

SECTION TWO:

Hypertension

Up to 90% of dialysis patients have elevated blood pressures. As in the general population, hypertension plays a major role in causing cardiac damage in ESRD patients. Daily dialysis can help to control blood pressure with fewer requirements for antihypertensive medications.

OVERVIEW

Hypertension (HTN) is an important independent risk factor for cardiac failure, and is a common problem in ESRD patients. Data from various studies indicate that 50% to 90% of patients with renal disease are hypertensive^{34,35}, and up to 90% of dialysis patients have a blood pressure greater than 140/90 mm Hg.^{36,37} In many patients, blood pressure does not decrease nocturnally as is normal. Therefore, hypertensive patients may be exposed to an increased blood pressure burden 24 hours a day.^{34,37}

Extra fluid and sodium accumulated by ESRD patients during interdialytic periods leads to increased blood pressure.^{38,39} Recent clinical and experimental studies indicate that sleep apnea^{40,41} and overactivity of the sympathetic nervous system responding to signals from the diseased kidneys^{34,37} also contribute to the development of HTN in ESRD patients. Elevated levels of parathyroid hormone, and asymmetric dimethylarginine may also be related to HTN.^{36,37} Experiments have demonstrated that both treatment time and dry weight reduction are important in normalizing blood pressure, suggesting that improved blood pressure control may be the result of more effective elimination of both excess fluid and vasoactive uremic factors.^{35,37,42,43}

HTN has been linked to development of left ventricular hypertrophy (LVH) and cardiac failure. Each 10 mm Hg rise in mean arterial blood pressure has been associated with an increased presence of LVH (OR 1.48, P=0.02) and the development of de novo cardiac failure (RR 1.44, P=0.007).⁴⁴ HTN also accelerates the decline in renal function in pre-dialysis patients.³⁷

Although many patients regularly take antihypertensive medications and restrict fluid intake to control blood pressure, non-compliance is high⁴⁵. The number and cost of antihypertensive medications can be a burden to patients. In addition, it is widely believed that the blood pressure medications themselves make blood

pressure control more challenging. Regardless of the cause, blood pressure remains too high in a significant number of patients.³⁴⁻⁴⁴

POTENTIAL BENEFITS OF MORE FREQUENT THERAPY

More frequent therapy reduces the interval between dialysis sessions, which in turn reduces the extent of fluid fluctuations resulting from interdialytic weight gains. This in itself can reduce blood pressure and may reduce overactivity of the sympathetic nervous system.

Although less well characterized, kinetics predict that certain vasoactive uremic factors that are cleared less efficiently than urea during conventional dialysis may be more effectively removed as therapy frequency and/or duration increases.

Patients on more frequent renal replacement therapies may discontinue or reduce the number of antihypertensive medications. This has potential clinical and economic benefits: it reduces the risk of side effects of such medications; decreases problems with compliance; and translates into lower treatment costs.

SUMMARY OF PUBLISHED RESULTS

Nearly all clinical studies have demonstrated a significant decrease in pre-dialysis blood pressure after patients start more frequent therapy, and fewer or no medications are required to maintain blood pressure in the acceptable therapeutic range. Both short daily and long nocturnal therapies appear to improve hypertensive status. When hypertensive patients were analyzed separately from the whole group of dialysis patients, there were greater declines in both systolic and diastolic blood pressure measurements.^{27, 46} Normalization of blood pressure in these studies was often accompanied by a regression of LVH and a decrease in episodes of sleep apnea.

Parameter Measured	Observations
Mean Blood Pressure	Reduced from 9.7% to 14%, 21-23, 27-30, 47-49
Systolic Blood Pressure	Reduced by 4.86% to 16.3% 9, 11, 18, 25, 27, 30, 46, 50-54
Diastolic Blood Pressure	Reduced by 4.6% to 12.5% 9, 11, 18, 25, 27, 30, 46, 50-55
Antihypertensive Medications	<p>From 20% to 85% of patients completely discontinued the use of antihypertensive drugs 6, 8, 11, 18, 22, 27, 29, 49, 52, 53, 56-58</p> <p>Significant percentage of patients decreased the number of pills and/or types of antihypertensive medications needed 5, 6, 8, 9, 11, 18, 21, 22, 25, 27-30, 47-49, 52-62</p>

TABULATED STUDY FINDINGS ON HYPERTENSION

Study & Design	Supporting Points
<p>Jaber, BL. Blood Purif. 2004; 22:481⁵⁴</p> <p>Daily HF 12 pts; 4 wk Prospective</p>	<ul style="list-style-type: none"> • Mean systolic blood pressures declined significantly from 143 ± 19 to 133 ± 16 mm Hg (p=0.002) • Mean diastolic blood pressures declined significantly from 79 ± 11 to 72 ± 12 mm Hg (p=0.002) • Mean number of blood pressure medications per day decreased from 2.1 to 1.1 (p=0.002)
<p>Lockridge Jr, RS. Hemodial Int. 2004; 8:61⁹</p> <p>Nocturnal HD 25 pts; 1-5 yr Prospective</p>	<ul style="list-style-type: none"> • Mean systolic/diastolic blood pressures declined significantly from 159/90 to 134/74 (p=0.003 for systolic and p=0.0001 for diastolic) • Mean number of blood pressure medications per day decreased from 2.15 to 0.73 (p=0.001)
<p>Reynolds, JT. Blood Purif. 2004; 22:320⁵⁵</p> <p>Daily HD 11 pts; 12 mo Prospective</p>	<ul style="list-style-type: none"> • Mean systolic blood pressures declined significantly from 153 ± 5.6 to 140 ± 6 mm Hg (p=0.017) • Mean diastolic blood pressures declined significantly from 79 ± 2.3 to 73 ± 2.9 mm Hg (p=0.022) • Mean number of blood pressure medications per day decreased from 2.0 to 1.0 (p=0.16)
<p>Williams, AW. Am J Kid Dis. 2004; 43:90⁵³</p> <p>Daily HD 20 pts; 4 wk Prospective</p>	<ul style="list-style-type: none"> • Mean predialysis systolic blood pressure declined during daily HD from 140 ± 23 to 132 ± 22 mm Hg. (p=0.0005) • Two patients discontinued blood pressure medication
<p>Chan, CT. Hypertension.2003; 42:925⁴⁷</p> <p>Nocturnal HD 18 pts; 2 mo Prospective</p>	<ul style="list-style-type: none"> • Mean arterial pressure decreased from 102 ± 3 to 90 ± 2 mm Hg (p=0.01) • Antihypertensive medications/patient decreased from 2.5 to 0.2 (p<0.001)
<p>Goldfarb-Rumyantzev, AS. J Am Soc Nephrol. 2003; 14:233A⁶³</p> <p>Daily HD 8 pts; 8 wk Prospective</p>	<ul style="list-style-type: none"> • Predialysis mean blood pressure declined from 111 ± 11 to 106 ± 11 mm Hg • Number of antihypertensive medications was unchanged

<p>Koshikawa, S. Nephron Clin Pract. 2003; 95:c23⁵²</p> <p>Daily HD 21 pts; 3 mo Prospective</p>	<ul style="list-style-type: none"> • Mean systolic and diastolic blood pressures declined significantly ($p < 0.01$); systolic (152.3 ± 23.5 to 136.6 ± 22.2 mm Hg); diastolic (84.3 ± 14.8 to 77.2 ± 13.1 mm Hg) • Of patients taking antihypertensive medication while on conventional HD, 2 patients discontinued and 4 decreased usage during daily HD
<p>Kunz, KW. J Am Soc Nephrol. 2003; 14:233A⁶⁴</p> <p>Daily HD 8 pts; 9 mo Prospective</p>	<ul style="list-style-type: none"> • Blood pressure was normalized in all patients • Antihypertensive drug consumption was reduced by 50% to 75%
<p>Lorch, J. J Am Soc Nephrol. 2003; 14:232A⁶⁵</p> <p>Nocturnal HD (4.8 times/wk) 5 pts; 2-23 mo Prospective</p>	<ul style="list-style-type: none"> • In two patients, blood pressure decreased dramatically (149/72 to 114/54 and 115/63 to 80/56) and antihypertensive drug use was decreased; blood pressure did not change significantly in 3 patients
<p>Maduell, F. Kidney Int. 2003; 64:305²⁰</p> <p>Daily HDF 8 pts; 6 mo Prospective</p>	<ul style="list-style-type: none"> • Reductions in systolic and diastolic blood pressures and mean arterial pressure were observed but were not statistically significant • During the first month on HDF, patients who had been taking antihypertensive medications discontinued their use
<p>Nesrallah, G. Am J Kid Dis. 2003; 42:S13⁴⁹</p> <p>Daily HD 11 pts Nocturnal HD 12 pts; 1.5 yr Prospective</p>	<ul style="list-style-type: none"> • Predialysis mean arterial pressure declined from 106.5 ± 13.7 to 100.9 ± 6.9 mm Hg ($p < 0.05$) during DHD and from 117.1 ± 22.6 to 97.1 ± 8.4 mm Hg. ($p < 0.05$) during NHD • Of patients taking antihypertensive medication while on conventional HD, 2 patients discontinued and 4 decreased usage during DHD and 5 patients discontinued and 3 decreased usage during NHD
<p>Ting, GO. Am J Kid Dis. 2003; 42:1020.¹¹</p> <p>Daily HD 42 pts; 1.5 yr Prospective</p>	<ul style="list-style-type: none"> • Mean systolic blood pressure decreased significantly ($p < 0.01$), while diastolic pressures remained about the same • There was a significant decline in both the number of different antihypertensive medications (1.3 ± 0.4 to 0.4 ± 0.5, $p = 0.004$) used and the number of pills/week (12.6 ± 5.8 to 5.3 ± 5.5, $p = 0.003$) taken on a per patient basis

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<p>Zimmerman, DL. <i>ASAIO Journal</i>. 2003; 49:426⁶⁶</p> <p>Daily HF 11 pts; 4 wk Prospective</p>	<ul style="list-style-type: none"> • Compared to measurements during conventional HD, blood pressure declined during daily HF: <ul style="list-style-type: none"> • Mean arterial pressure from 96 ± 11 to 86 ± 12 mm Hg ($p=0.001$) • Systolic blood pressure from 139 ± 18 to 128 ± 19 mm Hg ($p=0.001$) • Diastolic blood pressure from 74 ± 9 to 66 ± 11 mm Hg ($p=0.01$) • All patients who were on antihypertensive medications had a reduction in dosage
<p>André, MB. <i>Am J Nephrol</i>. 2002; 22:473⁴⁸</p> <p>Daily HD 5 pts; 2 yr Prospective</p>	<ul style="list-style-type: none"> • Mean blood pressure declined significantly during daily HD ($p<0.05$) • Of patients taking antihypertensive medication while on conventional HD, 3 decreased usage during daily HD
<p>Chan, C. <i>Nephrol Dial Transplant</i>. 2002; 17:1518³⁰</p> <p>Nocturnal HD 6 pts; 3.2 yr Prospective</p>	<ul style="list-style-type: none"> • Systolic blood pressure decreased from 138 ± 10 to 120 ± 9 mm Hg ($p=0.04$) • Mean arterial pressure decreased from 99 ± 6 to 86 ± 7 mm Hg ($p=0.01$) • Number of prescribed cardiovascular medications decreased from 2.2 to 0.7 ($p=0.02$)
<p>Chan, CT. <i>Kidney Int</i>. 2002; 61:2235²⁵</p> <p>Nocturnal HD 28 pts; 3.4 yr Prospective</p>	<ul style="list-style-type: none"> • Systolic blood pressure decreased from 145 ± 20 to 122 ± 13 mm Hg ($p<0.001$) • Diastolic blood pressure decreased from 84 ± 15 to 74 ± 12 mm Hg ($p=0.02$) • Number of prescribed antihypertensive medications decreased from 1.8 to 0.3 ($p=0.001$)
<p>Cagle, J. <i>ASAIO J</i>. 2001;47:470⁶⁷</p> <p>Nocturnal HD 1 patient; ~3 yr Case report</p>	<ul style="list-style-type: none"> • Personal account: blood pressure normalized to 110/70 within 1 day of long nocturnal HD
<p>Fagugli, RM. <i>Am J Kid Dis</i>. 2001; 38:371¹⁸</p> <p>Daily HD 12 pts; 1 year (6 mo random crossover)</p>	<ul style="list-style-type: none"> • Blood pressure during 6 months on daily HD decreased as compared to a crossover period on conventional HD: systolic from 148 ± 19.2 mm Hg to 128 ± 11.6 mm Hg ($p<0.01$) and diastolic blood pressure decreased from 73 ± 5.4 mm Hg to 67 ± 8.3 mm Hg ($p<0.01$) • 7 of 8 patients who previously needed anti-hypertensive medication, required none on daily HD; the number of medications needed by the other patient was decreased ($p<0.01$)

<p>Galland, R. J Am Soc Nephrol. 2001;12:265A¹⁹</p> <p>Daily HD 14 pts; 1 yr Prospective</p>	<ul style="list-style-type: none"> • Mean blood pressure decreased significantly from 107 ± 16.2 mm Hg to 92 ± 15.6 mm Hg ($p < 0.05$) on daily HD
<p>Galland, R. Am J Kid Dis. 2001;37Suppl 2:S95²¹</p> <p>Daily HD 10 pts; 13-38 mo Prospective</p>	<ul style="list-style-type: none"> • Blood pressure normalized in 5 hypertensive patients on daily HD and medications were stopped (no BP values given)
<p>Lindsay, RM. ASAIO J. 2001;47:449⁵</p> <p>Daily HD 9 pts Nocturnal HD 10 pts; 1-18 mo Prospective/ Case-control</p>	<ul style="list-style-type: none"> • No significant differences in blood pressure measurements between conventional HD and DHD periods • Blood pressure medication was significantly decreased from conventional HD to DHD (2.8 to 0.7 tablets/day; $p = NS$) and NHD (1.9 to 0.6 tablets/day; $p < 0.05$)
<p>Nesrallah, G. J Am Soc Nephrol. 2001;12:273A⁵⁹</p> <p>Nocturnal HD, Daily HD 18 pts; 18 mo Prospective</p>	<ul style="list-style-type: none"> • Mean arterial blood pressure was significantly reduced in daily HD patients at 6 months ($p < 0.05$) and in nocturnal HD patients at 1 year ($p < 0.05$) • There was a significant decrease in antihypertensive medications at 1 month on nocturnal HD ($p < 0.02$) and at 3 months on daily HD ($p < 0.05$) • Interdialytic weight swings were reduced on daily HD ($p < 0.05$) but not in nocturnal HD
<p>Traeger, J. Dial Transplant. 2001;30:76²²</p> <p>Daily HD 15 pts; ≥ 1 yr Prospective</p>	<ul style="list-style-type: none"> • Antihypertensive medications were stopped in 8 patients within 2 months • Mean normalized blood pressure was 106.5 ± 16.2 at baseline and 92.9 ± 13 at 1 year (no p values given)
<p>Cacho, C. Nephrol News Issues. 2000;14:36²</p> <p>Nocturnal HD 6 pts; 6 mo Prospective</p>	<ul style="list-style-type: none"> • Blood pressure was normal or low on decreased amounts of antihypertensives

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<p>Buoncristiani, U. Miner Electrolyte Metab. 1999;25:90³²</p> <p>Daily HD 20 pts; 6-12 mo Retrospective & Prospective</p>	<ul style="list-style-type: none"> • Blood pressure decreased significantly in patients on daily HD • Previously hypertensive patients were able to reduce blood pressure medications significantly on daily HD
<p>Pierratos, A. Nephrol Dial Transplant. 1999;14:2835⁶</p> <p>Nocturnal HD 37 pts; 5 yr Prospective</p>	<ul style="list-style-type: none"> • Most patients discontinued antihypertensives within 2 weeks of starting nocturnal HD • Only 6 of 30 current patients are on small doses of antihypertensives
<p>Pinciaroli, AR. Sem Dial. 1999;12:455²⁶</p> <p>Daily HD 22 pts; 1 yr Retrospective</p>	<ul style="list-style-type: none"> • Systolic blood pressure decreased from 174 to 141 mm Hg (no p values or std. dev. given) • Diastolic blood pressure decreased from 94 to 82 mm Hg (no p values or std. dev. given)
<p>Williams, AW. Sem Dial. 1999;12:431⁶²</p> <p>Daily HD 5 pts; 8 wk Prospective</p>	<ul style="list-style-type: none"> • Blood pressure control was achieved with fewer antihypertensives
<p>Williams, AW. J Am Soc Nephrol. 1999;10:270A⁶⁸</p> <p>Daily HD 20 pts; 8 wk Crossover</p>	<ul style="list-style-type: none"> • Pre-dialysis blood pressure decreased on daily HD
<p>Woods, JD. Kid Int. 1999;55:2467⁴⁶</p> <p>Daily HD 72 pts; 1 yr Retrospective</p>	<ul style="list-style-type: none"> • Predialysis systolic blood pressure decreased by 7 mm Hg in whole group (<0.01) and by 13 mm Hg in hypertensive patients (p<0.01) • Predialysis diastolic blood pressure decreased by 4 mm Hg in whole group (p=0.02) and by 7 mm Hg in hypertensive patients (p=0.02) • Percentages of patients taking hypertensive drugs decreased as did the number of medications taken

<p>Fagugli, RM. Int J Artif Org. 1998;21:429 ²⁷</p> <p>Daily HD 23 pts; 1 yr Retrospective</p>	<ul style="list-style-type: none"> • After 1 year on daily HD, systolic blood pressure decreased from 144.9 ± 22.9 mm Hg to 127.5 ± 18.6 mm Hg ($p < 0.001$) and diastolic blood pressure decreased from 83.4 ± 15.2 to 74.7 ± 11.6 mm Hg ($p < 0.001$) • Results were more striking in hypertensive patients • 9 of 15 patients who previously needed anti-hypertensive medication required none on daily HD; the number of medications needed by 4 patients decreased and remained unchanged for 2 patients
<p>Kooistra, MP. Nephrol Dial Transplant. 1998;13:2853 ⁵¹</p> <p>Daily HD 13 pts; 6 mo Prospective</p>	<ul style="list-style-type: none"> • Systolic blood pressure decreased significantly from 141.1 ± 17.2 mm Hg on conventional HD to 130.9 ± 19.2 mm Hg on daily HD ($p < 0.001$) • Diastolic blood pressure decreased insignificantly • Number of antihypertensive drugs was reduced from 1.88 ± 0.35 to 0.75 ± 0.17 on daily HD ($p < 0.005$)
<p>O'Sullivan, DA. Mayo Clin Proc. 1998;73:1035 ⁵⁶</p> <p>Nocturnal HD 5 pts; 8 wk Prospective</p>	<ul style="list-style-type: none"> • Mean arterial blood pressure decreased during period of nocturnal HD (no values given) • Antihypertensive medication was eliminated for 1 patient and decreased for the others after 2 months on nocturnal HD
<p>Pierratos, A. J Am Soc Nephrol. 1998;9:859 ⁶⁹</p> <p>Nocturnal HD 11 pts; 3 yr Prospective</p>	<ul style="list-style-type: none"> • Average number of hypertensive medications decreased from 2.67 ± 1.12 on conventional HD to 1.67 ± 1.17 on nocturnal HD ($p = 0.03$) • Of 10 patients taking antihypertensives when starting nocturnal HD, only 5 were still taking such medication at last time checked
<p>Ting, G. J Am Soc Nephrol. 1998;9:228A ⁶¹</p> <p>Daily HD 7 pts; 6 mo Prospective</p>	<ul style="list-style-type: none"> • Number of blood pressure medications required per patient was insignificantly reduced
<p>Traeger, J. Artif Org. 1998;22:558 ²³</p> <p>Daily HD 4 pts; 1 yr Prospective</p>	<ul style="list-style-type: none"> • Mean blood pressure decreased from 107.75 ± 8.13 mm Hg on conventional HD to 96 ± 5 mm Hg on daily HD ($p < 0.01$)

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<p>Buoncrisiani, U. J Am Soc Nephrol. 1997;8:216A ²⁸</p> <p>Daily HD 50 pts; 1 yr Retrospective</p>	<ul style="list-style-type: none"> • Mean blood pressure of all patients decreased from 105.2 ± 15.4 mm Hg on conventional HD to 95.2 ± 15.4 mm Hg on daily HD • For the 29 hypertensive patients, mean blood pressure decreased from 117.8 ± 13.2 mm Hg on conventional HD to 103.7 ± 9 mm Hg on daily HD • 69% of hypertensive patients were able to reduce their antihypertensive medications
<p>Buoncrisiani, U. Contrib Nephrol. 1996;116:152 ²⁹</p> <p>Daily HD 34 pts; 2 yr Retrospective</p>	<ul style="list-style-type: none"> • Mean blood pressure of all patients decreased from 106 ± 21.7 mm Hg on conventional HD to 95.5 ± 15.6 mm Hg on daily HD • For the 20 hypertensive patients, mean blood pressure decreased from 120 ± 12.9 mm Hg on conventional HD to 103.4 ± 9.36 mm Hg on daily HD • 13 formerly hypertensive patients stopped taking medication; the others reduced their doses
<p>Twardowski, ZJ. Adv Ren Repl Therap. 1996;3:124 ⁷⁰</p> <p>Daily HD 3 pts; 6 mo Prospective</p>	<ul style="list-style-type: none"> • Dramatic improvements in control of blood pressure (no values given)
<p>Uldall, R. Adv Ren Repl Therap. 1996;3:133 ⁵⁸</p> <p>Nocturnal HD 5 pts; 6-16 mo Prospective</p>	<ul style="list-style-type: none"> • 2 patients discontinued blood pressure medications
<p>Buoncrisiani, U. Kid Int. 1988;33:S137 ⁵⁰</p> <p>Daily HD 12 pts; ~2 yr Prospective</p>	<ul style="list-style-type: none"> • Blood pressure normalized in all patients on daily HD; changes were statistically significant for both systolic (157.22 ± 9.72 mm Hg vs. 131.6 ± 11.18 mm Hg) and for diastolic (92 ± 5.07 mm Hg vs. 83.33 ± 4.33 mm Hg) pressures