Renal Dysfunction in Heart Failure Is Due to Congestion but Not Low Output

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ABSTRACT

Background: Renal dysfunction in heart failure is thought to be due to poor perfusion of the kidney.

Hypothesis: We tested the hypothesis that passive congestion is more important than poor perfusion.

Methods: We retrospectively studied the data on 178 patients who underwent right heart catheterization for evaluation of heart failure and had serum creatinine (Cr) measured on the same day.

Results: Serum Cr and glomerular filtration rate (GFR) correlated with central venous pressure ($r = 0.22$, $P = 0.001$ and $r = -0.55$, $P < 0.0001$, respectively) and renal perfusion pressure ($r = 0.21$, $P = 0.001$ and $r = 0.27$, $P = 0.015$, respectively). Neither correlated with cardiac index or left ventricular ejection fraction. Serum Cr was significantly higher and GFR was significantly lower in the upper tertile of central venous pressure, pulmonary capillary wedge pressure as well as in the lower tertile of renal perfusion pressure.

Conclusions: Renal dysfunction in heart failure is determined more by passive congestion than by low perfusion.

Introduction

Renal insufficiency is highly prevalent in heart failure (HF). It is associated with poor outcomes. In patients hospitalized with acutely decompensated HF, 60% have moderate or severe renal insufficiency. Mortality rates, length of hospitalization, and the need for mechanical ventilation, intensive care, and cardiopulmonary resuscitation increase with the degree of baseline renal dysfunction in this patient population.¹

In the setting of HF, renal dysfunction is usually considered as secondary to renal hypoperfusion due to decreased cardiac output. This has been challenged by the recent published results of the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE). Nohria et al² found that baseline serum creatinine (Cr) and estimated glomerular filtration rate (GFR) in patients hospitalized with advanced HF correlated weakly with right atrial pressure, but not with other hemodynamic parameters including the cardiac index (CI).

In this retrospective study, we have investigated the possible correlation between renal dysfunction and invasive and noninvasive hemodynamic parameters. In particular, we tested the hypothesis that venous congestion was more strongly associated with renal dysfunction than with low cardiac output.

Methods

We retrospectively examined data obtained for 178 sequential patients who underwent right heart catheterization for

HF evaluation. Serum Cr levels were measured for all patients on the same day as, but prior to, the catheterization procedure. Patients on hemodialysis were excluded. We analyzed the correlation of serum Cr and calculated GFR with hemodynamic measurements including central venous pressure (CVP), right ventricular pressure, pulmonary artery systolic and diastolic pressures, pulmonary capillary wedge pressure (PCWP), CI, and cardiac output. GFR was estimated using the abbreviated Modification of Diet in Renal Disease formula. Renal perfusion pressure was calculated as the difference between mean arterial pressure and CVP.

Left ventricular ejection fraction (LVEF), tricuspid regurgitant velocity, and parameters of diastolic function were measured in patients who had an echocardiogram performed within 6 months prior to the right heart catheterization. The Pearson correlation coefficient (r) was calculated.

Mean serum Cr and GFR in the upper, middle, and lower tertiles of CVP, renal perfusion pressure, PCWP, CI, and LVEF were compared using the Student t test. A P value <0.05 was considered statistically significant.

Results

Patients included in this study represented consecutive hospital admissions for HF exacerbation who underwent right heart catheterization as part of HF evaluation for clinical indications. There were 178 patients, age range 19 to 81 years, mean 66 ± 12.1 (standard deviation), 58% men.

Etiology of HF was considered ischemic in 64% and nonischemic in 46%. LVEF $<55\%$ was present in 71%

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of patients. Medications most commonly included loop diuretics (92%), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (69%), and β -blockers (61%).

Baseline hemodynamic variables (mean $\pm$ standard deviation) were as follows: CVP 10.6 ± 6.5 , PCWP 18.7 ± 9.3 , pulmonary artery systolic and diastolic pressure 41.6 ± 15.6 and 19.8 ± 10.9 mm Hg, cardiac output and CI 3.9 ± 2.8 L/min and 2.3 ± 0.73 L/min/m², respectively. Mean EF was $39.5 \pm 12.1\%$ and serum Cr 1.15 ± 0.7 mg/dL. Values of serum Cr at the baseline (before the procedure but during the same admission) were available in 83% of patients, and were all within 0.3 mg/dL difference.

Serum Cr correlated with invasively measured CVP ($r = 0.22$, $P = 0.001$), PCWP ($r = 0.2$, $P = 0.003$), pulmonary artery systolic and diastolic pressure ($r = 0.29$, $P = 0.00012$ and $r = 0.18$, $P = 0.007$, respectively), and renal perfusion pressure ($r = 0.21$, $P = 0.001$), but not with CI or cardiac output. GFR correlated with CVP ($r = -0.55$, $P < 0.0001$) and with renal perfusion pressure ($r = 0.27$, $P = 0.015$). Similar to Cr, GFR did not correlate with either CI or cardiac output.

Out of the 178 patients, 156 had echocardiograms performed within 6 months of the procedure. Serum Cr correlated with velocity of tricuspid regurgitation ($r = 0.19$, $P = 0.03$), but not with LVEF. GFR also correlated with peak tricuspid regurgitation velocity ($r = -0.26$, $P = 0.01$), as well as end diastolic pulmonary regurgitation velocity ($r = -0.57$, $P < 0.0001$), but not with LVEF.

The values of serum Cr and GFR for the tertiles of CVP, PCWP, renal perfusion pressure, CI, and LVEF (by echocardiogram) are shown in Table 1 and Figures 1–3. Serum Cr was significantly higher and GFR was significantly lower in the upper tertile of CVP and PCWP, as well as in the lower tertile of renal perfusion pressure. There were no significant differences in GFR across the tertiles of CI or LVEF. Surprisingly, Cr was significantly higher in the upper tertile of CI than in the lower and medium tertiles (Table 1).

Discussion

In this study, we have found that renal dysfunction (as defined by serum Cr level/GFR) is related to high filling pressures (CVP, PCWP) and to lower renal perfusion pressure. However, renal dysfunction appears to occur independently from systolic function and forward flow (ejection fraction [EF] and CI, respectively) in patients with clinically diagnosed HF. Our results add to some data that implicate “kidney congestion,” rather than poor forward flow, as the principal etiologic factor for renal dysfunction in patients with HF.

Other authors have recently reported similar findings. In the ESCAPE trial, the strategy of pulmonary artery catheter-guided therapy with treatment based on clinical assessment alone was compared in patients admitted with advanced HF. Nohria et al² reported a weak correlation between serum Cr/GFR and right atrial pressure ($r = 0.165$, $P = 0.03$), but found no correlation between serum Cr/GFR and PCWP, CI, or systemic vascular resistance. The authors concluded that poor forward flow may contribute to,

Table 1. Serum Creatinine and Estimated GFR for the Tertiles of CVP, PCWP, and Cardiac Index

	Serum Cr, mg/dL, mean $\pm$ SD	GFR, mL/min, mean $\pm$ SD
CVP lower tertile	1.1 ± 0.5	96.3 ± 24.7
CVP medium tertile	1.1 ± 0.4	66.6 ± 20.6^a
CVP upper tertile	1.3 ± 1.0	54.6 ± 29.6^b
PCWP lower tertile	1.0 ± 0.3	79.9 ± 18.2
PCWP medium tertile	1.0 ± 0.4	74.8 ± 31.7
PCWP upper tertile	1.4 ± 1.0^a	59.3 ± 30.0^c
RPP lower tertile	1.3 ± 1.0	52.8 ± 28.6
RPP medium tertile	1.1 ± 0.4	73.7 ± 29.2^c
RPP upper tertile	1.1 ± 0.5	81.5 ± 24.2^b
CI lower tertile	1.1 ± 0.4	77.2 ± 23.0
CI medium tertile	1.0 ± 0.4	61.5 ± 32.4
CI upper tertile	1.4 ± 1.0^c	71.0 ± 32.4
EF lower tertile	1.1 ± 0.4	69.4 ± 30.3
EF medium tertile	1.1 ± 0.4	66.8 ± 24.5
EF upper tertile	1.4 ± 0.9	74.4 ± 36.0

Abbreviations: CI, cardiac index; Cr, creatinine; CVP, central venous pressure; EF, ejection fraction; GFR, glomerular filtration rate; PCWP, pulmonary capillary wedge pressure; RPP, renal perfusion pressure; SD, standard deviation.

^a $P < 0.01$.

^b $P < 0.001$.

^c $P < 0.05$.

Figure 1. Glomerular filtration rate vs central venous pressure.

Abbreviations: CVP, central venous pressure; GFR, glomerular filtration rate.

but is not the primary cause of, renal dysfunction in patients with advanced HF.

Most recently, Mullens et al³ evaluated the data from 145 consecutive patients who were admitted with

Figure 2. Glomerular filtration rate vs pulmonary capillary wedge pressure. Abbreviations: GFR, glomerular filtration rate; PCWP, pulmonary capillary wedge pressure.

Figure 3. Glomerular filtration rate vs ejection fraction. Abbreviations: GFR, glomerular filtration rate; EF, ejection fraction.

decompensated HF and treated with intensive medical therapy guided by pulmonary artery catheter. The purpose of their study was to determine whether venous congestion or impaired cardiac output was primarily associated with the development of worsening renal function in patients with advanced decompensated HF. They found that both increased CVP upon admission, and lack of sufficient reduction of CVP to values <8 mm Hg were associated with a greater incidence of worsening renal function during hospitalization. Impaired CI upon admission or improvement in CI during hospitalization were determined to have little impact on the incidence of worsening renal function. Estimated renal perfusion pressure upon admission was similar in patients who did and did not develop worsening renal function.³ Our study was carried out on a different patient population, with less-advanced HF. Very few of our patients required Swan-Ganz catheter for hemodynamic management and the majority received right heart catheterization as part of the routine HF workup.

Association of CVP was also reported by Damman et al.⁴ They found that although both CVP and CI were associated with GFR in a univariate analysis ($r = -0.259$ and $r = 0.123$, respectively), only CVP remained associated with renal function in multivariate analysis.

Further studies should be focused on interventions resulting in decreased cardiac filling pressures and observations of changes in renal function. If the hypothesis of venous congestion as a leading factor of kidney dysfunction in cardiorenal syndrome is correct, in volume-overloaded patients serum Cr and GFR should be improving in response to any manipulations causing decrease of intracardiac pressures. Such interventions can include loop diuretics, intravenous nitroglycerine, or ultrafiltration. Dobutamine or milrinone would not be appropriate interventions because they also increase cardiac contractility, and therefore provide not only decongestion but also increased cardiac output.

The uncoupling of renal function and LVEF has been reported by several previous studies.^{1,5–7} Heywood et al retrospectively analyzed the data from 118 465 hospitalizations for HF and found no association between renal dysfunction and left ventricular systolic dysfunction. The average EF was similar for all kidney function stages except stage V, where it was 40.3%.¹ Data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program⁸ also failed to identify an association between EF and GFR, despite a greater proportion of patients with low GFR having worse New York Heart Association class.

Study Limitations

This study is limited by its retrospective character. The echocardiograms were obtained at different times, sometimes several months apart from the cardiac catheterization and the renal function assessment. We also assumed that serum Cr obtained on the day of the procedure reflected the steady state of renal function, although in a minority of patients the values prior to the day of the procedure were unavailable.

Conclusion

In the present study, we found no association between renal dysfunction and decreased systolic function or CI. We did observe an association of renal dysfunction with higher filling pressures. In contrast to Mullens' report, we identified a strong correlation between renal perfusion pressure and renal function. This apparent incongruity may be a result of our data having been obtained from a single time point and the fact that we did not follow hemodynamic parameters or renal function during the period of hospitalization. Therefore, our results do not contradict those of Mullens. The mechanisms that cause renal dysfunction in HF are not well understood, but our results definitely challenge the accepted assumption that renal dysfunction in patients with heart failure is due to low forward flow to the kidneys.

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