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ABDOMINAL AORTIC CALCIFICATION ON A PLAIN X-RAY AND THE RELATION WITH SIGNIFICANT CORONARY ARTERY DISEASE IN ASYMPTOMATIC CHRONIC DIALYSIS PATIENTS

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ABSTRACT

Background

Coronary artery disease (CAD) is common in asymptomatic chronic dialysis patients and plays an important role in their poor survival. Early identification of these high risk patients could improve intervention and mortality. Abdominal aortic calcification (AAC), which can be quantified using a lateral abdominal X-ray, has been associated with CAD in dialysis patients. We hypothesized that the extent of AAC as assessed on a plain abdominal X-ray might be predictive of the presence of significant CAD in dialysis patients.

Methods

A subset of patients currently enrolled in the ICD2 trial, without a history of CABG or a PCI with stent were included in this study. All patients underwent CT-angiography (CTA) and a lateral X-ray of the abdomen. AAC on X-ray was quantified using a previously validated visual scoring system. The predictive value of AAC score for the presence of CAD was subsequently assessed.

Results

A total of 90 patients were included in this study (71% male, 67 ± 8 years old). Forty-six patients were found to have significant CAD following CTA. AAC-score was significantly higher in patients with CAD (10.2 ± 4.8 vs 6.3 ± 4.6; $p<0.05$). AAC-score is an independent predictor for the presence of CAD with a 1.2 fold higher risk per point increase ($p=0.001$) (Table). The AAC-score has a sensitivity of 85% and a specificity of 57% for predicting the presence of significant CAD.

Conclusion

This study shows that abdominal aortic calcification as assessed on a lateral abdominal X-ray is predictive for the presence of significant coronary artery disease in asymptomatic dialysis patients. This simple, non-invasive and cheap screening method could contribute to early identification of patients eligible for further screening for CAD.

INTRODUCTION

Coronary artery disease (CAD) plays an important role in the poor survival of chronic dialysis patients.[1-3] Optimizing treatment strategies for CAD could therefore substantially improve the outcome in this patient group. Although it is known that CAD is highly prevalent among dialysis patients, the currently reported prevalence is probably an underestimation of the actual prevalence. Several studies have indicated that also among asymptomatic dialysis patients CAD is prevalent in approximately 40-50% of the patients.[4-6] Identification of these patients would allow for earlier and better treatment. In dialysis patients it has been recently demonstrated that aortic calcification is an independent predictor of cardiovascular morbidity and mortality. It was therefore suggested that this screening modality could be used for accurate cardiovascular risk estimation in dialysis patients.[7, 8] Next to this relationship with cardiovascular events it has also been demonstrated, in an autopsy study performed in >600 middle-aged adults, that the degree of abdominal calcification is associated with the extent of calcified coronary plaques.[9]

Given these relationships we hypothesized that the extent of aortic calcification as assessed on a plain lateral abdominal X-ray might be predictive of the presence of significant CAD in dialysis patients. The purpose of this study was to assess the predictive value of abdominal calcification for the presence of significant CAD using a previously validated scoring system.[7]

METHODS

Study population

For this analysis all patients currently enrolled in the ICD2 trial (ISRCTN20479861) were included. The background, objectives and methods of this study have been previously reported.[10] In summary, this study will evaluate the effectiveness of prophylactic ICD implantation in chronic dialysis patients. Before patients are randomized an intensive screening protocol is performed including computed tomography angiography (CTA) and a lateral X-ray of the abdomen. All patients provided written informed consent and the design of the trial was approved by the local ethics committee. Not included were patients with previous

CABG or PCI with stent, patients with an aortic prosthesis and patients in whom the CT-scan was not feasible or considered uninterpretable.

Multi Slice CT protocol and MSCT data analysis

Prior to CT acquisition patients with a high heart rate, defined as >65 bpm, received oral oral β-blockers (metoprolol 50 or 100 mg, single dose, 1 hour before examination), if tolerated. Furthermore, depending on the patients residual kidney function pré and post-procedural measures were taken in order to prevent further deterioration. These

measures included pre- and post-procedural hydration (dose and route depending on the patients residual kidney function) and moreover in hemodialysis patients the scan was performed on the day prior to the next dialysis session.

Examinations were performed with a 64-detector row CT Scanner (Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) or a 320-detector row CT scanner (Aquilion ONE, Toshiba, Tokyo, Japan) as previously described.[11]

Data analysis was performed by two experienced CT observers. If there was no consensus between these 2 reviewers, a 3rd independent reviewer was consulted. Data of all major epicardial segments (in the RCA segments 1-3; in the LAD segments 5-8; and in the LCx segments 11 and 13 (see figure 1)) was analyzed as previously described. [11]

Quantification of abdominal aortic calcification

The extent of aortic calcification was calculated on a lateral X-ray of the abdomen. The lateral X-ray was taken in a standing position using standard radiographic equipment. The grading was performed using a previously validated grading system[12, 13] in which the extent of calcific deposits is graded on a per segment basis using the lumbar vertebral segments L1-L4. Per segment a score between 0 and 3 was given for both the anterior and posterior wall of the aorta. These 8 scores resulted in a composite abdominal aortic calcification score (AACscore) ranging between 0 and 24 points. See figure 2.

Statistical analysis

Continuous data were compared using the 2-tailed Student's t-test. Categorical data were compared using the Chi-square test. Using logistic regression analysis the univariate predictive value of the baseline parameters, for the presence of CAD, was assessed. Subsequently a multivariate analysis (controlling for all univariate predictors

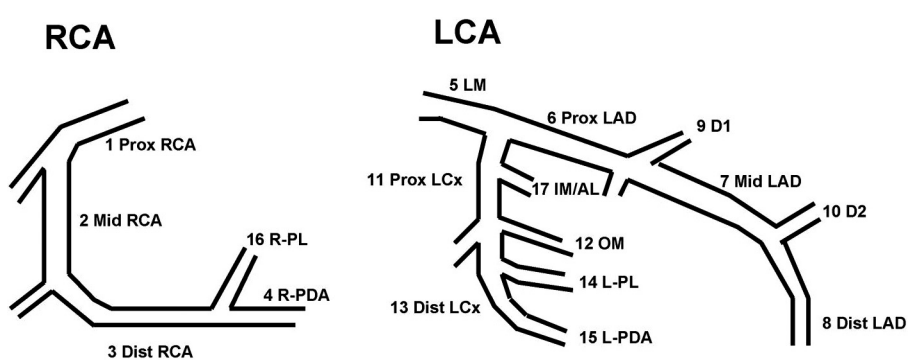

Figure 1: Coronary anatomy. RCA: Right coronary artery, R-PL: Right posterolateral branch, R-PDA: Right posterior descending artery, CA: Left coronary artery, LM: Left main, LAD: Left anterior descending artery, LCx: Left circumflex artery, L-PL: Left posterolateral branch, L-PDA: Left posterior descending artery.

Abdominal Aortic Calcification Score
For all segments both the anterior and the posterior walls are graded for the extent of vascular calcification.

Grading:
0 Points: No calcific deposits
1 Point: Less than 1/3 of the wall calcified
2 Points: Between 1/3 and 2/3 of the wall affected
3 Points: More than 2/3 of the wall affected

Figure 2: Grading of abdominal aortic calcification.

with p<0.2) was performed. All statistical analyses were performed using SPSS (version 20, IBM Corp, Amonk, NY, USA). A p-value <0.05 was considered statistically significant.

RESULTS

For this study 90 out of 142 patients that who are currently enrolled in the ICD2 study were eligible for this analysis; 23 patients were not included because of history of CABG, 10 patients because of history of PCI with stent, 6 patients because of a high/irregular heart rate, 4 patients had an non-diagnostic CTA, 3 patients had an aortic prosthesis, and 4 patients refused CTA. Furthermore in 2 patients no X-ray was obtained due to logistic reasons.

Patients were predominantly male (71%) with an average age of 67 ± 7 years. Most patients were on hemodialysis (69%) for a median duration for 18 [9, 29] months. The average abdominal aortic calcification score was 8.2 ± 5.0 points (range 0 – 20.5 points). The baseline characteristics are summarized in table 1.

CAD

Significant CAD was documented in 46 (51%) of the patients. Compared to patients with no significant CAD these patients were significantly older (69 ± 7 vs. 65 ± 7 years, p <0.05). Furthermore, patients with CAD were predominantly male (80 vs.

Table 1: Baseline characteristics of all patients and in two groups of patients with or without significant CAD

	All (n=90)	No CAD (n=44)	CAD (n=46)
Age, yrs	67 ± 8	65 ± 7	69 ± 7*
Male gender, nr.(%)	64 (71%)	27 (61%)	37 (80%)
Hemodialysis, nr.(%)	62 (69%)	29 (66%)	33 (72%)
Dialysis Vintage, months	18 [9, 29]	17 [9, 33]	18 [8, 25]
BMI, kg/m^2	26.8 ± 4.4	26.8 ± 4.5	26.8 ± 4.3
Hypertension, nr (%)	70 (77%)	32 (73%)	38 (83%)
Diabetes, nr (%)	26 (29%)	12 (27%)	14 (30%)
History of smoking, nr (%)	60 (67%)	25 (57%)	35 (76%)
Beta-Blocker, nr (%)	45 (50%)	23 (52%)	22 (48%)
ACEi/ARB, nr (%)	48 (53%)	23 (48%)	27 (59%)
Statin, nr (%)	45 (50%)	21 (48%)	24 (52%)
CACS	690 [133, 2085]	279 [20, 1691]	912 [441, 2217]*
AAC-score	8.2 ± 5.1	6.3 ± 4.6	10.2 ± 4.8*

CAD: coronary artery disease; BMI: body mass index; ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CACS: coronary artery calcification score; AAC: abdominal aortic calcification; * student T-test comparing "CAD" versus "No CAD" = p <0.05

61%, p<0.05). The AAC score was significantly higher in patients with significant CAD measured by CTA than in patients without CAD (10.2 ± 4.8 vs 6.3 ± 4.6 points, p <0.05). As could be expected the coronary artery calcium score assessed by CT was also higher in patients with CAD than in patients without CAD.

Prediction of the presence of CAD

Using logistic regression analysis the univariate predictive value of the baseline parameters, for the presence of CAD, was assessed. Older age, male gender and AAC score were significant univariate predictors for the presence of significant CAD. Multivariate analysis demonstrated that the AAC score was a significant and independent predictor for the presence of significant CAD with a 1.2-fold higher risk per point increase. See table 2.

Sensitivity and specificity

Using ROC curve analysis the optimal cut-off for the abdominal aortic calcification score was assessed: with a cut-off of 6.5 points the AACscore had a sensitivity of 85% and a specificity of 57% for predicting the presence of significant CAD. Furthermore when this cutoff is used the AAC score has a negative predictive value of 78% and a positive predictive value of 67%. See table 3. ROC curve analysis demonstrated an area under the curve of 0.72 (p <0.05). See figure 3.

Table 2: Uni- and multivariate predictors for the presence of CAD

	Univariate	Multivariate
Age	1.06 (1.00 – 1.13), p <0.05	
Male gender	2.59 (1.00 – 6.68), p<0.05	1.02 (0.95 – 1.09), p = 0.64
Hemodialysis	1.31 (0.54 – 3.20), p = 0.55	2.53 (0.88 – 7.27), p = 0.09
Dialysis vintage	1.0 (0.99 – 1.00), p = 0.42	
AACscore (per point)	1.19 (1.07 – 1.30), p <0.05	
Diabetes	1.17 (0.47 – 2.90), p = 0.74	1.20 (1.18 – 1.32), p = 0.001
History of smoking	2.42 (0.98 – 5.97). p = 0.055	
Hypertension	1.78 (0.65 – 4.89), p = 0.26	2.42 (0.88 – 7.27), p = 0.09
BMI	1.0 (0.91 – 1.10), p = 0.95	

AAC = abdominal aortic calcification; BMI = body mass index

Table 3: Presence of significant CAD using an AACscore cutoff of 6.5 points

	CAD (n=46)	No CAD (n=44)	
AACscore ≥6.5 (n=58)	39	19	*PPV :* 67%
AACscore <6.5 (n=32)	7	25	*NPV :* 78%
	Sensitivity : 85%	*Specificity* : 57%	

CAD: Coronary Artery Disease, AACscore: Abdominal Aortic Calcification score

When this cutoff was entered in the multivariable model, as described previously, an AACscore ≥ 6.5 was associated with a 6.28 (95% CI 2.17 – 18.22, p = 0.001) fold increased risk for the presence of significant CAD.

DISCUSSION

This study demonstrates that the extent of abdominal aortic calcification, assessed on a plain lateral abdominal X-ray, is predictive for the presence of significant CAD in chronic dialysis patients.

The necessity to detect significant CAD in dialysis patients

CAD is highly prevalent among dialysis patients and is a major contributor to the poor outcome of dialysis patients.[2, 14] Optimal treatment of CAD could, however, lead to significantly improved outcomes. For instance, it has been demonstrated that revascularization in dialysis patients in whom significant CAD is detected may indeed increase survival.[15-17] Nevertheless, despite these observations, it should be noted that invasive treatment for CAD is currently underused in dialysis patients.[18]

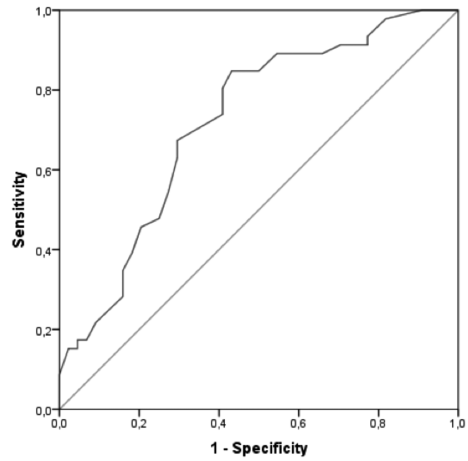

Figure 3: ROC curve for the sensitivity and specificity of the AAC score to detect CAD

Since significant CAD is highly prevalent among asymptomatic dialysis patients, a substantial number of patients is probably not optimally treated. These patients may benefit from more intensive medical treatment or even revascularization. Some controversy remains on this topic, however, since optimal treatment in this patient group is not well defined. Further studies are needed in the future to address this problem. It is clear though, that screening of dialysis patients for the presence of significant CAD is warranted in order to optimize treatment.

Abdominal aortic calcification and CAD

Already in the 1950s it was reported, based on autopsy studies of > 600 middle aged adults, that the degree of abdominal aortic calcification is strongly associated with the presence of calcified plaque in the coronary arteries.[9] Following these findings it was demonstrated, in the general population, that using a plain lateral abdominal x-ray the severity of aortic calcification can be predicted. Moreover a relationship between the extent of aortic calcification found on x-ray and cardiovascular morbidity and mortality was reported.[19, 20] Consequently this relationship was also documented in dialysis patients.[7] To our knowledge this is the first study that demonstrates that aortic calcification on X-ray is predictive of the presence of significant CAD in dialysis patients.

Other modalities to detect significant CAD

Many modalities to detect CAD are currently available, although each with its own limitations. The gold standard for the diagnosis of CAD, coronary angiography (CAG), has been suggested as a routine screening tool of CAD in dialysis patients.[21] However, given its invasive nature, the high costs and the risks of complications, other

diagnostic tools may be preferable in this asymptomatic population. Other imaging modalities have been proposed as well, such as dobutamine stress echocardiography and myocardial perfusion scintigraphy (MPS).[22]

Although no true comparison can be made between the screening modality presently investigated and other diagnostic tools for CAD, a plain lateral abdominal X-ray obviously has financial and logistical advantages over the other diagnostic screening modalities mentioned.

Clinical implications

CAD is highly prevalent among dialysis patients but it has not yet been decided which diagnostic modality is preferable. However routine screening for CAD, using one of the many available screening modalities, is warranted in order to improve the abysmal outcome of this patient group. We showed that aortic calcification on plain lateral abdominal X-ray is predictive for the presence of significant CAD. Using this inexpensive, non-invasive screening method, patients with significant CAD can be easily identified . Subsequently the most optimal diagnostic or treatment strategy can be initiated.

Limitations

CT-angiography was used to detect the presence of significant CAD instead of CAG. Although it has been recently reported by our group that CT-angiography is feasible to detect CAD in dialysis patients, coronary angiograms still should be considered the gold standard.[11] Therefore, future studies should compare the AAC score to CAG in order to confirm these findings.

Conclusions

Aortic calcification as assessed on a plain lateral abdominal X-ray is predictive for the presence of significant CAD in asymptomatic chronic dialysis patients. Using this X-ray patients with high risk for CAD in whom treatment could be optimized can be identified.

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