SECTION ONE:
Left Ventricular Hypertrophy

Left ventricular hypertrophy is present in most dialysis patients, and is an important independent risk factor for cardiac failure and mortality. Daily therapy has been shown to halt or reverse the deterioration of cardiac activity.

OVERVIEW

Left ventricular hypertrophy (LVH) is a frequent cardiovascular complication that is present in as many as 75% of patients with chronic renal disease at the time they start renal replacement therapy and in as many as 90% of patients who have been on maintenance renal replacement therapy for at least 5.5 years. [14] Of the 1836 patients in the HEMO study, 80% had cardiac disease at baseline. [15]

Common conditions associated with traditional ESRD therapies (e.g, anemia, hypertension, fluid overload) tax the cardiovascular system. To compensate, the heart enhances cardiac output by increasing the number of myofibrils and the thickness of the ventricle wall. However, this chronic stress on the heart can eventually lead to cardiomyopathy and fibrosis. This can reduce the efficiency of the heart and increase the risk of heart failure.

LVH is an important, independent risk factor for cardiac failure. In a prospective study of 91 dialysis patients, the relative risk of mortality, adjusted for age, systolic blood pressure, diabetes, and known coronary artery disease, was 2.7 for patients in the highest quintile of left ventricular mass (LVM) compared to those in the lowest quintile. [16] Another prospective study of 254 ESRD patients revealed that LVM indexed by either height or BSA was a good predictor of cardiovascular mortality. [17]

Halting or reversing this deterioration of cardiac activity may have significant benefits. A prospective study of 153 dialysis patients with LVH found that medications that reduced hypertension and anemia partially reversed the progression of LVH. Some patients responded well to the medication and LVM decreased by >10%; others did not respond well and experienced a smaller decrease, or even an increase, in LVM during 4-5 years of follow up. Mortality from cardiovascular disease was 14.3% among the responders and 57.8% among the nonresponders. [14]

POTENTIAL BENEFITS OF MORE FREQUENT THERAPY

More frequent therapy is reported to improve the conditions believed to play a role in LVH progression (hypertension, fluid overload, and anemia – see sections on each), so the progress of LVH in patients may be halted and/or reversed. As noted above, this may prolong the lives of ESRD patients and improve quality of life.

SUMMARY OF PUBLISHED RESULTS

Daily renal replacement therapy has been shown to significantly improve LVH in several trials as measured by its key clinical indicators. Improvements in LVH parameters are reported whether more frequent therapy is administered in a short daily or a long nightly format.

Reports of 15 trials (including 4 to 50 patients each) have demonstrated regression of several parameters of LVH.

Parameter Measured	Observations
Left Ventricular Mass	Reductions from 13.8% to 31% [18-25]
Left Ventricular End Diastolic Diameter	Reductions from 4.9% to 12.6% [19, 21, 22, 25-29]
Posterior Wall Thickness	Reductions from 11.6% to 20.9% [20, 22, 25-29]
Interventricular Septum Thickness	Reductions from 13.2% to 15.5% [20, 26-28]
Cardiac Output	Improved by 28 to 41% [24, 30, 31]

Not all parameters were measured in all studies but all reports indicated significant decreases in at least one of these measurements.

Significant improvements have been observed as early as 6 months from initiation of daily therapy. [20, 32] Follow-up data on a cohort of 13 patients treated for as long as six years demonstrated that improvements in LVH persisted. [33]

TABULATED STUDY FINDINGS ON LVH

Study & Design	Supporting Points
Maduell, F. Kidney Int. 2003; 64:305 [20] Daily HDF 8 pts; 6 mo Prospective	• Left ventricular mass index decreased significantly from 97.9±45 to 68.9±22 g/m^2 (p<0.01) • Left ventricular mass decreased significantly from 166.9±76 to 118.1±37 g (p<0.01) • Posterior wall thickness decreased significantly from 11.9±2.2 to 9.8±2.3 mm (p<0.05) • Septal wall thickness decreased significantly from 15.0±3.9 to 12.7±1.8 mm (p<0.05)
Chan, CT. Kidney Int. 2002;61:2235 [25] Nocturnal HD 28 pts; 3.4 yr Prospective	• Left ventricular mass index decreased significantly from 147±42 to 114±40 g/m^2 (p<0.05) • End diastolic diameter decreased significantly from 50.7±7.8 to 48.4±7.0 mm (p<0.05) • Posterior wall thickness decreased significantly from 10.8±2.1 to 9.4±2.4 mm (p<0.05) • Septal wall thickness decreased significantly from 10.9±2.4 to 9.6±2.2 mm (p<0.05)
Chan, C. Nephrol Dial Transplant.2002; 17:1518 [30] Nocturnal HD 6 pts; 3.2 yr Prospective	• Patients had known cardiac systolic dysfunction. After nocturnal HD, ejection fraction improved significantly from 28 ± 12 to 41 ± 18% (p=0.01) • There was a reduction in the number of prescribed cardiovascular medications (2.2 to 0.7, p=0.02)
Chan, CT. J Am Soc Nephrol. 2001;12:262A [24] Nocturnal HD 7 pts; 2.6 yr Prospective	• Patients had LV dysfunction but after nocturnal HD, ejection fraction increased significantly (30.3% ± 12.9% to 45% ± 18.4%, p=0.004) • There was a reduction in the number of prescribed cardiovascular medications (2.1 ± 0.8 to 0.5 ± 0.8, p<0.001) • Left ventricular mass index tended to decrease from 182 ± 50 g/m2 to 139 ± 43 g/m2 (p=0.08)
Fagugli, RM. Am J Kid Dis. 2001;38:371 [18] Daily HD 12 pts; 1 yr (6 mo random crossover)	• Left ventricular mass index during 6 months on short daily HD decreased significantly as compared to a crossover period on conventional HD from 148.7 ± 59.7 g/m^2 to 120.1 ± 60.4 g/m^2 (p<0.01)

Galland, R. Am J Kid Dis. 2001;37 Suppl 2:S95 [21] Daily HD 10 pts; 13-38 mo Prospective	• LVH was present in 8 patients before daily HD • Left ventricular mass index decreased from 190 ± 72 g/m^2 to 131 ± 28 g/m^2 and left ventricular diastolic diameter (LveDD) from 3.33 ± 0.43 to 3.05 ± 0.37 cm/m2 after 1 year on short daily HD
Galland, R. J Am Soc Nephrol. 2001;12:265A [19] Daily HD 14 pts; 1 yr Prospective	• LVeDD decreased from 5.8 ± 0.5 cm to 5.11 ± 0.7 cm (p<0.01) • PW thickness and interventricular septum thickness did not change significantly • Left ventricular mass index decreased significantly from 204 ± 76.6 g/m^2 to 165 ± 55.8 g/m^2 (p<0.05)
Odar-Cederlof, IE. J Am So Nephrol. 2001;12:404A [31] Daily HD 32 pts Prospective	• Brain natriuretic peptide (BNP) is released from cells in the ventricle wall in response to stress and has been reported to be a marker of cardiac stress and left ventricular dysfunction • Plasma BNP levels in 22 patients were inversely correlated with left ventricular ejection fraction on conventional HD (p<0.0001) • On daily HD, fluid overload and cardiac stress decreased and BNP levels decreased from 235 ± 69 ng/L (on conventional HD) to 143 ± 62 ng/L (p<0.007) (normal BNP level<22 ng/L)
Traeger, J. Dial Transplant. 2001;30:76 [22] Daily HD 15 pts; ≥1 yr Prospective	• Left ventricular mass index decreased from 188 ± 76.6 g/m^2 to 156 ± 55.8 g/m^2 (p<0.05) • Left ventricular diastolic diameter (LveDD) decreased from 5.54 ± 0.9 cm/m2 to 4.99 ± 0.7 cm/m2 (p<0.01) • Left ventricular posterior wall (PW) thickness decreased from 1.13 ± 0.25 cm to 1.09 ± 0.2 cm (p<0.05)
Buoncristiani, U. Miner Electrolyte Metab. 1999;25:90 [32] Daily HD 20 pts; 6-12 mo Retrospective & Prospective	• After 6-12 months on short daily HD, echocardiographic parameters were significantly reduced indicating improvement in LVH
Pinciaroli, AR. Sem Dial. 1999;12:455 [26] Daily HD 22 pts; 1 yr Retrospective	• PW decreased from 11 mm to 8.7 mm (no p values or std. dev. given) • LVeDD decreased from 56.3 mm to 49.2 mm (no p values or std. dev. given) • Interventricular septum thickness (IVS) decreased from 11.6 mm to 9.8 mm (no p values or std. dev. given)

Fagugli, RM. Int J Artific Org. 1998:21:429 [27] Daily HD 23 pts; 12 mo Retrospective	• On daily HD, interventricular septum (IVS) thickness decreased from 12.9 ± 3.2 mm to 11.2 ± 2.2 mm ($p<0.01$) • PW thickness decreased from 11.3 ± 2.1 mm to 10.1 ± 1.3 mm ($p<0.01$) • LveDD decreased from 53.3 ± 7.1 mm to 50.7 ± 6.2 mm ($p=0.1$) • Results were more striking in hypertensive patients
Traeger, J. Artif Org. 1998;22:558 [23] Daily HD 4 pts; 1 yr Prospective	• At 6 months there was a significant reduction in left ventricular mass index from 164 g/m^2 to 132 g/m^2 ($p<0.01$)
Buoncristiani,U. J Am Soc Nephrol. 1997;8:216A [28] Daily HD 50 pts; 1 yr Retrospective	• LVeDD decreased from 53.9 ± 6.1 mm on conventional HD to 50.9 ± 6.1 mm on daily HD • IVS thickness decreased from 12.9 ± 3.3 mm on conventional HD to 11.1 ± 1.8 mm on daily HD • Left ventricular PW thickness decreased from 11.7 ± 2.1 mm on conventional HD to 10.3 ± 1.1 mm on daily HD
Buoncristiani, U. Contrib Nephrol. 1996;116:152 [29] Daily HD 34 pts; 2 yr Retrospective	• After 1 year of daily HD, LVeDD decreased significantly ($p<0.01$) • After 2 years of daily HD, LVPW, LVeDD, and IVS decreased significantly ($P<0.01$)