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Focus on renal congestion in heart failure

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Abstract

Hospitalizations due to heart failure are increasing steadily despite advances in medicine. Patients hospitalized for worsening heart failure have high mortality in hospital and within the months following discharge. Kidney dysfunction is associated with adverse outcomes in heart failure patients. Recent evidence suggests that both deterioration in kidney function and renal congestion are important prognostic factors in heart failure. Kidney congestion in heart failure results from low cardiac output (forward failure), tubuloglomerular feedback, increased intra-abdominal pressure or increased venous pressure. Regardless of the cause, renal congestion is associated with increased morbidity and mortality in heart failure. The impact on outcomes of renal decongestion strategies that do not compromise renal function should be explored in heart failure. These studies require novel diagnostic markers that identify early renal damage and renal congestion and allow monitoring of treatment responses in order to avoid severe worsening of renal function. In addition, there is an unmet need regarding evidence-based therapeutic management of renal congestion and worsening renal function. In the present review, we summarize the mechanisms, diagnosis, outcomes, prognostic markers and treatment options of renal congestion in heart failure.

Key words: acute kidney injury, fluid management, heart failure, hypervolemia, renal congestion

Introduction

Deterioration of renal function is common in both acute and chronic heart failure (HF) settings lately described as 'cardiorenal syndromes'. Renal congestion (RC) has become increasingly recognized as a potential contributor to cardiorenal syndromes, and adequate control of congestion with simultaneous improvement/preservation of renal function has been proposed as a central goal of patient management in HF [1]. The pathophysiologic mechanisms, prognostic markers and treatment options regarding RC and deterioration of kidney function in HF are not fully elucidated, despite significant research. In the present review, we summarize data on mechanisms, diagnosis, outcomes, prognostic markers and treatment options for RC in HF.

Renal congestion is a fairly new concept and its importance is just beginning to be realized. Congestion—either clinical or identified with echocardiography—allows stratification of HF patient prognosis [2, 3]. As part of systemic congestion, RC is of special interest due to the physiology of glomerular filtration. Indeed,

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the kidney plays a major role in fluid overload compensation and, at the same time, glomerular filtration, a key component of kidney function, partly depends on venous pressure, which is elevated in patients with systemic congestion [4]. Thus, RC is more than a mandatory manifestation of systemic congestion and may *per se* have prognostic implications beyond those of systemic congestion.

The prognostic impact of renal congestion in HF

Congestion has a negative impact on clinical outcomes in patients with HF. In 2557 patients undergoing right heart catheterization, elevated central venous pressure predicted mortality and was associated with low estimated glomerular filtration rate (eGFR), independent of cardiac index [5]. In 1684 HF patients, decongestion (assessed as hemoconcentration: a ≥3% absolute increase in hematocrit) was associated with a greater risk of in-hospital worsening renal function as defined increase in SCr ≥ 0.3 mg/dL, worsening blood urea nitrogen (BUN) was defined as a ≥25% increase and worsening estimated glomerular filtration rate (eGFR) was defined as a ≥25% decrease, but this effect disappeared 4 weeks post-discharge. More importantly, after a median follow-up of 9.9 months, every 5% increase in hematocrit was associated with a 19% decreased risk of all-cause death {hazard ratio [HR] 0.81 [95% confidence interval (CI) 0.70–0.95]}, after adjustment for baseline clinical risk factors. An increase in hematocrit change was also associated with decreased cardiovascular mortality or HF hospitalization at ≤100 days post-randomization [HR 0.73 (95% CI 0.71–0.76)] [6]. Such data were confirmed in 336 patients with acute decompensated HF, in whom hemoconcentration was associated with a lower risk of mortality, despite an increased risk for worsening renal function (WRF) [7]. In another study, hemoconcentration correlated with favorable prognosis despite a decrease in renal function in 1969 patients with acute decompensated HF [8]. In 6080 patients with HF after myocardial infarction enrolled in the EPHESUS trial, plasma volume decrease, which was indirectly estimated using the Strauss formula, was associated with better outcomes [9]. In patients with chronic HF enrolled in the GISSI-HF trial, increased estimated plasma volume was associated with worse clinical outcomes, independent of body weight changes [10].

Importantly, in acute decompensated HF there was a strong association between an increased urine volume in the first 24 h and a lower incidence of WRF (defined as an increase in serum creatinine >0.3 mg/dL above baseline) [11]. This finding is extremely relevant since it overcomes prejudice regarding the fear of decreasing renal plasma flow and deterioration of kidney function. In addition, WRF was less frequent in patients who achieved decongestion as measured by low central blood pressures [4].

In fact, existing data suggest that congestion is more relevant than WRF for outcomes. A prospective study investigated the relative impact of WRF versus the presence of congestion on post-discharge mortality and readmission in 599 patients with acute decompensated HF [12]. Congestion was defined as the persistence at discharge of one or more signs or symptoms of fluid overload (third heart sound, pulmonary rales, jugular venous stasis, hepatomegaly and peripheral edema). There was no difference with respect to outcomes between patients with WRF and no congestion and patients without WRF and no congestion. In contrast, outcomes were worse in patients with congestion alone (with or without WRF). The authors concluded that WRF alone, when detected using serial serum creatinine measurements, is not an independent determinant of outcomes in patients with acute HF; it has an additive prognostic value only when it occurs in patients with persistent signs of congestion [12]. Taken together, these data suggest that residual congestion is perhaps a key variable underlying prognosis in HF patients with cardiorenal syndromes.

The pathophysiology of renal congestion and WRF in heart failure

The pathophysiology of renal congestion in HF is complex and involves multiple simultaneous pathways (Figure 1).

Ageing, hypertension and diabetes may be cofactors both in HF and in renal dysfunction. Their coexistence can accelerate atherosclerosis, myocardiopathy and chronic kidney disease (CKD) [13]. Use of iodinated radiocontrast agents or nonsteroidal anti-inflammatory drugs may predispose to renal dysfunction and renal congestion [14].

Arterial underfilling contributes to WRF during HF. When low aortic pressure results in a renal perfusion pressure ≤80 mmHg, kidney autoregulation is no longer possible [15]. Hemodynamic responses depend on endothelial function, which is impaired in CKD and in HF. Reduced kidney perfusion pressure upregulates the sympathetic nervous and renin angiotensin aldosterone (RAS) systems. Both angiotensin II and catecholamines further induce glomerular arteriolar vasoconstriction, decreasing renal plasma flow (RPF) [16]. However, angiotensin II has a disproportionate vasoconstrictive effect on the efferent arteriole, preserving GFR despite reduced RPF [17]. Thus, initially, the filtration fraction and GFR are preserved but eventually increased angiotensin II and/or catecholamine levels become maladaptive, causing more preglomerular vasoconstriction and decreasing GFR [18]. This in turn activates proximal tubular sodium and water reabsorption, leading to more systemic and renal congestion [19].

Elevated central venous pressure in HF promotes renal congestion (also known as backward failure). Indeed, classic experiments demonstrate that (i) there is a steeply graded relationship between change in renal venous pressure and reduction in urine flow and (ii) kidney blood flow is reduced more by an increase in venous pressure than by an equivalent decrease in arterial pressure [20]. These changes occur independently of any reduction in cardiac output and/or mean arterial pressure, changes that occur much later in the progression of HF [21]. In healthy individuals without HF, a transient hypervolemic state leads to increased renal fluid and salt excretion, which decreases both blood volume and cardiac output, returning the pressure back to normal. However, in patients with HF despite an increase in blood volume (hypervolemic state) the elevated right atrial and central venous pressure impinge on salt excretion by the kidney, so that a vicious cycle of sodium retention, volume expansion and HF is initiated, leading to more renal congestion [22].

Increased intra-abdominal pressure and abdominal congestion (i.e. splanchnic) and interstitial congestion may also have a role. Renal blood flow is inversely related to intra-abdominal pressure [23, 24]. Intra-abdominal venous hypertension can also result in systemic hypotension and low cardiac output [25]. Compromised capacitance of the splanchnic vasculature and deficient abdominal lymph flow may also contribute to elevated cardiac filling pressures [26], which initiates/adds to the cascade of events causing WRF and renal congestion. In addition, recent evidence suggests that alteration of gut flora during HF may play an important role in WRF and renal congestion. Indeed, it has been suggested that the entrance of bowel toxins into the

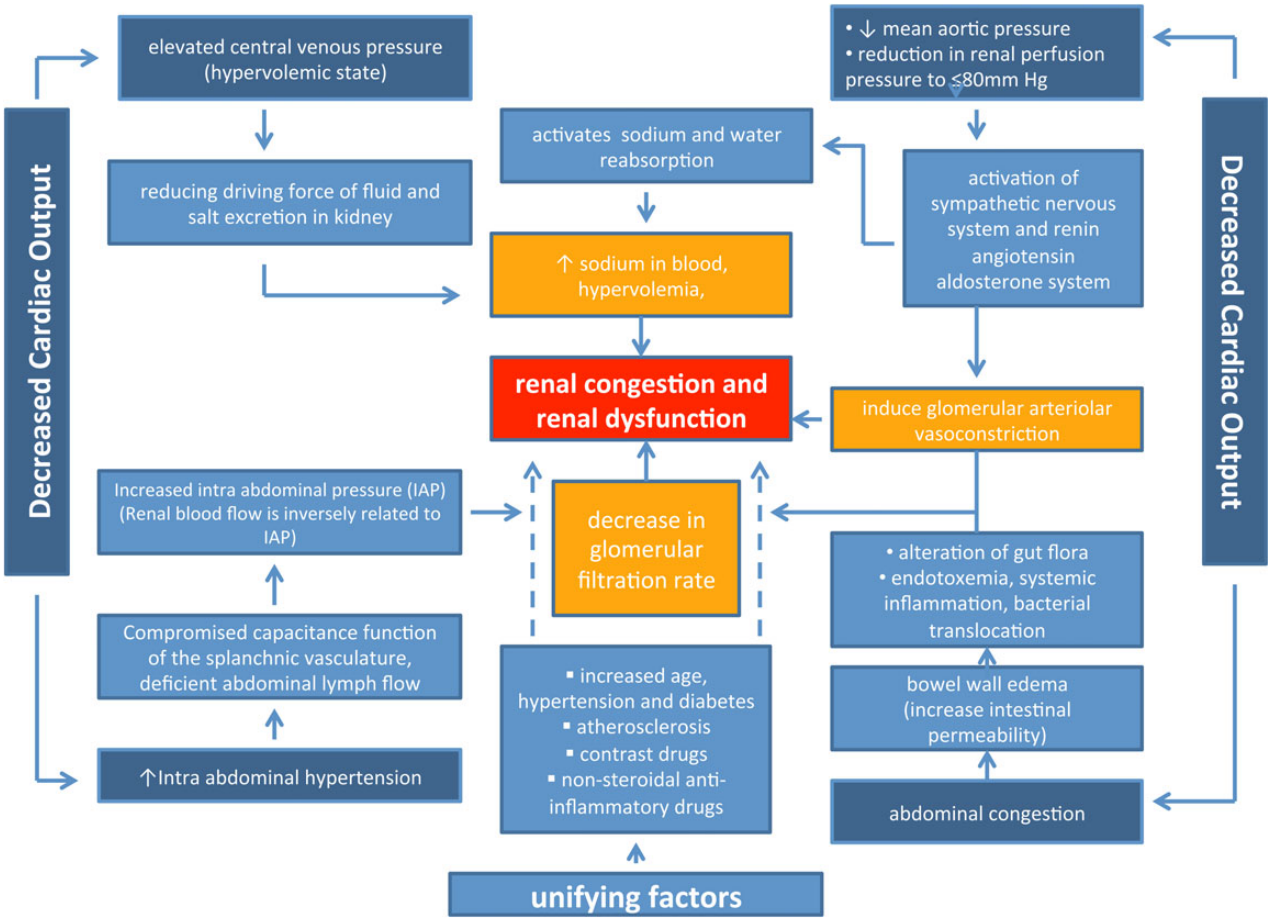

Fig. 1. Mechanisms involved in renal congestion in heart failure.

circulatory system—as a result of impaired intestinal barrier function secondary to congestion—may cause a further depression of cardiac and renal function. These toxins are mainly produced by microorganisms in the gut lumen and are altered in advanced HF, especially when there is congestion [27].

What are the consequences of renal congestion?

Renal congestion leads to increased renal interstitial pressure that affects the entire capillary bed and the tubules, possibly also inducing local hypoxia. Tubular compression raises the luminal pressure, further attenuating the transglomerular pressure gradient, and lowering the GFR. It is important to appreciate that an increase in renal interstitial pressure due to venous congestion is physiologically different from that caused by elevations in arterial pressure, which is associated with natriuresis [28].

Inflammation may also promote and be a consequence of renal congestion [29]. Inflammation may cause vascular dysfunction via endothelial activation and enhanced arterial stiffness, reduce myocardial contractility through functional suppression of contractility and increased myocardial cell death, contribute to progressive renal dysfunction and fibrosis and increase endothelial permeability, thus facilitating fluid extravasation into lung alveoli and absorption of pro-inflammatory endotoxin from the bowel [29]. Conversely, in HF and venous congestion, activation of the RAS and sympathetic system promotes/enhances the inflammatory response. In addition, accumulating evidence suggests that volume overload *per se* and venous congestion independent of RAS and sympathetic system activation promote the expression of inflammatory mediators [29].

A very recent study evaluated the role of peripheral venous congestion, induced by the venous stress test, on inflammation and endothelial activation. Venous arm pressure was increased to 30 mmHg above baseline by inflating a cuff around the dominant arm (test arm). Plasma interleukin-6 (IL-6), endothelin-1 (ET-1), angiotensin II, vascular cell adhesion molecule-1 (VCAM-1) and chemokine (C-X-C motif) ligand 2 (CXCL2) were significantly increased in the congested arm as compared with the control (no cuff) arm (Figure 2) [30]. In HF, bacterial endotoxin production and bacterial translocation from the bowel lumen may increase [31, 32]. Indeed, in a recent prospective study, endotoxin levels were higher in CKD patients with fluid overload than in those without fluid overload [33].

Endothelial cells may become activated during venous congestion to a pro-oxidant, pro-inflammatory and vasoconstricting state. Once 'activated', the endothelium can promote additional congestion through humoral, renal and cardiac mechanisms, resulting in a deleterious positive feedback loop [20]. Venous stretch increased the release of ET-1, IL-6 and tumor necrosis factor α (TNF-α) [34] and endothelial reactive oxygen species (ROS) production [35]. ROS and cytokines may also trigger an inflammatory response through activation of nuclear factor κB [36].

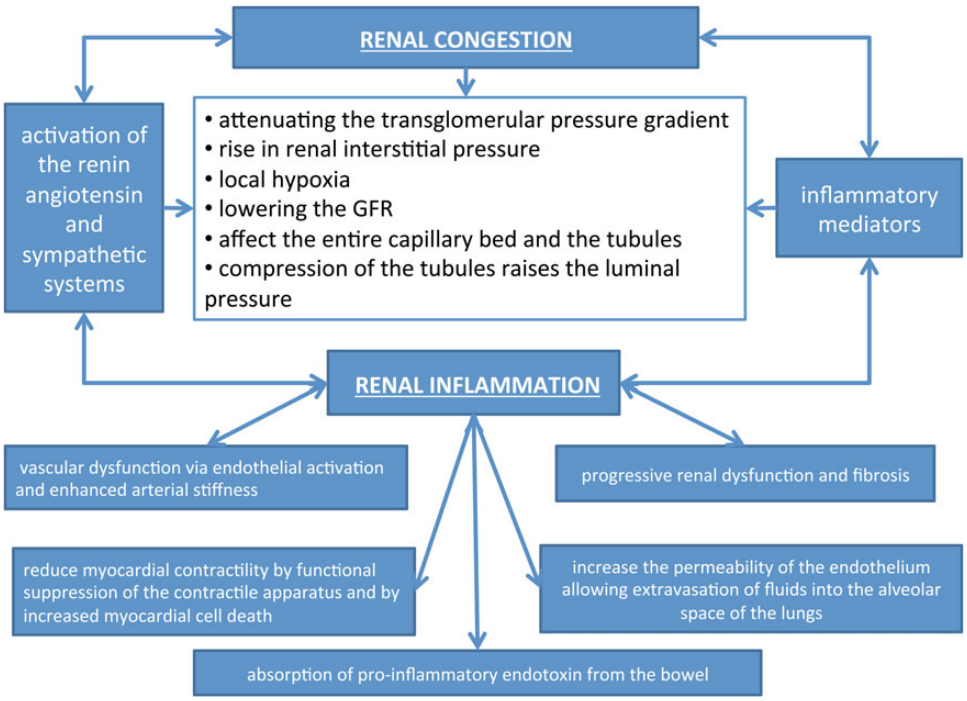

Fig. 2. Mechanisms of increased inflammation during venous congestion.

How to assess renal congestion?

Unfortunately there is no direct method to assess renal congestion. This is in contrast to the several possibilities for evaluating lung congestion. Indeed, visualization of B lines by lung ultrasound is now accepted as a valid method to assess pulmonary congestion in HF [37, 38]. Traditional markers such as eGFR and emerging markers such as cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1) and natriuretic peptides offer prognostic information in HF and renal dysfunction. However, none of these markers are specific for renal congestion. Natriuretic peptides are now routinely used and high values [>600 pg/ml B-type natriuretic peptide (BNP) or >6000 pg/ml N-terminal pro-BNP] are associated with high filling pressures secondary to volume overload [39]. BNP levels correlate with capillary wedge pressure and can also serve as an indirect marker for deterioration of kidney function during treatment of acute decompensated HF [40]. However, natriuretic peptides are not specific for renal congestion and can reflect congestion specifically related to HF. Echo/Doppler should be explored as a means to assess renal veins congestion. Thus, research is needed to find direct ways to measure renal congestion in HF.

Treatment of renal congestion and decongestion strategies in heart failure

There are various treatment options for renal congestion in HF that are beyond the scope of this review and will only be briefly mentioned (Table 1). Therapeutic strategies aim at eliminating excess fluid without compromising renal function.

Salt and water restriction

Salt and water restriction for routine management of HF is usually based on expert opinion rather than evidence-based proof [57]. Fluid restriction (1000 mL/day) in hyponatremic (serum sodium <137 mmol/dL) patients with HF improved the quality of life at 60 days after discharge [58]. In HF patients with preserved ejection fraction, sodium restriction was associated with favorable changes in ventricular diastolic function, arterial elastance and ventricular–arterial coupling [59]. A randomized trial (trial number NCT01896908) will investigate the effects of sodium and fluid restriction on neurohormonal activation in HF patients with preserved ejection fraction. However, another study failed to observe a clear benefit of sodium and fluid restriction in HF patients with preserved ejection fraction [60]. Likewise in another randomized trial, patients admitted for worsening HF did not benefit from aggressive fluid and sodium restriction [61]. The different findings may be due to patient characteristics, study design or not enough fluid and sodium restriction. On the other hand, sodium restriction may have a direct effect on extracellular volume, improving endothelial function and arterial stiffness [62, 63].

The effect of sodium and fluid restriction may differ in older and younger patients [64]. In elderly people, dietary sodium restriction might even cause harm through hypovolemia and increased neurohormonal activation, causing falls and their associated morbidity. Dietary sodium intake should be individually tailored based on HF severity and the physiologic response to sodium loading [57]. Thus, future clinical studies are needed to assess the effectiveness of sodium and fluid restriction in different stages and clinically divergent HF patients.

Loop diuretics, ultrafiltration and dialysis strategies

Loop diuretics are commonly used in patients with HF. In HF, the dose–response curve shifts downward and to the right. Thus, a higher dose is required to achieve the same therapeutic effect [65]. However, higher loop diuretic dosages in HF were associated with worse clinical outcomes, including WRF [66]. These studies were criticized since patients with more severe HF and preexisting renal disease require higher diuretic doses [41]. Indeed, in another trial involving 308 patients, after adjusting for cardiovascular risk

Table 1. Treatment strategies for venous congestion in heart failure

Loop diuretics	Use intravenous route
	Bolus dosing may be as effective as continuous infusion
	Start the initial dose at 2–2.5 times the home oral dose
	Increase the dose until the adequate symptom relief is achieved
	Avoid single dosing
	Consider adding thiazide diuretics or ACE-I and ARB in case of resistance
Ultrafiltration	Peripheral venovenous ultrafiltration
	Peritoneal dialysis
V2R antagonists	Increase free water excretion and improvement in sodium level
	Experimental evidence suggests an increase in survival
	Augment the diuretic and the natriuretic response to furosemide
Adenosine receptor blockers	Dilatation of afferent arteriole and preservation of GFR
	No effect on worsening renal function
	Had a favorable effect on dyspnea as well as short-term mortality
	May be associated with higher rates of seizures and stroke
Dopamine	Improve renal blood flow and diuresis at low doses
	In acute HF, use with caution
	No clear effect on mortality, rehospitalizations or prevention of renal damage
Natriuretic peptides	Decrease cardiac filling pressure, increase cardiac output, promote diuresis and decrease RAS and release of norepinephrine
	Borderline effect on dyspnea
	May have hypotensive effect
Novel therapies	Spliced BNPs
	Hypertonic saline with furosemide
	Relaxin
Left ventricular assist device	Was used refractory HF and cardiorenal syndrome
	Studies have demonstrated that creatinine levels decrease fast initially, then decrease gradually
	Early postoperative mortality correlates with the severity of preoperative renal dysfunction

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; V2R, vasopressin type 2 receptor; GFR, glomerular filtration rate; RAS, renin angiotensin aldosterone system; BNP, B-type natriuretic peptide.

and clinical stability, diuretic dose was not associated with increased risk [41]. The frequency of dosing of loop diuretics is another issue. A single dose of furosemide elicits transient natriuresis [67, 68] and loop diuretics may be given two or more times per day or continuously. However, continuous dosing was not more effective than an optimally prescribed bolus regimen, as proven in the Diuretic Optimization Strategies Evaluation (DOSE) trial [41]. The addition of nonloop diuretics (i.e. thiazide or potassium-sparing diuretic) may overcome the escape phenomenon due to activation of the RAS and sympathetic system and sodium reabsorption by more distal sodium transporters [65].

Several guidelines state that ultrafiltration is another reasonable approach for patients with refractory congestion not responding to diuretic therapy [69, 70]. It is currently unclear which strategy is safer and more effective [71]. Some important differences are obvious. First, the amount of urine produced in response to intravenous (i.v.) diuretics is not predictable, whereas fluid removal by ultrafiltration is completely controllable and adjustable. Second, the ultrafiltrate is isotonic, removing more sodium than loop diuretics, which induces hypotonic urinary output [72]. Third, since ultrafiltration can be controlled by machines and the amount of fluid removal is strictly controlled, excess fluid removal and neurohumoral activation can be prevented [73]. Also, the adequacy of intravascular refill during ultrafiltration can be assessed by continuous monitoring of the hematocrit. Finally, elimination of pro-inflammatory cytokines [74] or sodium-retaining vasoconstrictive agents may occur during ultrafiltration, theoretically leading to an improvement in urinary output or restoration of diuretic responsiveness during ultrafiltration [75].

Bearing all issues in mind, one may think that ultrafiltration is superior to diuretics, albeit it is an invasive procedure. However, there are no strict recommendations regarding the preferential use of diuretics, ultrafiltration or in combination, as stated earlier. In fact, the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) trial showed that the use of a stepped pharmacologic therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 h. While a similar amount of weight loss was achieved with the two approaches, ultrafiltration was associated with a higher rate of adverse events [76]. The AVOID-HF randomized study was designed to determine whether ultrafiltration as an initial strategy reduces hospitalizations for acute HF before the onset of worsening renal function as compared with i.v. diuretics [77]. Unfortunately, it was recently prematurely terminated due to patient recruitment challenges ('No interim analyses were completed; study closure was not related to any concerns about safety or futility, as stated by the sponsor'; ClinicalTrials.gov NCT01474200).

Peritoneal dialysis is another option in HF [78] and improves quality of life in HF [79]. However, these studies must be interpreted with caution due to the small number of patients, lack of a control group and advanced renal failure. Furthermore, there are no studies available comparing head-to-head peritoneal dialysis, diuretic therapy and salt restriction in congestive HF [80] and peritoneal dialysis has adverse effects such as peritonitis, increased intra-abdominal pressure and hyperlipidemia. In a very recent review, Lu *et al.* [81] suggested that peritoneal dialysis decreased hospitalization days and improved heart function in patients with congestive HF [81].

Continuous ultrafiltration strategies [48, 43] may also have a potential beneficial role in HF. It was suggested that cardiovascular tolerability is better with continuous venovenous hemodiafiltration in patients with acute HF [48]. However, there are no large-scale head-to-head comparison studies with regard to diuretics, conventional dialysis and continuous therapies. This is the reason that ultrafiltration should not be used as a quicker way to achieve a sort of mechanical diuresis nor as a remedy for inadequately prescribed and administered diuretic therapy. Instead, it should be reserved for selected patients with advanced HF and true diuretic resistance, as part of a more complex strategy aimed at adequate control of fluid retention [42].

Vasopressin type 2 receptor antagonists

Vaptans are recently marketed drugs. Since vaptans increase free water excretion and increase serum sodium levels (which are usually low in advanced HF), they may have potential benefits in HF [44, 45]. In animal models of HF, tolvaptan increased urine volume, decreased lung congestion and improved survival but did not modify blood pressure. Additionally, renal histopathologic damage, including tubular fibrosis and glomerulosclerosis, was ameliorated [46].

There are also human studies. In the EVEREST trial, tolvaptan caused an early and sustained reduction in body weight and improved serum sodium but did not improve mortality or morbidity [46].

In another study, conivaptan and loop diuretics (either alone or combined with conivaptan) were compared in stable HF patients. There were no differences with regard to hemodynamics, neurohormonal activation, renal blood flow and GFR. Conivaptan and furosemide similarly increased urine volumes, but only furosemide increased urinary sodium excretion. Conivaptan significantly augmented both the diuretic and the natriuretic response to furosemide when both were combined [47].

Adenosine receptor blockers

Adenosine is secreted by juxtaglomerular cells in response to increased distal sodium load and is usually increased in HF. Intensive diuretic treatment increases distal sodium load, leading to increased adenosine secretion. This in turn may cause decreased GFR by constricting afferent arterioles [82].

The PROTECT trial (a placebo-controlled randomized study of the selective A1 adenosine receptor antagonist rolofylline for patients hospitalized with acute HF and volume overload to assess treatment effect on congestion and renal function) randomized 2033 patients admitted for acute HF to rolofylline or placebo. Rolofylline had a favorable effect on dyspnea and short-term mortality, but no beneficial effect on WRF was observed [82]. However, rolofylline was associated with higher rates of seizures and stroke and drug development was stopped [49].

Dopamine

Renal dose dopamine has been traditionally used to increase urine volume [50, 51]. The recent Dopamine in Acute Decompensated Heart Failure (DAD-HF) trial randomized 60 acute HF patients to high-dose furosemide or low-dose furosemide plus low-dose dopamine. Although the 60-days outcomes were similar in both groups, deterioration of kidney function and hypokalemia were more frequent with high-dose furosemide. The major limitation of the study was small sample size [51]. Thus, there is no evidence to recommend dopamine administration for the protection of renal function in HF patients with fluid overload and the need of diuretic treatment [83].

Natriuretic peptides

Recombinant human BNP (nesiritide) decreases cardiac filling pressure, RAS activity and norepinephrine release while increasing diuresis and cardiac output [84]. In the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial in patients with acute HF, nesiritide had a borderline effect on dyspnea but no effect on outcomes when compared with placebo [52]. Also, concerns have been raised regarding untoward effects on renal function and mortality with nesiritide infusion [85]. Alternatively, spliced BNPs such as ASBNP and ASBNP.1 lack the hypotensive side effects of nesiritide and increased GFR, suppressed plasma renin and angiotensin and induced natriuresis and diuresis [53]. Randomized trials are warranted for these new agents in HF.

Neprilysin is a neutral endopeptidase that degrades several endogenous vasoactive peptides, including natriuretic peptides, bradykinin and adrenomedullin. Inhibition of neprilysin increases the levels of these peptides, countering the neurohormonal overactivation that contributes to vasoconstriction, sodium retention and maladaptive remodeling. A recent trial comparing the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in HF patients with reduced ejection fraction was stopped early due to the obvious superiority of LCZ696 with respect to the primary outcome, a composite of death from cardiovascular causes or hospitalization for HF, as well as to cardiovascular death, symptoms and physical limitations of HF [54].

Novel therapies

A combination of hypertonic saline and furosemide was thought to prevent rebound sodium reabsorption and promote effective diuresis. Indeed, a combination of high-dose furosemide with bolus hypertonic saline infusion in patients with New York Heart Association class IV HF resulted in improved diuresis, shortened hospital stay, decreased BNP levels and reduced readmissions compared with i.v. diuretic therapy alone [86].

Relaxin induces systemic and renal vasodilatation through actions on nitric oxide and endothelin B receptors. In a phase II trial (pre RELAX), relaxin was associated with relief of dyspnea and a tendency to greater weight loss with smaller doses of diuretics and nitrates [87]. The RELAX-AHF (Efficacy and Safety of Relaxin for the Treatment of Acute HF) trial compared serelaxin with placebo, with a primary endpoint of dyspnea relief [55, 56]. In 1161 patients with acute HF, serelaxin was associated with decreased other (non-HF, non-sudden death) cardiovascular deaths [hazard ratio (HR) 0.29 (95% CI 0.12–0.73), P = 0.005] and sudden death [HR 0.46 (95% CI 0.20–1.07), P = 0.065], but did not impact HF deaths or non-CV deaths. There was no specific comment on renal function and renal congestion [56].

Implantation of a left ventricular assist device for refractory HF and cardiorenal syndrome was associated with an initial fast decrease in creatinine levels, followed by a more gradual decrease. However, it is interesting to note that early postoperative mortality correlated with the severity of preoperative renal dysfunction, implying the importance of renal function [88, 89].

Conclusions

Renal congestion is now acknowledged as a major contributing factor for worse outcomes in HF patients. The management of

renal congestion in cardiac failure remains an important but unresolved clinical challenge. Among existing hurdles, renal congestion cannot be directly measured. In addition, the pathophysiology of renal congestion is still incompletely understood. Several pathways may be involved, but there may be interpatient variability in activation of the involved systems and companion diagnostics to individualize the management of HF are needed, with a focus on preventing renal injury and decreasing renal congestion. Various treatment strategies alone or in combination can be used for this purpose. More randomized clinical trials are needed to investigate imaging strategies, therapeutic options and individualization of therapy strategies for renal congestion in HF.

Ethical approval

This is a review and thus there was no need for ethical approval. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest statement

None declared.

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