest that the burden of subclinical atherosclerosis in the renal arteries may be linked to the kidney's influence on blood pressure. Additionally, because RAC was significantly associated with HTN after adjustment for the extent of atherosclerosis in other vascular beds, it appears that the local effects of atherosclerosis on renovascular HTN may be independent of the CVD risk factors and the systemic burden of atherosclerosis as reflected by calcium in the other (nonrenal) vascular beds.

The presence of RAC may also be clinically important for detection of those at increased risk for concomitant CVD in other vascular areas. In support of this hypothesis, we have recently found (21) strong and significant correlations between RAC and calcium in the coronaries, carotids, thoracic aorta, abdominal aorta and iliac arteries, as well as the aortic and mitral annuli. Furthermore, it is generally acknowledged that the risk factors for coronary artery disease (CAD) and atherosclerotic renal artery stenosis are similar (38,39). Additionally, the mortality of patients with CAD and atherosclerotic renal artery stenosis is doubled compared with patients with suspected CAD undergoing catheterization (41,42). Notably, the literature on subclinical atherosclerosis in the renal arteries is quite modest; therefore, further research into the potential association between RAC and CVD is recommended.

This report is based on data from a cross-sectional study design. Therefore, it is possible that reverse causality (i.e., HTN resulting in RAC) is responsible for the significant association between RAC and HTN. Indeed, HTN has been shown to be a risk factor for RAC (43) as well as calcified atherosclerosis in other vascular beds (26,27). However, we believe the evidence suggests that RAC is also a risk factor HTN. Specifically, we found that RAC was much more specific for HTN that calcified atherosclerosis in the other (nonrenal) vascular beds. Also, although the numbers are small, compared to patients with no calcium in any of the vascular beds, and after adjustment for age, gender, and CVD risk factors, those with calcium only in the renal arteries had nearly a 7-fold higher odds for the presence of HTN, whereas those with calcium limited to the nonrenal vasculature had only 2-fold odds for HTN. Finally, in our analyses the association between RAC and HTN was adjusted for the extent of calcified atherosclerosis in the nonrenal vasculature. Because HTN is a significant risk factor for calcified atherosclerosis, inclusion of nonrenal calcium in the multivariable models should account for some (but likely not all) of the confounding due to HTN. A prospective study is underway to further investigate the association between RAC and HTN.

Study limitations. Patients in this study were either self-referred or referred on the advice of their personal physician. Typically, these individuals tend to be from higher socioeconomic status and more concerned with health-related issues and therefore are probably engaged in more preventive health strategies. Also, the study population was free of clinical CVD. Therefore, the sample for this study may not be representative of the general population or populations from community-based samples, and the results of this study may not be generalizable to those groups. This study employed only a single measure of blood pressure. This may lead to misclassification with respect to HTN. In this case, the misclassification would not be systematic, and, therefore the association between RAC and HTN would be underestimated. Also, the association between RAC and HTN was largely driven by the inclusion of those individuals who were taking blood pressure medications. Notably, the prevalence of HTN in this study was similar to that for the U.S. population (44). Because the definition of diabetes in this study relied on self-report of medication use for this condition and not a fasting plasma glucose, there is the potential for misclassification. Calcium detected by EBCT is primarily due to intimal changes associated with atherosclerosis. However, this technique does not distinguish between intimal calcium due to atherosclerosis and Mockeberg's medial calcinosis. Because the latter occurs principally in those with diabetes (45) or chronic kidney disease (46) and is located primarily in the lower extremities (below the knee), we believe the probability of misclassification is low in our study.

Reprint requests and correspondence: Dr. Matthew A. Allison, 3855 Health Sciences Drive, Mailcode 0817, La Jolla, California 92093-0817. E-mail: mallison@ucsd.edu.

REFERENCES

1. Guyton AC. Blood pressure control—special role of the kidneys and body fluids. Science 1991;252:1813–6.
2. Goldblatt H. The renal origin of hypertension. Physiol Rev 1947;27: 120–65.
3. Reudelhuber T. Renin. In: Oparil S, Weber M, eds. Hypertension—A Companion to Brenner's and Rector's The Kidney. Philadelphia, PA: Elsevier, 2005:89–94.
4. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension. Ann Intern Med 2003;139:761–76.
5. Stary HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Arterioscler Thromb Vasc Biol 1995;15:1512–31.
6. Stary HC, Chandler AB, Glagov S, et al. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation 1994;89:2462–78.
7. Grundy SM, Becker D, Clark LT, et al. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143–421.
8. Galle J, Hansen-Hagge T, Wanner C, Seibold S. Impact of oxidized low density lipoprotein on vascular cells. Atherosclerosis 2006;185: 219–26.
9. Kawashima S. The two faces of endothelial nitric oxide synthase in the pathophysiology of atherosclerosis. Endothelium 2004;11:99–107.
10. Bolz S-S, Galle J, Derwand R, de Wit C, Pohl U. Oxidized LDL increases the sensitivity of the contractile apparatus in isolated resistance arteries for Ca2+ via a rho- and rho kinase-dependent mechanism. Circulation 2000;102:2402–10.
11. Stary HC. Natural history of calcium deposits in atherosclerosis progression and regression. Z Kardiol 2000;89 Suppl 2:28–35.
12. Stary HC. The development of calcium deposits in atherosclerotic lesions and their persistence after lipid regression. Am J Cardiol 2001;88:16E–9E.
13. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
14. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. J Am Coll Cardiol 1998;31: 126–33.
15. Rifkin RD, Parisi AF, Folland E. Coronary calcification in the diagnosis of coronary artery disease. Am J Cardiol 1979;44:141–7.
16. Alexopoulos D, Toulgaridis T, Davlouros P, Christodoulou J, Sitafidis G, Vagenakis AG. Prognostic significance of coronary artery calcium in asymptomatic subjects with usual cardiovascular risk. Am Heart J 2003;145:542–8.
17. Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. J Am Coll Cardiol 2000;36:1253–60.
18. Georgiou D, Budoff MJ, Kaufer E, Kennedy JM, Lu B, Brundage BH. Screening patients with chest pain in the emergency department using electron beam tomography: a follow-up study. J Am Coll Cardiol 2001;38:105–10.
19. Kondos GT, Hoff JA, Sevrukov A, et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. Circulation 2003;107:2571–6.
20. Raggi P, Shaw LJ, Berman DS, Callister TQ. Prognostic value of coronary artery calcium screening in subjects with and without diabetes. J Am Coll Cardiol 2004;43:1663–9.
21. Allison MA, DiTomasso D, Criqui MH, Langer RD, Wright CM. Renal artery calcium: relationship to systemic calcified atherosclerosis. Vascular Med 2006;11:232–8.
22. Allison MA, Michael Wright C. Body morphology differentially predicts coronary calcium. Int J Obes Relat Metab Disord 2004;28: 396–401.
23. Allison MA, Wright CM. A comparison of HDL and LDL cholesterol for prevalent coronary calcification. Int J Cardiol 2004;95:55–60.
24. Allison MA, Wright CM. Age and gender are the strongest clinical correlates of prevalent coronary calcification (R1). Int J Cardiol 2005;98:325–30.
25. Allison MA, Wright M, Tiefenbrun J. The predictive power of low-density lipoprotein cholesterol for coronary calcification. Intl J Cardiol 2003;90:281–9.
26. Allison MA, Cheung P, Criqui MH, Langer RD, Wright CM. Mitral and aortic annular calcification are highly associated with systemic calcified atherosclerosis. Circulation 2006;113:861–6.
27. Allison MA, Criqui MH, Wright CM. Patterns and risk factors for systemic calcified atherosclerosis. Arterioscler Thromb Vasc Biol 2004;24:331–6.
28. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2004;27:S5–S10.
29. Pischon T, Girman CJ, Sacks FM, Rifai N, Stampfer MJ, Rimm EB. Non-high-density lipoprotein cholesterol and apolipoprotein b in the prediction of coronary heart disease in men. Circulation 2005;112: 3375–83.
30. Frost PH, Havel RJ. Rationale for use of non-high-density lipoprotein cholesterol rather than low-density lipoprotein cholesterol as a tool for lipoprotein cholesterol screening and assessment of risk and therapy. Am J Cardiol 1998;81:26B–31B.
31. Wilder LB, Bachorik PS, Finney CA, Moy TF, Becker DM. The effect of fasting status on the determination of low-density and high-density lipoprotein cholesterol. Am J Med 1995;99:374–7.
32. Natarajan S, Glick H, Criqui M, Horowitz D, Lipsitz SR, Kinosian B. Cholesterol measures to identify and treat individuals at risk for coronary heart disease. Am J Prev Med 2003;25:50–7.
33. Freedman BI, Hsu FC, Langefeld CD, et al. Renal artery calcified plaque associations with subclinical renal and cardiovascular disease. Kidney Int 2004;65:2262–7.
34. Hosmer DW Jr., Lemeshow S. Applied Logistic Regression. 2nd ed. New York, NY: John Wiley & Sons, 2000.
35. Safian RD. Atherosclerotic renal artery stenosis. Curr Treat Options Cardiovasc Med 2003;5:91–101.
36. Farmer CKT, Cook GJR, Blake GM, Reidy J, Scoble JE. Individual kidney function in atherosclerotic nephropathy is not related to the presence of renal artery stenosis. Nephrol Dial Transplant 1999;14: 2880–4.
37. Siegel CL, Ellis JH, Korobkin M, Dunnick NR. CT-detected renal arterial calcification: correlation with renal artery stenosis on angiography. AJR Am J Roentgenol 1994;163:867–72.
38. Alhaddad IA, Blum S, Heller EN, et al. Renal artery stenosis in minority patients undergoing diagnostic cardiac catheterization: prevalence and risk factors. J Cardiovasc Pharmacol Ther 2001;6: 147–53.
39. Gross CM, Kramer J, Waigand J, Luft FC, Dietz R. Relation between arteriosclerosis in the coronary and renal arteries. Am J Cardiol 1997;80:1478–81.
40. Missouris CG, Papavassiliou MB, et al. High prevalence of carotid artery disease in patients with atheromatous renal artery stenosis. Nephrol Dial Transplant 1998;13:945–8.
41. Conlon PJ, Athirakul K, Kovalik E, et al. Survival in renal vascular disease. J Am Soc Nephrol 1998;9:252–6.
42. Conlon PJ, Little MA, Pieper K, Mark DB. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. Kidney Int 2001;60:1490–7.
43. Allison M, DiTomasso D, Criqui M, Langer R. Renal artery calcium: relationship to systemic calcified atherosclerosis. Vascular Med 2006; 11:232–8.
44. Thom T, Haase N, Rosamond W, et al., for the members of the Statistics Committee and Stroke Statistics. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2006;113:e85–151.
45. Edmonds ME. Medial arterial calcification and diabetes mellitus. Z Kardiol 2000;89:101–4.
46. Raggi P. Cardiovascular calcification in end stage renal disease. Contrib Nephrol 2005;149:272–8.