Simple Renal Cysts as Markers of Thoracic Aortic Disease

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Background—Thoracic aortic aneurysm is usually a clinically silent disease; timely detection is largely dependent upon identification of clinical markers of thoracic aortic disease (TAD); (bicuspid aortic valve, intracranial aortic aneurysm, bovine aortic arch, or positive family history). Recently, an association of simple renal cysts (SRC) with abdominal aortic aneurysm and aortic dissection was established. The aim of our study was to evaluate the prevalence of SRC in patients with TAD in order to assess whether the presence of SRC can be used as a predictor of TAD.

Methods and Results—We evaluated the prevalence of SRC in 842 patients with TAD (64.0% males) treated at our institution from 2004 to 2013 and compared to a control group of patients (n=543; 56.2% males). Patients were divided into 4 groups: ascending aortic aneurysm (456; 54.2%); descending aortic aneurysm (86; 10.2%); type A aortic dissection (118; 14.0%); and type B aortic dissection (182; 21.6%). SRC were identified by abdominal computed tomography or magnetic resonance imaging of these patients. Prevalence of SRC is 37.5%, 57.0%, 44.1%, and 47.3% for patients with ascending aneurysm, descending aneurysm, type A dissection, and type B dissection, respectively. Prevalence of SRC in the control group was 15.3%. Prevalence of SRC was not significantly different between male and female aortic disease patients, despite reported general male predominance (2:1), which was also observed in our control group (1.7:1).

Conclusions—This study establishes an increased prevalence of SRC in patients with TAD. SRC can potentially be used as a marker for timely detection of patients at risk of TAD. (***J Am Heart Assoc***. 2016;5:e002248 doi: 10.1161/JAHA.115.002248)

Key Words: aortic dissection • marker • simple renal cyst • thoracic aortic aneurysm

A ccording to the latest data from the Centers for Disease Control and Prevention, ≈13 000 people die annually in the United States of aortic aneurysms in various anatomical localizations, with almost 80% of these deaths among people 65 years and older. This makes aortic aneurysms the 18th leading cause of death in all individuals and the 15th most common in individuals older than 65 years.[1] Thoracic aortic aneurysms (TAAs) are "silent killers" because, in the absolute majority of the patients, they do not cause early warning symptoms; often, the first symptom is death or a major complication that threatens to produce death, such as aortic rupture or dissection.[2] Thus, timely detection of patients at risk of developing a TAA is bound to save many lives. Such timely detection of patients at risk can be achieved by identifying certain medical or anatomical conditions that have been linked to aneurysm development. Recent studies have shown that such medical conditions as bicuspid aortic valve,[3] intracranial aneurysm,[4] inguinal hernia,[5] and anomalies of the aortic arch vessels (such as bovine aortic arch and isolated left vertebral artery)[6,7] are associated with TAA,[8] and a family history of thoracic aortic disease[9] confers an increased risk of developing a thoracic aortic aneurysm.

A simple renal cyst (SRC) is a fluid collection in the kidney that is usually benign in nature. Overall prevalence of SRCs in the general population has been reported to be in the range of 5% to 41%, depending on the imaging study, ethnic background, and other influencing factors. Higher percentages of SRC prevalence are observed in the elderly and in males[10–19] (Table 1). Yaghoubian et al.[20] have shown an association of SRCs and abdominal aortic aneurysm development. A higher prevalence of SRCs has also been observed in patients with aortic dissection, suggestive of a common manifestation of connective tissue degeneration.[21] However, the association of simple renal cysts and thoracic

Table 1. Previous Reports on the Prevalence of Simple Renal Cysts (SRC) in the General Population

Source	No. of Subjects	Mean Age (Range)	Overall Prevalence of SRC	Male-to-Female Ratio in the Prevalence of SRC
Laucks et al. (1981)[13]	103	57.0	24.3%	—
Tada et al. (1983)[14]	542	51.3*	19.9%	2.72
Caglioti et al. (1993)[15]	1526	52.5	17.2%	1.85
Pedersen et al. (1993)[16]	675	48.9* (30–70)	5.2%	2.86
Ravine et al. (1993)[17]	729	52.7*	9.5%	2.15
Pal et al. (1997)[18]	1500	45.7*	5.1%	2.04
Terada et al. (2002)[10]	14 314	52.1 (26–91)	11.9%	1.90
Carrim et al. (2003)[19]	617	64.2 (17–92)	41.2%	1.39
Suher et al. (2006)[11]	684	65.7 (28–82)	13.7%	1.52
Chang et al. (2007)[12]	577	48.8 (20–94)	10.7%	2.81

*Approximated mean age, exact data not provided in original manuscript by authors.

aortic aneurysm has not, to the best of our knowledge, been established before.

Therefore, the aim of our study was to determine whether an association between thoracic aortic aneurysms and simple renal cysts exists. We evaluated the prevalence of SRCs in patients with TAAs and compared that to the prevalence of SRCs in patients with thoracic aortic dissection and to a control group of patients without thoracic aortic disease (TAD); (aneurysm or dissection).

Methods

Study Population

All consecutive patients treated for TAD at the Aortic Institute of Yale–New Haven Hospital (New Haven, CT) during the years 2004–2013 were included in this study. The total number of patients with TAD was 1177. Reliable radiological imaging studies that included the kidneys were available for 842 patients (71.5%), who comprised our study population. Mean age of the study population was 63.5 ± 14.2 years (range, 17–96), and 539 patients (64.0%) were males. The 335 excluded patients (28.5%) were statistically similar to the study population in the basic demographic and clinical characteristics with the exception of age (excluded patients were slightly older: 65.3 ± 11.9; $P=0.034$).

According to the type and location of TAD, patients in the study group were subdivided into 4 subgroups:

1. Ascending aortic aneurysm group: 456 patients (54.2%) with aneurysms of the aortic root, ascending aorta, or aortic arch, mean age 61.7 ± 13.9, 310 males (68.0%);
2. Descending aortic aneurysm: 86 patients (10.2%) with aneurysms of the descending aorta, including thoracoab-

dominal aneurysms, mean age 64.4 ± 13.7, 47 males (54.7%);
3. Stanford type A aortic dissection: 118 patients (14.0%), mean age 65.0 ± 15.5, 76 males (64.4%);
4. Stanford type B aortic dissection: 182 patients (21.6%), mean age 66.5 ± 14.3, 106 males (58.2%).

Diagnosis of TAD was confirmed by imaging studies (computed tomography [CT], magnetic resonance imaging [MRI], or echocardiography). Patients were considered as having an aortic aneurysm if the size of the aorta was greater than 4.0 cm. Baseline clinical characteristics of patients were obtained by our Aortic Database, hospital medical records, and outpatient medical records.

Control Group

A control group was identified by searching the Yale–New Haven Hospital Radiology database for all patients admitted through the emergency department with a diagnosis of trauma or motor vehicle accident during the 2004–2013 period who also had an imaging study (CT and/or MRI) performed at admission. This control group was selected because trauma patients would not be expected to present any inherent bias favoring either TAD or renal cysts. Patients with known or identified aortic disease of any location or with known or identified predisposing factor for renal cyst formation (autosomal-dominant polycystic kidney disease [ADPKD], end-stage renal disease, and hydronephrosis) were excluded from the study. The control group included 543 patients (mean age, 41.4 ± 17.8 years; range, 20–87), of whom 305 patients (56.2%) were male. Because of the specifics of the radiology database, detailed clinical or demographic information was not available for the control subjects.

Evaluation of Radiology Imaging Studies for Determining the Presence of Simple Renal Cysts

Only CT and MRI studies were used to analyze the presence of simple renal cysts in patients of the study population and control group. All imaging studies were read, analyzed, and reported by an experienced radiology attending physician as part of clinical care and without knowledge of this study. A patient was considered to have a simple renal cyst if a round or oval low-attenuation lesion with a thin wall and a size ≥4 mm was identified on a CT or MRI scan without obvious evidence of radiographic enhancement or septations.

Definition of Risk Factors and Comorbidities

The following risk factors and comorbidities were evaluated in the study population and were defined as:

1. Hypertension: diastolic blood pressure of 90 mm Hg and higher or treatment with at least 1 antihypertensive medication;
2. Hyperlipidemia: total cholesterol level over 200 mg/dL (5.17 mmol/L) or treatment with lipid control medications;
3. Diabetes: medically recorded diagnosis of diabetes either diet-controlled, controlled by oral medications, or requiring insulin;
4. Tobacco smoking: history of ever smoking for the duration of 2 years (consecutive or in total) or more;
5. Marfan syndrome: diagnosed according to the revised Ghent nosology[22];
6. Chronic kidney disease: history of chronic kidney disease or elevated creatinine (>2);
7. Neurological deficit: history of significant pathological conditions affecting the central or peripheral nervous systems;
8. Pulmonary/respiratory disease: history of significant pathological conditions affecting the lung parenchyma, the pleura, or the tracheobronchial tree;
9. Positive family history: the presence of confirmed family history of aneurysm disease (aortic, peripheral vascular, or cerebral) among first-, second-, or third-degree relatives;
10. Previous cardiac/aortic surgery: history of previous open surgical intrapericardial interventions, or aortic (thoracic and abdominal) interventions (open or endovascular).

Statistical Analysis

Pearson's chi-square test was used to compare proportions (categorical variables). The 2-tailed unpaired *t* test was used to compare continuous variables. Multivariate logistic regression was performed using SAS software (SAS Institute Inc., Cary, NC) and according to principles previously described by Rizzo et al.[23] Multivariate analysis was specifically designed to control for the age variable in order to permit reliable comparisons between the study population and the control group given the difference in the mean age of these groups. The potential confounding effects of differences in age were controlled by estimating multivariate logistic regression models that included age along with all anatomical groups in the study population (ascending aortic aneurysm, descending aortic aneurysm, Stanford type A aortic dissection, and Stanford type B aortic dissection). This model also controlled for sex because an increased prevalence of SRC among males was expected from the literature.[10–12,14–19] The control population was used as the reference group in logistic regression. A *P* value ≤0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the human investigation committee of Yale University. Requirement for informed consent was waived.

Results

Overall Prevalence of SRC

Among the 842 patients of the study population, 358 patients (42.5%) had at least 1 simple renal cyst. In the control group, prevalence of SRC was 15.3% (84 of 543), which was significantly lower than in the study population (*P*<0.0001).

Presence of SRC was then evaluated separately for all 4 groups of the study population. Overall prevalence of SRC was 37.5% (171 of 456), 57.0% (49 of 86), 44.1% (52 of 118), and 47.3% (86 of 182) in patients with ascending aortic aneurysm, descending aortic aneurysm, and type A and type B aortic dissection, respectively (Figure 1). In all 4 groups, the prevalence of SRC was significantly higher than in the control group (*P*<0.0001).

Age-Controlled Prevalence of SRC

Prevalence of SRC was also calculated separately for all age groups of patients with TAD and controls (10-year age periods). This analysis showed a higher rate of SRC in the study population than in our control group in the seventh (*P*=0.03), eighth (*P*=0.05), and ninth decade of life and beyond (*P*=0.01; Figure 2). The prevalence of SRC in study population patients was also higher than control levels among patients in their fifth and sixth decades of life, although no statistical difference was identified because of small sample size (*P*=0.31 and 0.22, respectively). Study patients also showed a statistically higher rate of SRC than historical controls from the literature for all decades, 40 years of age and above.
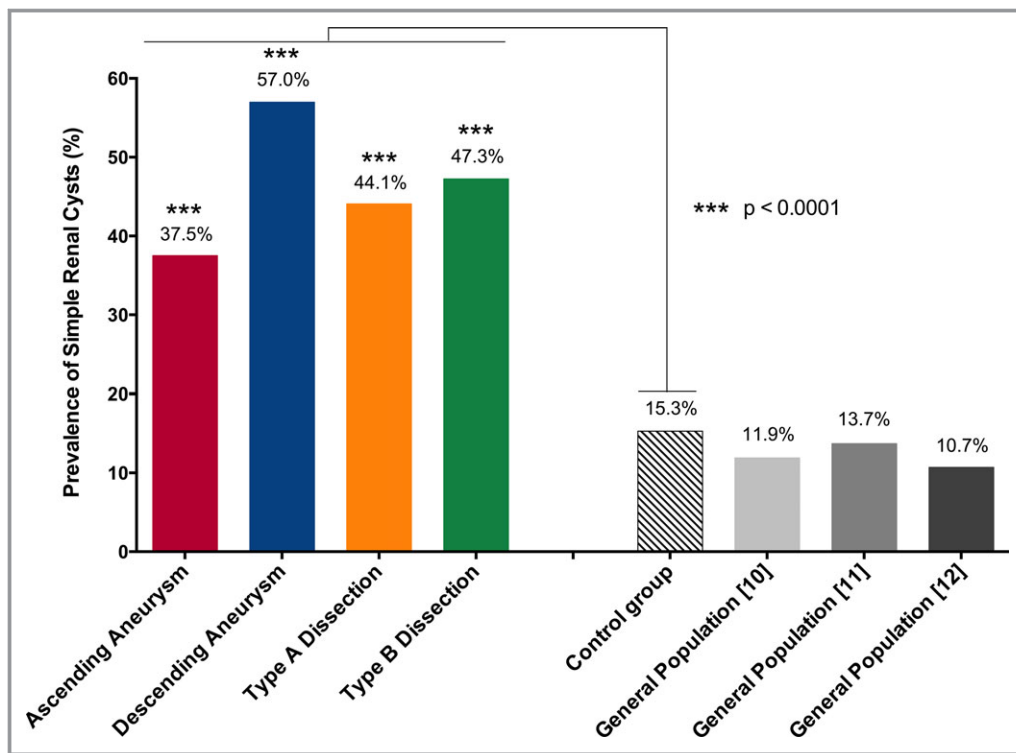
Figure 1. Overall prevalence of simple renal cysts in patients with thoracic aortic disease in comparison to the control group and the general population. ***Significantly different from control group.

Multivariate logistic regression, used to control for the difference in mean age between the study population (63.5±14.2) and control group (41.4±17.8), confirmed a statistically higher prevalence of SRC between all anatomical groups of the study population compared to the control group (*P*<0.05; Table 2). Statistical significance was strongest for the group of patients with descending aneurysm (odds ratio [OR]=3.15±0.84; *P*<0.001) and type B dissections (OR=1.84±0.38; *P*=0.004).

Sex-Controlled Prevalence of SRC

Prevalence of SRC was evaluated separately for males and females in both the study population and control group (Figure 3). In the group of patients with ascending aortic aneurysm, prevalence of SRC was 37.4% (116 of 310) and 37.7% (55 of 146) for males and females, respectively (*P*=1.0). In the group of patients with descending aortic aneurysm, prevalence of SRC was 57.5% (27 of 47) for males and 56.4% (22 of 39) for females (*P*=0.92). In the group of patients with type A dissections, prevalence of SRC was 46.1% (35 of 76) and 40.5% (17 of 42; *P*=0.56), and in the type B dissection group, it was 43.4% (46 of 106) and 52.6% (40 of 76) for males and females (*P*=0.22), respectively. In all anatomical groups of the study population, no statistically significant difference was observed between prevalence of SRC in males and females (*P*>0.05 for all 4 groups). In the control group, prevalence of SRC was higher in males (as expected from the literature[10–12,14–19]): 18.7% (57 of 305) for males and 11.3% (27 of 238) for females (*P*=0.004).

Incidence of SRC in Ascending and Descending Aortic Disease

Because of our understanding that diseases of the ascending and descending aorta are fundamentally different in etiology and pathogenesis,[24,25] we grouped the ascending aneurysm group together with type A dissections (ascending group) and the descending aneurysm group with type B dissections (descending group) in order to determine whether there is any difference in the incidence of renal cysts within the groups of TAD. Overall incidence of simple renal cysts in patients with ascending aortic pathology is 38.3% (223 of 583), which is significantly smaller than 50.4% (135 of 268) in the descending aortic pathology group (*P*=0.0009). Similar results were shown in multivariable analysis (see Table 2).

Clinical Characteristics

Detailed baseline clinical characteristics were evaluated for patients in the study population. These were not available for the control group because of the nature of the radiology
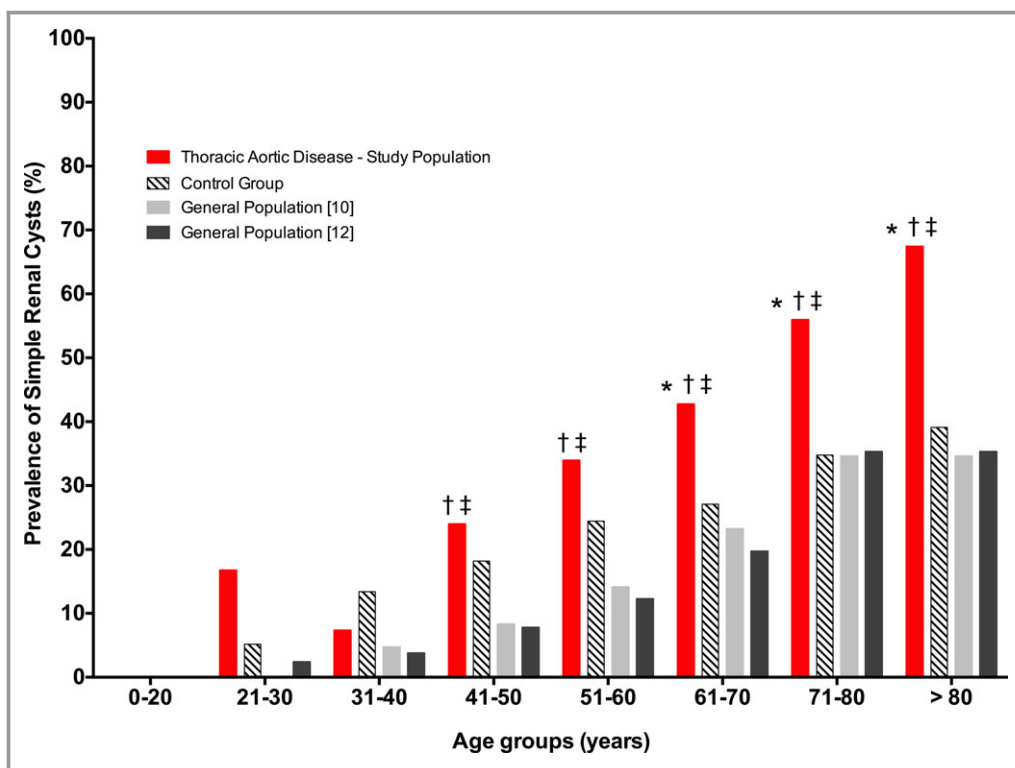
Figure 2. Prevalence of simple renal cysts in patients with thoracic aortic disease by the age groups compared to the control group and the general population. Symbols denote statistically significant difference between the study population and: *The control group, †prevalence reported by Terada et al.,[10] and ‡prevalence reported by Chang et al.[12] (*P*<0.05).

database. Clinical characteristics were compared between patients with TAD that had (358; 42.5%) and did not have (484; 57.5%) a SRC (Table 3). Complete clinical information was available for 304 of 358 (84.9%) patients with SRC and 408 of 484 (84.3%) without SRC (*P*=0.81). Mean age of patients with SRC was significantly higher than for those without renal cysts (68.5±12.1 vs 59.8±14.5, respectively; *P*<0.0001). Patients with SRC in comparison to patients without SRC were also more likely to have hypertension

Table 2. Results of Multivariate Logistic Regression Analysis Controlled for Patient Age Between the Study Population and the Control Group

Presence of a Simple Renal Cyst	Odds Ratio±SE	95% Confidence Interval	P Value
Age	1.05±0.00	1.04 to 1.06	<0.001
Male sex	1.50±0.20	1.15 to 1.96	0.003
Ascending aneurysm	1.43±0.25	1.02 to 2.02	0.038
Descending aneurysm	3.15±0.84	1.87 to 5.31	<0.001
Type A dissection	1.67±0.41	1.03 to 2.69	0.036
Type B dissection	1.84±0.39	1.21 to 2.80	0.004

(82.9% vs 69.9%; *P*<0.0001), dyslipidemia (54.3% vs 38.7%; *P*<0.0001), history of tobacco smoking (49.7% vs 40.7%; *P*=0.017), chronic kidney disease (13.5% vs 8.1%; *P*=0.019), and neurological comorbidities (14.1% vs 8.6%; *P*=0.019). Interestingly, patients with SRC were less likely to have Marfan syndrome (0.66% vs 3.9%; *P*=0.006), although the numbers were small. No differences were observed between patients with and without SRC in the prevalence of diabetes (11.5% vs 10.0%; *P*=0.53), pulmonary/respiratory disease (17.1% vs 17.2%; *P*=1.0), or presence of a positive family history of aortic disease (15.5% vs 19.1%; *P*=0.20), or a history of previous cardiac/aortic surgery (16.1% vs 15.7%; *P*=0.89).

Clinical characteristics were also evaluated separately for patients with and without SRC in each of the 4 study groups. In the ascending aneurysm group, hypertension (*P*<0.0001), dyslipidemia (*P*<0.0001), and neurological deficit (*P*=0.02) were found to be statistically greater among patients with SRC. In the descending aneurysm group, statistically significant difference was observed only in the prevalence of Marfan disease, which was higher in patients without SRC (*P*=0.01). In the group of patients with type A dissections, hypertension was significantly more prevalent in patients with SRC (*P*=0.03), whereas in the type B dissection group all
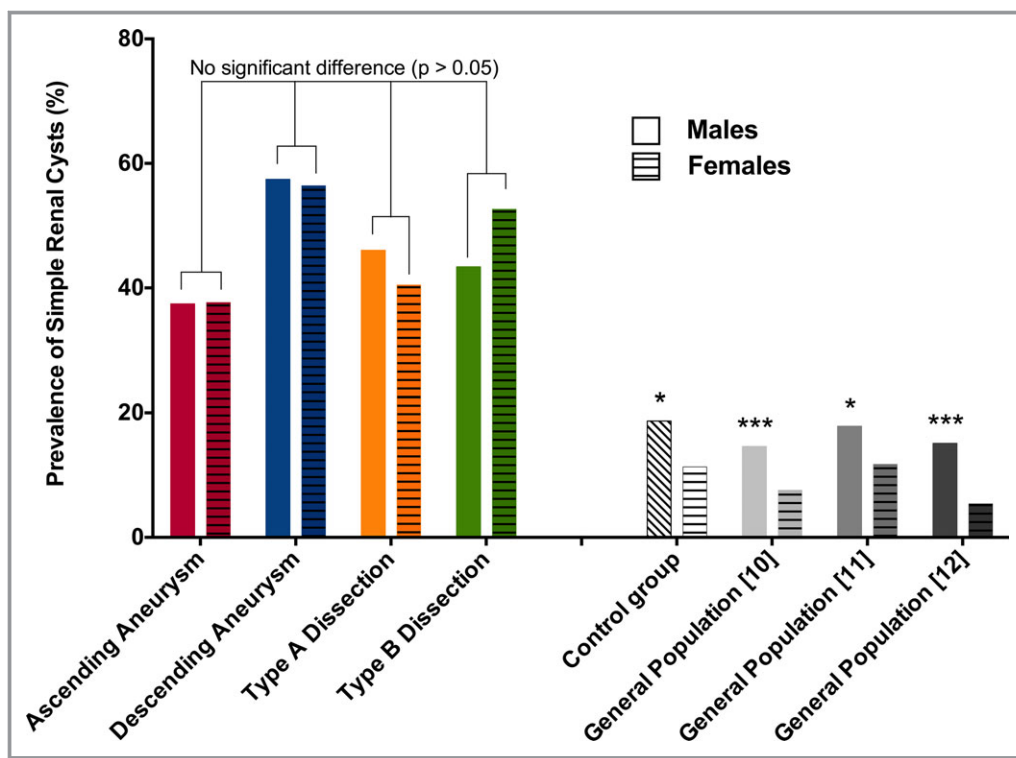
Figure 3. Prevalence of simple renal cysts in male and female patients with thoracic aortic disease compared to the control group and general population. *P<0.05 significance level; ***P<0.0001 significance level.

baseline clinical characteristics were statistically identical (P>0.05).

Relationship of Aortic Size and the Presence of SRC

In the 2 aneurysm groups—ascending and descending—aortic sizes were analyzed in relation to the presence or absence of renal cysts. Aortic sizes were available for analysis for 80.3% (366 of 456) of patients with ascending aortic aneurysm and for 95.3% (82 of 86) with descending aortic aneurysm. In the ascending aortic aneurysm group, mean size of the aorta was 5.15±0.71 cm and 4.98±0.67 cm in those with and without SRC, respectively (P=0.025). A similar trend was observed for descending aortic aneurysm—mean aortic size was 6.27±1.81 cm in patients with simple renal cysts and 5.97±1.55 cm in those without renal cysts. However, this difference was not statistically significant (P=0.426).

Discussion

This study shows that simple renal cysts are found with significantly higher frequency in patients with TAD than in our

control group or the general population, reported in most studies[10–19] (Table 1). These results suggest that patients found to have simple renal cysts are at increased risk of having TAD, namely, aortic aneurysm and/or dissection. This finding puts SRC in line with other clinical markers that have been associated with TAD, namely, bicuspid aortic valve,[3] intracranial aneurysm,[4] inguinal hernia,[5] aortic arch branching anomalies such as bovine aortic arch[6] and isolated left vertebral artery,[7] and a positive family history of aortic disease.[9] Such clinical markers make it possible to identify patients at risk of having TAD.[8] Such identification may be expected to pay dividends in lives saved by diagnosis before rupture, dissection, or death.

Our results also correlate with previous reports showing an association of simple renal cysts with abdominal aortic aneurysm and aortic dissection.[20,21] However, the natural history of simple renal cysts is associated with an increase in their prevalence in the older population as well as a higher prevalence in males.[10–12,16] Knowing this, and the fact that our study population of patients with TAD was predominantly male (64.0%) with a mean age of 63.5, we controlled for the age and sex factors in our study to make certain that the increased prevalence that we were observing was not merely attributed to the baseline characteristics of our thoracic aortic aneurysm population.

Table 3. Table With Baseline Clinical Characteristics of TAD Patients With and Without SRC

Variable	Thoracic Aortic Disease With Simple Renal Cysts		Thoracic Aortic Disease Without Simple Renal Cysts		P Value
	Absolute Value	Percentage	Absolute Value	Percentage	
Total No. of patients	358	42.5%	484	57.5%	—
Males	224	62.6%	315	65.1%	0.45
Mean age	68.5±12.1	—	59.8±14.5	—	<0.0001*
Clinical information available	304	84.9%	408	84.3%	0.81
Hypertension	252	82.9%	285	69.9%	<0.0001*
Diabetes	35	11.5%	41	10.0%	0.53
Dyslipidemia	165	54.3%	158	38.7%	<0.0001*
History of smoking	151	49.7%	166	40.7%	0.017*
Marfan syndrome	2	0.66%	16	3.9%	0.006*
Chronic kidney disease	41	13.5%	33	8.1%	0.019*
Neurological deficit	43	14.1%	35	8.6%	0.019*
Pulmonary/respiratory disease	52	17.1%	70	17.2%	1.0
Positive family history	47	15.5%	78	19.1%	0.20
Previous cardiac/aortic surgery	49	16.1%	64	15.7%	0.89

*Statistically significant.

Age Factor for SRC Development

Several studies that evaluated the natural history of simple renal cysts in the general population noted that increasing age is a risk factor for their development.[10–12,16] Terada et al.[10] in a study of over 14 000 individuals found that prevalence of renal cysts increased more than 7-fold with age from 5.1% in the fourth to 36.1% in the eighth decade of life. Therefore, in order to control for age, we split all patients of the study population and of the control group into age groups and analyzed the prevalence of SRC separately for each age group (Figure 2). These data were compared with the prevalence reported for similar age groups in studies reporting on the general population as well as with the prevalence established in our control group. In all age groups of patients with TAD starting from the seventh decade of life, the overall prevalence of SRC was statistically greater than in the control group ($P \leq 0.05$), and significantly different from the levels of the general population (for all age groups starting from the fifth decade and older) reported by Terada et al.[10] ($P < 0.0001$) and Chang et al.[12] ($P < 0.05$). This was also confirmed in multivariable analysis, where we controlled for the difference in age of the study and control populations (Table 2). It is possible that the slightly elevated incidence of simple renal cysts in the fourth, fifth, and sixth decade groups of our control population may have masked statistical significance in the analysis in those groups.

These findings are suggestive that age, although a contributing factor, is not the main factor influencing the development of SRC in patients with TAD. It appears that TAD itself is a predictor of SRC development.

No SRC Male Preponderance in TAD Patients

Another important factor in the natural history of SRC that differs significantly in the TAD patients, compared to the general population, is the male preponderance. All studies that looked at the prevalence of SRC in the general population have reported the male-to-female ratio to be in the 1.5 to 2.8 range (Figure 4). SRC is approximately twice as common in males in the general population.[10–12,16] Interestingly, we did not see this male predominance in our population of patients with TAD. The loss of the male preponderance suggests that the development of SRC may be fundamentally different in patients with TAD than in individuals without thoracic aortic pathology.

Ascending and Descending Aortic Aneurysm: 2 Different Diseases

More and more evidence is being accumulated in support of the observation that ascending and descending aortic aneurysm are 2 different diseases: descending aortic pathology is much more atherosclerotic in nature, whereas ascending aortic pathology is largely genetic and lacks the classic atherosclerotic features[24] (Figure 5). This is supported by the fact that during embryological development the ascending aorta and arch are formed from the neural crest, whereas the
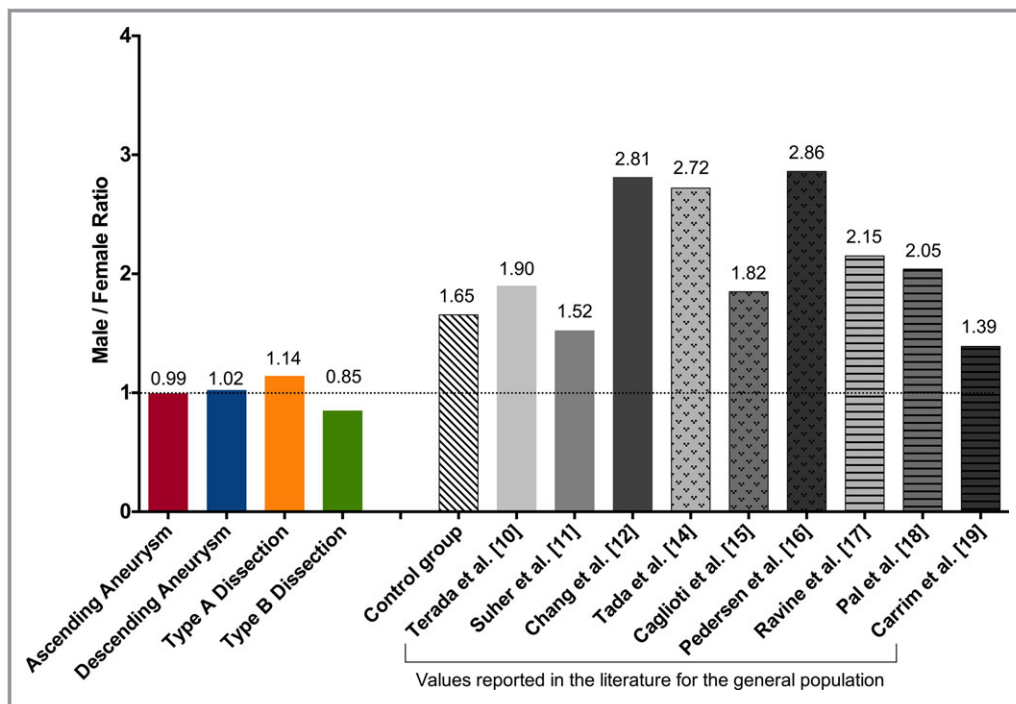
Figure 4. Male-to-female ratio in the prevalence of simple renal cysts in patients with thoracic aortic disease compared to the control group and the literature reports for the general population.

descending thoracic aorta is formed from the mesoderm, the ligamentum arteriosum being the separating point.[25] In this study, we found a higher overall incidence of SRC in patients with descending aortic pathology, compared to patients with ascending aortic disease. Also, in multivariable analysis the strongest association with SRC was found in the group of patients with descending aortic aneurysm (OR, 3.15±0.84; CI [1.87–5.31]; $P<0.001$) and type B dissection (OR, 1.84±0.39; CI [1.21–2.80]; $P=0.004$), both descending aortic pathologies. Therefore, the link between SRC and TAD seems to be even stronger for the descending aorta (and for patients with the traditional atherosclerotic risk factors of smoking, hypertension, and dyslipidemia[26]).

Possible Common Genetic or Pathophysiological Link

It is possible that TAD shares a common genetic defect also responsible for SRC formation as well. To date, more than 20 genes have been confirmed to be causative factors of syndromic and nonsyndromic cases of thoracic aortic aneurysm and dissection.[27–30] It is possible that some of these genes are causative factors for SRC development as well. Kim et al.[21] suggest that a genetic variation of the 8202A/G in the matrix metalloproteinase-9 (MMP-9) gene could be the common genetic defect causing TAD and renal cyst formation.[31] However, because molecular genetics of SRC formation have not been fully elucidated, it is difficult to

make definitive conclusions about the exact location of any possible common genetic defect.

It is quite plausible that a defect in MMP-related genes could be the link between TAD and SRC. MMPs are proteolytic enzymes that degrade the main structural proteins of the aortic wall (elastin, collagen, fibrillin, and so on) and are known to play an important role in the pathogenesis of thoracic aortic aneurysm and dissection.[2,32] The imbalance of MMP activity and their tissue inhibitors—favoring net lysis—leads to cystic medial degeneration and weakening of the aortic wall. At the same time, there is growing evidence that MMPs may play a role in cystic renal disease.[33] Specifically, MMP-2 and MMP-9 have been shown to be present in the cystic fluid of both benign simple renal cysts, as well as in cystic renal cell carcinomas.[34] MMP-14 has been found in the cyst-lining epithelium of an experimental animal polycystic kidney disease model; treatment with a metalloproteinase inhibitor results in a significant reduction of cyst number and kidney weight.[35] This is suggestive that MMPs may be the common link between TAD and SRC. The role of MMP overactivity may be detectable in future studies using whole-exome sequencing[36] or our RNA Signature test.[37]

Another possible explanation of the link between TAD and renal cysts may be in the recently described hypomorphic alleles (alleles with reduced levels of gene activity) of the *PKD1* and *PKD2* genes, mutations of which cause ADPKD.[38,39] Presence of a heterozygous hypomorphic allele of one of these genes results in a significantly milder cystic
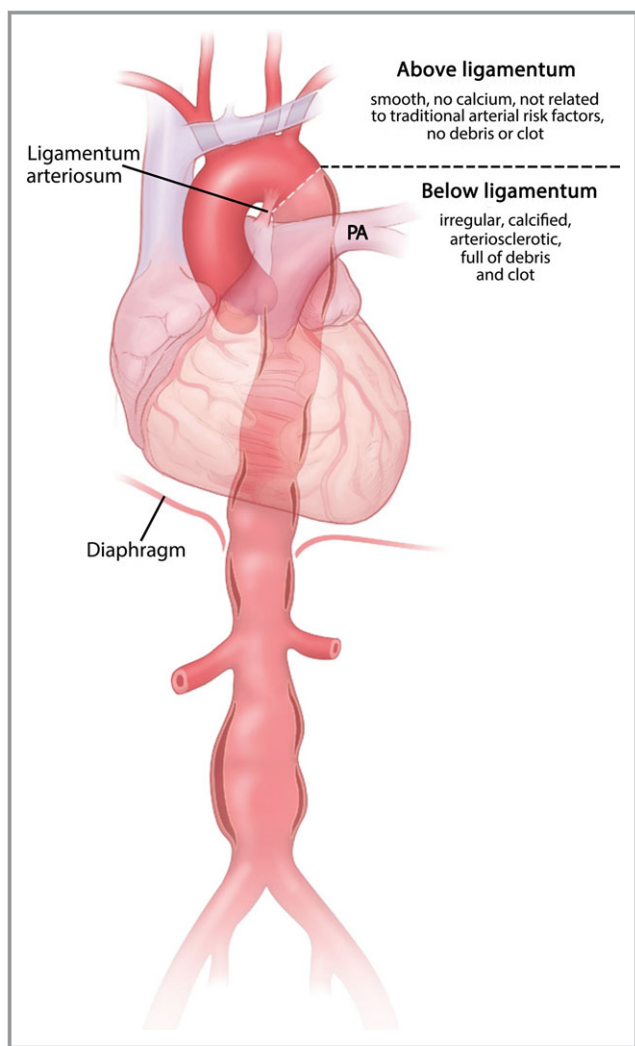
Figure 5. Aortic aneurysm is really 2 diseases: Ascending/arch disease differs markedly from descending/abdominal disease (reprinted with permission from Elefteriades and Farkas[24]).

disease,[38,40] which could manifest in a few kidney cysts and be radiologically interpreted as SRC. Clinically, the presence of an association between thoracic aortic dissection and ADPKD,[41–43] as well as abdominal aortic aneurysm and ADPKD,[44] has been modestly proposed in the literature based on a very small number of case reports; however, no cohort studies of these patients have yet been performed. It is possible that some of the patients in our study had a hypomorphic ADPKD allele, which would explain the presence of cysts in the kidneys of patients with thoracic aortic aneurysm and dissection.

Clinical Recommendation

Because thoracic aortic aneurysm is a silent condition with such devastating, often lethal, complications, this study raises the question whether patients with documented renal cysts should be screened for TAA. This has important cost/benefit considerations and may be premature based on this single study. Abdominal CT already includes the lower third of the thorax. However, extending an abdominal image (CT or MRI) in a patient with SRC to include the thoracic segment as well (only a few inches higher) would have the potential to detect silent thoracic aortic aneurysms and thus save considerable lives. Because renal cysts are so common, especially in the elderly, we are not yet ready to make such a recommendation. With this report, we simply wish to convey to clinicians a heightened awareness of the association between renal cysts and TAD.

Study Limitations

The limitations of this study include its retrospective nature and the fact that the control group is significantly younger than the study population, although we were able to control for age using appropriate statistical methods of analysis. Missing data of patients from the study population were handled using complete-case analysis, which can introduce additional bias. Another limitation of this study is in the unavailability of data on baseline risk factors and comorbidities for the control group. This is an inherent characteristic of the radiology database, which was developed specifically to permit comparative studies of this sort. Because of these data limitations, we were able to control only for age and sex as potential confounders (although we feel that these are the most important ones). Other confounders may exist that could potentially bias the estimated effects of the anatomical groups on SRC. However, to warrant inclusion in the model as confounders, such variables would need to be meaningfully correlated with at least one of these anatomical groups as well as with SRC itself. It is unclear a priori what additional variables may satisfy these requirements, but this is an important direction for further study. Finally, the statistical method of inverse probability weighting could not be utilized to address the missing data because of the absence of a variable that would strongly predict the probability of an observation missing the data.

Most important, this study merely shows an association between renal cyst and TAD. This association does not imply causation. This study is a clinical observation and was not designed to provide insight into the molecular and pathophysiological mechanisms that might explain the link between TAD and SRC. We hope that these clinical observations may prompt detailed pathophysiological and genetic investigations into potential shared pathways.

Conclusion

In this study, we established an increased prevalence of simple renal cysts in patients with TAD compared to the

general population. The highest prevalence of simple renal cysts is observed in patients with descending aortic aneurysms. There appears to be no male preponderance of simple renal cyst in the TAD population, in contradiction to the pattern observed in the general population. These results are suggestive that simple renal cysts can be used as a marker for detection of patients at risk of developing TAD. It is possible that thoracic aortic aneurysm and dissection share a common genetic pathway with simple renal cysts, as well a common pathogenesis, possibly through MMP abundance.

Disclosures

None.

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