

BRINGING THE BENEFITS OF HIGH-DOSE HAEMODIALYSIS TO THE HOME WITH A NOVEL HAEMODIALYSIS SYSTEM

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Dialysis Inadequacy: Understanding the Limitations of Conventional Haemodialysis

Professor Chris McIntyre

Haemodialysis (HD) is a haemodynamically traumatic practice that is known to cause ischaemic insult to a variety of organs. Reductions in perfusion pressure as well as the stress of ultrafiltration are thought to give rise to these ischaemic insults. In turn, these stresses are associated with an increased risk of mortality.¹

Investigations have been assessing the haemodynamic stress of dialysis and its effects on a number of organs, specifically the heart, gut, and brain. As HD patients exhibit a high incidence of heart failure and cardiovascular death, two studies were conducted to determine whether HD was capable of driving recurrent myocardial ischaemia.^{2,3} Four patients had measurements of myocardial perfusion using a positron emission tomography (PET) scanner during dialysis.

Myocardial blood flow (MBF) was acutely reduced during dialysis and became progressively worse over time.² Two-dimensional (2D) echocardiography was performed to evaluate regional wall motion abnormalities (myocardial stunning) before, during, and after dialysis.² In a second study, approximately two-thirds of the 70 patients analysed had significant regional wall motion abnormalities during and after dialysis.³

Factors associated with the development of myocardial stunning were ultrafiltration volume and blood pressure (BP) levels during dialysis.³ At 12-month follow-up there was a marked reduction in contractile function in the regions of the heart that stunned upon dialysis with almost half the contractile function lost.^{3,4} In contrast, heart regions that did not stun showed no reduction in contractile function. Patients with myocardial stunning also displayed significantly lower left ventricular ejection fraction at rest and on HD (Figure 1). Myocardial stunning also has an impact on survival, with decreased survival in the patient group that exhibited stunning. Other studies have

HD-Induced Myocardial Stunning Leads to Myocardial Hibernation and Reduction in Overall Systolic Function

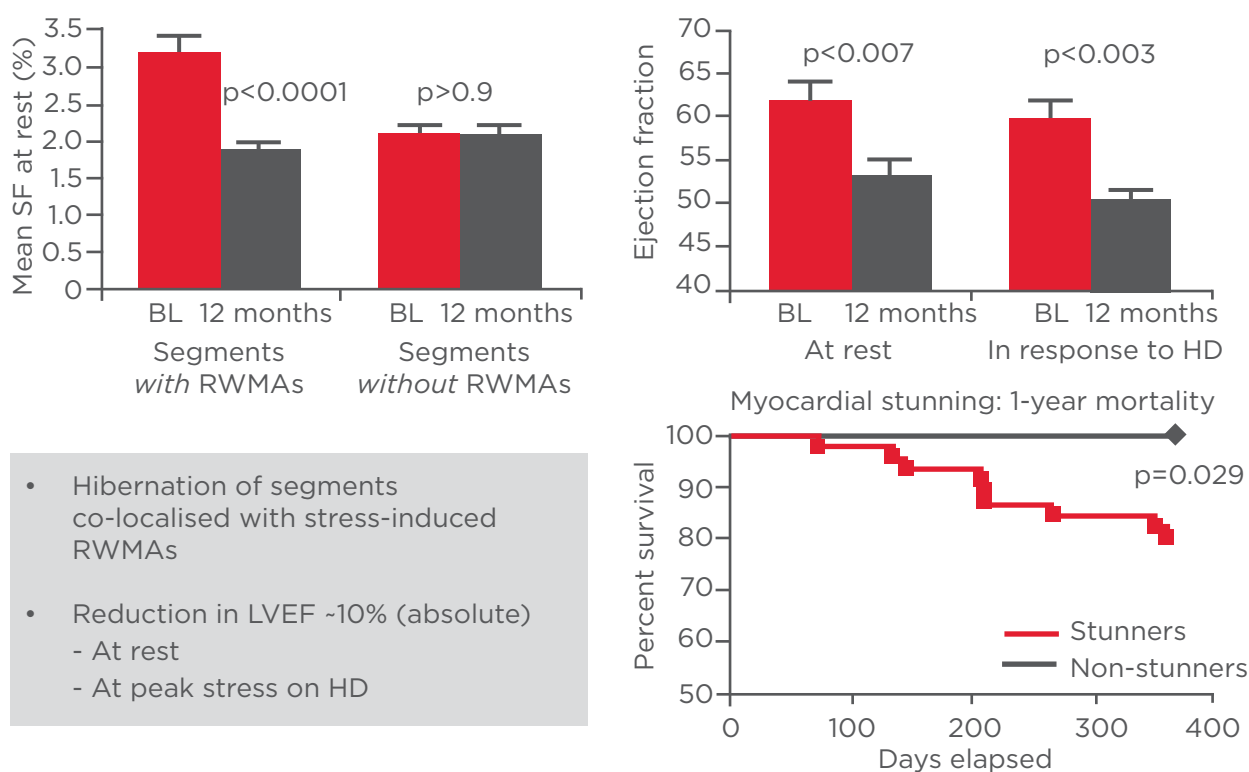


Figure 1: The consequences of haemodialysis (HD)-induced myocardial stunning.

BL: baseline; LVEF: left ventricular ejection fraction; SF: systolic function; RWMA: regional wall motion abnormality.

Modified from Burton et al.³ and Burton et al.⁴

shown a gradation between myocardial stunning and death; a greater number of stunned segments being associated with higher mortality.⁵

To assess uraemia and dialysis in a patient population where diabetes, smoking, and epicardial large vessel disease are not factors, a paediatric sample was used. Using the same echo-based methods, all 12 children tested exhibited significant myocardial stunning.⁶ A link between stunning and post-dialysis fatigue has also been shown where patients who experience increased myocardial stunning are more likely to feel exhausted in between treatments.⁷ Serum endotoxin levels were assessed in 250 patients including those with chronic kidney disease (CKD) Stage 3, Stage 4, Stage 5, those receiving peritoneal dialysis (PD), HD, and a comparison group of non-CKD patients. Significantly high endotoxin levels were observed in the HD and PD groups (*p* < 0.001), in comparison to CKD patients not receiving dialysis. These effects were also associated with mortality.⁸ Dialysis has also been shown to have effects on the brain.

Specifically, HD patients exhibit an increase in generalised cerebral atrophy, silent cerebral infarcts, effects on cerebral blood flow, and leukoaraiosis.

To measure white matter ultra-structural injury, a cohort of 55 HD-naïve patients underwent diffusion tensor imaging, matched with 25 normal volunteers for age, BP, and arterial stiffness (McIntyre personal comm.). The scans of all patients were merged to generate a 3D organisational map of the brains and similarly for the volunteers, and both data sets were analysed for areas that were significantly more disrupted. The patients' cohort displayed widespread white matter ultrastructural injury (Figure 2). Functional significance was tested by subjecting patients to cognitive function testing, specifically the Montreal Cognitive Assessment Test and trail-making tests. Dialysis patients were markedly worse, with the biggest difference seen in the subcortical white matter tests, showing that it was functionally significant and correlated to the level of brain injury (McIntyre personal comm.).

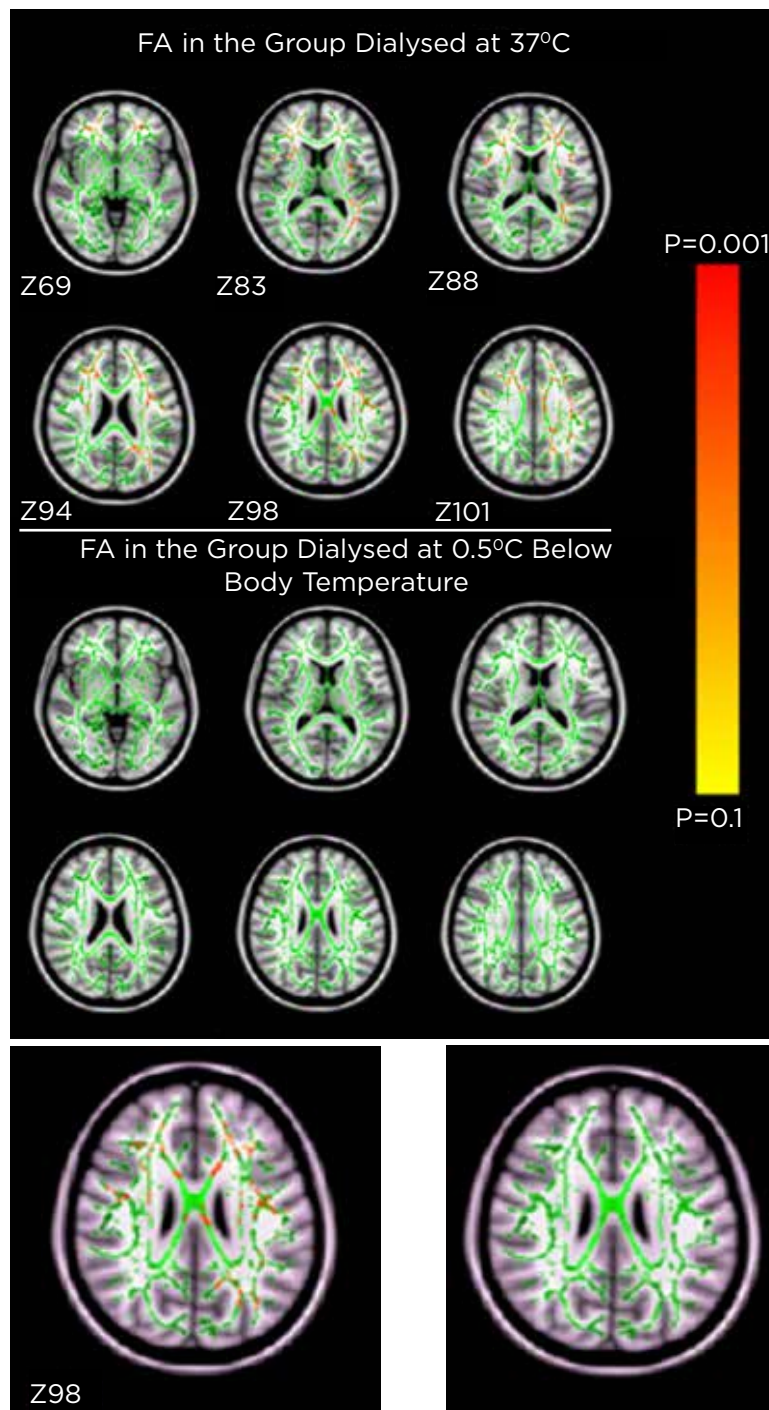


Figure 2: Brain - protection against progressive white matter ultrastructural injury.
McIntyre, personal communication.

A systematic analysis revealed that cooling the dialysate may be an effective and safe way to resolve ischaemic insults to the heart, gut, and brain. In initial studies, individuals were cooled to 35 °C; however, it is difficult for patients to experience this temperature in the long term,⁹ and in further studies patients were cooled sequentially. The tympanic temperature appears to be the ideal temperature. A randomised controlled trial was then

conducted in 72 HD-naïve patients randomised to conventional temperature or individualised cooling. At 12-month follow-up, brains of patients who were not cooled had evidence of progressive brain injury, whereas patients who were cooled had no evidence of brain injury (McIntyre personal comm.). Cardio-protection was evidenced by ventricular size, preservation of systolic function, and protection of diastolic dysfunction.⁹

The effect of dialysis on weight gain was assessed in patients receiving treatment in-centre three times a week (CHD3), in-centre five times a week (CSD), short daily (SDHD), and nocturnal (NHD) at home.¹⁰ The SDHD and NHD groups showed a much lower weight gain and less change in BP during dialysis. Echocardiography revealed that all the patients in the CHD3 group displayed myocardial stunning. In addition, intensive dialysis resulted in normalised serum endotoxin levels (as shown by the endotoxin levels in the short daily and nocturnal groups). Dialysis results in recurrent ischaemic injury with the heart and brain being particularly vulnerable. It is possible to protect against this stress and thus increase survival.

Improving Clinical Endpoints and Health-Related Quality of Life with High-Dose HD

Doctor Tom Cornelis

Studies have shown that high-dose HD has several clinical benefits such as optimised anaemia control, left ventricular systolic function, arterial compliance, sleep apnoea, autonomic nervous system functioning, and improvements in phosphate control.¹¹

Using conventional dialysis modalities such as HD and PD, patients at CKD Stage 5 remain at this stage with clearances of 15 mL/minute, which results in suboptimal volume and phosphate control. Upon kidney transplantation, CKD Stage 3 or even 2 can be achieved, resulting in optimised phosphate and volume control. In between conventional HD and transplantation, high-dose HD modalities such as SDHD, NHD can result in a decrease of CKD Stage from 5 to 3. Observational studies conducted in the USA, Australia, and New Zealand comparing intensive HD to conventional HD show significantly reduced mortality ratios in intensive cohorts.¹²⁻¹⁶

It is assumed that patients on high-dose HD have an improved quality of life (QoL) as they are not dependent on HD schedules within a dialysis unit, enabling them to have increased autonomy/independence.¹⁷ Furthermore, such patients also experience the clinical benefits of high-dose HD, have a reduced pill burden as they require fewer hypertensive pills and phosphate binders,^{18,19} and have a more liberal diet and fluid intake.²⁰ Travel to and from the hospital is eliminated; instead they experience the convenience of dialysing at home,

allowing them to alter the treatment schedule as they wish. When dialysis is conducted in a nocturnal fashion it enables them to continue with employment.²¹ High-dose HD also decreases the incidence of sleep apnoea, resulting in improved sleep quality and consequently reduced daytime sleepiness.²² Furthermore, there is evidence to support that high-dose HD produces a reduction in uraemic symptoms and inflammation.^{23,24} All of these factors contribute to an improvement in QoL in high-dose HD.

Multiple studies have shown that high-dose HD has resulted in improvements in kidney-specific QoL and burden of kidney disease.²⁵⁻²⁸ Moreover, the FREEDOM study showed a reduction in depression score (Beck Depression Inventory [BDI]) after 12 months of SDHD.²⁹ The Daily FHN trial showed no significant change in BDI but an improvement in mental health composite ($p=0.007$) and emotional subscale ($p=0.01$) scores.³⁰

A meta-analysis conducted by Susantitaphong et al.³¹ included studies on frequent HD and extended HD on left ventricular hypertrophy, and showed a significant reduction in left ventricular mass index to -31 g/m^2 and an improvement in left ventricular ejection fraction with high-dose HD.

Gene expression in rat cardiomyocytes showed a significant downregulation of genes involved in cardiac apoptosis and fibrosis and a significant upregulation of *S100a*, a gene involved in cardiac contractility when exposed to plasma from patients converted from conventional to nocturnal HD.³² Another study showed a significant improvement in endothelial function;³³ microvascular perfusion of ischaemic rat hindlimb tissue was improved after injection of endothelial progenitor-like cells from nocturnal HD patients and healthy controls compared with saline (negative control), whereas cells derived from conventional HD patients had no beneficial effect when compared with saline.

A randomised cross-over trial was conducted in HD patients who underwent a single session of 4-hourly HD, 4-hourly haemodiafiltration, 8-hourly HD, and 8-hourly haemodiafiltration with a 2-week interval when they underwent conventional HD.³⁴ The results showed a reduction in the change of peripheral and central systolic BP, also a decrease in the change of cardiac output and relative blood volume. These results provide further evidence of the cardioprotective effects of high-dose HD (Table 1). Uraemic toxin studies showed that

Table 1: Acute haemodynamic (HD) effects in extended dialysis.

Parameter	4h HD	4h HDF	8h HD	8h HDF
Peripheral SBP, mmHg	-21.7	-23.3	-6.7*	-0.5*†
Peripheral DBP, mmHg	-5.0	-11.5	-1.1†	-1.2†
Central SBP, mmHg	-19.2	-24.2	-7.1	-3.8
Central DBP, mmHg	-5.0	-12.1*	-2.6	+3.5†
CO, L/minute	-1.4	-1.6	-0.4†	-0.5†
RBV, %	-1.8	-9.1	-4.4†	-3.3*†
ET rate, W	-13.1	-16.2	-14.2	-14.5

*p<0.05 vs 4h HD; †p<0.05 vs 4h HDF

CO: cardiac output; DBP: diastolic blood pressure; ET: energy transfer; RBV: relative blood volume; SBP: systolic blood pressure; HDF: haemodiafiltration.

Cornelis et al.³⁴

extending dialysis optimised the reduction in β 2 microglobulin and fibroblast growth factor (FGF)-23,³⁴ providing further evidence of the improved cardiovascular outcomes in extended dialysis. However, longer-term studies are required to confirm this.

The benefits of high-dose HD, such as reduction of uraemic toxin levels, peripheral vascular resistance, hypervolaemia, BP, and endothelial dysfunction, were thought to result in improved pregnancy outcomes such as optimisation of placental development, reduction of pre-eclampsia, prevention of polyhydramnios, and better fetomaternal outcomes. A recent study investigated pregnancy outcomes in a nocturnal home HD cohort in Toronto and compared these with conventional HD pregnancy outcomes in the American Registry of Pregnancy in Dialysis.³⁵ A significant dose-response relationship was established between hours of HD and live birth rate. This was further confirmed in a time-to-event analysis where the higher dose showed a greater cumulative survival compared to the lower-dose HD group. There is also evidence from a single study that sex hormones may be better regulated in high-dose HD.³⁶

Despite the many beneficial effects of high-dose HD, there are some adverse events. The Frequent Haemodialysis Network (FHN) trial showed an increased loss of residual renal function after 12 months in nocturnal patients in comparison to conventional patients,³⁷ and not in the short daily trial. Furthermore, an in-depth review showed

that patients in the high-dose or intensive group exhibited an increase in vascular access events in comparison to the conventional group, which may be related to cannulation.³⁸

A Canadian study, investigating adverse events in the home setting, found that although adverse events are minimal, human errors do occur such as lapses in protocol adherence.³⁹ This points to the need for a quality assurance framework where programmes and cases are discussed as well as techniques of patients, among other issues.

In conclusion, there appears to be much evidence to support high-dose HD as an option for patients with end-stage renal disease; however, this method is still underutilised. Potential adverse events of high-dose HD still require further study. However, randomised controlled trials are difficult to perform and this raises the question of whether we should be relying on observational studies and day-to-day clinical experience. The option of incremental home HD should also be considered, where patients are started conventionally and up-titrated in the intensity of the dose while monitoring residual kidney function as well as other clinical parameters.

Overcoming Barriers to the Growth of Home HD through Device Innovation

Doctor Bruce Culleton

High-dose HD is associated with numerous clinical benefits, and a better QoL.^{13,18,27} However, it has

also been established that high-dose and home HD have associated risks to the patient.⁴⁰ It is important to remember that some of these risks are inherent to the HD procedure itself. Similarly, there are inherent risks to the user-device interaction, which could be reduced or prevented with improved innovation in HD devices.

A survey conducted by Dr Sandip Mitra along with the European Renal Association found that 70% of nephrologists believed that there was sufficient evidence in the literature in favour of longer, more frequent HD schedules. Of the respondents, 75% believed that the HD modality that offers the best patient outcome in any setting was either frequent nocturnal, alternate nightly, or short daily HD.⁴¹ Only 6% opted for three times per week haemodiafiltration. Using data published in registries and internal data, a wide variance in the prevalence of home HD was observed, with 10% use in Australia, 3% in the Netherlands, and <1% in France and Germany.

There are several reasons why home HD is not more widespread, including lack of education of the patient and carer to be able to make an informed choice of the different types of treatment modality, and patients may not feel motivated or confident enough to perform the therapy in the home/themselves.⁴²⁻⁴⁴ There is also a general fear surrounding cannulation, and 'learned helplessness', where patients feel helpless as they are well looked after within the dialysis unit. Increased comorbidity plays a role as patients get older and sicker. On the organisational side, healthcare practitioners are in need of more education on the different dialysis modalities and also how to perform these procedures.⁴⁴ Misaligned economic incentives is another contributing factor as is operation and infrastructure demands, and uncertainties such as questions around how to actually initiate/grow a programme determine how many nurses/technicians are needed, etc.⁴⁴ These factors make it difficult to send patients to the home environment for HD.

When Baxter Healthcare came to designing an HD device for the home, three main goals were set: 1) deliver superior clinical and health-related QoL outcomes through device design and services; 2) deliver best-in-class safety, simplicity, and support services; and 3) deliver favourable economics for all stakeholders.

Baxter, in partnership with other key companies, developed a HD device named Vivia™. One of the

key features of the device is a tablet/screen that plays animated clips to help guide the patient through set-up and resolving alarms. In an effort to limit the fear associated with venous access disconnection, the device includes a built-in access-disconnect sensor. Wires are embedded within the arterial and venous tubing, meaning that if a needle should fall from the venous or arterial access then the blood pump will stop automatically, resulting in minimal blood loss in the patient. The device also includes an extended-use dialyser, allowing short daily treatments at least 5 days per week for sessions that typically run for fewer than 4 hours, or as nocturnal treatments where sessions are conducted for >6 hours while the patient sleeps, thereby reducing the burden of home treatment. Multiple uses of the blood treatment-set combined with hot water disinfection mean the device is environmentally friendly. Furthermore, Vivia comes with a web-based connectivity platform called Sharesource™ which allows communication to and from the clinic, enabling healthcare professionals to monitor their patient's treatment data and remotely edit device settings as required. As well as keeping the clinic informed, the aim is also to give the patient confidence in performing dialysis in the home. It is hoped that these features will tackle some of the barriers for patients to conduct HD in the home.

A first-in-human clinical study using the Vivia system was conducted in the USA with 22 subjects who were dialysed four times per week for 10 weeks. The standard weekly Kt/V urea was above the values stated by the guidelines, blood flow on average was 316 mL/minute, and the dialysate flow was 395 mL/minute.^{45,46} The feasibility of extending use of the dialyser and blood set was also studied. Approximately 40% of the treatments (269) were delivered on dialysers that were used ten or more times, and about 25% of the treatments with dialysers were used five-to-nine times (Figure 3).

Over the course of extending the use of the dialyser, there was only a minimal change in small molecule clearance as assessed using urea clearance, even after more than ten uses. Middle molecule clearance declined after several uses of the dialyser; however, the baseline mean β_2 clearance was 77 mL/minute, which is considered very good, meaning that a 10% reduction in this value over time is not a significant decline, especially if patients receive longer treatments. None of the

Extended Use of the Dialyser by Category of Treatments Achieved

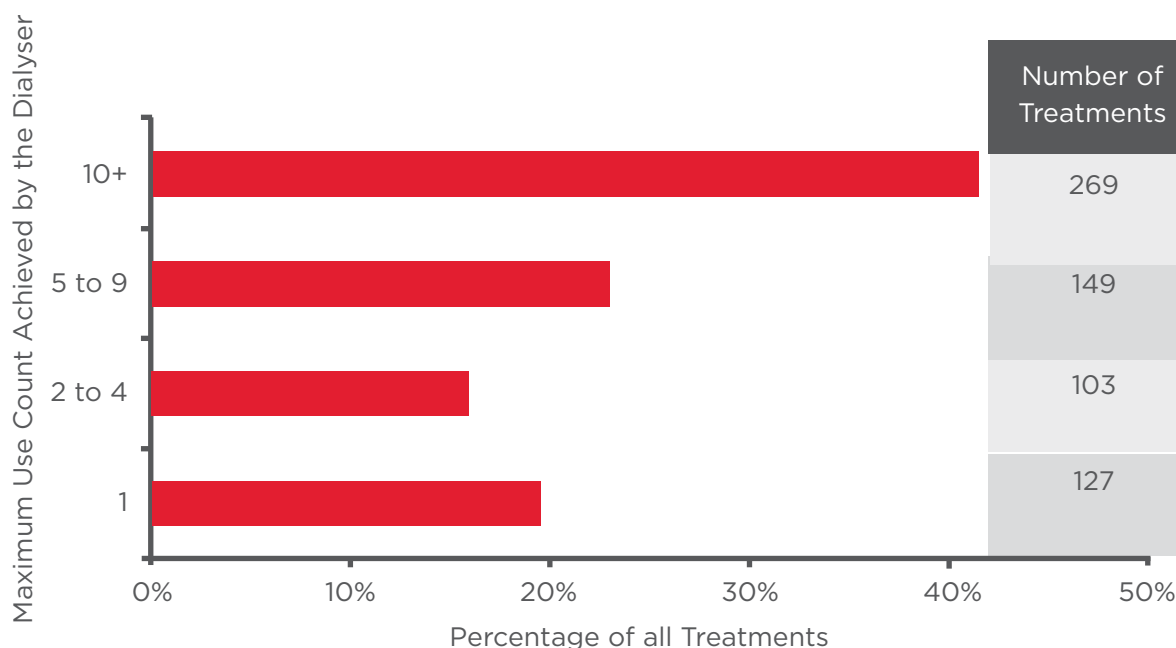


Figure 3: Safety and efficacy of the Vivia™ HD system; results from the first-in-human clinical study. 2014 ERA-EDTA Annual Meeting; SP415.

271 dialysate samples taken at different counts of dialysis use (ranging from first use to more than ten times) revealed any bacteria, and all samples met the international standards for bacteria as well as endotoxin.

A nocturnal clinical study assessed the feasibility of extending dialyser use under longer treatments.⁴⁶ All subjects underwent three treatments per week for 6 weeks. Results revealed that a large between-patient and within-patient variability exists for dialyser use, with some patients using only 3 dialysers during treatment and others using up

to 17. This variability points to the importance of establishing an optimal anticoagulation blood circuit in order to extend the use of the dialyser and blood set.

In conclusion, high-dose HD has numerous clinical and QoL benefits, yet relatively few patients are provided this therapy due to a number of factors. Some of these issues could be addressed with improved HD device innovation and design as well as improvement in the services and support patients receive.

REFERENCES

- McIntyre CW. Effects of hemodialysis on cardiac function. *Kidney Int.* 2009;76:371-5.
- McIntyre CW et al. Hemodialysis-induced cardiac dysfunction is associated with an acute reduction in global and segmental myocardial blood flow. *Clin J Am Soc Nephrol.* 2008;3:19-26.
- Burton JO et al. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol.* 2009;4:914-20.
- Burton JO et al. Hemodialysis-induced repetitive myocardial injury results in global and segmental reduction in systolic cardiac function. *Clin J Am Soc Nephrol.* 2009;4:1925-31.
- Assa S et al. Hemodialysis-induced regional left ventricular systolic dysfunction: prevalence, patient and dialysis treatment-related factors, and prognostic significance. *Clin J Am Soc Nephrol.* 2012;7:1615-23.
- Hothi DK et al. Hemodialysis-induced acute myocardial dyssynchronous impairment in children. *Nephron Clin Pract.* 2013;123:83-92.
- Dubin RF et al. Association of segmental wall motion abnormalities occurring during hemodialysis with post-dialysis fatigue. *Nephrol Dial Transplant.* 2013;28:2580-5.
- McIntyre CW et al. Circulating endotoxemia: a novel factor in systemic inflammation and cardiovascular disease in chronic kidney disease. *Clin J Am Soc Nephrol.* 2011;6:133-41.
- Odudu A et al. Rationale and design of a multi-centre randomised controlled trial of individualised cooled dialysate to prevent left ventricular systolic dysfunction in haemodialysis patients.

10. Jefferies HJ et al. Frequent hemodialysis schedules are associated with reduced levels of dialysis-induced cardiac injury (myocardial stunning). *Clin J Am Soc Nephrol*. 2011;6:1326-32.

11. Perl J et al. Home hemodialysis, daily hemodialysis, and nocturnal hemodialysis: Core Curriculum 2009. *Am J Kidney Dis*. 2009;54:1171-84.

12. Johansen KL et al. Survival and hospitalization among patients using nocturnal and short daily compared to conventional hemodialysis: a USRDS study. *Kidney Int*. 2009;76:984-90.

13. Marshall MR et al. Home hemodialysis and mortality risk in Australian and New Zealand populations. *Am J Kidney Dis*. 2011;58:782-93.

14. Lockridge RS et al. Nightly home hemodialysis: outcome and factors associated with survival. *Hemodial Int*. 2011;15:211-8.

15. Nesrallah GE et al. Intensive hemodialysis associates with improved survival compared with conventional hemodialysis. *J Am Soc Nephrol*. 2012;23:696-705.

16. Weinhandl ED et al. Survival in daily home hemodialysis and matched thrice-weekly in-center hemodialysis patients. *J Am Soc Nephrol*. 2012;23:895-904.

17. Hall YN et al. Effects of six versus three times per week hemodialysis on physical performance, health, and functioning: Frequent Hemodialysis Network (FHN) randomized trials. *Clin J Am Soc Nephrol*. 2012;7:782-94.

18. Chertow GM et al. In-center hemodialysis six times per week versus three times per week. *N Engl J Med*. 2010;363:2287-300.

19. Daugirdas JT et al. Effects of frequent hemodialysis on measures of CKD mineral and bone disorder. *J Am Soc Nephrol*. 2012;23:727-38.

20. Sikkes ME et al. Improved nutrition after conversion to nocturnal home hemodialysis. *J Ren Nutr*. 2009;19:494-9.

21. Pierratos A. Nocturnal home haemodialysis: an update on a 5-year experience. *Nephrol Dial Transplant*. 1999;14:2835-40.

22. Pierratos A et al. Nocturnal hemodialysis improves sleep quality in patients with chronic renal failure. *J Am*

Soc Nephrol. 1997;8:169A.

23. Manohar NL et al. Success of frequent short hemodialysis. *Trans Am Soc Artif Intern Organs*. 1981;27:604-9.

24. Ayus JC et al. Effects of short daily versus conventional hemodialysis on left ventricular hypertrophy and inflammatory markers: a prospective, controlled study. *J Am Soc Nephrol*. 2005;16:2778-88.

25. Manns BJ et al. Nocturnal hemodialysis does not improve overall measures of quality of life compared to conventional hemodialysis. *Kidney Int*. 2009;75:542-9.

26. Finkelstein FO et al. At-home short daily hemodialysis improves the long-term health-related quality of life. *Kidney Int*. 2012;82:561-9.

27. Culleton BF et al. Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. *JAMA*. 2007;298:1291-9.

28. Heidenheim AP et al. Patient quality of life on quotidian hemodialysis. *Am J Kidney Dis*. 2003;42:36-41.

29. Jaber BL et al. Effect of daily hemodialysis on depressive symptoms and postdialysis recovery time: interim report from the FREEDOM (Following Rehabilitation, Economics and Everyday-Dialysis Outcome Measurements) Study. *Am J Kidney Dis*. 2010;56:531-9.

30. Rocco MV et al. The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial. *Kidney Int*. 2011;80:1080-91.

31. Susantitaphong P et al. Effect of frequent or extended hemodialysis on cardiovascular parameters: a meta-analysis. *Am J Kidney Dis*. 2012;59:689-99.

32. Chan CT et al. Impact of frequent nocturnal hemodialysis on myocardial mechanics and cardiomyocyte gene expression. *Circ Cardiovasc Imaging*. 2012;5:474-80.

33. Yuen DA et al. Nocturnal hemodialysis is associated with restoration of early-outgrowth endothelial progenitor-like cell function. *Clin J Am Soc Nephrol*. 2011;6:1345-53.

34. Cornelis T et al. Acute hemodynamic response and uremic toxin removal in conventional and extended hemodialysis and hemodiafiltration: a randomized crossover study. *Am J Kidney Dis*. 2014.

35. Hladunewich MA et al. Intensive hemodialysis associates with improved pregnancy outcomes: a Canadian and United States cohort comparison. *J Am Soc Nephrol*. 2014;25:1103-9.

36. van EC et al. Changes in serum prolactin, sex hormones and thyroid function with alternate nightly nocturnal home haemodialysis. *Nephrology (Carlton)*. 2012;17:42-7.

37. Daugirdas JT et al. Effect of frequent hemodialysis on residual kidney function. *Kidney Int*. 2013;83:949-58.

38. Cornelis T et al. Vascular access vulnerability in intensive hemodialysis: a Significant Achilles' Heel? *Blood Purif*. 2014;37:222-8.

39. Wong B et al. Procedure-related serious adverse events among home hemodialysis patients: a quality assurance perspective. *Am J Kidney Dis*. 2014;63:251-8.

40. Pauly RP et al. Patient and technique survival among a Canadian multicenter nocturnal home hemodialysis cohort. *Clin J Am Soc Nephrol*. 2010;5:1815-20.

41. Jayanti A MS. Home Hemodialysis: Survey Results. <http://ndt-educational.org/hhd.htm>. Accessed: 2014.

42. Cafazzo JA et al. Patient-perceived barriers to the adoption of nocturnal home hemodialysis. *Clin J Am Soc Nephrol*. 2009;4:784-9.

43. Young BA et al. How to overcome barriers and establish a successful home HD program. *Clin J Am Soc Nephrol*. 2012;7:2023-32.

44. Golper TA et al. Systematic barriers to the effective delivery of home dialysis in the United States: a report from the Public Policy/Advocacy Committee of the North American Chapter of the International Society for Peritoneal Dialysis. *Am J Kidney Dis*. 2011;58:879-85.

45. Bernardo A et al. Safety and performance of a home haemodialysis device: results from the first in-human study with a novel home HD system. 2014; Abstract SP415. Presented at: the 51st ERA-EDTA Congress, 31 May-3 June 2014, Amsterdam, the Netherlands.

46. McFarlane P et al. Nocturnal haemodialysis with the vivia haemodialysis system. 2014; Abstract SP431. Presented at: the 51st ERA-EDTA Congress, 31 May-3 June 2014, Amsterdam, the Netherlands.