

# Renal function in acute heart failure: what can go wrong and what we can do about it

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## Abstract

Renal dysfunction frequently occurs during treatment for acute heart failure. Baseline renal dysfunction and worsening renal function confer a poor prognosis in patients with acute heart failure. Renal dysfunction may be due to disturbances in intrinsic renal function, inadequate arterial pressure, excessive renal venous and intracapsular pressure, and/or the impact of therapy on intrarenal autoregulatory mechanisms. Distinguishing the precise mechanism or mechanisms that may be operative in each case of renal dysfunction in acute heart failure is critical to avoid further worsening of renal function and to provide optimum therapy for both the heart and the kidney. ■ *Heart Metab.* 2017;74:13-16

**Keywords:** acute heart failure; kidney; afterload/preload

## Introduction

Acute heart failure (AHF) is characterized most commonly by an increase in left and right ventricular filling pressures. The vast majority of severe or acutely decompensated heart failure (HF) patients suffer primarily from congestion and elevated filling pressures and not from low blood pressure or decreased cardiac output.<sup>1</sup> Increased filling pressures are transmitted to the pulmonary and systemic circulation and result in circulatory congestion. A primary change in cardiac function due to myocardial infarction or arrhythmia may initiate this sequence. However, circulatory congestion may develop independent of primary changes in cardiac function and in turn cause increases in cardiac filling pressures. Such congestion may arise from many different causes, including increased total body volume expansion,

shifts of blood from reservoirs in the splenic and splanchnic beds to the central circulation,<sup>2</sup> and/or a rise in blood pressure, which increases left and right ventricular afterload and may compromise systolic and/or diastolic function. Frequently, many of these mechanisms occur together and set up a number of feedback loops whereby they magnify their individual adverse effects.

Simple volume retention is probably the most common mechanism of circulatory congestion, and by far the most common treatment involves diuretics. The kidney is therefore at the center of the problem for most cases of AHF both as a contributor to congestion and as the target of therapy. The signal for volume retention arises from activation of the sympathetic nervous system (SNS) and the renin-angiotensin aldosterone system (RAAS), as well as secretion of the antidiuretic hormone arginine vasopressin, all of

### Abbreviations

**AHF:** acute heart failure; **GFR:** glomerular filtration rate; **HF:** heart failure; **RAAS:** renal-angiotensin aldosterone system; **SNS:** sympathetic nervous system; **WRF:** worsening renal function

which contribute to sodium and water reabsorption. As left ventricular filling pressure increases, causing increased respiratory rate and dyspnea, SNS activity rises further with additional stimulation of the RAAS and vasopressin, setting the stage for a vicious cycle. Data from several recent trials conducted by the National Heart, Lung, and Blood Institute Heart Failure Network demonstrate heightened activity of the RAAS in severely congested patients with AHF.<sup>3</sup> In these studies, activation of the RAAS was linked to worsening renal function (WRF), suggesting a bidirectional relationship between neurohormonal activation and renally mediated congestion as AHF develops.

### A physiological approach to the heart and kidneys

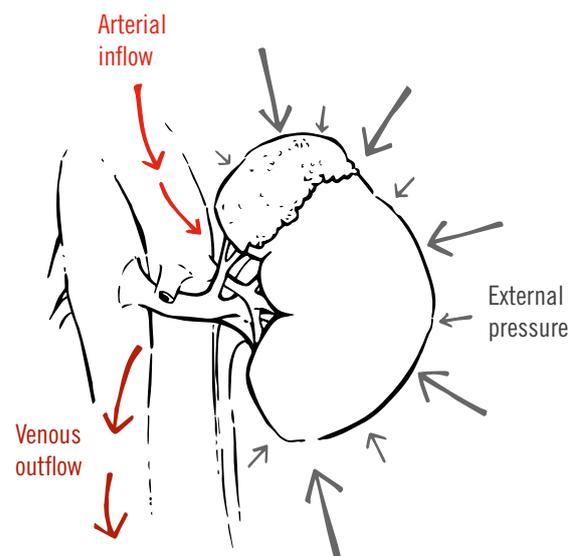
When we treat AHF, therapy is directed at removing volume and reducing arterial pressure (if elevated). Although it has not been a major focus of recent trials, therapy should probably include an attempt to mitigate the effects of neurohormonal activation.<sup>4</sup> All of these interventions have effects on the kidney. A sound understanding of the influences on renal function in AHF and how it is affected by therapy is therefore critical in the treatment of AHF. Lack of appreciation of the ways in which AHF and the treatment for AHF may affect renal function may lead to failure to correct renal dysfunction when present, or worse, to WRF, which in turn may further aggravate volume retention and vasoconstriction.

When we approach a patient with AHF, we analyze the problem in terms of changes in preload, afterload, and ventricular function. This is because it makes little sense to give diuretics to a patient with acute diastolic HF whose main problem is hypertension from non-compliance with blood pressure medications. That patient primarily and perhaps only needs a reduction in blood pressure to alleviate the increase in cardiac filling pressure and pulmonary venous congestion. On the other hand, it may be risky to further lower blood pressure in a patient with a dilated ventricle and low ejection fraction presenting with a 30-kg weight

gain, anasarca, and a blood pressure of 90/60 mm Hg. Furthermore, neither approach may be useful to a patient who had a normal blood volume and arterial pressure immediately before a massive myocardial infarction or the onset of an arrhythmia, such as atrial fibrillation, with rapid ventricular response. A similar analysis should occur when approaching renal function in a patient with AHF.

### Renal preload and afterload

The kidney may be regarded as a sophisticated filtration system with many intrinsic components. However, for any given level of intrinsic renal function, renal loading conditions are important, just as they are for the left ventricle.<sup>5</sup> One can therefore view renal function in AHF in terms of renal “preload,” intrinsic renal function, and renal “afterload” (Figure 1). Renal “pre-



**Fig. 1** The main function of the kidney is to maintain volume and electrolyte homeostasis. Although intrarenal function is highly complex, ultimately, renal function depends on adequate perfusion pressure. Perfusion pressure in turn relates to the gradient between arterial inflow pressure, which can be considered as “renal preload,” and venous outflow pressure, which can be viewed as “renal afterload.” Although the kidney is a retroperitoneal structure, transmission of intra-abdominal pressure, if increased, may also influence perfusion and glomerular filtration and so may also be a component of renal “afterload.” In severe or acutely decompensated heart failure, renal function may decline purely on a hemodynamic basis, though typically used heart failure therapies may also influence intrarenal function. See the body of the paper for more detail.

load” is the arterial inflow pressure and it has to be adequate to allow filtration to occur, although there are important autoregulatory factors that may preserve glomerular filtration rate (GFR) even when arte-

rial pressure falls. As most patients with AHF are not overtly hypotensive, maintaining renal “preload” is not generally the most pressing problem in maintaining or improving renal function while treating AHF, though it does come into play with hypotensive patients or those who are in cardiogenic shock.

Frequently, however, one observes that despite a normal arterial pressure or renal “preload,” and with no known intrinsic renal disease, patients with AHF exhibit a decrease in GFR that reverses when they are decongested. The mechanism of this effect relates to renal “afterload”—the renal venous pressure, which in turn is related to the central venous pressure. A component of this renal afterload also seems to be related to the intra-abdominal pressure which may be transmitted to the retroperitoneal space and increase intracapsular pressure.<sup>6</sup> It has been known for decades that an increase in renal venous pressure has an adverse effect on GFR, but until comparatively recently, the importance of this mechanism in both the presentation and treatment of AHF had been overlooked.<sup>7</sup> The key to understanding renal dysfunction and WRF in many patients and its subsequent improvement with decongestive therapy lies with the beneficial effects from reducing renal “afterload” as a response to decongestive therapies whether they be pharmacologic, such as loop diuretics, or mechanical, such as ultrafiltration. To continue the analogy with HF, renal dysfunction due to increased renal venous/abdominal/intracapsular pressures might well be termed “congestive kidney failure.”

We can therefore modulate renal “preload” and “afterload” by paying attention to the mean arterial pressure and the central venous pressure, as well as to the intra-abdominal pressure if conditions such as tense ascites are present. Under most circumstances in AHF we may not be able to directly improve renal function because of renal injury from hypoxia, contrast dye, or intrinsic renal disease. However, our therapies may also have effects that appear independent of “preload” and “afterload,” as assessed by mean arterial and central venous pressure. As noted, autoregulatory factors allow for maintenance of GFR when arterial inflow pressure is decreased. Angiotensin II figures prominently here as it is a potent constrictor of the efferent arteriolar circulation within the glomerulus. When arterial pressure falls, and activation of the RAAS occurs, efferent arteriolar constriction may help to maintain intraglomerular filtration pressure. When

an angiotensin II antagonist or angiotensin-converting enzyme inhibitor is given, GFR may then actually fall slightly because of a decrease in the glomerular filtration pressure despite a normal arterial pressure. This may occur more commonly at low arterial pressures where preferential dilation of the efferent arterioles occurs in response to these agents. This sort of renal “dysfunction” as reflected by a fall in GFR is generally not clinically important since the effect for the most part is small, and sodium and water excretion may continue because of a fall in the filtration fraction (GFR declining out of proportion to renal blood flow); also, since angiotensin II may constrict overall renal arterial input and limit intrarenal flow or renal “preload,” the net effect of using these drugs on renal filtration and excretory function may be neutral or even positive. It is not recommended that ACE inhibitor and angiotensin receptor blocker (ARB) be stopped in AHF unless severe renal dysfunction is present.<sup>8</sup>

### Respecting the heart and kidneys

It is therefore very helpful to approach the kidney in AHF in the same manner as we approach the heart and attempt to identify the mechanisms leading to renal dysfunction and address them selectively. Just as attempting to treat all AHF in the same manner will not produce uniformly positive results, lumping all cases of abnormal or WRF together will lead to misunderstanding and inappropriate or inadequate therapy. If the patient is hypotensive, arterial pressure must be raised. If the patient is grossly volume overloaded, aggressive diuresis is critical. RAAS inhibition should continue even if a transient fall in GFR due to efferent arteriolar dilation is seen.

One variable that does not seem to be important is cardiac output, since the kidney doesn’t respond to cardiac output per se, but rather to perfusion pressure.<sup>9</sup> As elegantly shown by studies from the Cleveland Clinic, regardless of cardiac output, it is the renal perfusion pressure, ie, the difference between diastolic blood pressure and central venous pressure, that is the key determinant in maintaining GFR.<sup>7</sup>

This point is illustrated nicely in an elegant brief review by Jessup and Costanzo.<sup>5</sup> Considering the various factors that influence renal function in AHF, improving cardiac output (even if low) with the use of vasodilators and inotropes would probably not be of value, independent of improvement in arterial pressure.

## Thinking beyond loop diuretics

Why is attention to the kidney so important in treating patients with AHF? As already stated, it is the kidney that causes much of the congestion in congestive HF. If renal function is inadequate, diuresis will be very difficult, particularly with loop diuretics, which themselves directly and adversely affect both renal function and neurohormonal imbalance.<sup>10</sup> And if the patient is congested to the point of an increase in central venous pressure, this may be very difficult to overcome since more and more loop diuretics may simply cause more and more renal dysfunction, aggravating what has been called type I cardiorenal syndrome.<sup>11</sup> It is for this reason that newer therapies, such as ultrafiltration and vasopressin antagonism, have been and are being explored in AHF, a topic beyond the scope of the current discussion.<sup>4</sup> However, the “bottom line” is that without adequate renal function, successful treatment of AHF is often very difficult.

## Is worsening renal function always bad?

The last point to emphasize is the prognostic importance of renal function in AHF. Many studies have shown that abnormal or WRF is associated with an adverse prognosis.<sup>12</sup> More recent studies have suggested that transient WRF, or WRF without persistent congestion, may not have the same adverse effects.<sup>13,14</sup> Although these observations have not been substantiated or studied prospectively, it does seem that transient or mild WRF, if not associated with persistent congestion, may be acceptable. It is perhaps likely that in many of these situations, the WRF is due to the effects of neurohormonal inhibition triggered by the use of agents that interfere with activity of the RAAS. However, at least in theory, our goal in treating AHF should be to achieve adequate decongestion while improving or at least not significantly worsening renal function. We can do this most successfully by improving the loading conditions for both the heart and the kidney if we understand the impact of our treatments on each. ■

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