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## CARDIOVASCULAR COMPLICATIONS IN DIALYSIS

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### Abstract

An increasing number of patients require renal replacement therapy through dialysis and renal transplantation. Chronic kidney disease (CKD) affects a large percentage of the world's population and has evolved into a major public health concern. Patients in advanced stages of CKD have varying degrees of cardiovascular damage. Comorbidities of these patients, include, on the one hand, hypertension, hyperlipidemia, hyperglycemia, hyperuricemia and, on the other hand, the presence of mineral-bone disorders associated with CKD and chronic inflammation, which contribute to cardiovascular involvement. Acute complications occur quite frequently during dialysis. Among these, the most important are cardiovascular complications, which influence the morbidity and mortality rates of this group of patients. Chronic hemodialysis patients manifest acute cardiovascular complications such as intradialytic hypotension, intradialytic hypertension, arrhythmias, acute coronary syndromes and sudden death.

**Keywords:** Chronic kidney disease, hemodialysis, intradialytic hypotension, high blood pressure, arrhythmia, unstable angina, acute coronary syndrome, sudden death

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### 1. Introduction

Chronic kidney disease (CKD) represents a public health concern as it affects over 50 million people worldwide, and is more and more commonly encountered, especially due to the increased incidence of high blood pressure (HBP) and diabetes mellitus (DM). Over 1 million CKD patients require renal replacement therapy (RRT) through dialysis and renal transplantation [1]. DM, HBP and a family history of kidney failure are all major risk factors for CKD [2, 3]. Official data in the USA reported over 661,000 patients with advanced stage CKD, out of which 468,000 receive RRT through dialysis and 193,000 have a functional kidney transplant [4, 5].

Cardiovascular disease (CVD) is the major cause of morbidity and mortality in patients with end-stage renal disease (ESRD) on hemodialysis (HD). Since ESRD frequently results from hypertension and diabetes mellitus, the increased CVD risk in these patients has been assumed to be the result of these underlying diseases. Nevertheless, it has been elucidated how ESRD represents per se a CVD risk factor independently by both hypertension and diabetes mellitus [6, 7]. CVD is present in >50% of patients undergoing dialysis and the relative risk of death due to CVD events in HD patients is reported to be 20 times higher than in the general population. In fact, in patients on renal replacement therapy (RRT) the prevalence of coronary heart disease and ventricular hypertrophy has been described to be 40% and 70%, respectively [8]. The acute complications occur quite frequently during dialysis, and are caused by complex mechanisms, which are insufficiently known. Among these, the most important are cardiovascular complications, which influence the morbidity and mortality rates in this group of patients [5].

### 2. Cardiovascular complications of hemodialysis

Advanced stage CKD is associated with the increased risk of cardiovascular affection. Thus, in the case of chronic dialysis patients, cardiovascular

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disease is identified in a large percentage of patients. An important role in its onset, in addition to factors such as mineral bone disease and patient comorbidities (e.g., HBP, hyperlipidemia, hyperglycemia, homocysteine, hyperuricemia), is chronic inflammation [9, 10].

Research particularly described a smaller total antioxidant capacity (TAC) in healthy controls than in diabetic hemodialysis patients; oxidative stress is one of the main factors leading to the onset of CKD in this group of patients [11]. Acute intradialytic cardiovascular complications besides chronic cardiovascular affection are identified in chronic hemodialysis patients.

**Table 1. Cardiovascular complications**

Cardiovascular complications
1. Intradialytic hypotension
2. High blood pressure
3. Arrhythmias
4. Acute coronary syndrome (unstable angina/myocardial infarction)
5. Sudden death

### 3. Intradialytic hypotension

IDH is quite commonly encountered. It has an impact on the quality of lives of these patients, on the cost of dialysis and is associated with mortality. There is no clear definition of IDH; two factors are taken into account in clinical practice: The decrease in systolic pressure under 90 mmHg or the symptomatic intradialytic decrease in systolic pressure by more than 20 mmHg compared to the value from the beginning of dialysis. Studies have demonstrated the strong association between the decrease in systolic pressure under 90 mmHg during dialysis in over 30% of treatments and an increase in mortality [12, 13]. Patients of advanced age ( $\geq 65$ ), with diabetic nephropathy, cardiovascular illnesses, or autonomic dysfunction, are at risk for developing IDH [1, 6, 8].

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Furthermore, clinical features such as low blood pressure levels before hemodialysis session (<100 mmHg), poor nutritional status (hypoalbuminemia), or severe anemia also predispose chronic dialysis patients to IDH occurrence [14].

There are several groups of risk factors for IDH onset, and they concern the patient, the dialysis machine or the medical manoeuvres (iatrogenic factors). Hemodialysis patients with direct or indirect cardiovascular affectation, that is to say elderly patients undergoing dialysis for a long time, diabetic patients, patients with low arterial pressure prior to dialysis, patients with systemic infections, arrhythmias, valvulopathy, myocardial infarction, hemorrhage, or patients with hypoalbuminemia are predisposed to IDH [15, 16]. Most researchers concur that IDH frequently occurs during dialysis, when large volumes of fluid are removed within one session. Rapid ultrafiltration then fails to elicit compensatory cardiovascular (CV) responses, such as vasoconstriction and rising cardiac output, while the combination of inadequate peripheral vascular tone and plasma refilling insufficiency leads to the drop of BP [3].

**Table 2. Different definitions of intradialytic hypotension.**

	Decrease in SBP (mmHg)	Decrease in MAP (mmHg)	Symptoms or need for intervention
KDOQI clinical practice guidelines (2005)	$\geq 20$	$\geq 10$	Symptoms.
European Best practice (2007)	$\geq 20$	$\geq 20$	Symptoms and intervention.
UK renal association guidelines (2011)	Any	Any	Immediate intervention

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### 4. Intradialytic hypertension

Intradialytic hypertension (HBP) has been defined as an increase in intradialytic systolic pressure by  $\geq 10$  mmHg compared to pre-dialysis systolic pressure and it has been confirmed to be associated with increased mortality in dialysis patients [17]. Some patients develop HBP during the last part of the dialysis session, a moment when the hydric excess has been ultrafiltered. The frequency of intradialytic HBP varies, even in the same patient, and the mechanisms are not clear; there are proofs related to the alteration of the nitric oxide/endothelin-1 balance and/or endothelial dysfunction [18]. Hypertension promotes cardiovascular stiffening, which impairs left ventricular (LV) diastolic function, and contributes to an overall increased risk for cardiovascular comorbidities such as heart failure, myocardial infarction and stroke. Hypertension is an extremely common (~90%) syndrome in patients with end-stage renal disease on hemodialysis, and contributes to a higher risk of cardiovascular morbidity and mortality in these patients [19, 20].

### 5. Arrhythmias

Hemodialysis patients quite frequently present with hydroelectrolytic and acid base imbalances both during and between treatment sessions, which can cause heart rhythm disorders. In 2013, United States Renal Data System (USRDS) reported a mortality rate of 198/1,000 patients/year, 40% of the deaths having a cardiovascular cause. Among the cardiovascular causes, 26% were cardiac arrhythmias [21]. In addition, atrial fibrillation (AF) was the most commonly found heart abnormality in clinical practice and affected more hemodialysis patients than the general population, with percentages varying between 14% and 27% [22]. The Framingham Study reported an incidence of 0.2% per year for AF in the general population, for 20 years. In comparison, the Afi incidence in the hemodialysis patients reaches 1.25 episodes/100 patient-year [21,22].

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Cardiac rhythmic abnormalities, especially AF, occur in 7-27% of all ESRD patients and increase over higher dialysis vintage [26]. Thromboembolic events (cerebrovascular accidents) and the preload reduction from AF might precipitate hemodynamic alterations and myocardial ischemia, leading to adverse prognosis. Development of AF in dialysis patients is associated with more hospitalization, CV events, and poorer survival. Incident AF also impairs renal prognosis in CKD patients [23, 26].

Intradialytic arrhythmias are generated by hydroelectrolytic and acid base disorders which occur quite frequently in the dialysis patients; all of these, along with the composition of the dialysate, create an 'arrhythmogenic environment'. On the other hand, dialysis patients present cardiovascular comorbidities, such as myocardial ischemia and secondary anemia, which increase the risk for intradialytic arrhythmias [23]. A range of acid-base (pH) and electrolytic (especially in potassium, calcium and magnesium) changes, causing prolongation of the QT interval and associated with an increased risk of arrhythmias occur in the dialysis patients, both during and post-dialysis [24]. Dialysis patients can develop atrial fibrillation during dialysis. The risk factors for the onset of Afib in these patients include ischemic coronary disease, old age, enlarged left atrium, the value of systolic pressure before the beginning of dialysis and the presence of peripheral vascular disease [21, 22].

### 6. Acute coronary syndrome

CKD is associated with a high death risk of cardiovascular pathology. Most often patients with CKD have an acute myocardial infarction as the initial manifestation of ischemic heart disease, without previous signs of stable angina [24]. SCD accounted for approximately 25% of all deaths in dialysis patients in the 2010 United States Renal Data System (USRDS) report. Findings in a post-hoc analysis of the EVOLVE trial, a large randomized study enrolling

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3883 hemodialysis patients, were similar- cardiovascular causes were responsible for 54% of deaths and SCD accounted for 24,5% [25].

There are several types of CHD risk factors in the dialysis patients. In this respect, CHD onset can be favored by traditional risk factors or by uremia-related risk factors. The traditional risk factors include: DM (54%), low serum high density lipoprotein (HDL) cholesterol (33%), HBP (96%), HVS diagnosed by electrocardiographic criteria (22%), sedentary life style (80%), old age, and smoking [23, 24]. CKD is an independent CHD risk factor. Uremia and hemodialysis as treatment methods increase oxidative stress and the production of proinflammatory factors, and so creates a favorable environment for the fast development of atherosclerosis [24].

### Conclusion

Intradialytic cardiovascular complications are commonly encountered in clinical practice and influence the quality of life, such as morbidity and the mortality rate of dialysis patients. In order to have detailed knowledge concerning the risk factors and the pathogenic mechanisms and to ensure an optimal management of these complications, more studies must be conducted.

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