

Hypertension in HD Patients

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HTN is **common** among **dialysis** patients.

Prevalence **estimates vary widely** due to

Differences in the definition of HTN
&

Methods of measuring BP (either before & after dialysis or using ambulatory BP recordings).



50 to 85% of HD patients & 30% of PD patients are hypertensive.

In one multicenter trial that included 2535 adult HD patients,
the prevalence of HTN, (defined as one-week average predialysis systolic BP 150 mmHg or diastolic BP 85 mmHg or use of antihypertensives) was 86%.

80% Of patients who are just initiating dialysis had HTN due to overloaded.

HTN often reflects inadequate volume control.

PATHOGENESIS



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Volume expansion **major cause** (supported by studies that have shown improvement in BP with volume reduction). Removal of the

excess Na & reduction in target dry weight can result in the normalization of BP in >60% of & in many PD patients.

In combination of

A **rise in cardiac output** &

High systemic vascular resistance.

Sympathetic overactivity,

Activation of the RAAS, &

Arteriosclerosis

Changes in **endothelium-derived vasoactive peptides**,

Increases in intracellular Ca,

Decreases in renalase (Renalase is a catecholamine-metabolizing enzyme released by the kidney in response to catecholamine surge).

ESAs, NSAIDs, illicit drugs such as **cocaine**, and **herbal remedies** such as ma-huang and St. John's wort.

DIAGNOSIS

ABPM is the **gold standard** &
Correlates with outcomes.



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Another way is **self-recorded home BP monitoring**

that is **efficient, accurate & correlate with ABPM** & outcomes.

Check home BP readings **twice daily** for (at least) **4 days** after the **mid-week dialysis treatment**.

The **optimal frequency** of monitoring **is not known**.

Pre- & postdialysis BP measurements don't be recommended, because

**Correlate only weakly with ABPM &
Associate inversely with outcomes.**

Predialysis BP readings tend to **overestimate** &
Postdialysis readings **underestimate** BP
readings obtained by **ABPM**.

ABPM & self-recorded home measurement are directly related to all-cause mortality.

ABPM is best performed over 44 hours during the interdialytic period.

ABPM generally shows a linear increase in BP as volume accrues.

Another way to diagnosis is to use median intradialytic systolic BP.

In a HD patient who dialyzes Monday-Wednesday-Friday, if the systolic BP is 146 mmHg on Wednesday, (in our country Monday) the patient is very likely to be hypertensive.

In one study, the **midweek median intradialytic BP of 140 mmHg** was **approximately 80% sensitive & approximately 80% specific in diagnosing HTN among dialysis patients.** (For median diastolic BP of 80 mmHg, the **sensitivity & specificity** was approximately 75% each.)

Albeit, median intradialytic systolic BP has wide limits of agreement with 44-hour ambulatory systolic BP ranging from 16 to 20 mmHg.

BENEFITS OF TREATING HTN



Multiple studies & meta-analyses of RCTs in have suggested a benefit of using antihypertensives to lower BP on **cardiovascular- events & mortality.**

The best data are from two meta-analyses:

A **2009** systematic review & meta-analysis of **eight** RCTs that enrolled **1679** dialysis patients found that **lowering BP** with antihypertensive therapy was associated with **decreased risks of:**

- Cardiovascular events** (RR 0.71, 95% CI 0.55-0.92),
- All-cause mortality** (RR 0.80, 95% CI 0.66-0.96), and
- Cardiovascular mortality** (RR 0.71, 95% CI 0.50-0.99).



A second 2009 meta-analysis including five randomized trials

1202 HD patients showed that, **compared with placebo or control therapy, BP lowering with antihypertensive therapy resulted in a 31% reduction in the risk of cardiovascular events**

(pooled HR 0.69, 95% CI 0.56-0.84).

TREATMENT



BP target

The **threshold BP** that should be **treated is not known**. BP target ranges for dialysis patients have been **extrapolated** from studies in the **nondialysis** patients. According to these data target an **interdialytic self-measured home BP of <140/80 mmHg**.

If **interdialytic** self-measured home BP is not available, targeting a **median midweek BP of <140/80 mmHg** appears to be a reasonable alternative strategy.

Calculate the median midweek BP from all the BPs measured during a midweek dialysis session (eg, on Wednesday for a patient receiving dialysis on Mondays, Wednesdays, and Fridays). **Do not** use a **predialysis** BP target to control HTN.

In an observational study of 150 HD patient
BP was recorded by 3 methods:



- Pre- & post-dialysis BP by routine automated oscillometric recordings;
- 44-hour ambulatory BP by monitoring during the midweek interdialytic interval
- Home BP by self-measurement over one week.

The BPs obtained by **home & ambulatory monitoring** (as opposed to those obtained pre- and post-dialysis) **were associated with mortality.**

Home systolic BP of 125 to 145 mmHg &
Ambulatory systolic BP of 115 to 125 mmHg
appeared to be associated with the **lowest risk of mortality.**

Similar findings were noted in another observational study in which

Home systolic BP of 120 to 130 mmHg &
Ambulatory systolic BP of 110 to 120 mmHg
were associated with the **lowest mortality.**

Targeting predialysis BPs is not helpful. As an example, one pilot trial evaluated the target predialysis BP in dialysis patients. The trial randomly assigned 126 long-term HD patients to one of two BP goals:

An intensive arm (predialysis systolic BP of 110 to 140 mmHg) &

A standard arm (predialysis systolic BP of 155 to 165 mmHg).

Those in the intensive arm had a **higher risk of recurrent hospitalization, vascular access thrombosis, & intradialytic hypotension.**

Thus, until trial data becomes available, **targeting a BP of <140/80 among dialysis patients is reasonable. Self-measured home BP to achieve this target is better.**

Treatment



-Reducing the target dry weight to achieve euvolemia
&

-Antihypertensive medications • If possible, the target dry weight should be adjusted before antihypertensive agents are added.

Achieving optimal dry weight

gradually can **normalize** the BP or make the HTN easier to control. The exact definition of target dry weight remains uncertain.

The **best definition** is the **lowest tolerated postdialysis weight** at which there are **minimal signs or symptoms** of either **hypovolemia** or **hypervolemia**.



Assessment of volume status



-History & Ph exam

-**Orthostatic hypotension** (such as **lightheadedness** & occasionally **muscle cramps**) might indicate that the dry weight is **below desired**.

-Increased **JVP**, peripheral or pulmonary edema, & ascites.

-**Bioimpedance**, relative plasma volume (**RPV**) monitoring, **IVC** diameter, & plasma **ANP** & **BNP**.

-An **emerging strategy** to assess volume excess is **lung ultrasound**. (At 12 mo, lung US-guided dry weight reduction was greater in the US group (-2 vs +0.5 kg), & a greater **decline** in 44-h ambulatory systolic (6 vs 0.5 mmHg) & diastolic (4 vs 1 mmHg) BP, US B lines (metric of lung water; -5 lines vs +6 lines), & rate of intradialytic hypotension.

How to reduce target dry weight

Is best done gradually (over days to weeks) by 0.5 L/session even in who are unable to tolerate, 0.2 L/session.

Patients should **avoid** large interdialytic weight gain (ideally <2 to 3 L) & who gains **5 liters in between** dialysis sessions will have **difficulty** achieving the previous target dry weight.

Limit **salt intake** (because drives **thirst**) to a restricted (**1500 to 2000 mg of Na/day**), but adherence to a low-sodium diet is often **suboptimal**.



Increase dialysis time

Length or frequency of sessions

which was demonstrated in a Tassin, France, 8 h, 3 times/week

that was associated with the

maintenance of normotension

without medications in almost all patients.

The improved BP was largely attributed to volume control,

Other factors:

-Decreased afferent renal nerve activity & efferent sympathetic activation.

-More frequent dialysis (nocturnal HD, 6 or 7 nights a week during sleep usually 6 to 12 hours in total). Almost all patients become normotensive without medications.

-Short daily HD may also be associated with better BP control.

Reduce dialysate Na.



Standard Na prescriptions leads to decreased Na loss during dialysis & increases PNa & volume overload & thirst.

Dialysate Na should be reduced **gradually** (ie, 1 mEq/L every three to four weeks) **to** **approximately 136 mEq/L.**



The dialysate Na may be reduced in a fixed or variable fashion.



A variable reduction was evaluated in one study. A programmed decrease in Na dialysate from 155 to 135 mEq/L was compared with the standard stable Na dialysate concentration of 140 mEq/L.

Postdialysis BP & antihypertensive use were reduced when patients were dialyzed with a variable Na prescription.

A lower dialysate Na in combination with Na restriction was evaluated in a study.

Hypertensive HD patients were dialyzed against a

gradually lowered Na dialysate (140 to 135 mEq/L at a rate of 1 mEq/L every three to four weeks) &

encouraged to limit salt intake to <6 g/day.

At study end, **MAP** was **lower**, &

antihypertensives were no longer required in half of patients.

Adherence was difficult, & the frequency of muscle cramps during dialysis & risk of hypotension was increased.

Antihypertensive medications



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First-choice is a beta-blocker, even among patients previously controlled with another agent.

Atenolol (In HD, post-dialysis thrice weekly) **is better** but other BBs are acceptable •

Start in HD at **25 or 50 mg to 100 mg thrice weekly** & PD patients up to **50 mg once daily.**

Side effects include symptomatic bradycardia
(eg, lightheadedness, presyncope or syncope, exercise intolerance).

Second-choice

Dihydropyridine CCB, such as amlodipine 10 mg dosed daily. CCBs are not cleared by dialysis.

Third-choice

ACEi or ARB.



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Preference for BBs (as the first-line) is based upon HDPAL (HTN in HD Patients Treated with Atenolol or Lisinopril) trial in which 200 patients. At 12 months, **compared with lisinopril, atenolol** led to A greater reduction in BP using the 44-h interdialytic ABPM (mean reduction -21/-13 versus -18/-10 mmHg) & the self-measured home BPs (mean reduction -25/-12 versus -19/-10 mmHg); these differences were not statistically significant.

Over the course of the trial **those in the atenolol group required fewer antihypertensive medications despite a lesser degree of reduction in their dry weight & fewer serious CV events** (cardiovascular death, MI, stroke, & hospitalization for heart failure) in the atenolol group (20 events among 16 patients versus 43 events among 28 patients), leading to **early termination** of the trial.

Preference for CCBs is based upon their **efficacy & tolerance** in addition to their **beneficial effect on CV** outcomes in dialysis patients. In one trial, compared placebo, **those on amlodipine** had a **reduction in the composite of all-cause mortality and CV events** HR 0.53, 95% CI 0.31-0.93.

Amlodipine led to a clinically meaningful but statistically nonsignificant reduction in **all-cause mortality** (12% with amlodipine and 17% with placebo).

Do not use
nondihydropyridine CCBs
(verapamil or diltiazem)
because drug interactions
& bradycardia.

ACEis & ARBs only use in patients who have an elevated BP **despite** maximally tolerated doses of BBs and CCBs. **This is because ACEis or ARBs lead to modest reduction in BPs and no reduction in fatal and nonfatal CV events.**

Additionally ACEis & ARBs can cause hyperkalemia, hypotension, reduction in the effect of ESA, & anaphylactoid reaction in patients dialyzed with an AN69 dialyzer, thereby lowering the overall appeal of these agents.

RESISTANT HYPERTENSION

Some dialysis patients are resistant to both volume control & antihypertensive medications.

Factors include:

- Nonadherence to the antihypertensive regimen
- NSAIDs or ESA
- Inadequate dialysis
- Renovascular HTN
- ADPKD



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If a treatable cause cannot be found, use from

Minoxidil

Central sympathetic agonists

[Methyldopa & Clonidine,

(Guanfacine may be less sedating)].



Renal denervation

is an experimental therapy in which sympathetic nerves innervating the kidney are ablated for BP control. This method was evaluated in a small nonrandomized trial of 24 HD patients who had resistant HTN.

Bilateral nephrectomy is
no longer performed ever
since effective
antihypertensive
medications became
available.



HTN DURING HD

Some patients develop **paradoxical HTN** in the **later stages of dialysis**, a time at which most of the **excess fluid has already been removed**. This problem is intermittent in a given patient with a **widely variable frequency**. The **pathogenesis is unclear**, although some evidence suggests that **altered nitric oxide/endothelin-1 balance** and/or **endothelial dysfunction** may contribute.

Carvedilol, blocks endothelin-1 release & may also be effective. In a 12-week pilot study, carvedilol titrated to 50 mg twice daily was associated with a decrease in the frequency of intradialytic hypertensive episodes from 77 to 28% of HD sessions.

Use of a dialysate Na
lower than the patient's
PNa may decrease BP
during dialysis.



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