Incidental renal artery calcifications: a study of 350 consecutive abdominal computed tomography scans

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Abstract

Background. Calcifications in arteries are thought to represent atherosclerosis.

Methods. Consecutive abdominal tomographic scans performed during a 4-month period were evaluated and assessed for renal artery calcifications (RAC). Scans that showed calcifications were evaluated for renal artery narrowing and for various characteristics of the atherosclerotic plaque.

Results. Of 350 consecutive examinees, 43% were men, 40% had hypertension and 38% had hypercholesterolaemia. The age was 61 ± 13 years. Aortic calcifications were found in 54% and RAC in 102 (29%), of whom 53 had bilateral calcifications. Subjects with RAC were older, 72 ± 6 versus 55 ± 12 years. Adjusted odds ratios of RAC were 2.2 (95% CI 1.1–4.6) for male gender, 2.4 (1.2–4.8) for hypertension and 2.9 (1.4–5.8) for hypercholesterolaemia, whereas family history of hypertension was protective with 0.5 (0.3–0.9). All patients with calcified renal arteries had aortic calcifications, versus 35% of those without RAC. A significant correlation was found between the severity of calcifications and the degree of renal artery narrowing (r = 0.7), and also between the presence of bilateral calcifications and a high-grade narrowing.

Conclusions. RAC strongly relates to atherosclerosis. Calcifications and artery narrowing may have a role in the pathogenesis of hypertension. Bilateral calcifications suggest atherosclerotic renal artery stenosis.

Keywords: computed tomography; hypertension; renal artery calcification; renal artery stenosis

Introduction

Calcifications in arteries are thought to represent atherosclerosis. This was found in coronary arteries of asymptomatic hypertensive men [1,2], in carotid arteries [3,4] and cerebral arteries [5]. In most of these studies, calcifications had a relationship with male gender, hypertension, smoking and diabetes—all established atherosclerosis risk factors.

Histological studies found calcium to be deposited relatively late in the formation of the atherosclerotic plaque, propagated by inflammatory processes, smooth muscle cell changes and lipid core formation. It is within the lipid core where calcium granules can be seen, and later propagate to a calcified lesion. Indeed the calcified plaque is the hallmark of advanced atherosclerosis [6].

Computed tomography (CT)-detected calcification is also not a rare finding in renal arteries. Only few previously published studies explored the relationship of RAC with renal arterial stenosis (RAS). Siegel et al. reviewed abdominal CT of 70 patients and concluded that calcifications in the renal artery are not good predictors of stenosis or hypertension. However, RAC in hypertensive patients showed a stronger association with RAS, especially in patients younger than 65 years of age [7]. A smaller but prospective study of spiral CT with angiography in 42 patients revealed no correlation between aortic and renal arterial calcifications and RAS, regardless of age, with or without hypertension [8]. Moynahan et al. [9] reviewed lumbar CT of 93 sequential patients and found a significant association between hypertension and aortic or renal calcifications. The authors did not investigate actual narrowing of the renal arteries in these studies.

RAC were found to be strongly associated with older age, diastolic blood pressure, body mass index (BMI) and carotid artery intima-medial thickness and were found to be a useful noninvasive marker of subclinical atherosclerosis in type 2 diabetes mellitus [10]. In the largest study to date, Allison et al. [11] found that RAC were associated with hypertension, even after adjustment for confounders such as age, gender, BMI, smoking, diabetes, etc. However, this study was of subjects referred (including self referral) for cardiovascular risk assessment and did not use a contrast medium, and thus the relationship with RAS was not determined.

The association between RAS, peripheral vascular disease and coronary disease is well established [12,13], and one of the unresolved issues in the field is to what extent RAC is associated with RAS. This is a comprehensive study on a relatively large group of consecutive patients, referred for abdominal CT for a variety of reasons, investigating...
prospectively the association between calcifications in the main renal arteries, the presence of RAS by CT angiography and the relationship with hypertension and various risk factors for atherosclerosis.

Subjects and methods

During 4 months, all abdominal CT examinations performed at our institution for patients older than 35 years were evaluated and assessed for RAC. All patients signed informed consent forms approved by the Helsinki Committee for Human Studies of our institution. Indications for the CT examination were abdominal pain, lymphoma staging, assessment of a focal liver lesion found on ultrasound and search for abdominal abscesses or space-occupying lesions. Examinations for haematuria, renal lesions (calculi, infarcts, abscess, etc.) and renal vasculature were not included. Demographic details were obtained by questionnaires for ambulatory patients and by patient charts for inpatients. The patient’s age, gender, body weight, height and blood pressure were registered and information regarding hypertension, antihypertensive treatment, family history of hypertension, renal function, smoking, diabetes mellitus, hypercholesterolaemia, ischaemic heart disease (IHD) or cerebrovascular disease was recorded. Hypertension was defined as a physician diagnosis based on the patient’s age and blood pressure; IHD, ischaemic heart disease; CV A, cerebral vascular accident; family Hx, family history.

Data analysis

CT scans that showed calcifications were evaluated for renal artery narrowing and for various characteristics of the atherosclerotic plaque. The severity of calcifications was graded by the agreement of two radiologists as normal (no calcifications), mild (small flecks of calcium <1 mm in diameter), moderate (larger calcifications 1–3 mm in diameter) or severe (heavy calcifications >3 mm in diameter). The location of calcifications was recorded (ostial, proximal, mid-artery, distal or diffuse). The type of the plaque (calcified, soft or mixed) was assessed as well. Renal artery calibre was measured from the MIP images at the narrowest location and was graded as normal, <25%, 25–50%, 50–75% and >75% stenosis. The presence of abdominal aortic calcifications was documented.

Statistical analysis

Data presented are expressed as mean ± SD, unless stated otherwise. Analysis (SPSS 13.0, Chicago, IL, USA) included the chi-square or logistic regression of the association between renal artery calcification (presence/absence) and demographic, radiographic and clinical variables. Interactions between gender and BMI and between hypertension and hypercholesterolaemia were examined by introducing the appropriate interaction term. The assessment of the factors independently linked with RAS was done with multivariable logistic regression. Spearman’s method was applied to quantify the correlation between arterial calcification and narrowing severity. Logistic regression was used for the prediction of the hypertension status by the presence and severity of renal artery stenosis. For this analysis, each semi-quantitative level of stenosis determined from the computed tomography (none, <25%, 25–50%, 50–75% and >75%) was assigned a nominal value equal to the mean (0, 12.5, 37.5, 62.5 and 87.5%, respectively). Average narrowing was defined as the average of right and left artery narrowing, while largest narrowing refers to the narrowing of the more stenosed artery. Receiver–operator characteristic (ROC) curves predicting RAC were generated with age and reported blood pressure (systolic and diastolic) as predictors.

Results

There were 350 patients; 151 (43%) were men and 199 women with an average age of 61 ± 13 years. Demographic and comorbidity characteristics of the patients with and without RAC are summarized in Table 1. Average BMI was 27 ± 4.1 kg/m². Fifty-five patients (16%) patients were smokers. One hundred thirty-nine patients (40%) had
hypertension, of whom 123 (88.5%) were treated with antihypertensive medications.

Only seven (2%) patients had abnormal serum creatinine. Fifty-six (16%) patients had diabetes, 132 (38%) had hypercholesterolaemia, 30 (8.6%) had documented ischaemic heart disease (IHD) and 12 (3%) had a history of cerebrovascular accident. Aortic calcifications were found among 191 (54%) patients and RAC in 102 (29%), of whom 53 had bilateral RAC. Because we focused on RAC, when they were not observed angiographic reconstruction was not performed.

**Age, gender and RAC**

Univariable analysis showed a distinct connection between age and the presence of RAC ($P < 0.001$, Table 1 and Figure 1). A significant relationship was found between male gender and RAC ($P < 0.024$).

**Adiposity and RAC**

Simple analysis showed an insignificant connection between a high BMI and RAC (Table 1 and Figure 2), yet in a subgroup analysis a borderline interaction was found between gender and BMI. The odds ratio (OR) for RAC was 0.97 (0.86–1.11) for obese men and 1.12 (1.02–1.22) for obese women (Figure 2).

**Other cardiovascular risk factors and RAC**

An inverse relationship was found between a history of hypertension in the family and RAC, so that RAC were found more frequently in patients without a family history of hypertension. Hypercholesterolaemia and IHD—but not diabetes, smoking, stroke or kidney dysfunction—had significant associations with RAC (Table 2).

![Graph showing the prediction of RAC by age and blood pressure. The area under the curve for age is 0.88 ± 0.02 ($P < 0.001$). The area under the curve for systolic blood pressure is 0.71 ± 0.03 ($P < 0.001$). The area under the curve for diastolic blood pressure is 0.60 ± 0.03 ($P = 0.004$).](image)

**Fig. 2.** The connection between BMI below and above the median and renal artery calcifications. The median BMI was 26.8 and 26.6 for men and women, respectively. The odds ratio was 3.6 (1.3–9.6) for men below median BMI. The odds ratio was 2.8 (1.0–8.0) for men above the median. The odds ratio was 2.2 (0.8–5.9) for women below the median.

**Table 2.** Multivariable analysis of factors significantly associated with renal artery calcifications

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR (95% CI)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>1.17 (1.12–1.21)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male gender</td>
<td>2.06 (1.09–3.91)</td>
<td>0.026</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.47 (1.31–4.65)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>2.34 (1.24–4.42)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Odds ratios were computed by multivariate logistic regression, and are expressed per 1 year of age, per 1 BMI unit and for the other risk factors for the presence of the risk factor versus its absence. OR, odds ratio; CI, confidence intervals.

**Aortic calcifications and RAC**

All the patients with RAC had aortic calcifications, whereas only 46% of those with aortic calcifications had coexisting RAC ($P < 0.001$).

**Multivariable analysis of risk factors and RAC**

The association between RAC and age, gender, hypertension and hypercholesterolaemia was significant on multivariable analysis, but not that with IHD. Inclusion of aortic calcifications in the model abolished the associations of RAC with age and gender. Comorbidity with hypertension and hypercholesterolaemia had a greater impact on the presence of RAC than hypertension or hypercholesterolaemia alone (Figure 3).

**Renal artery characteristics**

Of the 102 patients with RAC, 23 patients (22.5%) had them in the right, 26 patients (25.5%) in the left artery and 53 patients (52%) had bilateral RAC. RAC were mild in 58%, moderate in 14% and severe in 5%. Calcifications arose predominantly at the arterial ostia (79%). Patients with bilateral RAC had a higher degree of stenosis ($P < 0.001$, Table 3). No significant association was found between the location of calcification in a renal artery and the degree of artery narrowing ($P = 0.138$). Mixed atherosclerotic plaques were more likely to have diffuse RAC (21%), than calcified or soft plaques (7%) ($P = 0.014$). A significant correlation, $r = 0.7$ ($P < 0.001$), was found between the RAC severity and the degree of arterial narrowing. This
Renal artery calcifications on CT

Fig. 3. The combination of hypertension and hypercholesterolaemia as risk factors for renal artery calcifications. In patients without hypertension and hypercholesterolaemia, 9.4% of arteries had calcifications (n = 14).

In patients with isolated hypertension or hypercholesterolaemia 40.5% (n = 28) or 32.2% (n = 20) of arteries were calcified, respectively. In patients with both hypertension and hypercholesterolaemia 57.1% (n = 40) of renal arteries had calcifications.

Discussion

RAC are common findings on CT scans. Our study, in which contrast-enhanced CT was used, is to our knowledge the largest to date.

A brief summary of our finding

RAC were identified in roughly one-third of unselected consecutive examinations; therefore, it is important to understand their significance in order to direct appropriate work-up and treatment. One of our most prominent findings is that when there were no aortic calcifications, RAC were virtually absent. Diffuse RAC, especially when bilateral, were associated with a higher grade of narrowing of the renal artery on the CT angiography. The degree of renal artery narrowing was significantly associated with hypertension. Diffuse RAC were more frequent when the plaques were of mixed type. There is an association between RAC and hypertension.

As in previous studies [7,11], RAC were significantly associated with older age and male gender. According to our findings, 40–70-year-old men have significantly more calcifications than women, but in older subjects the frequency of RAC becomes similar. These findings correspond to the well-known gap in cardiovascular morbidity between men and women that fades away with ageing.

Of importance is the significant association between RAC and systolic hypertension. Both systolic and diastolic blood pressures were related to RAC, but the former was more tightly related to RAC (Figure 1). This finding probably reflects the higher prevalence of isolated systolic hypertension in the older subjects with atherosclerosis.

Some previous studies found an association between a high BMI and RAC [7], though this association was not found in a much larger study [11]. We too, could not confirm this finding; nevertheless, in a subgroup analysis of women with high BMI there were more RAC than in lean women. This is rather surprising as the male central obesity is considered more of a risk factor than the female-type fat distribution. Perhaps if the waist circumference (considered to be a stronger risk factor than BMI) were used to define obesity, the results would have differed.

A significant association was found between hypercholesterolaemia and RAC, but in contrast to previous studies [7,9] we found no association between diabetes mellitus and RAC, confirming a similar finding in subjects free of cardiovascular disease [11]. Moreover, the significant association between IHD and RAC on a univariable analysis faded upon adjustment for atherosclerotic risk factors, probably reflecting shared atherosclerotic pathogenesis. Such discrepancies could be explained in part by the small number of IHD, smokers and diabetic patients included in our study, rendering it underpowered.

Table 3. Distribution of the narrowing observed in patients with calcified renal arteries, according to the presence of unilateral versus bilateral calcifications

<table>
<thead>
<tr>
<th>Degree of narrowing</th>
<th>With unilateral RAC(^a), n = 49</th>
<th>With bilateral RAC(^a), n = 53</th>
<th>Total number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>&lt;25%</td>
<td>43</td>
<td>34</td>
<td>77</td>
</tr>
<tr>
<td>25–50%</td>
<td>2</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>50–75%</td>
<td>1</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>&gt;75%</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

\(^a\)The distribution differed significantly for unilateral versus bilateral calcifications (P = 0.005, chi-square test).

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>History of hypertension</th>
<th>Antihypertensive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average narrowing</td>
<td>1.05 (1.01–1.08)</td>
<td>1.05 (1.02–1.09)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.009</td>
<td>0.005</td>
</tr>
<tr>
<td>(R^2)</td>
<td>0.170</td>
<td>0.233</td>
</tr>
<tr>
<td>Largest narrowing</td>
<td>1.03 (1.01–1.06)</td>
<td>1.04 (1.01–1.06)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.017</td>
<td>0.011</td>
</tr>
<tr>
<td>(R^2)</td>
<td>0.175</td>
<td>0.228</td>
</tr>
</tbody>
</table>

\(^a\)Odds ratios, 95% CI, P-values and overall model strengths (\(R^2\)) were computed by univariable logistic regression models. Odds ratios express the odds of hypertension or treatment with antihypertensive agents per 1% increase in renal artery narrowing.

Table 4. Renal artery stenosis as a predictor of hypertension: average narrowing versus maximal narrowing in the right and left renal arteries

<table>
<thead>
<tr>
<th>Predictor(^a) (assessment of stenosis)</th>
<th>History of hypertension</th>
<th>Antihypertensive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average narrowing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odds ratio (95% CI)</td>
<td>1.05 (1.01–1.08)</td>
<td>1.05 (1.02–1.09)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.009</td>
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<tr>
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</tbody>
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\(^a\)Odds ratios, 95% CI, P-values and overall model strengths (\(R^2\)) were computed by univariable logistic regression models. Odds ratios express the odds of hypertension or treatment with antihypertensive agents per 1% increase in renal artery narrowing.
to examine these subgroups. It is likely that for studies that involve contrast medium administration, diabetic subjects were selected more conservatively because of their higher renal risk. The lack of association with diabetes is likely explained here, as well as in the large study of Allison et al. [11], by the nature of the referral: for contrast-enhanced abdominal CT in our study and of cardiovascular disease-free subjects referred for electron beam computed tomography for prognostic evaluation in the study of Allison et al.

The association of RAC with age, male gender, hypertension and hypercholesterolaemia and especially their combination, as well as IHD and aortic calcification, strongly points to a more generalized form of atherosclerosis underlying RAC. Muntner et al. [14] showed that the prevalence of hypercholesterolaemia increases with the severity of hypertension. Despite the higher hypertension prevalence, African Americans are less likely to have occlusive atherosclerotic arterial disease, attributed to a more favourable lipid profile in comparison to Caucasians [15,16].

In this study, bilateral RAC were associated with a higher level of RAS, yet it should be noted that only 9.8% (10 of 102) of the patients had renal artery stenosis of 50% or more and only 2.9% (3 of 102) had stenosis of >75%. As expected from the atherosclerotic relations, a significant association was found between diffuse RAC and mixed plaques (a more advanced form of atherosclerosis) and the level of renal artery stenosis.

The association between RAC and hypertension reinforces previous findings [7,11] and probably expresses the role of hypertension in the atherosclerotic process and subsequent calcifications that may lead to RAS. However, among patients with a family history of hypertension RAC were significantly less frequent, suggesting that in patients with a family history, genetic factors may dominate the pathogenesis of hypertension, whereas among those with RAC, hypertension may be secondary to atherosclerotic stenosis, hinted at by RAC as well as aortic calcifications. Nevertheless, not all subjects with RAC have hypertension. Indeed atherosclerosis may progress in the absence of one risk factor or another. Also, hypertension may promote atherosclerosis and RAC, but atherosclerosis may also promote hypertension through RAS as well as through other mechanisms [17]. Remodelling of a renal artery with stenotic plaque (see below) may prevent the critical degree of flow impediment that will cause renovascular hypertension.

Our findings are at variance with the pioneering study of Siegel et al. [7], where RAC had no relationship with RAS. There are probably several reasons for this discrepancy: (a) the study of Siegel et al. was five times smaller than ours, and thus the lack of association may be purely due to the lack of power in that study. (b) The relationship between an atherosclerotic plaque and long-term anatomy is complex: the majority of arteries (including renal arteries) undergo remodelling secondary to the flow changes. This remodelling could be of an expansive nature, rendering the stenosis of little haemodynamic consequence, but for poorly understood reasons, some arteries undergo a constrictive remodelling accentuating the stenosis [18]. Indeed, in coronary arteries it was found that there may be poor relations between a degree of calcifications and stenosis [19], probably in relation to the remodelling issue [16].

In summary, the absence of aortic calcification may rule out atherosclerotic renal artery stenosis, mitigating the need for contrast medium-enhanced studies in the search of this finding. The more diffuse RAC, especially when bilateral, may suggest a renovascular aetiology of hypertension in patients without such family history. If our findings are substantiated by additional observations, it might enable us to form a policy in the now agonizing approach [17] towards patients suspected of having atherosclerotic renovascular disease: not using contrast when there are no aortic calcifications and using contrast when RAC are diffuse and bilateral. Such a policy will obviously not be relevant when RAS from fibromuscular dysplasia is sought.

Conflict of interest statement. None declared.

References
Risk of acute kidney injury in patients with severe aortic valve stenosis undergoing transcatheter valve replacement

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Abstract

Background. Transcatheter aortic valve implantation (TAVI) for high-risk and inoperable patients with severe aortic stenosis is an emerging procedure in cardiovascular medicine. Little is known of the impact of TAVI on renal function.

Methods. We analysed retrospectively renal baseline characteristics and outcome in 58 patients including 2 patients on chronic haemodialysis undergoing TAVI at our institution. Acute kidney injury (AKI) was defined according to the RIFLE classification.

Results. Fifty-eight patients with severe symptomatic aortic stenosis not considered suitable for conventional surgical valve replacement with a mean age of 83 ± 5 years underwent TAVI. Two patients died during transfemoral valve implantation and two patients in the first month after TAVI resulting in a 30-day mortality of 6.9%. Vascular access was transfemoral in 46 patients and transapical in 12. Estimated glomerular filtration rate (eGFR) increased in 30 patients (56%). Fifteen patients (28%) developed AKI, of which four patients had to be dialyzed temporarily and one remained on chronic renal replacement therapy. Risk factors for AKI comprised, among others, transapical access, number of blood transfusions, postinterventional thrombocytopenia and severe inflammatory response syndrome (SIRS).

Conclusions. TAVI is feasible in patients with a high burden of comorbidities and in patients with pre-existing end-stage renal disease who would be otherwise not considered as candidates for conventional aortic valve replacement. Although GFR improved in more than half of the patients, this benefit was associated with a risk of postinterventional AKI. Future investigations should define preventive measures of peri-procedural kidney injury.

Keywords: acute kidney injury; severe inflammatory response syndrome; transcatheter aortic valve implantation

Introduction

Despite the proven benefit of surgical valve replacement, almost one-third of patients with severe valvular heart disease (VHD) do not undergo intervention because of end-stage disease, advanced age and multiple comorbidities, including chronic kidney disease (CKD) [1]. Transcatheter aortic valve implantation (TAVI) for high-risk patients has emerged as a new therapeutic option, first reported in 2002 by Cribier [2]. Meanwhile, more than 2000 TAVI have been performed using a transfemoral or a transapical approach in patients with an estimated excessive perioperative risk or in those with contraindications for conventional surgical aortic valve replacement [3–10]. Information about the impact of TAVI on renal function is scarce. Two studies have reported the necessity of renal replacement therapy (RRT) as a postoperative outcome in a total of 9 from 69 patients.