In-Depth Clinical Review

Left ventricular dysfunction in the haemodialysis population

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Abstract
Cardiovascular disease in the haemodialysis population continues to contribute to mortality and morbidity. Disorders of left ventricular geometry and function are highly prevalent and lead to increased mortality in this highly vulnerable population. Left ventricular dysfunction (LV Dys), often as a result of hypertension, ischaemic cardiac disease or dilated cardiomyopathy, has not been uniformly defined in the literature making diagnosis and therapy problematic. Although routinely available, screening by echocardiography is critically volume dependent and prone to underestimation in left ventricular ejection fraction. Few randomized control trials are available to guide management with the majority of evidence requiring extrapolation from the non-dialysis population. Beyond medication, interventional cardiac procedures such as implantable cardiac defibrillator implantation and cardiac resynchronization therapy show promise. Conversion to alternative dialysis modalities such as peritoneal dialysis, short-daily or nocturnal dialysis have been attempted and are actively being explored.

Keywords: beta blockers; cardiac defibrillators; haemodialysis; left ventricular dysfunction; nocturnal haemodialysis

Left ventricular dysfunction in the haemodialysis population
Cardiovascular disease remains the primary culprit for poor health outcomes and high mortality in patients undergoing maintenance dialysis. In the haemodialysis (HD) population left ventricular dysfunction (LV Dys) is common with a rate 10–30 times greater than that in the general population [1–4]. The clinical diagnosis of congestive heart failure (CHF) in the HD population, which may be due to decreased left ventricular function, correlates strongly with mortality, having a reported 3-year survival of only 17% [5]. LV Dys is often preceded by left ventricular hypertrophy (LVH) that in itself carries a poor prognostic value for mortality in patients with ESRD [6–10]. Taken together, LV Dys (or its precursor, LVH) and its clinical correlate, CHF, confer a substantially increased risk of morbidity and mortality. These links are significant enough for National Kidney Foundation guidelines to recommend baseline and routine echocardiographic follow-up for all patients initiating dialysis [11].

The literature concerning disorders of left ventricular (dys)function in HD can be daunting since there is no uniform definition of the problem, multiple aetiologies exist and several methods of measurement are employed, making comparisons of individual studies difficult to interpret. For clarity, we will define LV Dys as a left ventricular ejection fraction <40% or endocardial left ventricular shortening <25% [12]. LVH is categorically defined as left ventricular mass index (LVMI) of >131 g/m2 in males and >100 g/m2 in females taken from the upper limits of normal used in the Framingham Study [13]. LVMI is simply the LVM normalized to body surface area. CHF is a clinical diagnosis based on the presence of dyspnoea and pulmonary oedema that may or may not involve LV Dys. This review will focus on various aspect of LV systolic dysfunction in the HD population. The incidence and prevalence, methods of measurement, pharmacological and interventional management, and alternative dialytic treatment strategies will be discussed.

Incidence, prevalence and mortality of LV dysfunction in haemodialysis patients
Early seminal studies by Foley et al. of 432 dialysis patients studied prospectively in the 1980s focused on distortions of left ventricular architecture, namely LVH, and clinical CHF [9,14–18]. They reported high rates of 75% and 31% of patients who had LVH and CHF at initiation of dialysis, respectively [14,16]. Furthermore, prevalent HD patients had rates of de novo CHF of 25% [17]. It seemed that left ventricular disorders were common in the HD patient population. This observation was solidified by other investigators who reported rates of 46–79% for LVH and 13–36% for LV systolic dysfunction [19–22]. Key studies reporting
rates of incidence and prevalence of left ventricular disorders in HD patients are summarized in Table 1.

Does LV systolic dysfunction confer an adverse prognosis? Foley et al. utilized a multivariate model to predict that the significant risk factors for recurrent CHF were ischaemic heart disease (RR 3.10), anaemia (RR 1.25/10 g fall), hypoalbuminaemia (1.37/5 g fall) and baseline systolic dysfunction on echocardiography (1.92). As expected, systolic dysfunction at baseline was the strongest predictor of CHF presence at the initiation of dialysis (OR 5.34). LVMI (per 20 g/m\(^2\)) was not a significant predictor of CHF (OR 2.9). LV dysfunction but not LVMI predicts CHF. In the Parfrey cohort, the echo timing was not specified and in the Mallamaci cohort the echo was performed midweek whereas in the Joki era effects, assorted study conditions and heterogeneous definitions of ‘systolic dysfunction’ render inter-study generalizations about exact numbers of incidence and prevalence for cardiac dysfunction problematic. Information bias (see the next section) further worsens the issue of comparison. Taking all of these factors into consideration, the fact remains that echocardiographic evidence of LV Dys and LVH remain important prognostic indicators for predicting cardiac demise in the dialysis population.

**Methods of measurement**

Information bias can occur when there is a random or systematic inaccuracy in measurement. Unfortunately, the most widely used means of measurement of left ventricular function, M mode, two-dimensional echocardiography is prone to significant information bias. While its benefits include wide availability, relatively low cost and good inter-observer reliability [32], errors may occur because many of the measurements are based on geometric assumptions. The calculated left ventricular mass (LVM) relies heavily on the measurement of left ventricular internal dimension (LVID) that, in turn, is susceptible to changes with plasma volume [33]. Thus, sensitivity to volume status at the time of measurement is crucial in obtaining an accurate measure. Failure to obtain a true dry weight or echocardiographic assessment prior to HD will lead to underestimations of LV function. In two small series, the average reductions for the classification of EF are mild dysfunction 41–49%, moderate 35–40% and <35% severe [31]. The large cohort study by Parfrey et al. [18] used a cutoff ejection fraction of 25% versus the Mallamaci et al. [19] study that uses 40%. Despite this, the Parfrey group reports a higher prevalence of systolic dysfunction at 16% versus 13% by Mallamaci et al. These contradictory results may be explained by the timing of the echocardiogram. In the Mallamaci cohort the echo was performed midweek whereas in the Parfrey cohort, the echo timing was not specified and may have been predialysis.

A further caveat in gauging prevalence of systolic dysfunction in this population surrounds the heterogeneity in cutoffs for what entails ‘dysfunction’. Current recommendations for the classification of EF are mild dysfunction 41–49%, moderate 35–40% and <35% severe [31]. The large cohort study by Parfrey et al. [18] used a cutoff ejection fraction of 25% versus the Mallamaci et al. [19] study that uses 40%. Despite this, the Parfrey group reports a higher prevalence of systolic dysfunction at 16% versus 13% by Mallamaci et al. These contradictory results may be explained by the timing of the echocardiogram. In the Mallamaci cohort the echo was performed midweek whereas in the Parfrey cohort, the echo timing was not specified and may have been predialysis.

**Table 1.**

| Author/year | Study type | Key findings (pertaining to systolic dysfunction) | Imaging/definition of LV dysfunction | Considerations |
|-------------|------------|---------------------------------------------------|-------------------------------------|----------------|
| Greaves et al. 1994 [21] | 84 prevalent patients (mean = 3.9 years on HD/CAPD) | 36% systolic dysfunction | Echocardiography (FS ≤ 25%) | Mean HCT 0.28, no report of CHF med use |
| Foley, Parfrey, Harnett et al. [19,14,15,17,18] | 432 patients prospective over 41 months | LV dysfunction but not LVMI predicts CHF | Echocardiography (FS ≤ 25%) | Mean haemoglobin 8.7 g/dL, no report of CHF med use |
| Joki et al. 2003 [20] | 88 incident HD patients followed for 3 years | 27% had systolic dysfunction that predicted cardiac death | Echocardiography (FS ≤ 25%) | Mean haemoglobin 8.7 g/dL, no report of CHF med use |
| Mallamaci et al. 2001 [19] | 246 prevalent patients (HD/PD). No clinical CHF. Biomarker study | 79% LVH 13% systolic dysfunction | Echocardiography (LVEF ≤ 45%) | Minimal use of ACE/ARB/B-blockers/EPO Hgb not reported |
| Zoccali et al. 2000 [8] | 254 prevalent patients (HD/PD) | 77% LVH 22% systolic dysfunction by LVEF measurement 48% systolic dysfunction by midwall fractional shortening | Echocardiography (LVEF < 50%, fractional shortening <28%) | No report of CHF med use |
in LVMi and end-diastolic diameter from pre- to post-dialysis were 26.2–36.1 g/m² and 4–8.4 mm, respectively [34,35].

From the nephrologists’ perspective, newer techniques of visualization of cardiac structures are emerging that may minimize information bias. In experimental settings, cardiac magnetic resonance imaging (MRI) is becoming more readily available and directly measures cardiac mass, thereby circumventing the geometric assumptions and calculations used in echocardiography. Indeed in head to head comparisons of cardiac MRI versus echocardiography, MRI detected lower LV mass (122.3 versus 177 g/m² for men, 133.5 versus 89.6 g/m² for women) and better intra-observer variability (4.3% versus 9.6%) [36]. Of note, the same study found that as left ventricular dilatation increased, so did the overestimation of LV mass by echocardiography. Cardiac MRI is greatly limited by cost, availability, claustrophobia, contraindications such as pacemakers and, lastly, concerns with gadolinium use and its association with nephrogenic systemic fibrosis. Thus, cardiac MRI is still used primarily in the experimental setting.

Real-time 3D echocardiography (RT3DE) and cardiac CT (CCT) are potential future modalities for cardiac structural assessment. RT3DE, when compared to 2D echocardiography, can be performed without geometric modelling, thereby foregoing the need for error magnifying calculations [37]. In direct comparisons, RT3DE has better correlation with cardiac MRI versus CCT ($r^2 = 0.93$ versus 0.85) for measurements of ejection fraction and less bias by the Bland–Altman analysis (0.3% versus $-2.8\%$) but a higher rate of intra- and interobserver variability.

With cardiac MRI as the gold standard for cardiac structure, positron emission tomography (PET) is considered the gold standard for cardiac tissue perfusion. Preliminary studies have shown PET imaging to be highly sensitive and specific in detecting regional wall motion abnormalities and changes in myocardial blood flow during haemodialysis [38]. Future studies combining the two techniques could elucidate myocardial perfusion in the dilated ventricular and its response to various pharmacologic and interventional therapies.

Pharmacological management of LVDys in HD

A paucity of literature exists on the use of pharmacological agents in HD patients with LVDys as often elevations in creatinine and the presence of ESRD are used as exclusion criteria. Discussions regarding the extrapolation of evidence for usage of pharmacologic therapy have been recently reviewed elsewhere [20,39]. To date, only a few small randomized studies have shown pharmacologic benefit in HD patients in prevention of CHF and established LVDys.

The strongest evidence of benefit exists for the utilization of beta-blockers. A small open-label RCT examined the effect of carvedilol versus placebo on cardiovascular disease in dialysis patients with symptomatic, NYHA Class 2 or higher CHF and echocardiographic evidence of impaired left ventricular systolic function (ejection fraction <35%). The investigators showed improvement in clinical NYHA class and ejection fraction in the carvedilol group at 1 year [40]. Based on these favourable findings, the protocol was continued for another year at which point an impressive 50% relative risk reduction (RRR) in all cause death, a 55% RRR in hospitalization and a 68% RRR in cardiovascular death were observed with carvedilol [41]. While these results are broadly congruent with the previously cited observational data and with the known benefit of BB in non-dialysis patients with CHF, several methodological concerns have been raised, including a small and possibly non-representative patient sample characterized by an unusually high mortality rate (70% at 2 years in the placebo group) and an open label design. Nevertheless, the data presented do support the use of carvedilol in a small subset of haemodialysis patients with symptomatic dilated cardiomyopathy (NYHA 2 or 3 heart failure and EF <35%). Whether the benefits observed can be generalized to other BB, to peritoneal dialysis patients, or to patients without symptomatic heart failure or dilated cardiomyopathy will need to be addressed in future.

Angiotensin blocking agents are a mainstay of therapy of LVDys in the non-dialysis population; however, their role in the HD population appears much less clear. Evaluation of the evidence is hampered by the lack of studies stratifying HD patients according to the presence of LVDys. Several studies have documented a favourable effect on surrogate outcomes. RAS antagonists are effective in reducing hypertension, regressing LVH, improving large vessel compliance and preserving residual renal function in dialysis patients [42–45]. One randomized controlled trial (RCT) by Zannad et al. examined the effect of fosinopril on the reduction of cardiovascular events (CVE) in 397 dialysis patients with LVH [46]. A 7% reduction in CVEs was observed, but it was not statistically significant due to the low statistical power of the study. The composite endpoint of CVE included CHF requiring hospitalization (6% of the total who reached primary endpoint); however, it is unclear whether fosinopril truly confers any benefit. In a small RCT, candasartan therapy resulted in CVE of 16.3% versus 45.9% in those not treated ($P < 0.01$) [47]. At baseline, the average LVEF was 61 ± 2.8% in the treatment arm with 5/43 patients reaching the endpoint of CHF requiring hospitalization versus 11/37 patients in the control arm. In a small, single centre RCT, ARB therapy appears to decrease de novo CHF in patients with normal ejection fraction at baseline. Whether ACEI or ARB improves prevalent LVDys, mortality or morbidity remains unknown.

More recently, data in dialysis patients and the general population have suggested that ASA use may be associated with increased risk of de novo and recurrent heart failure [48,49]. This effect persisted even after adjustment for other risk factors including prevalent CAD. Important limitations to this data include the observational design of the studies, which cannot establish causation, and the problem of residual confounding due to incomplete adjustment for the effect of confounding variables. Nevertheless, these findings remain a concern, because heart failure is a major mechanism of death in dialysis patients, and so a negative
impact on this event could diminish the overall benefit of ASA in preventing death.

**Interventional management**

Left ventricular dysfunction is associated with sudden cardiac death and one quarter of all cardiac deaths in HD patients are due to arrhythmogenic sudden cardiac death [50]. However, the role of ICD implantation in haemodialysis patients with left ventricular dysfunction has not been well established [51]. Current recommendations by the American College of Cardiology state that ICDs should be used as primary prevention in patients with good functional capacity, an EF <30% with mild to moderate symptoms of heart failure and expected survival to be >1 year (level of evidence B) [52]. The role of ICD insertion for primary prevention in patients with EF 30–40% is, in general, much more controversial; however, patients post-ACS with non-sustained ventricular tachycardia or significant symptoms appear to benefit (level of evidence B) [3]. A reasonable number of dialysis patients with severe reductions in EF can be expected to survive >1 year. In the trial by Cice et al, the 2-year mortality for patients with an average EF of 26% on carvedilol was found to be 52% [41]. Using an EF <30% as criteria for ICD implantation in HD patients may be too stringent a criterion as HD patients suffer higher event rates compared to the general population and thereby may benefit the most by their use. As secondary prevention, ICD use appears to be beneficial as Herzog et al. showed a 42% relative risk reduction [RR 0.58 (95% CI 0.50, 0.66)] with ICD implantation in HD patients [53].

Ejection fraction was not available as the data were derived from Medicare claims. Furthermore it appears that ICD usage in HD patients is underutilized as only 8% of eligible HD patients in Herzog’s study received an ICD as secondary prevention. In a small, single-centre study, 8 of 46 (17%) patients with an EF <40% had an ICD implantation; however, indications for ICD insertion were not provided. To date, there are no randomized studies looking at the benefit of ICD implantation as either primary or secondary prevention in HD patients with LV Dys.

Cardiac resynchronization (CRT) with or without ICD implantation is being more frequently utilized for heart failure management in select populations. CRT involves the use of a specialized pacemaker to resynchronize the actions of the left and right ventricle. Benefits include improvements in quality of life, EF, functional class and survival [54,55]. Indications for implantation include EF <35%, a QRS interval of 130 ms and persistent symptoms. Currently no studies have delineated the potential role of CRT in the HD population. A *post hoc* analysis of the COMPANION trial, found among patients who underwent cardiac resynchronization, that renal dysfunction was associated with an increased risk of sudden cardiac death [HR 1.69 (95% CI 1.06–2.69)] but whether this pertains to the ESRD population remains unknown [56]. CRT seems like a viable treatment option in suitable patients with HD; however, studies of clinical outcomes are lacking.

Underutilization of interventional cardiology procedures on HD patients is likely related to under-referral and an increase in complication rate. There is no literature on underutilization in HD; however, the suspicion exists [57]. Increased rates of complication have been shown by Dasgupta et al. They conducted a retrospective, single-centre study finding an overall complication rate of 39% in ESRD patients versus 11% for controls (*P < 0.001*) [58]. Haematomas, thrombosis and other device-related complications were more common in the ESRD group while infection rates were not statistically different. Of note, thrombosis to an access graft or fistula occurred in 3/6 patients when the device was placed ipsilateral and 19% when placed contralateral to the access. Dialysis patients were more likely to have diabetes, hypertension, low albumin and a higher INR versus controls partially explaining these results. Insertion of these devices requires contrast administration for adequate visualization that may damage residual renal function. Overall, complication rates appear to be higher, albeit with a paucity of data on the subject, in HD patients requiring cardiovascular intervention. A careful risk versus benefit assessment in individual patients should guide therapeutic decision making.

**Alternative dialysis modalities**

Hypotension and inability for adequate ultrafiltration often limit effective intermittent haemodialysis therapy with LDYs. This has lead to the exploration of alternative dialysis modalities and techniques.

**Peritoneal dialysis**

Advocates of peritoneal dialysis (PD) have long suggested that this modality is better suited to manage patients with LDYs on account of its continuous, gentle ultrafiltration that avoids the significant haemodynamic fluctuations associated with conventional haemodialysis. However, the validity of this assumption is likely confounded by an era effect, the influence of residual renal function, the type of PD performed (i.e. continuous ambulatory peritoneal dialysis, automated peritoneal dialysis or a hybrid approach) and the choice of dialysate (dextrose only versus dextrose plus icodextrin). To our knowledge there are no randomized controlled trials comparing PD to conventional haemodialysis in the management of CHF or asymptomatic LDYs. Data from a large observational cohort of >100 000 incident ESRD patients between 1995 and 1997 suggest that mortality is actually higher for PD-treated patients with CHF and gets worse with increasing duration of follow-up [59]. This may be related to declining residual renal function, inadequate ultrafiltration with changing membrane characteristics over time or some other PD-specific factor. In fact, sub-clinical overhydration is more common in PD than originally thought and certainly more pronounced than in haemodialysis patients or renal transplant recipients [60,61]. This subtle but significant expansion of extracellular fluid volume in PD is associated with hypertension and left ventricular hypertrophy (LVH), both of which are determinants of LDYs [61,62]. Notwithstanding these findings, good volume and blood pressure control is achievable in the modern PD era with liberal use of icodextrin and hypertonic
dialysate resulting in stabilization of LVH [63,64]. However, it appears that this occurs at the expense of residual renal function and whether the latter offsets the presumed cardiac benefits is not known. In light of this observational evidence, no definitive statement concerning the preferential use of PD in the management of LVDys in ESRD can be made.

New dialysis strategies

Patients undergoing short daily haemodialysis (SDHD) usually receive 1.5–2.5 h of dialysis 5–6 days per week. In comparison to three times per week conventional haemodialysis, SDHD is consistently associated with a decrease in blood pressure, antihypertensive use and LVMi [65,66]. The mechanism underlying this improvement is likely multifactorial but reduced extracellular fluid volume is a probable determinant [65]. Though it is assumed that improved left ventricular geometry mitigates the cardiac dysfunction of ESRD, no studies involving SDHD have demonstrated this to date.

Nocturnal home haemodialysis (NHD) is a treatment paradigm whereby patients self-administer their dialysis on 4–6 nights per week with each session lasting between 6 and 8 h. This strategy combines both high frequency treatments with long duration and has well-documented physiological restorative properties [67]. The cardiovascular benefits were among the first recognized advantages of NHD with a reduction in LVMi of 22% observed in ESRD patients after converting to NHD. Conversely, control subjects remaining on a conventional three times weekly haemodialysis demonstrated a 6% progression of LVMi [68]. This may be particularly relevant for patients with CHF and depressed ejection fraction (EF). In fact, EF improved from 28% to 41% in a small cohort of ESRD patients with CHF [69]. The consistent reduction in blood pressure and antihypertensive medication use, as well as the regression of left ventricular mass associated with NHD, was recently confirmed in a randomized controlled trial comparing cardiovascular characteristics between NHD and conventional haemodialysis [70]. Attenuated LVMi likely results from a decrease in total peripheral resistance and mean arterial pressure, possibly mediated by decreased circulating catecholamines and improved flow-mediated vascular responsiveness [71]; diminished extracellular fluid volume was not demonstrated but cannot be ruled out [68]. Certainly, NHD represents a promising novel approach to manage ESRD patients with LVDys.

Conclusions

LVDys is highly prevalent in HD patients and confers a worse prognosis in this already highly co-morbid population. The most commonly used measurement technique, 2D echocardiography, can lead to underestimation of LV function rendering interpretation of the literature problematic. The routine use of modern measurement techniques will hopefully allow for more accurate estimates of prevalence.

Limited evidence exists regarding therapeutic options for management in these patients. The most robust data support the use of beta-blocker therapy; however, there remains a paucity of studies to support the routine use of renin–angiotensin system blockade or ASA. Interventional therapies are potentially underutilized in the HD population due to increased rates of complications and under-referral. ICDs appears to be beneficial as a secondary prevention measure; however, the question of its use in primary prevention remains unknown and their widespread adoption is at present cost prohibitive. The benefit of novel management strategies such as cardiac resynchronization and the use of home nocturnal haemodialysis have shown promise for managing these patients; however, larger trials need to be carried out to confirm original findings in these areas.

In conclusion, much work remains to be done in this high-risk patient group with a significant burden of illness pertaining to LVDys. Large randomized controlled trials are necessary to establish evidence-based guidelines in management of these patients, as therapeutic interventions with demonstrable benefit may not reliably be extrapolated from studies involving LVDys in the non-HD population.

Conflict of interest statement. None declared.

References

1. USRDS. USRDS 2006 Annual Data Report. The National Institute of Health. Am J Kidney Dis 2006; 49(Suppl 1): s1
2. Jassal S, Trpskí L, Zhu N et al. Changes in survival among elderly patients initiating dialysis from 1990 to 1999. CMAJ 2007; 177: 1033–1038
3. Stack AG, Bloembergen WE. A cross-sectional study of the prevalence and clinical correlates of congestive heart failure among incident US dialysis patients. Am J Kidney Dis 2001; 38: 992–1000
4. Collins AJ. Impact of congestive heart failure and other cardiac diseases on patient outcomes. Kidney Int Suppl 2002; 8: S3–S7.
5. Trespalacios FC, Taylor AJ et al. Heart failure as a cause for hospitalization in chronic dialysis patients. Am J Kidney Dis 2003; 41: 1267–1277
6. Silberberg JS, Barre PE et al. Impact of left ventricular hypertrophy on survival in end-stage renal disease. Kidney Int 1989; 36: 286–290
7. Zoccali C, Benedetto FA. Prognostic impact of the indexation of left ventricular mass in patients undergoing dialysis. J Am Soc Nephrol 2001; 12: 2768–2774
8. Zoccali C, Benedetto FA et al. Prognostic value of echocardiographic indicators of left ventricular systolic function in asymptomatic dialysis patients. J Am Soc Nephrol 2004; 15: 1029–1037
9. Foley RN, Parfrey P et al. The prognostic importance of left ventricular geometry in uremic cardiomyopathy. J Am Soc Nephrol 1995; 5: 2024–2031
10. London GM, Pannier B et al. Alterations of left ventricular hypertrophy in and survival of patients receiving hemodialysis: follow-up of an interventional study. J Am Soc Nephrol 2001; 12: 2759–2767
11. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Am J Kidney Dis 2005; 45(Suppl 3): S1–S153.
12. SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med 1991; 325: 293–302
13. Levy D, Savage DD et al. Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart Study. Am J Cardiol 1987; 59: 956–960
14. Foley RN, Parfrey PS et al. Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 1995; 47: 186–192
15. Foley RN, Parfrey PS et al. Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 1998; 54: 1720–1725
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60. Enia G, Mallamaci F et al. Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than haemodialysis patients. Nephrol Dial Transplant 2001; 16: 1459–1464

61. Konings CJ, Kooman JP et al. Fluid status, blood pressure, and cardiovascular abnormalities in patients on peritoneal dialysis. Perit Dial Int 2002; 22: 477–487

62. Koc M, Toprak A et al. Uncontrolled hypertension due to volume overload contributes to higher left ventricular mass index in CAPD patients. Nephrol Dial Transplant 2002; 17: 1661–1666

63. Konings CJAM, Kooman JP et al. Effect of icodextrin on volume status, blood pressure and echocardiographic parameters: a randomized study. Kidney Int 2003; 63: 1556–1563

64. Ascì G, Ozkahya M et al. Volume control associated with better cardiac function in long-term peritoneal dialysis patients. Perit Dial Int 2006; 26: 85–88

65. Fagugli R, Reboldi G et al. Short daily hemodialysis: blood pressure control and left ventricular mass reduction in hypertensive hemodialysis patients. Am J Kidney Dis 2001; 38: 371–376

66. Traeger J, Galland R et al. Six years’ experience with short daily hemodialysis: Do the early improvements persist in the mid and long term? Hemodialysis Int 2004; 8: 151–158

67. Pauly RP, Chan CT. Reversing the risk factor paradox: Is daily nocturnal hemodialysis the solution? Semin Dial 2007; 20: 539–543

68. Chan CT, Floras JS et al. Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. Kidney Int 2002; 61: 2235–2239

69. Chan C et al. Improvement in ejection fraction by nocturnal haemodialysis in end-stage renal failure patients with coexisting heart failure. Nephrol Dial Transplant 2002; 17: 1518–1521

70. Culleton BF et al. Effect of frequent nocturnal hemodialysis versus conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. JAMA 2007; 298: 1291–1299

71. Chan CT et al. Short-term blood pressure, noradrenergic, and vascular effects of nocturnal home hemodialysis. Hypertension 2003; 42: 925–931

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