Original Paper

Clinical Manifestation, Management and Prognosis of Acute Myocardial Infarction in Autosomal Dominant Polycystic Kidney Disease

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Key Words

Autosomal dominant polycystic kidney disease (ADPKD) • Acute myocardial infarction (AMI) • Cardiovascular complications

Abstract

Background/Aims: Cardiovascular complications are the most common cause of death in individuals with autosomal dominant polycystic kidney disease (ADPKD), yet there is no substantial data concerning the clinical characteristics of acute myocardial infarction (AMI) in this population. This study thus aimed to investigate AMI in persons with ADPKD. **Methods:** A retrospective analysis of ADPKD patients admitted to our hospital over a 13 year period was conducted. Age and gender-matched control patients without ADPKD were also selected at a ratio of 1: 10. **Results:** A total of 52 ADPKD and 520 non-ADPKD patients were enrolled in the present study, with those in the former group exhibiting significantly poorer kidney function. The distribution of AMI types differed significantly between these two groups. The incidence of ST-segment elevation myocardial infarction (STEMI) was higher (75.0%) and the incidence of non-ST segment elevation myocardial infarction (NSTEMI) was lower (25.0%) in the ADPKD group. At the onset of AMI, sudden cardiac death (SCD) was more common in ADPKD patients (11.5% vs. 4.6%). In terms of risk factors, the occurrence of hypertension was greater in ADPKD patients (78.8% vs. 39.6%). With regard to subsequent management, ADPKD patients had a higher prevalence of triple-branch coronary lesions (21.1% vs. 11.2%), undergoing more coronary artery bypass grafting (CABG) (7.7% vs. 5.4%) and fewer percutaneous coronary interventions (PCI) (73.1% vs. 84.6%). Overall, ADPKD patients had higher rates of mortality (13.5% vs. 6.2%). **Conclusion:** ADPKD patients with AMI suffer from more severe conditions and difficult therapies, resulting in a poorer prognosis.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease [1], with a prevalence of 1/1000 to 1/400 [2]. Patients often present with bilateral renal cysts as they grow older. These renal cysts grow over time, gradually degrading renal structure and function. Even when appropriate treatment is applied, end-stage renal disease (ESRD) still eventually develops in about half of ADPKD patients by the age of 60 [3]. Because of an increased incidence of early-onset hypertension, left ventricular hypertrophy and valvular abnormalities, cardiovascular complications are the most common cause of death in the ADPKD population [4]. Recent data have demonstrated that the frequencies of acute myocardial infarction (AMI) in ADPKD patients from America and Taiwan were up to 6% and 2.91% respectively [5, 6]. To the best of our knowledge, there has been no published study to date regarding the clinical manifestations, management, and prognosis of AMI in patients with ADPKD. We therefore conducted a retrospective analysis of the clinical characteristics of ADPKD patients with AMI and compared these findings to a non-ADPKD population based on a single-center review of 13 years' worth of clinical data.

Materials and Methods

Data sources and study population

We retrospectively analyzed ADPKD patients with AMI admitted to Peking University People's Hospital from January 2004 through December 2016. We searched the patient database for ADPKD patients between 18 and 75 years of age, who had been diagnosed with AMI and underwent subsequent treatment in our hospital. Additionally, age- and gender-matched non-ADPKD patients with AMI were included as a control group at a 1:10 ratio. Exclusion criteria were: patients with severe infections, pulmonary diseases, active immune diseases, or advanced malignant tumors. The definition of hypertension was a systolic pressure ≥ 140 mmHg and/or a diastolic pressure ≥ 90 mmHg. Chronic kidney disease was defined as kidney damage or glomerular filtration rate (GFR) < 60 ml/min/1.73m² for 3 months or more, irrespective of cause. CKD classification was as follows: CKD 1 indicated GFR ≥ 90 ml/min/1.73m²; CKD 2 indicated GFR 60–89 ml/min/1.73m²; CKD 3 indicated GFR 30–59 ml/min/1.73m²; CKD 4 indicated GFR 15–29 ml/min/1.73m²; CKD 5 indicated GFR < 15 ml/min/1.73m² or dialysis. In this study, dialysis patients were separated from CKD 5 patients for statistical analyses.

Statistical analysis

All analyses were conducted using SPSS version 16. All measured data are presented as mean $\pm$ standard deviation. Enumerated data are presented as percentages. Differences in measurement data were compared using an independent t-test, while differences in enumerated data were assessed via the Chi-squared test or Fisher's exact test. A P-value < 0.05 was considered being statistically significant.

Results

Clinical features and risk factors

A total of 52 patients with ADPKD and 520 patients without ADPKD were eligible for our study (Table 1). The study group and the control group had a male to female ratio of 3:1, with mean ages of 49.2 ± 13.5 and 51.1 ± 12.6 years in the ADPKD and control groups, respectively. Difference in gender and age were not significant between groups. All patients were Asian. Among the ADPKD patients, 39 (75.0%) were diagnosed with ST-segment elevation myocardial infarction (STEMI) and 13 (25.0%) were diagnosed with non-ST segment elevation myocardial infarction (NSTEMI), while 308 (59.2%) were STEMI and 212 (40.8%) were NSTEMI in the control group. The distribution of STEMI and NSTEMI diagnoses was statistically different between these groups ($p=0.026$). At the onset of AMI,

ADPKD patients were more likely to suffer sudden cardiac death (SCD) than were controls (11.5% vs. 4.6%, $p=0.033$). An analysis of cardiovascular risk factors revealed that ADPKD patients had a significantly increased prevalence of hypertension (78.8% vs. 39.6%, $p<0.001$). In contrast, non-ADPKD patients were significantly more likely to have a history of smoking and were more likely to be obese (53.8% vs. 69.0%, 26.9% vs. 33.1%, $p=0.026$, 0.001, respectively). Patients with ADPKD had significantly poorer renal function than did non-ADPKD controls ($p<0.001$). 41 patients in the ADPKD group had hypertension, while 206 patients in the control group had hypertension. Detailed information regarding patient antihypertensive treatments is listed in Table 2.

Management and prognosis

Patients all underwent coronary artery angiography to identify the culprit vessel, with the exception of 10 ADPKD patients and 52 non-ADPKD patients, who either did not have the opportunity to undergo examination or refused further examination. The coronary angiography findings indicated that ADPKD patients had higher rates of multiple-branch artery lesions, particularly triple-branch lesions (21.2% vs. 11.2%, $p=0.012$). Operative treatments were performed on the majority of patients, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). ADPKD patients underwent CABG significantly more often and PCI significantly less often than did non-ADPKD patients (7.7% vs. 5.4%, 73.1% vs. 84.6%, $p=0.007$, 0.032, respectively). There were also significant differences in the application of subsequent therapies during convalescence in intensive care units (ICU). A significantly higher percentage of patients with ADPKD underwent continuous renal replacement therapy (CRRT) and temporary pacemaker therapy than did non-ADPKD controls (13.5% vs. 2.5%, 7.7% vs. 1.0%, $p<0.001$, 0.005, respectively). Importantly, patients with ADPKD had significantly higher mortality rates than did non-ADPKD patients (13.5% vs. 6.2%, $p=0.046$). We followed all patients for one additional year, and found that during that time the occurrence of cardiac adverse events, such as new-onset acute coronary syndrome (ACS), heart failure, arrhythmia or SCD, were similar between these two groups (Table 3).

Table 1. Clinical features and AMI risk factors. * indicates a statistically significant difference

Parameter	ADPKD (N=52)		Non-ADPKD (N=520)		χ^2	P-value
	N	%	N	%		
AMI					4.926	0.026*
STEMI	39	75.0	308	59.2		
NSTEMI	13	25.0	212	40.8		
Symptom						
SCD	6	11.5	24	4.6	4.559	0.033*
Cardiogenic shock	12	23.1	76	14.6	2.600	0.107
Risk factors						
Hypertension	41	78.8	206	39.6	46.944	<0.001*
Diabetes mellitus	10	19.2	41	7.9	2.442	0.118
Hyperlipemia	11	21.2	92	17.7	0.878	0.349
History of smoking	28	53.8	359	69.0	4.986	0.026*
Obesity	14	26.9	172	33.1	11.014	0.001*
Family history of coronary heart disease (CHD)	18	34.6	104	20.0	3.424	0.064
Renal function					78.079	<0.001*
Normal	27	51.9	477	91.7		
CKD 1	11	21.1	21	4.0		
CKD 2	5	9.6	10	1.9		
CKD 3	4	7.7	3	0.6		
CKD 4	1	1.9	1	0.2		
CKD 5	2	3.8	2	0.4		
Dialysis	2	3.8	6	1.2		

Table 2. Antihypertensive therapy. ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor antagonist; CCB: calcium channel blocker; FDC: fixed-dose combination

Parameter	Numbers of antihypertensive drugs						Kinds of antihypertensive drugs				
	0 -1		2 -3		>3		ACEI/ARB	CCB	diuretic	α/β -blocker	FDC
	N	%	N	%	N	%					
ADPKD (N=41)	9	22.0	28	68.3	4	9.8	32	27	25	11	5
Non-ADPKD (N=206)	105	51.0	89	43.2	12	5.8	128	131	45	27	28

Discussion

ADPKD is the most common inherited renal disease. Two genes (PKD1 and PKD2) have been implicated in its development [7]. The disease is characterized by both renal and extra-renal involvement with cystic and non-cystic manifestations. Cardiovascular complications have emerged as a major cause of death in patients with ADPKD [3]. Hypertension occurs in 50-70% of patients [8] and manifests at a much earlier age than it does in the general population [9]. 50% of hypertensive patients with ADPKD exhibit left ventricular hypertrophy (LVH) [10]. Additionally, cardiac valvular abnormalities occur in more than 20% of patients, with defects of the aortic root, annulus, and mitral valve being the predominant irregularities [11]. As one of the most serious complications of ADPKD, AMI must be a topic of greater research focus as it is a cause of mortality in approximately 10% of the world population [12]. Previous articles have reported that patients with ADPKD have higher AMI rates than do those without ADPKD [5, 6]. Fick et al. [13] investigated the causes of mortality in ADPKD patients based on autopsy data and found that 81% of ADPKD patients had history of coronary artery disease, with moderate to severe arteriosclerosis commonly found in the aorta. To the best of our knowledge, there has not been substantial clinical research concerning AMI in ADPKD patients. We therefore compiled the clinical information available from our hospital in order to complete a retrospective single center analysis of this important medical topic.

In our study, patients with ADPKD suffered from more serious heart conditions than did non-ADPKD controls. ADPKD affected patients had a higher incidence of both STEMI (75.0% vs. 59.2%) and SCD (11.5% vs. 4.6%), indicating that the myocardium in these patients suffered more severe injury and associated necrosis. As a consequence, these individuals were subject to a poorer prognosis and a lower quality of life. Li et al. [14] have recently reported that in 2011 the median age of STEMI onset is 65 years old (55-74 years old) in China in the population at-large. The age at which AMI first appeared was earlier in those with ADPKD. This finding may be attributable to the higher prevalence and earlier onset of hypertension and LVH in ADPKD patients. A significant correlation between hypertension and LVH has been demonstrated in those with ADPKD [15]. Since LVH was a powerful independent risk factor for cardiovascular morbidity and mortality, it may also be a predictor of AMI severity in ADPKD patients. In addition, disrupted renal function and structural damage may also drive AMI in those with ADPKD. In our study, ADPKD patients had, on average, significantly poorer kidney function and a higher percentage of ESRD. Although there has been some evidence indicating that renin-angiotensin-aldosterone system (RAAS) blockade may be effective for the treatment of LVH, vascular remodeling, and renal endothelial dysfunction in ADPKD patients [16], death from AMI always remains unpredictable and difficult to prevent.

Table 3. AMI Management and prognosis. * indicates a statistically significant difference

Parameter	ADPKD (N=52)		Non-ADPKD (N=520)		χ^2	P-value
	N	%	N	%		
Culprit vessel						
Anterior descending branch	11	21.2	178	34.2	2.318	0.128
Left circumflex branch	2	3.8	48	9.2		0.413
Right coronary artery	3	5.8	72	13.8		0.177
Two branches	15	28.8	112	21.5	2.861	0.091
Three branches	11	21.2	58	11.2	6.271	0.012*
Therapy						
PCI	38	73.1	440	84.6	4.583	0.032*
CABG	4	7.7	28	5.4		0.007*
Thrombolysis	3	5.8	15	2.9		0.212
Conservative treatment	7	13.5	37	7.1	3.045	0.081
Supportive treatment						
Intra-aortic balloon pump (IABP)	5	9.6	24	4.6	2.285	0.131
Mechanical ventilation	4	7.7	18	3.5		0.130
CRRT	7	13.5	13	2.5	16.603	<0.001*
Temporary pacemaker	4	7.7	5	1.0		0.005*
Cardiac function (Killip classification)					3.845	0.279
I	32	61.5	382	73.5		
II	13	25.0	98	18.8		
III	4	7.7	21	4.0		
IV	3	5.8	19	3.7		
Mortality	7	13.5	32	6.2	3.973	0.046*
Cardiac adverse events	4	7.7	19	3.7		0.147

Among the analyzed AMI risk factors, there was a higher incidence of hypertension in ADPKD patients (78.8% vs. 39.6%), whereas rates of smoking and obesity were higher in those without ADPKD (53.8% vs. 69.0%, 26.9% vs. 33.1%, respectively). Blood pressure levels are elevated on average by 4–6 mmHg in pediatric patients with ADPKD as compared to unaffected age and gender matched controls [17]. The average age of hypertension onset is 30–34 years in these individuals, with men being more commonly affected than women [18]. Hypertension contributes not only to an increased incidence of cardiovascular mortality but also to faster ESRD progression, which is itself an independent risk factor for AMI [19]. Previous studies have reported that the most effective therapy for ADPKD patients is the control of hypertension via RAAS inhibition [20]. However, a meta-analysis by Xue et al. [21] recently demonstrated that there is little evidence to indicate that different antihypertensive treatments alter ADPKD kidney disease progression. Furthermore, only rigorous blood pressure control is likely to be associated with any measurable decline in left ventricular mass index (LVMI) [16]. There is a clear need for additional studies regarding the management of blood pressure in ADPKD patients.

Coronary artery angiography was performed on 42 ADPKD and 468 non-ADPKD patients, revealing that multiple-branch lesions, especially triple-vessel lesions, occurred more frequently in ADPKD patients (21.2% vs. 11.2%). Beyond hypertension, other metabolic abnormalities have also been reported to occur more frequently in ADPKD patients relative to a healthy control population, resulting in coronary artery disease [22]. Several articles have reported that ADPKD patients exhibit an increased incidence of post-transplant diabetes mellitus or new-onset diabetes after transplantation [23–25], indicating that an increased diabetogenic state arises due to ADPKD itself. HLA-B27 has been reported to be a potential risk factor for post-transplant diabetes mellitus in those with ADPKD [26]. ADPKD patients with diabetes mellitus have larger renal volumes, earlier age of hypertension diagnosis and an increased risk of early death as compared to those patients with ADPKD alone [27], and cardiovascular disease has been shown to be a dominant cause of death in ADPKD patients with diabetes [28]. Additionally, insulin resistance is often observed in ADPKD patients and is significantly associated with LVMI [29]. Abnormal lipid metabolism can drive a deterioration of renal function in ADPKD patients, thereby contributing to AMI progression. An inverse correlation between serum high-density lipoprotein levels and both the rate of kidney growth and the decline in glomerular filtration rate has been observed in ADPKD patients [30]. Furthermore, several clinical studies have demonstrated that oxidative modification of low-density lipoprotein in patients with early stage ADPKD can drive the deterioration of renal function and hypertension [31, 32]. Consequently, ADPKD patients exhibit more severe coronary lesions and more frequently undergo CABG. Similarly, patients with ADPKD had greater rate of CRRT (13.5% vs. 2.5%) and temporary pacemaker therapy (7.7% vs. 1.0%) after a heart attack. As a result, the rate of AMI-associated mortality was significantly higher in ADPKD patients (13.5% vs. 6.2%).

Conclusion

Cardiovascular complications are common and have emerged as a major cause of death in ADPKD patients. ADPKD patients with AMI suffer from more severe condition and difficult therapies, resulting in a poorer prognosis. Due to the prevalence of AMI in ADPKD patients, early diagnosis and clinical intervention are recommended to improve patient outcomes.

Disclosure Statement

The authors declare they have no conflict of interest.

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