The Pattern of Aggravated Renal Dysfunction in Patients with Advanced Heart Failure

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ABSRACT

Advanced Heart Failure (AHF) is associated with significant mortality which could be affected by renal dysfunction The objective of the study was to describe the pattern of renal dysfunction in patients with AHF and I investigate whether the dysfunction is a predictor of mortality. Fifty-four patients with AHF who underwent intravenous diuretic therapy were studied. Aetiology of AHF was determined clinically and by echocardiography. Baseline renal functions were determined before and after treatment. The glomerular filtration rate(GFR) was determined using the Cockcroft-Gault equation. Correlation was determined using Pearson's correlation coefficient and risk of death estimated using Cox regression analysis. We found out that aggravated renal dysfunction(ARD) occurred in 18(33%) of all the patients and was associated with increased mortality (RR 3.23 $p<0.05$). The baseline GFR of the patients was 68.5±25.5 ml/min and also correlated with mortality ($r = -.486$, $p< 0.05$). Patients with GFR <40ml/min had more than 2 times risk of death than those with GFR > 40ml/min (RR 2.65, $p<0.05$).The other parameters that correlated with mortality included baseline creatinine($r = .671$, $p=0.002$) and presence of atrial fibrillation ($r = .532$, $p = 0.045$). NYHA classification did not correlate with mortality in this study. In conclusion, ARD is common in our patients with AHF and it is associated with increased mortality as some other renal parameters.

KEY WORDS: *Advanced heart failure, Aggravated renal dysfunction, Mortality, Glomerular filtration rate.*

INTRODUCTION

Advanced Heart Failure (AHF) which can be defined as symptoms limiting daily life activities (NYHA class III/IV) despite previous therapy with angiotensin converting enzyme inhibitors (ACEI), diuretics, digoxin and more recently B-aderenergic receptor blockers, when tolerated [1] accounts for over 25% of all heart failures [2]. Heart failure patients with left ventricular ejection fraction (LVEF) less than 25% are also said to have AHF, if they conformed to previous therapy as stated above [2], or corresponds to stage D of the new American College of Cardiology/ American Heart Association (ACC/AHA) classification of chronic heart failure (CHF).[3].

It is a known fact for over a decade that the cardiovascular risk is increased in patients who are on renal replacement therapy [4]. Accelerated cardiovascular disease is now recognized as the leading cause of death in patients with progressive renal disease [5]. Minor renal dysfunction as reflected by an increase in serum creatinine or estimated glomerular filtration rate (GFR) has major impact on cardiovascular risk [6]. Studies have shown that patients exhibited a 1% increase in mortality for each 1ml/min decrease in creatinine clearance [7] and that in a patient with slight reduction in renal function the cardiovascular risk is in the magnitude of that conferred by diabetes mellitus[8].

Aggravated renal dysfunction (ARD), defined as at least 25% increase in serum creatinine or values equal or greater than 2mg/dl has been reported to be common in patients with AHF undergoing intensive treatment [9].

GFR which is the standard indicator of renal function has been shown to be a stronger predictor of mortality than LVEF and NYHA classification in patients with AHF [10]. Furthermore the activation

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of the renin angiotensin aldosterone system that occurs when renal perfusion pressure is reduced in heart failure might not be just a primary response to preserve cardiovascular homeostasis but a renal compensatory reaction to preserve renal function [11]. Therefore renal function and GFR can be used as a pointer of cardiovascular status and prognostic indicator [9], since the activity includes both cardiovascular and haemodynamic properties [10].

The aim of this study therefore was to describe the pattern of aggravated renal dysfunction in our patients with advanced heart failure and also to investigate renal function as a predictor of mortality in this cohort of patients.

PATIENTS AND METHODS

We studied 54 patients admitted to our medical wards in advanced heart failure who had intravenous diuretic therapy with at least a weight loss of 2kg [9] during admission. Weights were measured on admission and on discharge or death. Baseline biochemical indices were also measured. The serum creatinine was measured on admission and a 25% increase or a serum creatinine of at least 2mg/dl after treatment was adjudged as ARD. The GFR was calculated using the Cockcroft-Gault equation [12], which has been validated worldwide [11] and also in Nigerian patients [13] as representative of the actual determined GFR. Patients who were primarily admitted for chronic renal disease who later developed heart failure were excluded from the study as were patients whose admission serum creatinine was at least2mg/dl. Diabetic patients with microalbuminuria were also excluded in order not to include patients with diabetic nephropathy. *The inclusion criteria included all patients with AHF as defined irrespective of the aetiology of the AHF. Echocardiography was performed using ALOKA SSD 1700 machine. Measurements were made according to the recommendations of the American Society of Echocardiography. The Ejection Fractions were calculated automatically by the machine using the TEICHOZ calculation formula.*

The aetiology of the heart failure was deemed to be hypertension, if the patient was a known hypertensive patient or had clinical features of hypertensive heart disease as demonstrated by heaving displaced apex beat,atrial S4 and loud A2. The echocardiogram also showed concentric hypertrophy with normal valves and/or diastolic dysfunction. Dilated cardiomyopathy was diagnosed by clinical evidence of normal blood pressure, displaced and diffused apex beat and some had evidence of mitral and/or tricuspid regurgitation. They were confirmed on echocardiogram by the finding of globally dilated chambers with thin walls and systolic dysfunction. Some had evidence of mild regurgitation. The patients with rheumatic heart disease had left ventricular hypertrophy and left atrial enlargement on echocardiography. The mitral valves were thick and fibrotic with grade III regurgitation. Ischaemic heart disease was diagnosed in patients who had classical history of myocardial infarction confirmed on ECG.Other patients were admitted primarily as a complication of HIV/AIDS.

STATISTICAL ANALYSIS

All the data were entered into SPSS 11.0 data editor. All data were reported as mean $\pm$ SD and frequencies expressed as percent. Continuous variables were compared by the Student's t-test. Pearson's coefficient was used to test correlation between relevant variables.Cox regression was also used to investigate the influence of baseline renal function on survival. Level of significance was put at $p< 0.05$.

RESULTS

Fifty-four patients satisfied the entry criteria for the study. The mean age was 51.4$\pm$15.6 years made up of 25(46.3%) males. The basic characteristic data were as shown in Table1. Thirty-eight (70.3%) of the patients were in NYHA functional class III while the rest were in class IV. Forty-two(77.8%) of the patients had echocardiography to confirm clinical aetiology and also to measure the left ventricular ejection fractions (LVEF).

The mean LVEF was 22.3$\pm$ 5.1%. Hypertension was the commonest clinical aetiology of the AHF occurring in 42.6% followed by dilated cardiomyopathy in 27.8%. There were 2 patients each with Ischaemic Heart Disease and HIV cardiomyopathy. Eleven patients (20.4%) were in atrial fibrillation. Mortality rate was 31.5% with an average hospital stay of 17.9$\pm$9.2 days.

The mean GFR of all the patients was 68.5$\pm$25.5 ml/min. When the patients in the total cohort with GFR< 40ml/min were compared with those above 40ml/min, there was more than two times risk of death in those below 40ml/min (RR 2.65, p =0.02).

Table 1: Baseline characteristics of all the patients

Variables n (%)	54(100)
Age (years)	51.4±15.6
Sex(Male)	25(46.3%)
NYHA class	
III	38(70.3)
IV	16(29.7)
Cause of AHF	
Hypertension	23(42.6)
Dilated cardiomyopathy	15(27.8)
Cor Pulmonale	7(12.9)
Rheumatic Heart Disease	5(9.3)
Ischaemic Heart Disease	2(3.7)
HIV cardiomyopathy	2(3.7)
Serum urea(mg/dl)	46.8±23.2
Serum creatinine(mg/dl)	1.22±0.42
Serum sodium (mEq/L)	134.2±4.6
GFR (ml/min)	68.5±25.5
Atrial fibrillation	11(20.4)
LVEF	22.3±5.1
Admission(days)	17.9±9.2
Mortality	17(31.5)

Eighteen (33.0%) patients had ARD (Table 2). The mean age of the those without ARD was not statistically different from those with ARD. There was also no difference in the number of patients in each NYHA class. The baseline creatinine (0.99±0.26 vs 1.67 ±0.29) and GFR (78.9±25.0 vs 47.6±7.7) were significantly different when the 2 groups were compared . Atrial fibrillation was also significantly more common in those with ARD. The 72.2% mortality rate in those with ARD was significantly more than those without ARD. There was at least three times risk of death in those with ARD (RR 3.23, $p<0.05$). Out of the total mortality of 17 deaths, 13(76.4%) occurred in patients with ARD. The variables that correlated with mortality include baseline creatinine ($r=.671, p=0.002$), baseline GFR ($r=-.486$, $p=0.041$) and presence of AF ($r=.532$, $p=0.045$).

DISCUSSION

This study revealed that ARD is common in our patients with AHF. The prevalence of 33% is comparable to the 21% found in the work by Weinfeld *et al* in a Caucasian community [9] but unlike in that study there was no difference in the mean age of those with or without ARD. Our patients were younger. It is generally known that CHF occurs in older age group in Caucasians than Blacks [14] and also our patients are known to present in hospital late

TABLE 2: Comparison between patients with Ard and those without Ard

	ARD Absent	ARD Present	P Value
Variable n(%)	36(67)	18(33)	0.023
Age(years)	55.0±15.6	44.3±13.9	0.755
Sex(male)	16(52.0)	9(50.0)	0.807
NYHA class			
Weight (kg)	71.3±19.2	64.5±10.6	0.435
Serum urea(mg/dl)	42.0±24.3	56.3±19.4	0.228
Serum creatinine(mg/dl)	0.99±0.26	1.67±0.29	0.001
Serum sodium(meq/L)	135.2±4.6	132.3±4.3	0.224
GFR(ml/min)	78.9±25.0	47.6±7.7	0.009
Admission(days)	19.8±10.1	14.2±5.9	0.233
Mortality	4(11.1)	13(72.2)	0.007

The variables, urea, creatinine, sodium and GFR were baseline parameters)

also our patients are known to present in hospital late [15]. This might account for the lower age group observed in patients with ARD in this study. This could also explain the higher mortality rate we had in the total cohort and in those with ARD.

Biochemical markers including serum sodium, urea and creatinine have been shown to have prognostic values in patients with CHF [10, 16, 17]. Only creatinine had correlation with mortality in this study. Presence of ARD including reductions in GFR correlated with increased mortality in this study confirming the notion that patients with renal dysfunction usually have a poorer prognosis when compared with those with relatively preserved renal function [10]. In patients with severe CHF as one finds in AHF, GFR is dependent more on afferent arteriolar flow and the stimulation of haemodynamic and hormonal pathways. It has also been observed that in asymptomatic left ventricular dysfunction renal haemodynamics might have been already impaired even when the GFR may still be normal [10,18]. This requires that the renal status in patients with AHF need closer monitoring even when the biochemical indices seem normal as it has been shown here again that development of ARD increases the risk of death in these patients. The lower the GFR, the greater the risk of death as shown in this study. Patients with GFR< 40ml/min had more than 2 times risk of dying. This is similar to the observation of Hillege et al who found about 3 times the risk of death in patients with GFR< 44ml/min [10].

Other factor that had prognostic implication in this study is AF which occurred more frequently in patients with ARD as in the work of Weinfeld [9]. Atrial fibrillation, by loss of atrial contribution to end diastolic volume and decreased diastolic filling time makes heart failure worse and with the increased sympathetic activity in patients with renal dysfunction, it is likely to lead to increased mortality in ARD patients.

Unlike the study of Hillege et al where NYHA correlated, albeit weakly, with mortality, this was not the case in this study. NYHA functional class has been noted to be a weaker prognostic indicator than the renal indices of serum creatinine and GFR [6, 10].

Hypertension was the commonest cause of AHF in this study unlike the experience in Hillege et al where it came a distant third to Ischaemic Heart Disease and cardiomyopathy. Hypertension is the commonest non-communicable disease in Nigeria [19] and noted to be the commonest cause of CHF in our environment [20, 21]. It could be a cause or effect of chronic kidney disease. In any case it accelerates deterioration of renal function in patients where it occurs primarily as a causative factor of CHF. Its high prevalence in this study may have added to the high incidence of ARD and the more grievous outcome in patients with ARD. This association was not particularly investigated in this study; though Hillege et al found systolic blood pressure to be of a weak prognostic value for mortality.

The limitation of this study includes the fact that patients with AHF were of various aetiologies and some of the changes might have been due to the pre- morbid state. However we tried to correct for this by excluding from the study, patients with significant renal damage at the onset of study.

The conclusion of this study is that ARD is common in our patients with AHF and it is associated with increased mortality. The variables that correlate with mortality were baseline serum creatinine, decreased GFR and presence of AF.Unlike in some other studies the NYHA functional class and serum sodium did not correlate with mortality. We recommend that determination of renal function can help in identifying CHF patients at risk. This is of utmost importance in our environment where patients present late to hospital.

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