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Clinical Report

Autosomal dominant polycystic kidney disease (ADPKD) is associated with coronary arterial dilatation in end-stage renal failure patients

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Abstract

Autosomal dominant polycystic kidney disease (ADPKD) can affect several organs in addition to the kidney. There is paucity in the literature on the cardiac manifestations of this disease. This retrospective study aimed to assess whether ADPKD was associated with a larger coronary artery diameter and to evaluate for the presence of coronary artery aneurysm and ectasia. This study shows that subjects with ADPKD and end-stage renal failure have dilatation of coronary arteries independent of traditional coronary risk factors and medication use.

Keywords: autosomal dominant polycystic kidney disease; coronary angiogram; coronary artery size

Background

Autosomal dominant polycystic kidney disease (ADPKD) is associated with several extra-renal manifestations including coronary artery aneurysm and ectasia as well as cerebral aneurysms, hepatic and pancreatic cysts, cardiac valve disease, aortic root dilatation and colonic diverticulae [1–5]. Abnormalities in the polycystic kidney disease (PKD) gene manifested in arterial smooth muscle cells and myofibroblasts could explain the expression of these extra-renal complications of the disease [6]. Despite some case reports [1–5], there is paucity in the literature regarding the coronary artery manifestations of ADPKD. The aim of this retrospective study was to determine the incidence of coronary artery aneurysms and ectasia in the ADPKD population and to assess if the size of the coronary arteries was larger compared to a control population.

Case report

We retrospectively reviewed all end-stage renal failure (ESRF) patients on haemodialysis over a 10-year period (2000–2010) at Westmead Hospital using the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data. A total of 29 subjects ranging from 41 to 79 years old were studied. The study population had a diagnosis of ADPKD and ESRF at the time of coronary angiogram. The control group of 15 patients was selected from the hospital cardiology database if they had both a diagnosis of end-stage kidney disease not due to ADPKD at the time of catheterisation. Patients with previous coronary artery bypass grafting were excluded from the study. Relevant clinical details including patient medical history, medica-

tions at the time of angiography and coronary risk factors were obtained from the case records. Baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were obtained from the coronary angiography report. The study was approved by the Human Research Ethics Committee at Westmead Hospital.

Angiograms were analysed offline by a single observer (J.C.) using computerised edge-detection software (Xcelera, Philips Healthcare, Netherlands). The proximal left main coronary artery (LMCA), left anterior descending (LAD), left circumflex (LCX) and right coronary (RCA) arteries were analysed. The catheter of known diameter was used for calibration. Arterial segments were viewed in two orthogonal planes at end-diastole to maximise vessel diameter. The start and end points of a 5 mm segment of vessel were determined by the user. The average diameter within this 5 mm chosen segment was used to calculate the diameter of the proximal artery for each view. Figure 1 illustrates the method of analysis for the LMCA from one representative subject.

All data analysis was performed using commercially available software (SPSS Inc. Statistical Package for the Social Sciences, Version 18, Chicago, IL). Categorical data are reported in percentages and continuous data are represented as mean value $\pm$ SD. Continuous variables were compared using the Student's t-test and confirmed with a Mann–Whitney test. The Pearson Chi-square or the Fisher Exact Test was used as appropriate to compare categorical data. A value of $P < 0.05$ was considered significant.

The baseline demographics, prevalence of cardiac risk factors and use of aspirin, clopidogrel, β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors and statins between the groups were not statistically different (Table 1). The average diameters of the LMCA, LAD and RCA were significantly larger in the ADPKD group compared

to the control group (Table 1). The average diameter of the LCX was not significantly different between groups. There were no aneurysms or ecstatic vessels in the control group. The LAD, RCA and LCX were diffusely ectatic in one subject with ADPKD. There were no documented coronary artery dissections in either group.

Discussion

This retrospective study shows that subjects with ADPKD have larger diameter coronary arteries independent of coronary risk factors and medication use. To our knowledge, this has not been demonstrated previously.
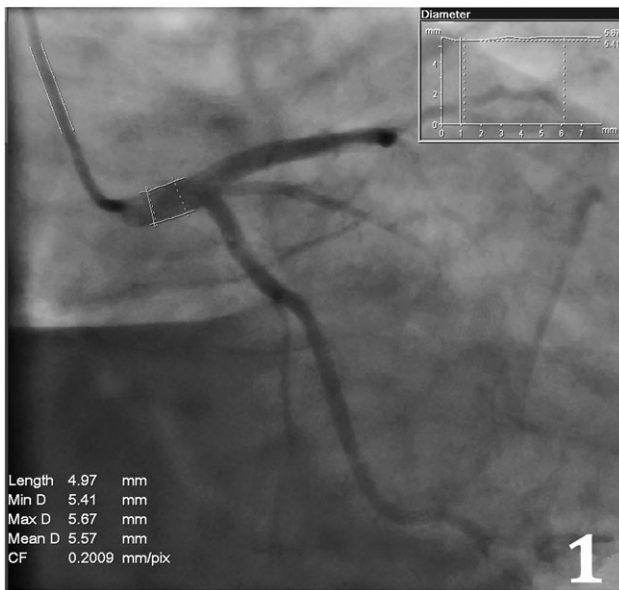

Fig. 1. Representative cine captures showing catheter calibration and measurement of the left main coronary artery. Figure 1 shows the Right Anterior Oblique 30° with 30° caudal angulation. The start and end points were chosen by the user and the length of vessel measured was 5 mm.

Dodge *et al.* [7] studied the normal lumen diameter of human coronary arteries. Our study showed that the ESRF group with no history of ADPKD had LMCA, LAD and RCA vessel diameters similar to this normal range in contrast to the ADPKD group whose average vessel diameter was larger. Interestingly, the LCX diameter was similar in both groups.

ADPKD is associated with abnormalities in vascular smooth muscle and myofibroblasts as well as the extra-cellular matrix and collagen through defects in the PKD gene [6, 8]. It is likely that polycystin has a role in maintaining the integrity of the arterial wall [9]. Dysfunction of polycystins regulate cell–cell and cell–matrix interactions in vascular cells, and in the vasculature, this may lead to abnormalities in endothelial function, vascular tone as well as vascular integrity [10]. These pathophysiological abnormalities support that PKD gene mutations may contribute to coronary artery dilatation; however, the mechanisms remain to be defined.

The significance of larger diameter coronary arteries is uncertain. It is thought that the presence of coronary aneurysmal segments leads to an increased risk of acute myocardial infarction and ischemia through the promotion of sluggish and turbulent blood flow in the relevant artery. It is possible that larger coronary arteries might precipitate coronary events due to a similar process; however, this requires further study.

Further studies examining the change in vessel size and presence of aneurysms and ectasia in ADPKD subjects at diagnosis and longitudinally over time using non-invasive imaging would be beneficial. In addition, it would also be of interest to examine the incidence of clinical events in the same population. A detailed understanding of the incidence and pattern of coronary artery disease in ADPKD patients will allow us to determine the optimal time to screen patients for the presence of coronary artery disease and may assist in choosing the most appropriate treatment strategy, especially if the risk of arterial dissection is greater.

Conflict of interest statement. None declared.

Table 1. Demographics and mean coronary artery size in the ADPKD and non-ADPKD groups[a]

	No ADPKD (*N* = 15)	ADPKD (*N* = 14)	P-value
Sex (male, %)	60	64	0.812
Age (years)	63.7 ± 9.8	65.2 ± 8.5	0.667
Systolic blood pressure (mmHg)	153.7 ± 28.2	140.4 ± 23.7	0.188
Diastolic blood pressure (mmHg)	69.6 ± 12.6	69.8 ± 10.6	0.974
Mean arterial pressure (mmHg)	100.2 ± 14.1	95.1 ± 14.2	0.351
Smoking (last 10 years, %)	40.00	21.43	0.429
Diabetes (%)	53.33	28.57	0.299
Hypertension (%)	93.33	78.57	0.330
Family history of coronary disease (%)	0.00	0.00	1.000
Dyslipidaemia (%)	46.67	42.86	1.000
Aspirin (%)	86.67	78.57	0.109
Clopidogrel (%)	26.67	7.14	0.330
β-blockers (%)	60.00	50.00	1.000
ACE inhibitors (%)	20.00	28.57	1.000
Calcium channel blockers (%)	20.00	21.43	1.000
Statins (%)	53.33	42.86	0.715
LMCA, mm	4.49 ± 0.80	5.06 ± 0.62	0.050
LAD artery, mm	3.57 ± 0.77	4.11 ± 0.49	0.027
LCX artery, mm	2.97 ± 0.73	3.36 ± 0.46	0.182
RCA, mm	3.59 ± 0.53	4.26 ± 0.86	0.026

[a]ACE, angiotensin-converting enzyme. Data are expressed as mean ± SD.

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