

# Role of different kinds of dialysis in the treatment of refractory heart failure

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## ABSTRACT

**Cardiorenal syndrome is a severe and potentially lethal disease in which heart and kidney failures coexist. The classic treatment with loop diuretics is ineffective due to the resistance of the kidney to those drugs, which requires the use of other therapies, such as extracorporeal ultrafiltration and peritoneal dialysis. This last technique is useful both in the acute treatment of acute heart decompensation and the chronic management of heart failure, because it improves heart function by reducing the volume overload, which in turn contributes to improving the kidney function with a limited number of side effects, which makes it the technique of choice for the treatment of diuretic-resistant heart failure. In this review, we present a description of the different kinds of cardiorenal syndrome, as well as the different treatments that are used, with special attention to the different modalities of peritoneal dialysis.**

## KEYWORDS

**Cardiorenal Syndrome; Peritoneal Dialysis; Extracorporeal Ultrafiltration**

## 1. EPIDEMIOLOGY

Heart failure is a common disease all over the world. It affects 5 million people in the United States [1], where more than 550,000 new cases are diagnosed each year, and it is the main cause of hospitalization in adults over 65 years old, so that 93% of the admitted patients present water retention, 42% are discharged without weight loss and 25% of the patients who are re-admitted develop resistance to diuretics [2].

Patients who suffer from heart failure present an increased incidence of chronic kidney failure: 30% to 50% suffer from chronic kidney disease with K/DOQI stages 3 to 5, which are associated with a higher hospitalization rate and higher mortality [3]. Mortality increases annually in patients with heart failure by 15% for each creatinine increase of 0.5 mg/dl, and by 7% for each decrease in the glomerular filtration rate of 10 ml/min.

In hospitalized patients, there is a worsening in the renal function due to the decompensation caused by the heart failure. Therefore, when the patient reaches stage NYHA class IV and heart failure becomes refractory to the treatment, the six-month mortality rate increases to 50% [1].

## 2. DEFINITION OF CARDIORENAL SYNDROME

The kidneys and the heart work together to regulate the volume of extracellular fluid, natriuresis, cardiac output, arterial pressure, and glomerular filtration rate.

This relation also becomes clear in the pathologic states, where the dysfunction of both organs coexists. The term “cardiorenal syndrome” has recently been coined [4], and it is defined as the set of clinical situations characterized by the existence of a heart condition that leads to organic renal damage or to renal dysfunction, or as the existence of a kidney condition that leads to organic heart damage or cardiac dysfunction. Therefore, these two organs affect each other and the damaging effects are promoted and receive mutual feedback, so that the progression of the damage in the kidneys and the myocardium quickens.

There are five types of cardiorenal syndrome, but the same patient can evolve from one type to another [3,4], as we describe in **Table 1**.

**Table 1.** Different types of cardiorenal syndrome.

CARDIORENAL SYNDROME	NAME	DESCRIPTION
TYPE 1	Acute cardiorenal syndrome	It appears after an abrupt worsening of cardiac function, mainly due to the acute decompensation of the chronic heart failure.
TYPE 2	Chronic cardiorenal syndrome	It is characterized by the chronic and progressive deterioration of renal function due to chronic heart failure.
TYPE 3	Acute renocardiac syndrome	It consists of acute heart disorder (acute heart failure, arrhythmia or ischemia) in the context of an acute kidney failure.
TYPE 4	Chronic renocardiac syndrome	It is characterized by the development of a chronic heart disease (with hypertrophy and left ventricular dysfunction, especially diastolic), and an increased risk of adverse cardiovascular events in the context of chronic kidney disease.
TYPE 5	Secondary cardiorenal syndrome	Both organs are affected simultaneously. It usually appears as a consequence of systemic diseases such as sepsis, vasculitis or amyloidosis, because the underlying disease causes a simultaneous failure of both organs.

### 3. PATHOPHYSIOLOGY

The simultaneous failure of heart and kidney, which is characteristic of cardiorenal syndrome, is associated with several pathophysiological mechanisms.

#### 3.1. Low Cardiac Output

A decrease in cardiac output such as what has been observed in heart failure causes a progressive deterioration of the glomerular filtration rate. Therefore, an inadequate renal blood flow or a decrease in the renal perfusion pressure lead to a release of *tensin* by the juxtaglomerular cells, with the resulting activation of the RAAS, which leads to the retention of sodium and water, the contraction of the renal afferent arterioles (thus causing a decrease in glomerular perfusion) and an increase in cardiac, vascular and renal fibrosis [2].

#### 3.2. Increase of Central and Intraabdominal Venous Pressure

Cardiac output depends on the existence of a sufficiently large pressure gradient through the capillary bed. In patients with heart failure, the increase in central venous pressure reduces the pressure gradient in the glomerular capillary network, which limits the renal blood flow and leads to a deterioration of the renal function.

When there is an increase of the intra-abdominal pressure, there is an increase in the pressure of renal veins, which leads to a phenomenon similar to the increase of the central venous pressure, which in turn results in the deterioration of the renal function [3,4].

#### 3.3. Hyperactivity of the Sympathetic Nervous System

An increase in the systolic dysfunction of the left ventricle leads to a decrease in the renal blood flow and the renal perfusion pressure, which causes an activation of

the renal sympathetic nerves and the release of catecholamines, which result in a decrease of glomerular filtration.

#### 3.4. Oxidative Damage and Endothelial Dysfunction

Neurohormones trigger and mediate an oxidative damage cascade that leads to endothelial dysfunction, inflammation and cell death in cardiorenal syndrome.

### 4. TREATMENT OF THE CARDIORENAL SYNDROME

#### 4.1. Loop Diuretics

The treatment of patients with type 1 or type 2 cardiorenal syndrome is extremely complicated, because the most important objectives are an improvement of cardiac function and the relief of the symptoms derived from the volume overload. This can be tried with the use of loop diuretics. However, diuretics are not always effective, because the decrease in renal perfusion prevents it from reaching its working site in the nephron, thus reducing its pharmacological action. This leads to a worsening of the heart failure and further reduces cardiac output, which means that this resistance to diuretics can lead to death. This happens when the ejection fraction drops below 35% [2].

This is the reason why other therapies need to be implemented, such as extracorporeal ultrafiltration or peritoneal dialysis which improve the clinical state and reduce the hospitalization rate, although they cannot reduce the mortality rates for this entity [5].

#### 4.2. Extracorporeal Ultrafiltration

Extracorporeal ultrafiltration, either by itself or combined with hemodialysis, is an optimal treatment to treat short-term volume overload. This technique can improve the

heart function by reducing the preload and eliminating neurohormonal substances. However, this technique presents the disadvantage that a fast and intermittent elimination of fluid is associated with hypotension, coronary ischemia and arrhythmias, which leads to a worsening of cardiovascular function [4]. Therefore, a more gradual elimination of the extracellular fluid is preferred, and in this case peritoneal dialysis can play a much more important role in acute cases and in long-term treatments.

### 4.3. Peritoneal Dialysis

This technique represents an optimal treatment to combat decompensate cardiac failure as a long-term therapy in patients with refractory heart failure with or without advanced chronic kidney disease; and also as a temporary support therapy until a heart transplant is performed (the only definitive treatment for type 1 and 2 cardiorenal syndrome).

Peritoneal dialysis can reduce the weight of the patient, volume overload and edema, which means that the heart function improves, and also the symptoms of hydric overload, hyponatremia and renal function, thus reducing the resistance to diuretics.

Therefore, the admission time is reduced [6,7], and so is the number of drugs used, while the quality of life significantly improves.

This technique provides considerable advantages compared with extracorporeal ultrafiltration of the dialysis, such as the fact that the fluid elimination is gradual and takes place over long periods of time, there is no need for anticoagulation and there is a possibility of an ambulatory treatment [8,9].

When the technique is implemented in a situation of acute heart decompensation, low volumes must be used (750 to 1000 mL), and the dialysis must be changed often (approximately every 1 - 2 hours), with dialysis solutions based on icodextrin (a glucose polymer with a high ultrafiltration potential) or hypertonic glucose, in order to prevent complications, such as the pericatheter leakage of peritoneal fluid [10,11].

In long-term treatments, both intermittent peritoneal dialysis and continuous ambulatory peritoneal dialysis may be used [11]. However, this last technique offers more advantages to the patients, because it provides hemodynamic stability and the slow and gradual control of nitrogen products [12].

The dialysis scheme must be adapted to the needs of each patient and it must take into account the peritoneal transport, the residual renal function, the degree of heart deterioration, the need of control of nitrogen products, the frequency of admissions caused by heart decompensation and the response to ultrafiltration [13].

It is recommended to start with continuous ambulatory peritoneal dialysis with solutions of hypertonic glucose

with short cycles and, once that the behavior of the peritoneal membrane has been assessed, this technique can be maintained or, if the patients present residual renal function or they do not need to eliminate nitrogen products, it can be replaced by automatic peritoneal dialysis with hypertonic glucose-based solutions or a night cycle of icodextrin two or three times per week [14].

In patients who do not present residual renal function and who, therefore, also need to eliminate nitrogen products, the most adequate option would be ambulatory continuous dialysis, with a night cycle of icodextrin or an automatic dialysis and the use of icodextrin in a cycle during the day [14].

The use of peritoneal dialysis in the treatment of cardiorenal syndrome is not without its complications. The amount and speed of the elimination of volume overload is less predictable than with extracorporeal ultrafiltration. Other complications are related to the insertion of a Tenckhoff catheter, pericatheter leakage, wall hematomas, surface or deep hemorrhage or peritonitis [12].

## 5. CONCLUSION

Patients who suffer from type 1 or type 2 cardiorenal syndromes present an inadequate response to high doses of diuretics, which means that other techniques are required, such as extracorporeal ultrafiltration and peritoneal dialysis. This last technique has some advantages compared with ultrafiltration, such as a higher preservation of residual renal function, a steady and slow extraction of extracellular fluid, which provides higher hemodynamic stability, a better clearance of molecules that depresses the myocardial function, a reduction of systemic inflammation, the possibility of implementing ambulatory treatment and lower costs. These advantages make this modality of dialysis the treatment of choice for cardiac failure refractory to diuretics and types 1 and 2 cardiorenal syndromes.

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