REVIEW ARTICLE

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Cardiovascular Consequences of Acute Kidney Injury

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Acute kidney injury is generally characterized by an abrupt rise in the serum creatinine level, decreased urinary output, or both.[1] Advances in critical care and renal replacement therapies have provided tools that can support patients through most of the immediate complications of acute kidney injury, such as uremia or hyperkalemia, which could be rapidly fatal. Yet mortality from acute kidney injury remains high. Up to 60% of patients with severe acute kidney injury who are admitted to an intensive care unit (ICU) die from the disorder[2]; the long-term risk of death associated with acute kidney injury is also increased.[3-5]

Acute kidney injury is associated with an increased risk of chronic and end-stage kidney disease[6] and has adverse effects on other organ systems, including the heart. Likewise, patients with chronic kidney disease are at high risk for acute kidney injury and adverse cardiovascular sequelae.[7-9] Accumulating evidence supports the notion that cardiovascular damage due to acute kidney injury leads to other poor outcomes,[10] independent of or intertwined with the risks associated with the development of chronic kidney disease (see Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).[11]

Interactions between cardiac and kidney diseases have been classified as cardiorenal syndromes. A current classification[10] includes five types of cardiorenal syndromes: acute cardiac impairment leading to acute kidney injury (type 1), chronic cardiac impairment leading to kidney impairment (type 2), acute kidney injury leading to cardiac impairment (type 3), chronic kidney disease leading to cardiac impairment (type 4), and systemic conditions leading to both cardiac and kidney impairment (type 5) (Fig. S1).

In this review, we discuss the current understanding of the cardiovascular consequences of acute kidney injury (i.e., type 3 cardiorenal syndrome). We also discuss potential preventive strategies that target acute and recovery phases, with the aim of reducing the risk of subsequent adverse clinical events.

EPIDEMIOLOGIC INSIGHTS

Chronic hypertension and heart failure are risk factors for acute kidney injury and can hamper recovery from kidney injury.[12] Certain systemic conditions leading to acute kidney injury, such as sepsis, are additional potential causes of cardiovascular damage.[7]

Conversely, acute kidney injury is associated with an increased risk of death and both short-term and long-term cardiovascular complications, such as decompensated heart failure (Fig. 1). The association between acute kidney injury and long-term cardiovascular events has been observed in several large cohort studies (Table S1), although direct comparisons of risk among available studies are of limited

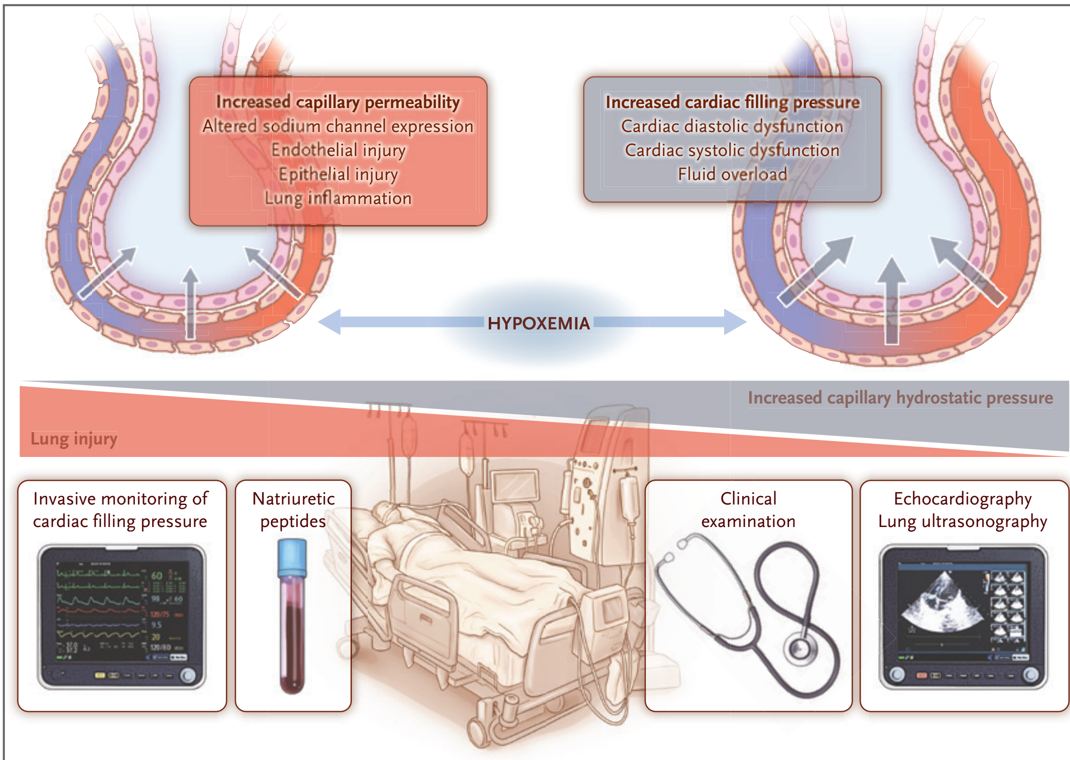

Figure 4. Pulmonary Edema after Acute Kidney Injury.

Mechanisms of pulmonary edema after acute kidney injury involve direct lung injury with increased lung capillary permeability and increased capillary hydrostatic pressure due to increased cardiac filling pressure. Fluid overload in patients with oliguria can contribute to the pathogenesis of pulmonary edema. A combination of clinical examination, measurement of plasma biomarkers such as natriuretic peptides, echocardiography, lung ultrasonography, and in challenging cases, invasive cardiac catheterization may be needed to identify the mechanisms of pulmonary edema in patients who have had an episode of acute kidney injury.

involved in phosphate homeostasis, has been described as a likely mediator of cardiovascular disease associated with chronic kidney disease. FGF-23 was observed to be rapidly up-regulated after an episode of acute kidney injury in a murine model.[51] In addition, reduced expression of klotho, a coreceptor of FGF-23, has been linked to secondary cardiac damage after acute kidney injury (as reviewed by Christov et al.).[52]

Electrolyte disturbances and metabolic acidosis are also thought to contribute to cardiac manifestations after acute kidney injury. Hyperkalemia can induce electrophysiological disturbances that alter cardiac conduction and potentially lead to cardiac arrest.[53] In rats, acute kidney injury increases the risk of ventricular arrhythmia after myocardial infarction because of distorted intracellular calcium homeostasis due to changes in the dihydropyridine receptor on the L-type calcium channel.[31] Profound metabolic acidosis alters myocyte contraction and excitability in vitro.[54]

DIAGNOSTIC FEATURES

Patients with, or recovering from, acute kidney injury often present with clinical signs and symptoms of heart failure, but the diagnosis can be challenging in such patients, since the symptoms are often nonspecific. Biomarkers and imaging techniques are frequently used for diagnostic purposes and to guide treatment decisions and monitor the response to therapy (Fig. 4). Capillary pulmonary pressure measured with a pulmonary-artery catheter can provide useful information regarding possible lung injury or cardiogenic pulmonary edema. Echocardiography, which has become the standard of care for

kidney injury and its effect on the cardiovascular system, if patients are to receive needed, potentially lifesaving treatments.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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