Cardiac Disease in Dialysis Patients in a Jamaican Hospital
Echocardiographic Findings that Predict Mortality
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ABSTRACT
The aim of the study was to assess, by echocardiography, the cardiac abnormalities in a group of patients with chronic renal failure and to determine the cardiovascular predictors of mortality. The study comprised forty-five patients from the Renal Unit, University Hospital of the West Indies, Kingston, Jamaica, and was undertaken between October 1, 1998 and July 31, 2000. All echocardiography was done by a single operator. The parameters assessed were systolic dysfunction, diastolic dysfunction, ejection fraction, regional wall motion abnormalities and valvular disease. Left ventricular cavity size, septal and posterior wall thickness were measured and left ventricular mass calculated. Demographic data were obtained directly from each patient by interview. The patients were mainly of African/mixed-African origin. Their mean age was 43.2±16.0 years. The average body mass index was 23.7±6.9. Twenty-eight (60.9%) patients were male and seventeen (39.1%) female. Hypertension, chronic glomerulonephritis and diabetes mellitus were the leading causes of chronic renal failure. Blood pressure was controlled at a mean value of 145/90 mm Hg pre-dialysis and 140/90 mm Hg post-dialysis. The mean duration of renal failure was 2.8 years. Echocardiographic M-mode and two dimensional apical, four chamber view measurements indicated that mean left ventricular internal diameter (LVID) diastole was 55.7±7.9 mm (normal 38–56 mm) and LVID systole was 38.9±9.8 mm (normal 24–45 mm); the mean thickness of the chamber walls was 10.3±2.8 mm and 10.6±2.4 mm for the interventricular septum (normal 6–11 mm) and left ventricular posterior wall (normal 6–11 mm) respectively. Diastolic dysfunction was seen in 15 (34%) patients and systolic dysfunction in 12 (23%) patients who had ejection fractions less than 50%. The mean left ventricular ejection fraction was 56.3%±16% (normal 65–85%), mean stroke volume was 82.9±27.2 mls (normal 51–96 ml). After 21 months enrolment in the study, Kaplan Meier analysis revealed a two-year mortality of 28.3%. Cox regression analysis indicated that a history of smoking current or past, low haemoglobin level, high aorta flow velocities, severity of mitral regurgitation and a negative association with serum creatinine were independent predictors of mortality. The correction of anaemia and control of other factors that impact negatively on cardiac function in dialysis patients is vital to enhance survival.

La enfermedad cardíaca en los pacientes de diálisis en un hospital de Jamaica: hallazgos ecocardiográficos que predicen la mortalidad
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RESUMEN
El objetivo del estudio fue evaluar, mediante ecocardiografía, las anormalidades cardiacas en un grupo de pacientes con fallo renal crónico, y determinar los predictores cardiovasculares de mortalidad. El estudio comprendió cuarenta y cinco pacientes de la Unidad Renal del Hospital Universitario de West Indies, Kingston, Jamaica, y se emprendió entre el 1ero de octubre de 1998 y el 31 de julio de 2000. Toda la ecocardiografía se realizó por un solo operador. Los parámetros evaluados fueron la disfunción sistólica, la disfunción diastólica, la fracción de eyecación, las anormalidades del movimiento de la pared regional, y la enfermedad valvular. Se midió el tamaño de la cavidad ventricular izquierda, el grosor de la pared posterior y septal, y se calculó la masa ventricular izquierda. Los datos demográficos se obtuvieron directamente de cada paciente mediante entrevista. Los pacientes eran principalmente de origen africano o mestizo-africano. Su edad mediana fue de 43.2±16.0 años. El índice de masa...
INTRODUCTION

Patients with end stage renal failure are living longer because of the availability of long term renal replacement therapy: dialysis and transplantation. It is reported that at the commencement of dialysis, 50 – 80% of patients already have left ventricular hypertrophy and 10% have coronary artery disease (1, 2). Cardiac disease has a major impact on morbidity and mortality in dialysis patients. Risk of death for dialysis patients is 3.5 times that of age-match individuals of the general population (1, 3).

Disorders of coronary perfusion caused either by coronary artery disease or non-atherosclerotic disease and disorders of the left ventricular myocardium leading to systolic and diastolic dysfunction often cause frequent morbidity events including heart failure, ischaemic syndromes, arrhythmias, dyskiensis and decreased longevity (4–7). Among dialysis patients, there is a high prevalence of the traditional cardiovascular risk factors such as hypertension, diabetes mellitus, hyperlipidaemia and physical inactivity (4). In addition, haemodynamic and metabolic factors related to chronic uraemia may be atherogenic and cardiomyopathic (8).

Anaemia, a feature of end stage renal disease, results in functional alterations aimed at maintaining optimal oxygen delivery to tissues and organs. The haemodynamic changes include increased cardiac output as a result of increased stroke volume and heart rate and the net result is left ventricular hypertrophy (9). Correction of anaemia by erythropoietin causes partial regression of left ventricular size.

Arteriovenous shunts for haemodialysis access also cause cardiomegal and left ventricular dilatation and therefore can contribute to cardiac morbidity.

In this study, the authors investigated, by echocardiography, the cardiac abnormalities in a group of patients with chronic renal failure and determined the cardiovascular predictors of mortality.

SUBJECTS AND METHODS

The study comprised all forty-five patients, from the Renal Unit, University Hospital of the West Indies, Kingston, Jamaica and was conducted between October 1, 1998, and July 31, 2000. Patients were revisited at least 21 months after initial enrolment in the study. All study patients provided informed consent.

Demographic data such as age, gender and occupation were obtained directly from the patients by interview. Values of systolic and diastolic blood pressure were measured during the course of their treatment, pre- and post-dialysis and at clinical reviews which were at least once monthly. Patients’ files were used to obtain clinical data on the underlying cause of chronic renal failure (CRF) and the type of treatment received, (haemodialysis, peritoneal dialysis, medical therapy ie drugs and diet without dialysis). Laboratory values such as haemoglobin, serum albumin, blood urea and creatinine levels were also documented. Echocardiography was performed by a single operator (AC). The occurrence of left ventricular diastolic dysfunction as evidenced by reduced compliance and a reversal of the E:A ratio, as well as that of systolic dysfunction as evidenced by a reduced left ventricular ejection fraction (EF) was noted. Regional wall motion abnormalities were categorized as being either hypokinetic, dyskinetic or akinetic. Valvular diseases (aortic stenosis (AS), aortic regurgitation (AR), mitral regurgitation (MR) and tricuspid regurgitation (TR) were assessed and graded as trivial, mild, moderate or severe. Flow velocities across the cardiac valves were measured and the pulmonary artery systolic pressure calculated.
Left ventricular cavity size, septal and posterior wall thickness were measured and their values used to calculate left ventricular mass utilizing the following formula: 
\[
V = \pi (b + t)^2 \left( \frac{2}{3} a + t \right) \left[ \frac{2}{3} (a + t)^2 - b^2 \right] - \frac{2}{3} a + t - \frac{2}{3} a^2
\]

where \(a\), \(b\), and \(d\) are the dimensions shown in the Figure below. Left ventricular (LV) mass was derived by multiplying the volume by myocardial density (1.05 g/ml). Thus mass = \(V \times 1.05\). \(V\) = LV cavity size; \(t\) = mean left ventricular wall thickness; \(a\) = length of semimajor axis of the LV cavity; \(b\) = radius of the semiminor axis of the LV cavity and \(d\) = length of the truncated semimajor axis of the LV cavity (10). Data were analyzed using SPSS and Microsoft Excel software. Survival was described using Kaplan Meier analysis.

![Diagrammatic representation of the left ventricle as a truncated ellipsoid.](image)

**RESULTS**

The demographic characteristics of the patient population, which was mainly of African descent, are summarized in Table 1. The mean age of the patients enrolled in the study was 43.2 ± 16.0 years. Their average body mass index (BMI) was 23.7 ± 6.9. Twenty-eight (60.9%) patients were male. The most common underlying cause of CRF in the study population was essential hypertension (33.3%), followed by chronic glomerulonephritis (30.6%). Other important causes included diabetes mellitus (16.7%), systemic lupus erythematosus (8.3%) and sickle cell disease (2.8%). Although many patients had family histories of diabetes mellitus (4.3%) and hypertension (30.4%), none of the patients had a family history of renal disease.

Clinical results showed that the patients’ blood pressure (BP) readings were relatively well controlled, with the mean pre-dialysis, systolic and diastolic blood pressure being 145 and 90 mm Hg respectively and the mean post dialysis systolic and diastolic blood pressure being 140 and 90 mmHg respectively. Mean laboratory values of note included, predialysis serum urea (37.3 ± 7.8 mmol/L) serum creatinine (1526 ± 512.7 µmol/L) and urea reduction ratio of 66. Patients were generally anaemic, with a mean haemoglobin of 7.5 g/dL; 13.6% of them used recombinant erythropoietin.

The mean duration of CRF on haemodialysis was 2.8 years with patients being admitted to the hospital at least once per year. The most popular type of access was the forearm arterio-venous fistula, used in 83% of patients. Other type of access was the subclavian catheter in 17%. Three of the major risk factors for coronary artery disease, hypertension, diabetes mellitus and smoking were present in 33.3%, 16.7% and 31.8% of patients respectively.

Echocardiographic, M-mode and two dimensional, apical, four-chamber view measurements showed that the majority of hearts were within the normal range, with the mean left ventricular internal diameter (LVID) diastole being 55.7 ± 7.9 mm (normal, 38–56 mm) and the LVID systole 38.9 ± 9.8 mm (normal 25–45 mm), the mean thickness of the chamber walls was 10.3 ± 2.8 mm and 10.6 ± 2.4 mm for the interventricular septum and the left ventricular posterior wall (LVPW) respectively. Evidence of diastolic dysfunction was seen in 15 (34%) patients, while systolic dysfunction was evident in 12 (23%) patients who had ejection fractions less than 50%, the mean LVEF was 56.3% ± 16% (normal >50). The average stroke volume was 82.9 ± 27.2 ml (normal 51–96 ml). At 21 to 26 months after initial enrolment in the study, patients were clinically reviewed and mortality ascertained. Kaplan Meier analysis revealed the two-year mortality as 28.3% with 80% dying of cardiovascular related diseases. Multiple regression analysis showed that ejection fraction, left ventricular mass, left ventricular thickness (interventricular septum and posterior wall) LVID (diastole) and LVID (systole) and haemoglobin were significantly associated with mortality. Utilizing Cox regression analysis, the independent predictors of mortality were history of smoking whether current or past, low haemoglobin levels, high aortic flow velocities, severity of mitral regurgitation and a negative association with serum creatinine i.e low creatinine was associated with increased mortality \((p < 0.001)\).

**DISCUSSION**

There was a mortality of 28.3% over two years in the study patients. Eighty per cent were related to ischaemic heart disease. There is a tremendous risk burden for cardiovascular disease in patients with CRF/End Stage Renal Disease (ESRD) and this is related directly to the degree of renal dysfunction (11). The underlying cause of the chronic renal failure adds its own risk and in dialysis patients the incidence of hypertension and diabetes mellitus as primary cause of the ESRD is increasing more rapidly than other diagnoses (12).

In the present study, about sixty-four per cent of patients had hypertension and/or diabetes mellitus as primary cause of CRF/ESRD. Three of the major risk factors for coronary artery disease, hypertension, diabetes mellitus and kidney disease, were present cumulatively in 81.8% of patients and smoking was an independent predictor of mortality. These are major risk factors which need to be modified by lifestyle changes in the general population.

Twenty-three per cent of patients had ejection fraction less than 50% and diastolic and systolic dysfunction was present in 34% and 23% of these respectively. In patients with ESRD without other cause for cardiac disease, the indices for systolic dysfunction may be normal but are particularly increased in those patients with hypertrophic hyper-
kinetic disease (4, 13, 14). On the other hand diastolic filling is frequently altered as a result of intramyocardial fibrosis and delayed relaxation. Concentric left ventricular hypertrophy or left ventricular dilatation may exhibit diastolic dysfunction which predisposes to congestive cardiac failure (15, 16). Systolic dysfunction is frequently observed in patients with cardiac disease pre-existing before ESRD or in patients with sustained and marked haemodynamic overload. It is believed that reduced cardiac contractility is the result of overload cardiomyopathy. While systolic dysfunction might be associated with the presence of ischaemic heart disease, it is also a manifestation of uraemia per se. In vitro studies indicate that uraemic serum reduces inotropy of cardiac heart cells in a concentration – dependent manner (4).

Grossman and Messerli (17, 18) concluded that patients with diabetes mellitus and hypertension have a higher incidence of coronary heart disease and that this was more pronounced in patients with either disease alone. They also found that diabetic patients have more systolic and diastolic dysfunction.

Patients with chronic renal failure must be considered in the highest risk group for the development of cardiovascular disease. While physicians need to be aggressive in the treatment of the traditional risk factors for cardiovascular disease, satisfactory control of uraemia is also vital.

Anaemia is associated with progressive cardiac enlargement (19). There is an independent association between falling haemoglobin and progressive left ventricular dilatation (9). In the present study, low haemoglobin level was an independent predictor of mortality. Anaemia may predict new and recurrent cardiac failure in patients on dialysis therapy and there is also a clear survival advantage for a haematocrit of 33–36% (20).

The majority of patients in this study had arteriovenous shunts (AV) which can cause left ventricular dilatation and cardiac failure especially in dialysis patients with underlying cardiac disease.

In summary, there was a 28.3 % mortality in this study with the majority dying of cardiovascular related disease and history of smoking, low haemoglobin, severe valvular disease and increased aortic flow velocities were independent predictors of mortality.

ACKNOWLEDGEMENTS
We wish to thank the Dialysis Nurses at the University Hospital of the West Indies, Kingston, Jamaica and the Staff of the Cardiac Unit, University Hospital of the West Indies, Jamaica. Gratitude to Dr Clifford Thomas, Dawn Williams, Donald Simeon and Ivan Vickers for valuable advice.

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