AYM Wang 王依滿
JE Sanderson 孫德生
KW Chan 陳錦榮
SF Lui 雷兆輝

Epidemiology of cardiovascular problems in Chinese continuous ambulatory peritoneal dialysis patients: prevalence, severity, and risk factors

Key Messages

1. Chinese end-stage renal disease patients on continuous ambulatory peritoneal dialysis (CAPD) show a high prevalence of cardiovascular diseases (CVD) including: left ventricular hypertrophy (95%) and dilatation (92%), left ventricular systolic (35%) and diastolic dysfunction (79%), congestive heart failure (39%), coronary artery disease (23.5%), and cardiac valve calcifications (24%).
2. Apart from traditional risk factors such as age, sex, diabetes, systolic hypertension, and anaemia, there are risk factors unique to CAPD patients that increase CVD incidence and predispose to mortality and cardiovascular death. These include: loss of residual renal function, increased calcium-phosphorus product, low diastolic blood pressure, and cardiac valve calcification.
3. A more proactive approach should be adopted to prevent cardiovascular complications and improve cardiovascular health of Chinese chronic renal failure and dialysis patients. All chronic kidney disease patients, especially those with a history of heart failure, should undergo echocardiography to identify early left ventricular hypertrophy or dysfunction, or valvular calcification with a view to more aggressive intervention.

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Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong:
Department of Medicine and Therapeutics
AYM Wang, JE Sanderson, SF Lui
Department of Diagnostic and Interventional Radiology
KW Chan

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Principal applicant and corresponding author:
Dr Angela YM Wang
Department of Medicine, Queen Mary Hospital, University of Hong Kong, 102 Pokfulam Road, Hong Kong SAR, China
Tel: (852) 2855 4949
Fax: (852) 2855 5411
E-mail: aymwang@hku.hk

Introduction

In Hong Kong, there are around 3000 dialysis patients, of whom 80% are on continuous ambulatory peritoneal dialysis (CAPD) and the remaining 20% receive haemodialysis. According to the Hong Kong Renal Registry, annual mortality in dialysis patients is approximately 11%; 44% are due to cardiovascular causes. In the general population cardiovascular morbidity and mortality have declined substantially, presumably due to risk factor modification and more effective treatment of coronary artery disease, congestive heart failure, cardiac hypertrophy and dysfunction. By contrast, the proportion of cardiovascular deaths in dialysis patients has risen rapidly, accounting for 27% of deaths in 1996, 38% in 1997, and 42% in 1998, a figure very comparable to reports from the western nations. Cardiovascular disease is also associated with significant morbidity; congestive heart failure is one of the most frequent causes of hospitalisation in dialysis patients. These observations have significant cost implications for the health service. However, data on the actual prevalence of cardiovascular disease in the Chinese CAPD population are lacking.

According to the Hong Kong Renal Registry, there is also an increasing incidence of diabetes mellitus as the cause of end-stage renal disease (ESRD) in the Hong Kong dialysis population. Little is known about the epidemiology of cardiovascular disease in local diabetic CAPD patients versus the non-diabetic counterparts.

Excess cardiovascular disease in dialysis patients is attributable, in part, to certain well-recognised risk factors for cardiovascular disease in the general population (age, sex, smoking history, hypertension, hyperlipidaemia, and diabetes). However, there are risk factors unique to dialysis patients that predispose to coronary artery disease, congestive cardiac failure, cardiac hypertrophy and dysfunction. They include anaemia, hyperfibrinogenaemia, hyperhomocysteinaemia, and hyperparathyroidism. Studies are therefore needed to determine their relative importance and significance as risk factors in local CAPD patients.

Furthermore, other important risk factors known to be associated with the outcome of dialysis patients (residual renal function, dialysis adequacy, and peritoneal membrane transport) have never been examined in relation to cardiovascular disease in CAPD patients.

Aims and objectives

This study aimed to determine the actual prevalence of coronary artery disease, congestive heart failure, cardiac hypertrophy and dilatation, systolic and diastolic dysfunction, and evaluate the relative importance of different risk factors for these conditions in local CAPD patients. Such risk factors include: anaemia, hypertension, diabetes, hyperlipidaemia, inflammation, hyperhomocysteinaemia, hyperfibrinogenaemia, hyperparathyroidism, residual renal function, dialysis adequacy, and peritoneal membrane transport.

Table 1. The prevalence of coronary artery disease, congestive heart failure, left ventricular hypertrophy and dilatation, systolic and diastolic dysfunction in Chinese continuous ambulatory peritoneal dialysis patients with stratification for diabetes mellitus

	Prevalence, % (unless otherwise specified)		
	All patients (n=268)	Diabetic patients (n=82)	Non-diabetic patients (n=186)
Coronary artery disease	20	35.4	12.9*
Congestive cardiac failure	39	61	29.6*
Left ventricular hypertrophy	95	93	100
Left ventricular dilatation	92	91	93
Left ventricular mass index (g/m^2), mean±standard deviation	227±85	238±81	222±87
Left ventricular volume index (cm^3/m^2) , mean±standard deviation	66±20	67±20	66±20
Systolic dysfunction	35	47	29
Diastolic dysfunction	79	85	75†
Abnormal relaxation pattern	69	70	68
Pseudonormal pattern	2	5	0
Restrictive filling pattern	8	10	7
Cardiac valve calcification	24	36.7	19.0†

* P<0.001
† P=0.005

Table 2. Multivariate analysis showing significant risk factors associated with left ventricular hypertrophy in Chinese continuous ambulatory peritoneal dialysis patients

	Unstandardised coefficient, B	Standardised coefficient, β	95% confidence interval	P value
Presence of residual renal function	-35.17	-0.203	-55.70 to -14.63	0.001
Systolic blood pressure (mm Hg)	0.98	0.201	0.40 to 1.57	0.001
Serum albumin (g/L)	-3.23	-0.194	-5.22 to -1.23	0.002
Calcium-phosphorus product ($mmol^2/L^2$)	11.75	0.187	4.32 to 19.19	0.002
Haemoglobin (g/L)	-8.90	-0.179	-14.95 to -2.86	0.004

Methods

This was a cross-sectional survey carried out in a single regional dialysis centre in Hong Kong from June 2000 to May 2003. Altogether 268 patients (140 men and 128 women) receiving CAPD for a mean±standard deviation [SD] duration of 38±29 months were recruited. Twelve patients did not provide informed consent for the study and were therefore excluded.

All study patients underwent echocardiography to define the presence and severity of left ventricular hypertrophy and dilatation and to assess left ventricular systolic and diastolic function. Persantin sestamibi scintigraphy (MIBI scan) was performed in clinically asymptomatic patients as a screening test to rule out coronary artery disease. Cardiac catheterization was reserved for patients with symptoms suggestive of ischaemic heart disease to assess whether it was present, and if so define its severity. Fasting venous blood was collected from all study patients to measure various blood parameters relevant to cardiovascular risk, including: haemoglobin, lipid profile, fibrinogen, C-reactive protein, homocysteine, parathyroid hormone, and glycosylated haemoglobin. Twenty-four urine and dialysate samples were collected to determine weekly urea and creatinine clearance and residual renal function. Peritoneal membrane function was assessed using a standard peritoneal equilibration test.

Results

Among local Chinese CAPD patients, we found an extremely high prevalence of left ventricular hypertrophy (95%) and dilatation (92%), and associated systolic (35%) and diastolic dysfunction (79%). Our patients showed a high prevalence of congestive heart failure (39%); especially among those with underlying diabetes mellitus, coronary artery disease, cardiac hypertrophy and dilatation (with associated systolic and diastolic dysfunction) as well as among those who had greater degrees of anaemia, hypoalbuminaemia, and high peritoneal transport. In patients undergoing persantin MIBI scans or cardiac catheterization, the prevalence of coronary artery disease was 24%. The prevalence of cardiovascular disease in Chinese CAPD patients with stratification for diabetes mellitus is shown in Table 1.

Apart from systolic hypertension, anaemia, and hypoalbuminaemia (well-known risk factors for cardiac hypertrophy), for the first time we identified loss of residual renal function and high calcium-phosphorus product as important risk factors associated with left ventricular hypertrophy in our CAPD patients (Table 2). Male sex, diabetes, higher fibrinogen and lipoprotein (a), as well as lower residual renal function and diastolic blood pressures were associated with coronary artery disease in these patients (Table 3).

Our most important finding in these Chinese CAPD patients was the high prevalence (24%) of cardiac valve calcification detected by echocardiography; our study was the first to demonstrate cardiac valve calcification to be an important, novel predictor of mortality and cardiovascular death in CAPD patients (Table 4). In our patients, presence of cardiac valve calcification carries

Table 3. Final multiple logistic regression model showing significant risk factors associated with coronary artery disease in Chinese continuous ambulatory peritoneal dialysis patients

Factors	Unit increase	Odds ratio	95% confidence intervals	P value
Diabetes mellitus	-	4.38	1.91-10.05	<0.001
Fibrinogen	1 g/L	1.62	1.26-2.07	<0.001
Lipoprotein (a)	1 mmol/L	1.02	1.01-1.04	0.002
Sex	Male	2.61	1.13-6.00	0.024
Diastolic blood pressure	1 mm Hg	0.96	0.92-1.00	0.035
Residual glomerular filtration rate	1 mL/min per 1.73 m^2	0.76	0.58, 0.99	0.039

Table 4. Multivariable Cox regression analysis showing important factors associated with all-cause and cardiovascular mortality in 192 Chinese patients in receipt of continuous ambulatory peritoneal dialysis

	Unit increase	Hazard ratio (95% confidence interval)	
		All-cause mortality	Cardiovascular mortality
Age	1 year	1.05 (1.01-1.08)*	1.07 (1.02-1.12)‡
Male sex	-	3.18 (1.57-6.44)†	3.60 (1.33-9.74)*
Duration of dialysis	1 year	1.27 (1.13-1.43)†	1.27 (1.13-1.60)†
Diabetes mellitus	-	2.48 (1.22-5.05)*	-
Atherosclerotic vascular disease	-	2.90 (1.46-5.76)‡	11.70 (4.35-31.52)†
Cardiac valve calcification	-	2.50 (1.32-4.76)‡	5.39 (2.16-13.48)†
C-reactive protein	1 mg/L	1.02 (1.00-1.04)*	-

* P<0.05
† P<0.001
‡ P<0.005

similar prognostic implications as other atherosclerotic vascular complications. Furthermore, other than diabetes mellitus and increased calcium-phosphorus product, cardiac valve calcification was significantly associated with inflammation and malnutrition in these patients. Thus, those with valve calcification had greater serum concentrations of C-reactive protein (median [interquartile range]: 4.5 [0.1, 13.4] vs 0.2 [0.1, 4.4] mg/L; P<0.005) and lower serum albumin levels (mean±SD: 26.6±3.6 vs 28.7±3.3g/L; P=0.001) than those without. These data suggest cardiac valve calcification is a marker of atherosclerosis in the dialysis patients.

Discussion

The rising epidemic of cardiovascular diseases as well as the increasing incidence of cardiovascular complications including coronary artery disease, congestive cardiac failure, cardiovascular calcification, ventricular hypertrophy with associated ventricular dysfunction among our local CAPD patients have significant implications for the utilisation of hospital care by ESRD patients and hence tremendous implications for health care cost. Our data provide important evidence to support the adoption of a more proactive approach to better manage or even prevent the development and progression of cardiovascular disease in our chronic renal failure and dialysis patients.

Our study identifies some important risk factors that operate uniquely in CAPD patients to increase their risk of cardiovascular diseases and mortality. These include an increased calcium-phosphorus product, loss of residual kidney function, inflammation, a low diastolic blood pressure, which reflects the degree of arterial stiffening and cardiac valve calcification.

As most of the cardiovascular problems are already well established and advanced by the time these patients start dialysis, our study demonstrates the importance of active and regular screening for these different cardiovascular risk factors in patients with chronic kidney disease, so as to allow early institution of treatment strategies. For instance, more attention should be focused on improving calcium-phosphorus control by ensuring adequate dialysis, education on dietary phosphorus restriction, regular dietetics visits to ensure compliance with respect to phosphorus intake, and encouraging the use of non-calcium instead of calcium-containing phosphate binders. At present, very little is known about ways to better preserve residual kidney function in CAPD patients. However, we should try to avoid the use of nephrotoxic drugs in such patients if possible. Further study is needed to evaluate whether renoprotective agents such as angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists may be useful in retarding the decline of their residual renal function. Whether more biocompatible peritoneal dialysis solutions can also slow the decline of residual renal function needs evaluation. In terms of inflammation, studies are urgently needed to evaluate whether drugs with anti-inflammatory property such as statins, glitazones or the angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists may be effective in reducing coronary artery disease and cardiac valve calcification and thus lower mortality of CAPD patients.

Such a high prevalence of cardiac hypertrophy and

dilatation with associated ventricular dysfunction and valvular calcification in peritoneal dialysis patients indicates the importance of routine echocardiography in all chronic renal failure and dialysis patients. From the health service point of view, therapeutic strategies should be targeted at improving calcium-phosphorus control, better preservation of residual renal function, reducing inflammation, and decreasing the stiffening of arteries. However, further study is needed to determine whether better control of calcium-phosphorus levels, better preservation of residual renal function, use of drugs with anti-inflammatory effects that can modify the arterial properties will influence different cardiovascular complications and lower mortality in CAPD patients. At present, very little is known about treatment strategies to reduce cardiovascular morbidity and mortality in CAPD patients. This will therefore form the scope for future studies.

Our data indicate that most of the cardiovascular complications in CAPD patients are multi-factorial and need a multi-dimensional approach to manage complications. We believe the adoption of a more proactive approach to the cardiovascular management of patients with chronic kidney disease (especially dialysis patients) will be more cost-effective in the long run and have a major impact on outcomes, with the potential of reducing utilisation of health services and corresponding health care cost.

For policy makers and health service managers, our study demonstrates the need to provide more funding and support to increase awareness of cardiovascular health in patients with chronic kidney disease and improve the cardiovascular management of such patients. Other than focusing on retarding the progression of chronic renal failure, funding should be targeted at initiating early screening for the different traditional and non-traditional cardiovascular risk factors and the different cardiovascular diseases occurring in patients with chronic kidney disease and those initiating long-term dialysis. Funding should also be provided to evaluate the efficacy of treatment strategies with the potential of reducing cardiovascular morbidity and mortality in chronic kidney disease and dialysis patients.

Conclusions

We observed a very high prevalence of left ventricular hypertrophy and dilatation with associated systolic and diastolic dysfunction among the Chinese CAPD patients. For the first time, loss of residual renal function and calcium-phosphorus product were identified as important novel risk factors associated with left ventricular hypertrophy in CAPD patients. A very high prevalence of congestive heart failure was also observed among such patients; its prevalence was especially high among those with underlying diabetes, coronary artery disease, left ventricular hypertrophy and dilatation and ventricular dysfunction. It was also high in those patients with higher peritoneal transport, as well as a greater degree of anaemia and hypoalbuminaemia. Chinese CAPD patients showed a high prevalence of coronary artery disease that was associated with higher fibrinogen and lipoprotein (a) as well as lower diastolic blood pressures and loss of residual renal function. An important novel finding was the high prevalence of cardiac valve calcification, an important predictor of mortality in CAPD patients and a marker of atherosclerosis, and importantly it was related to the calcium-phosphorus product and inflammation.

Our results are directly applicable to Hong Kong as our cohort of CAPD patients was representative of the local peritoneal dialysis population. This study contributes significantly to the current knowledge and understanding about the nature, prevalence, and severity of cardiovascular diseases in Hong Kong Chinese ESRD patients. Based on our findings, there is an urgent need to improve cardiovascular management of chronic kidney disease (including dialysis) patients. Apart from providing early screening for the different traditional and non-traditional cardiovascular risk factors and complications, more therapeutic strategies should be targeted at overcoming such cardiovascular disease. Such strategies should include better preservation of residual renal function, better control of calcium-phosphorus product, lowering inflammation, and reducing the calcification burden. Studies are also needed to evaluate whether treatment strategies that reduce cardiovascular mortality in the general population are effective in lowering cardiovascular mortality in CAPD patients.

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