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

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.
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 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/m²), mean±standard deviation | 227±85          | 238±81          | 222±87          |
| Left ventricular volume index (cm³/m²), 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*           |

| 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)                             | -2.33           | -0.194          | -5.22 to -1.23  | 0.002  |
| Calcium-phosphorus product (mmol²/L²)           | 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  |
Cardiovascular problems in peritoneal dialysis patients

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 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±3.3 g/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.

| 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 m² | 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
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
cardiовascular 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.

Acknowledgements

This study was supported by the Health Services Research
Fund (HSRF #931009). We are also indebted to the late Dr
Kam-wing Chan for providing expert technical support for
the persantin sestamibi investigations and to the patients
who participated in this study.