

Hypertension and the kidney

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PATHOGENESIS OF HYPERTENSION IN KIDNEY DISEASE

- Hypertension is a frequent finding in both acute and chronic kidney disease, particularly with glomerular or vascular disorders .
- The pathogenesis and preferred treatment of hypertension vary with the type of renal disease and its duration.

PATHOGENESIS OF HYPERTENSION IN KIDNEY DISEASE

- **Acute glomerular disease:**
 - *Patients with acute glomerular disease, and nephrotic syndrome*

Pathogenesis

Experimental studies of the nephrotic syndrome or glomerulonephritis suggest **that sodium retention** in these disorders is due to increased reabsorption in the collecting tubules

Collecting duct abnormalities

Two different abnormalities in collecting tubule function have been identified:-

- ✓ *Relative resistance to atrial natriuretic peptide*
- ✓ *increased activity of the Na-K-ATPase pump in the cortical collecting tubule but not in other nephron segments*

- **Acute vascular disease:-**
- *Examples: vasculitis or scleroderma renal crisis.*
pathogenesis: ischemia-induced activation of the renin-angiotensin system rather than volume expansion

Chronic kidney disease

- Hypertension is present in approximately 80 to 85 percent of patients with CKD
- Data from the Modification of Diet in Renal Disease Study, for example, showed that the prevalence of hypertension rose progressively from 65 to 95 percent as the GFR fell from 85 to 15 mL/min per 1.73 m²

factors that contribute to the increased prevalence of hypertension in patients with CKD:

- Sodium retention is generally of primary importance
- Increased activity of the renin-angiotensin system
- enhanced activity of the sympathetic nervous system
- Secondary hyperparathyroidism raises the intracellular calcium concentration, which can lead to vasoconstriction and hypertension
- Impaired nitric oxide synthesis and endothelium-mediated vasodilatation
- Patients with end-stage renal disease (ESRD) are more likely to have an increase in central pulse pressure and isolated systolic hypertension
Why this occurs is incompletely understood, but increased aortic stiffness probably plays an important role.

Treatment of hypertension in patients with CKD

BP goal <130/80 mm Hg
(Class I)

Albuminuria
(≥ 300 mg/d or ≥ 300 mg/g
creatinine)

Yes

No

ACE inhibitor
(Class IIa)

Usual "first-line"
medication choices

ACE inhibitor
intolerant

Yes

No

ARB*
(Class IIb)

ACE inhibitor*
(Class IIa)

UPT

algorithm on management of hypertension in patients with CKD

9.3. Chronic Kidney Disease

Recommendations for Treatment of Hypertension in Patients With CKD References that support recommendations are summarized in Online Data Supplements 37 and 38 and Systematic Review Report.		
COR	LOE	Recommendations
I	SBP: B-R ^{SR}	1. Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg (1-6).
	DBP: C-EO	
IIa	B-R	2. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥ 300 mg/d, or ≥ 300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression (3, 7-12).
IIb	C-EO	3. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥ 300 mg/d, or ≥ 300 mg/g albumin-to-creatinine ratio in the first morning void]) (7, 8), treatment with an ARB may be reasonable if an ACE inhibitor is not tolerated.

SR indicates systematic review.

Hypertension in dialysis patients

EPIDEMIOLOGY

- ✓ Hypertension is a common finding in dialysis patients
- ✓ Prevalence estimates vary widely among studies because of differences in the *definition of hypertension* and in *methods of measuring* blood pressure.
 - some reports up to 85 percent in hemodialysis patients
 - 30 percent of peritoneal dialysis patients

- **EPIDEMIOLOGY**

- In one multicenter trial that included 2535 adult hemodialysis patients, the prevalence of hypertension, defined as *one-week average predialysis systolic BP measurements 150 mmHg or,*
- *diastolic BP 85 mmHg or*
- *the use of antihypertensive medications,*
- *was 86 percent .*
- Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States.
Am J Med. 2003;115(4):291.

Intradialytic hypertension

Defenition

- Intradialytic hypertension is a condition where there is an increase in blood pressure (BP) from pre- to posthemodialysis
- intradialytic hypertension is defined as:-
- *an increase in systolic blood pressure ≥ 10 mmHg from pre- to post-hemodialysis. (Am J Kidney Dis 2011;58:794–803.)*

Intradialytic hypertension

- *Epidemiology*
- Over the course of 6 months, intradialytic hypertension occurred in over 90% of the patients at least once.

Intradialytic hypertension

- **clinical significance**
- among hypertensive hemodialysis patients, those with intradialytic hypertension appear to have some of the worst outcome.
- observational analysis showed that:-
- *compared to patients whose systolic BP decreased by at least 10 mm Hg from pre- to post-hemodialysis, those with increases in BP of that magnitude had a higher odds ratio for hospitalization or mortality after 6 months .*
- In a cohort of more than 100,000 hemodialysis patients followed for more than 5 years, a mean systolic BP decrease of 14 mm Hg represented the group with the best survival
- ***This important study highlights the risk associated with intradialytic hypertension and the need to identify the underlying mechanism responsible for it.***

Intradialytic hypertension

➤ Extracellular Volume Overload:-

-The paradoxical' increase in BP was related to dynamic changes in the cardiac output during dialysis

Reduction in end-diastolic volume that occurred through the process of ultrafiltration enabled BP to increase along with cardiac output.

The conclusion of a study published in *Nephrol Dial Transplant 2010* showed that the phenotype of intradialytic hypertension could be modified through adjustment in dry weight over time.

The findings demonstrated that those patients with BP increases during dialysis had higher ratios of extracellular water to total body water. These studies collectively support the practice that the initial approach to patients with intradialytic hypertension should include reassessment of dry weight.

In other study published in *Kidney Int 2015* showed that those patients with BP increases during dialysis had higher ratios of extracellular water to total body water

Intradialytic hypertension

- Vasoconstriction

in a study by Chou et al (*Kidney Int 2000*) the authors found there was a significant increase in vascular resistance from pre- to posthemodialysis in the intradialytic hypertension patients, also

there were no significant differences in the change in cardiac output.

These authors and others have sought to identify specific mediators of the increase in BP that may be related to endogenous vasoconstrictive pressors.:

- no evidence that surges in sympathetic nervous system activity or

- in renin-angiotensin-aldosterone system activity

They did find, however, imbalances in endothelial cell-derived mediators after dialysis in the intradialytic hypertension patients. Specifically endothelin-1 (ET-1)

Further studies showed that endothelial cell dysfunction appears to be greater in intradialytic hypertension patients.

the most recent research has focused on specific mechanisms by which the endothelial cells influence intradialytic BP.

Intradialytic hypertension

- Dialysate Sodium
- It was shown that low-dialysate sodium concentration (7% lower than serum) causes intradialytic hypotension with extracellular volume removal that exceeds the total fluid removed during hemodlysis . Movement of fluid from the extracellular space to the intracellular space accounted for the additional extracellular fluid loss

Intradialytic hypertension

- Dialysate Sodium
- One randomized crossover study investigated how dialysate sodium modification affected BP in patients with a history of recurrent intradialytic hypertension (*Am J Kidney Dis* 2015)
 - In this study, both serum sodium and BP measured throughout the dialysis treatment were much higher when subjects were exposed to high-dialysate sodium (pre-dialysis serum sodium + 5) compared to low dialysate sodium (pre-dialysis serum sodium – 5)
 - Evidence in endothelial cell culture show that high extracellular sodium concentration impairs nitric oxide release with higher ET-1

Management of intradialytic HTN

- ***Achieving optimal dry weight***
- Reducing the target dry weight can normalize the BP or make the hypertension easier to control in the great majority of dialysis patients.
- *the best definition of dry weight is the lowest tolerated postdialysis weight at which there are minimal signs or symptoms of either hypovolemia or hypervolemia*
- Patient history and physical examination are generally used to determine the optimal target dry weight.

Management of intradialytic HTN

- Methods to more accurately assess dry weight include :
 - Bioimpedance plethysmography
 - Measurement of the inferior cava diameter
 - plasma natriuretic peptides (particularly atrial and B-type) concentrations.

How to reduce target dry weight

The reduction in dry weight is best done gradually (over days to weeks), attempt 0.2 L per session The best way to limit interdialytic weight gain is to limit salt intake, (1500 to 2000 mg of sodium/day)

Increasing the length or frequency of sessions is often effective in reducing target dry weight

Management of intradialytic HTN

- **Reduce dialysate sodium**

The dialysate sodium should be reduced gradually (ie, 1 mEq/L every three to four weeks) to approximately 136 mEq/L.

- **Drugs**

In a 12-week pilot study, the initiation of carvedilol titrated to 50 mg twice daily was associated with a decrease in the frequency of intradialytic hypertensive episodes from 77 to 28 percent of hemodialysis session

carvedilol blocks endothelin-1 release,

Intradialytic hypotension (IDH)

Intradialytic hypotension (IDH)

- **INTRODUCTION**

_Hypotension during hemodialysis is common. In some patients, the development of hypotension necessitates intravenous fluid replacement before patients are able to safely leave the dialysis unit. Intradialytic hypotension may reduce the efficacy of the dialysis procedure and contributes to the excessive morbidity and mortality that is associated with hemodialysis.

Intradialytic hypotension (IDH)

- **DEFINITION OF INTRADIALYTIC HYPOTENSION**

There is no generally accepted definition of intradialytic hypotension (KDOQI) and European Best Practice Guidelines define intradialytic hypotension as

the presence of a decrease in systolic blood pressure ≥ 20 mmHg or a decrease in mean arterial pressure by 10 mmHg, provided that the decrease in blood pressure is associated with clinical events and need for nursing interventions .

Intradialytic hypotension (IDH)

- ***Incidence of IDH***

- In reviews, a 20% incidence of intra-dialytic hypotension is widely cited
- 75 percent of patients had at least one episode of intradialytic hypotension
- ***risk factors:***
 - old age, longer dialysis vintage, diabetes, lower predialysis blood pressure, female gender, Hispanic ethnicity, and higher body mass index, hyperphosphataemia, presence of coronary artery disease

Intradialytic hypotension (IDH)

- Ultrafiltration,
- erroneous target weight, and reduction in osmolality
- *Autonomic dysfunction*: occurs in over 50 percent of patients on maintenance dialysis
 - Mechanisms that prevent the homeostatic responses include:
 - Downregulation of alpha-adrenergic receptors, which diminishes the hemodynamic response to endogenous catecholamines .
 - A paradoxical decrease in sympathetic and increased parasympathetic nervous system activity during ultrafiltration

Intradialytic hypotension (IDH)

- Decreased cardiac reserve e.g ;
 - heart failure, cardiomegaly, or ischemic heart disease

(These conditions lead to poor left ventricular performance and a diminished cardiac reserve in the setting of a hemodynamic challenge.)

Intradialytic hypotension (IDH)

- **CLINICAL PRESENTATION** —
- Although occasionally asymptomatic, patients with hypotension usually have; lightheadedness, muscle cramps, nausea, vomiting, and dyspnea.
- Vagal symptoms, including yawning, sighing, and hoarseness, may be observed before the drop in blood pressure is detected

Intradialytic hypotension (IDH)

- **ACUTE MANAGEMENT**

- Ultrafiltration rate should be decreased or stopped, depending upon the severity of hypotension.
- The patient should be placed in the Trendelenburg position
- give an intravenous fluid bolus of 250 to 500 mL. (isotonic saline is commonly used . May use (hypertonic glucose, 5 percent dextrose, or albumin solutions)
- Oxygen should be administered

Intradialytic hypotension (IDH)

- *PREVENTION OF RECURRENT EPISODES*
- *Reassess target weight*
- *Avoid food during dialysis*
- *Withhold antihypertensive agents*
- *Limit interdialytic sodium intake*
- *Review dialysate composition*
- *Use of cool dialysate*
- *Increasing dialysis time*
- *Drugs (midodrine)*

Intradialytic hypotension (IDH)

- **OUTCOMES**
- Intradialytic hypotension has been associated with *increased mortality*
- High ultrafiltration rates (>13 mL/hour/kg) have also been associated with *increased cardiovascular mortality risk in hemodialysis patients*
- *Recommended UF rate of no greater than 13 mL/hour/kg*

Thanks