Update on Frequent Hemodialysis

Increased Hemodialysis Frequency Versus Increased Dialysis Duration

Berlin Dialyse Seminar 2009

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Objectives

- To discuss the rationale of Frequent HD
- To compare short daily HD (frequency) versus nocturnal HD (frequency + duration)

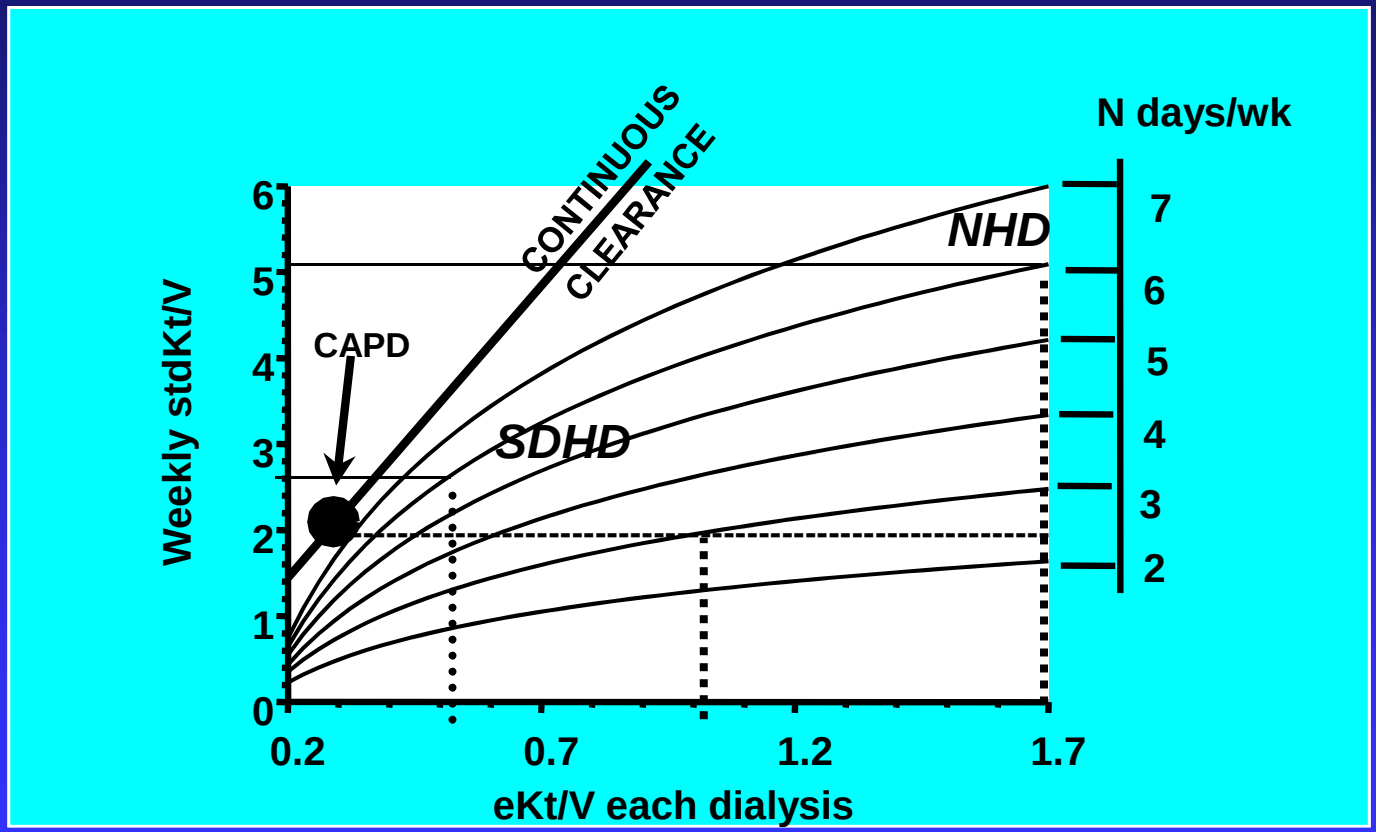
Possible solutions for poor ESRD Rx outcomes

- ***Higher dialysis dose***
  - ***Hemo study – no benefit***
  - ***ADEMEX study – no benefit***
- ***Alternative schedules***
  - ***Daily (quotidian HD)***
  - ***Intermittent long HD***
- ***Alternative modalities***
  - ***Hemo(dia)filtration***
  - ***Sorbents***
  - ***Other***
- ***Address the co-morbidities → RETURN TO NORMAL PHYSIOLOGY***

Typical Treatment Parameters During Quotidian Hemodialysis

	Conventional HD	Short Daily HD	Nocturnal HD	NxStage HD
Treatments/wk	3	6	5-6	6
Treatment time (hrs)	4	2-3	6-8	2.5-3.5
Blood Flow Rate (ml/min)	400	400	200	400
Dialysate Flow Rate (ml/min)	500	800	300	130

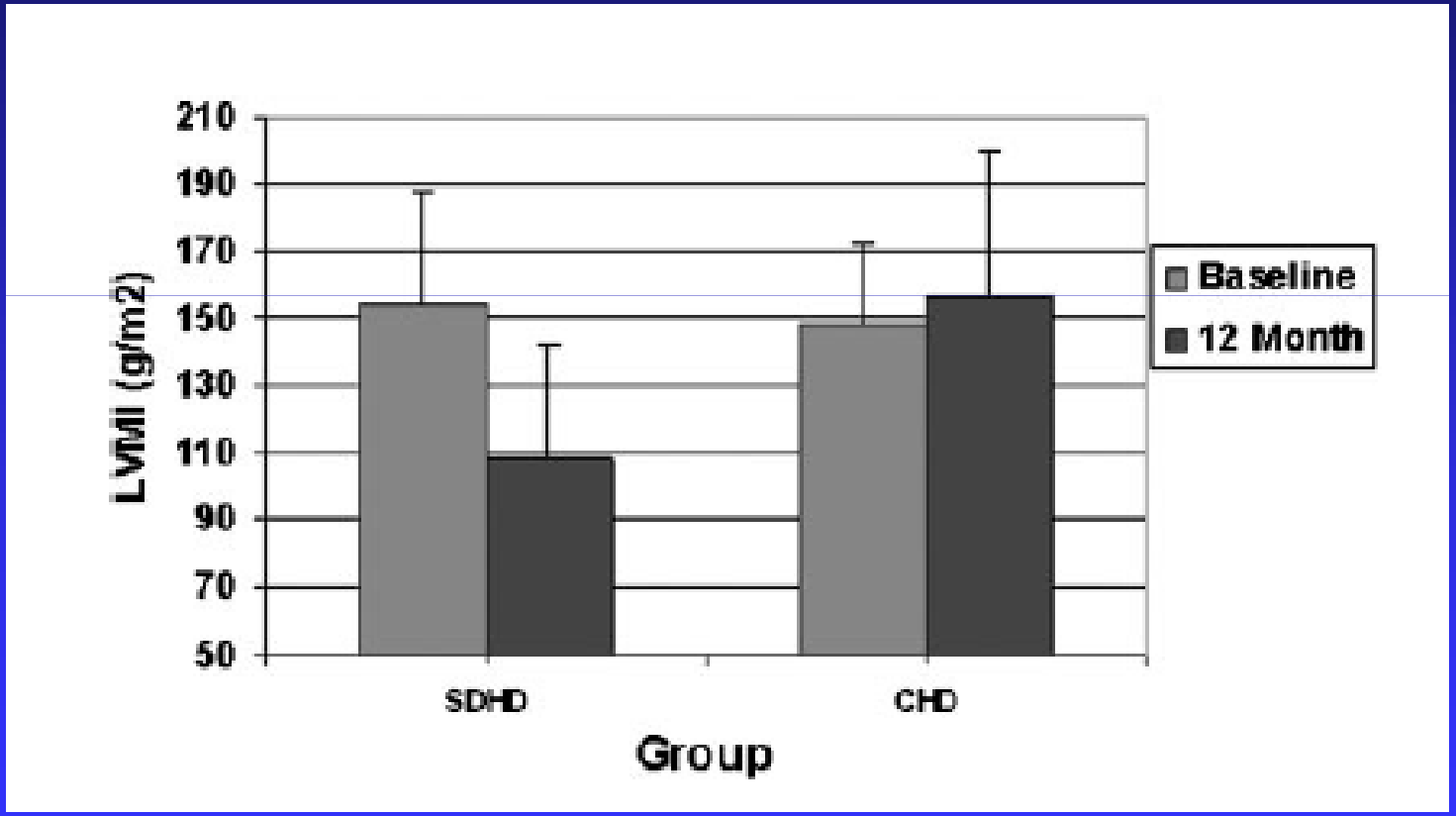
Weekly stdKt/V for different eKt/V and dialysis frequency



Gotch FA 1998 (modified)

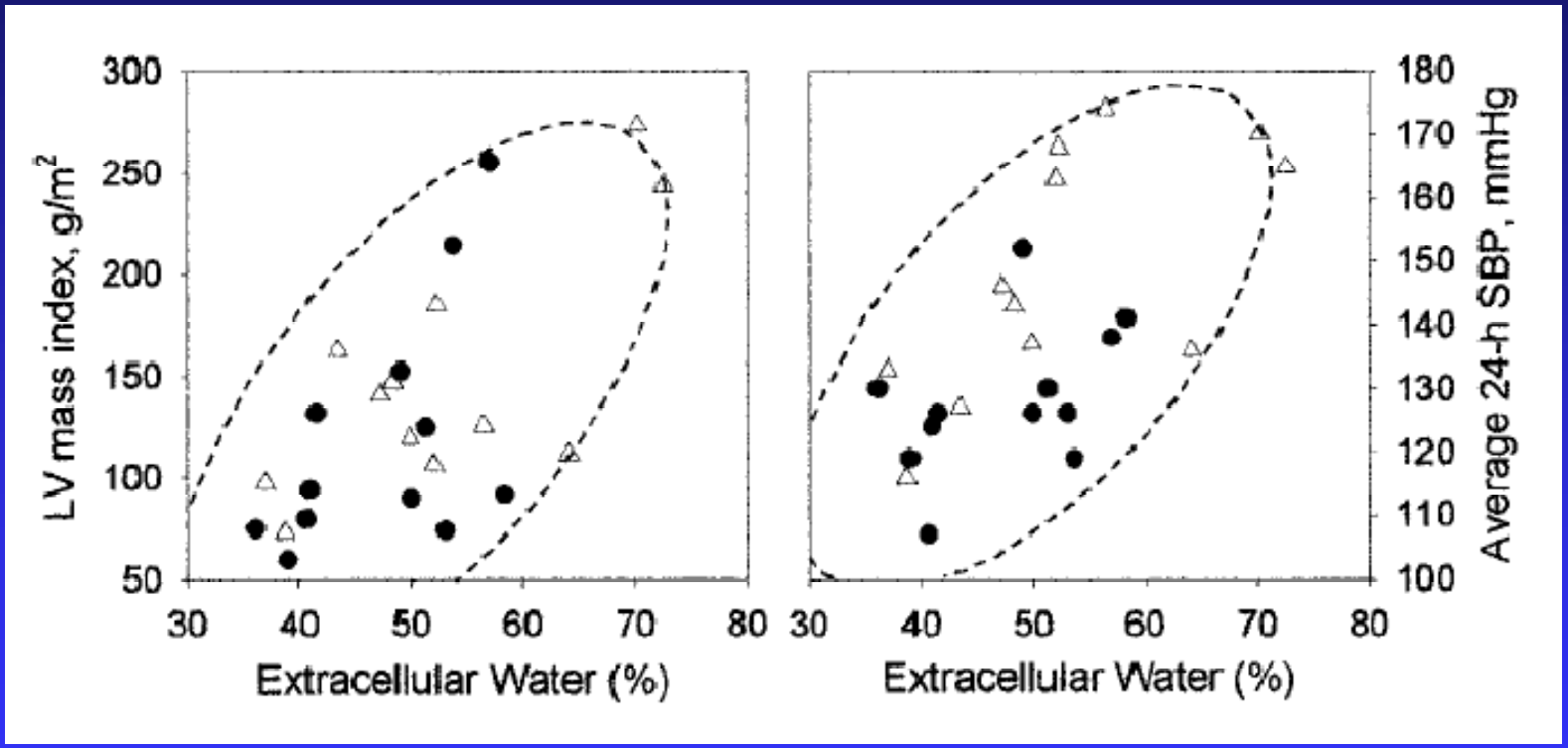
What are the clinical/physiological effects of frequent HD?

Reduction in LVMI via SDHD



Ayus et al JASN 2006

Reduction in ECFV -- SDHD



Fagugli et al:AJKD : 38, 2001: pp 371-376

Impact of long term NHD on LVMI, blood pressure, and anti-hypertensive therapy

Measurements	CHD (n=13)		NHD (n=28)	
	Initial	Final	Initial	Final
LVMI (g/m^2)	142 ± 33	150 ±56	147 ± 42	114 ± 40 *
SBP (mmHg)	136 ± 25	131 ± 20	146 ± 20	122 ±13*
DBP (mmHg)	82 ± 13	80 ± 15	84 ± 15	74 ± 12 *
PP (mmHg)	54 ± 22	51 ± 17	61 ± 12	49 ± 12 *
Anti-BP Meds	1.5	1.5	1.8	0.3*

* denotes $p < 0.05$

Chan CT et al, *Kidney Int* 61:2235-2239., 2002

Vascular Effects of NHD

	CHD	NHD - 1 month	NHD - 2 months
Resting systolic BP, mm Hg	140±5	124±3*	119±3*
Resting diastolic BP, mm Hg	82±3	75±3*	71±3*
Cardiac output, L/min	4.9±0.4	5.3±0.4	5.5±0.5
Stroke volume, mL	63±5	64±5	68±6
Heart rate, beats/min	78±3	75±3	80±4
Total peripheral resistance, dyne -s-cm-5	1967±235	1647±185*	1499±191*

Chan et al Hypertension 42(5):925-31 2003

Effect of Frequent Nocturnal Hemodialysis vs Conventional Hemodialysis on Left Ventricular Mass and Quality of Life

A Randomized Controlled Trial

Table 2. Outcomes for LV Mass, Blood Pressure, Anemia, and Mineral Metabolism[a]

Characteristic	Nocturnal Hemodialysis[b] (n = 26)	Conventional Hemodialysis[b] (n = 25)
LV mass, mean (SD), g		
Baseline	177.4 (51.1)	181.5 (92.3)
Exit	163.6 (45.2)	183.0 (84.2)
Change	−13.8 (23.0)	1.5 (24.0)
LV mass, mean (SD), g/m^2		
Baseline	92.4 (26.6)	101.8 (50.6)
Exit	85.3 (23.2)	102.8 (46.1)
Change	−7.1 (12.4)	1.0 (14.1)
Blood pressure, mean (SD), mm Hg		
Systolic		
Baseline	129 (23)	135 (19)
Exit	122 (23)	139 (20)
Change	−7 (29)	4 (17)
Diastolic		
Baseline	75 (14)	77 (16)
Exit	68 (16)	75 (12)
Change	−7 (16)	−2 (12)

Culleton et al – JAMA 2007

Change in LV Mass – Link with Pi

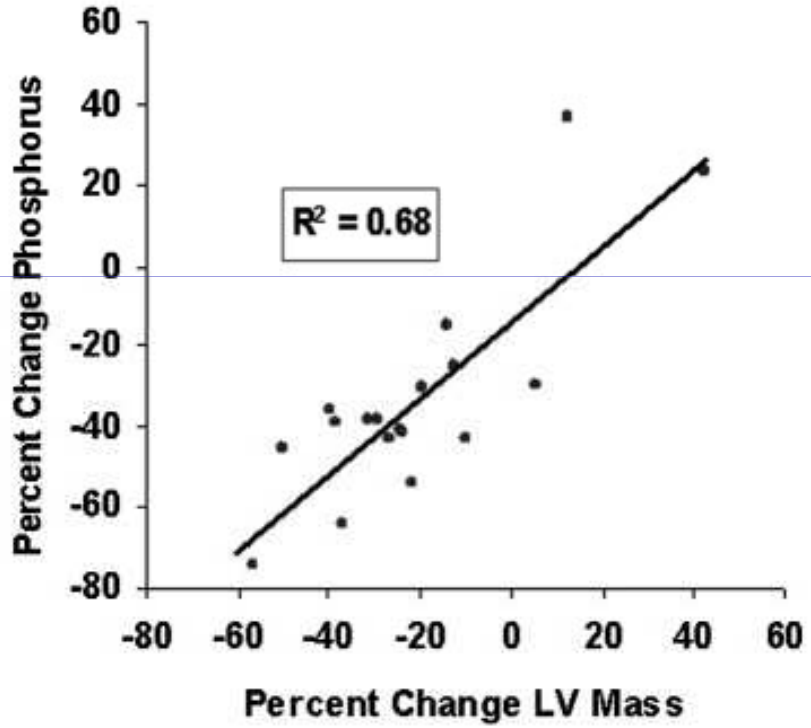


Figure 2. Correlation of percentage change in serum phosphorus (mg/dl) *versus* percentage change in LVMI (g/m^2).

Ayus et al JASN 2006

Fibroblast Growth Factor 23 and Left Ventricular Hypertrophy in Chronic Kidney Disease

Orlando M. Gutiérrez, MD, MMSc; James L. Januzzi, MD; Tamara Isakova, MD; Karen Laliberte, RN, MS; Kelsey Smith, BA; Gina Collerone, AS; Ammar Sarwar, MD; Udo Hoffmann, MD; Erin Coglianese, MD; Robert Christenson, PhD; Thomas J. Wang, MD, MPH; Christopher deFilippi, MD; Myles Wolf, MD, MMSc

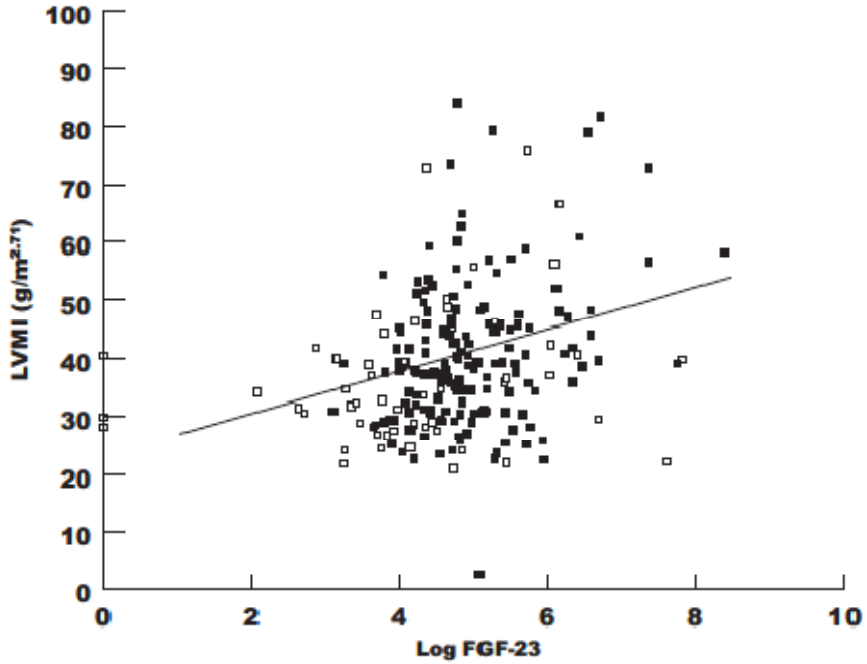
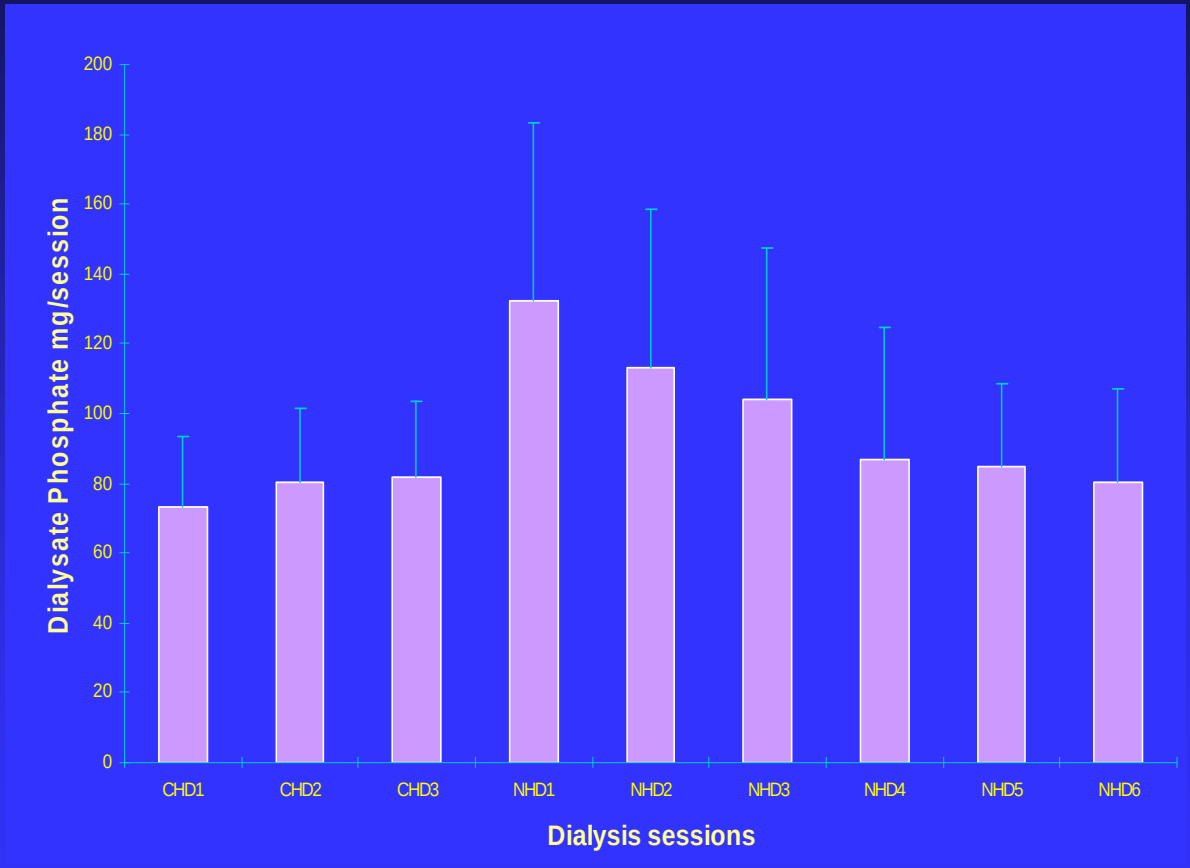


Figure 2. Correlation between log FGF-23 and LVMI (r=0.27, P<0.001). □ Indicates non-CKD subjects; ■, subjects with CKD.

Circulation. 2009;119:2545-2552.

Dialysate Phosphate on CHD and NHD



Weekly removal 2.2±0.6 vs. 4.8±1.7 gm

VSMC biology is improved after conversion to NHD

CHD

- ↓ VSMC proliferation
- ↑ VSMC apoptosis
- Runx 2 expression is increased

NHD: reversal of

- Proliferation/apoptosis ratio
- Reduction in Runx 2 expression

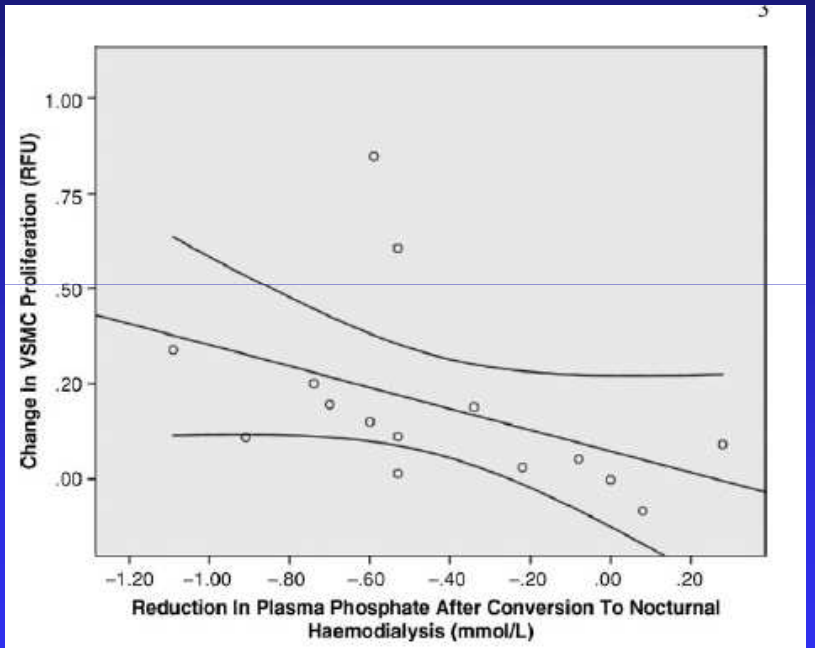


Fig. 1. This figure illustrates the significant relationship between reduction in plasma phosphate and changes in vascular smooth muscle cell (VSMC) proliferation before and after conversion from conventional to nocturnal haemodialysis. ($r = -0.71$, $P = 0.007$).

Chan et al (in press)

The natural history of coronary calcification progression in a cohort of nocturnal haemodialysis patients

Darren Yuen[1], Andreas Pierratos[2], Robert M.A. Richardson[1] and Christopher T. Chan[1]

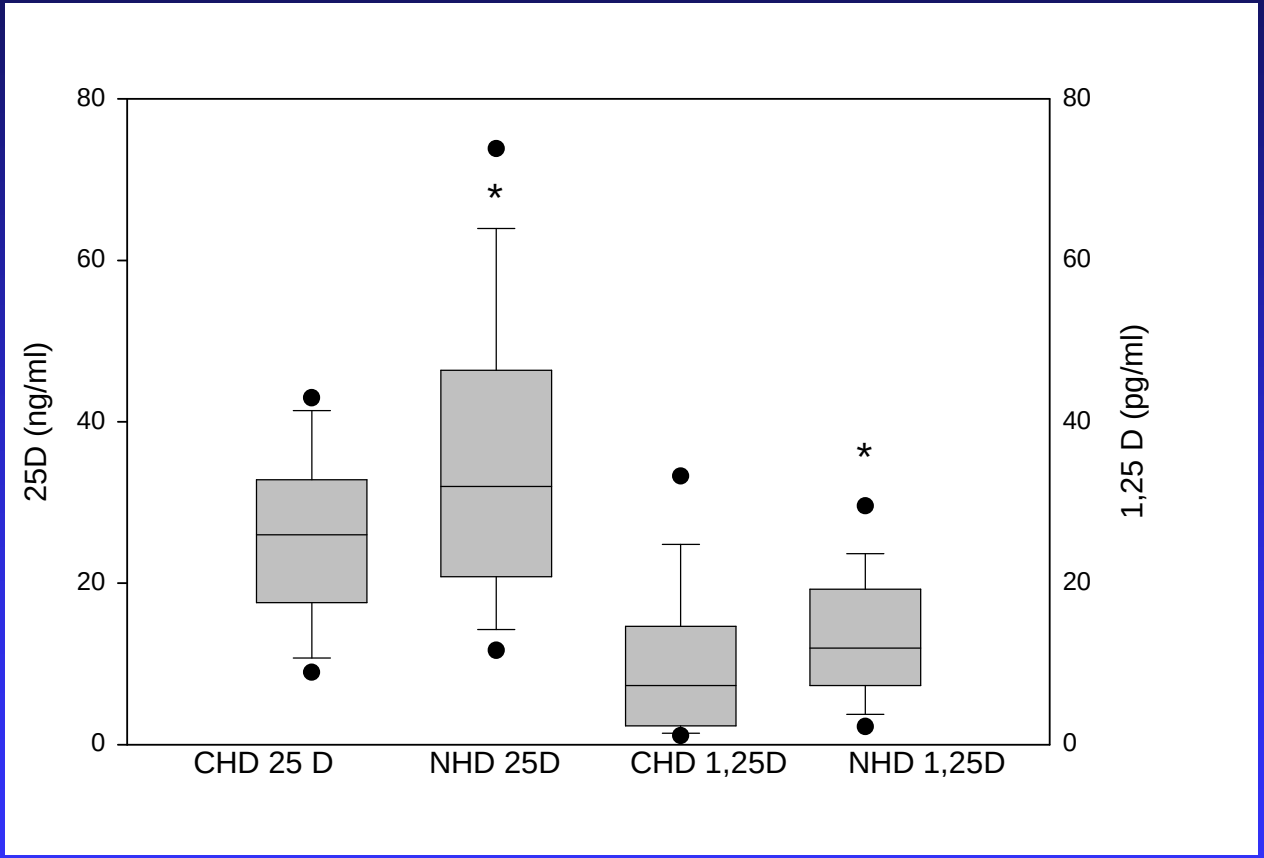
Table 1. Changes in CACS before and after conversion to NHD ($n=38$)

Variables	All Patients	Baseline CACS ≤10	Baseline CACS >10
Mean baseline CACS (range)	691 ± 295 (0–8217)	0.7 ± 0.5 (0–10)	1874 ± 697 (112–8217)
Mean follow-up CACS (range)	765 ± 316 (0 to 8356)	6 ± 4 (0–71)	2066 ± 739 (179–8356)
ΔCACS per year	64 ± 38	5 ± 3	164 ± 98
1 year standardized CACS[a]	755 ± 315	6 ± 3	2038 ± 740
Percentage change in CACS over 1 year	9%	762%	9%

Results are expressed as mean ± SEM, median (range).
[a]1 year standardized CACS refers to the change in CACS adjusted for a 1 year interval assuming a linear rate of CACS change (see Methods section).

Yuen et al : NDT 2006

NHD increases vitamin D levels



Nessim et al KI 2008

SDHD - CRP

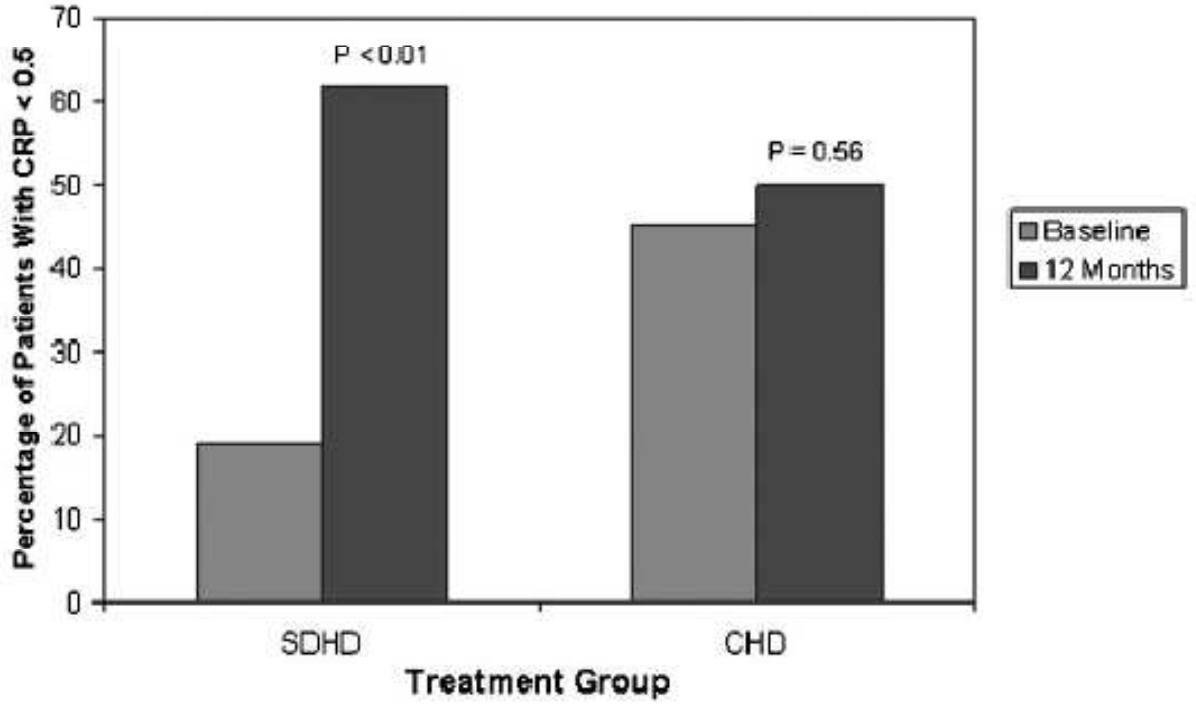


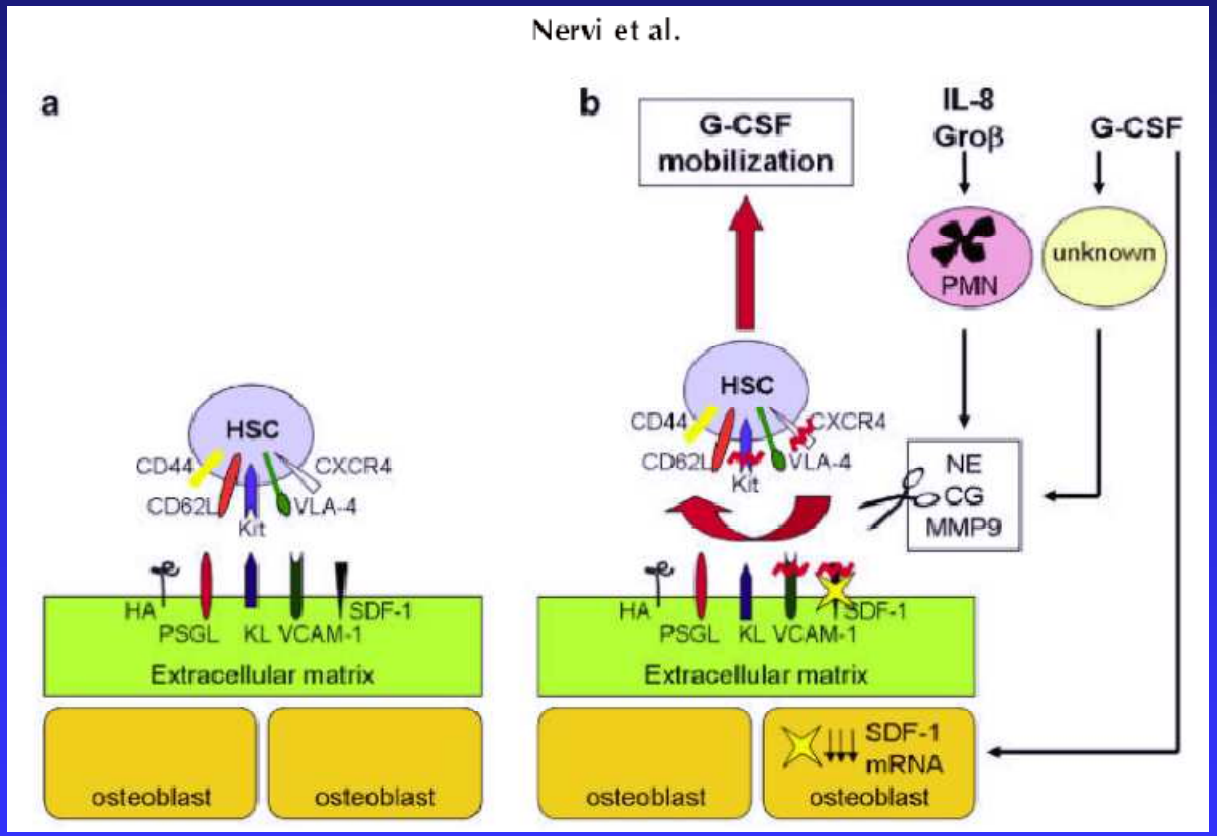
Figure 3. Percentage of patients with a normal C-reactive protein (CRP) level at baseline and at 12-mo follow-up.

Impact of NHD on EPO responsiveness

	Initial (CHD)	6 mos	12 mos	**p**
NHD				
Hb (g/L)	115 ± 2.3	122 ± 2.5	124 ± 2.3*	0.03
EPO dose (u/week)	10400 ± 1400	8500 ± 1300	7600 ± 1100	0.03
EPO free (%)	19	24	24*	NS
CHD				
Hb (g/L)	110 ± 2.2	115 ± 2.7	115 ± 2.2	NS
EPO dose (u/week)	8300 ± 1100	8100 ± 1300	8600 ± 1000	NS
EPO free (%)	13	13	9.4	NS

Schwartz et al: Clin Nephro, 2005

Bone – Blood Communication



NHD plasma facilitates the growth of HPC (both BFU-E and CFU-GM)

	BFU – E (# of colonies)	CFU – GM (# of colonies)
Normal	352 ± 76	189 ± 11
CHD (20%)	61 ± 30*	34 ± 16*
NHD (20%)	190 ± 54†	94 ± 25†

Chan et al JASN 2009

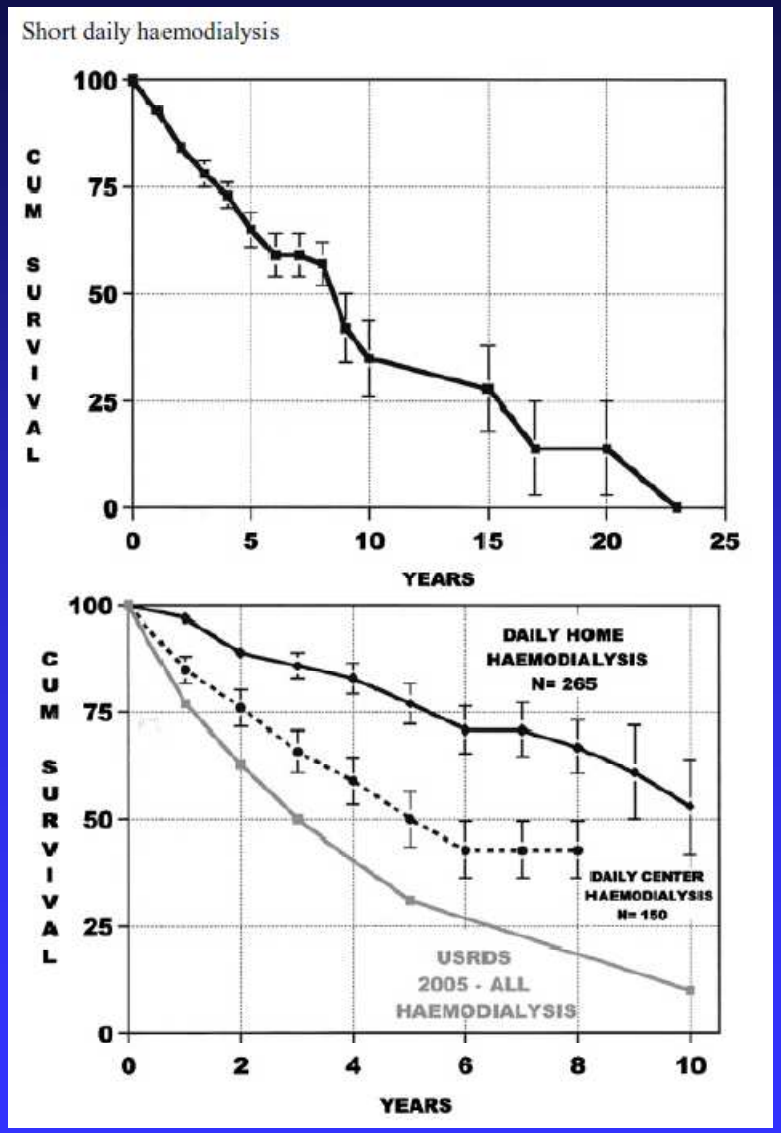
Gene expression of cultured HPC

- Total RNA derived from cultured HPCs
- What are the genes that were differentially expressed:
  - Genes responsible for HPC mobilization and RBC synthesis

Chan et al JASN 2009

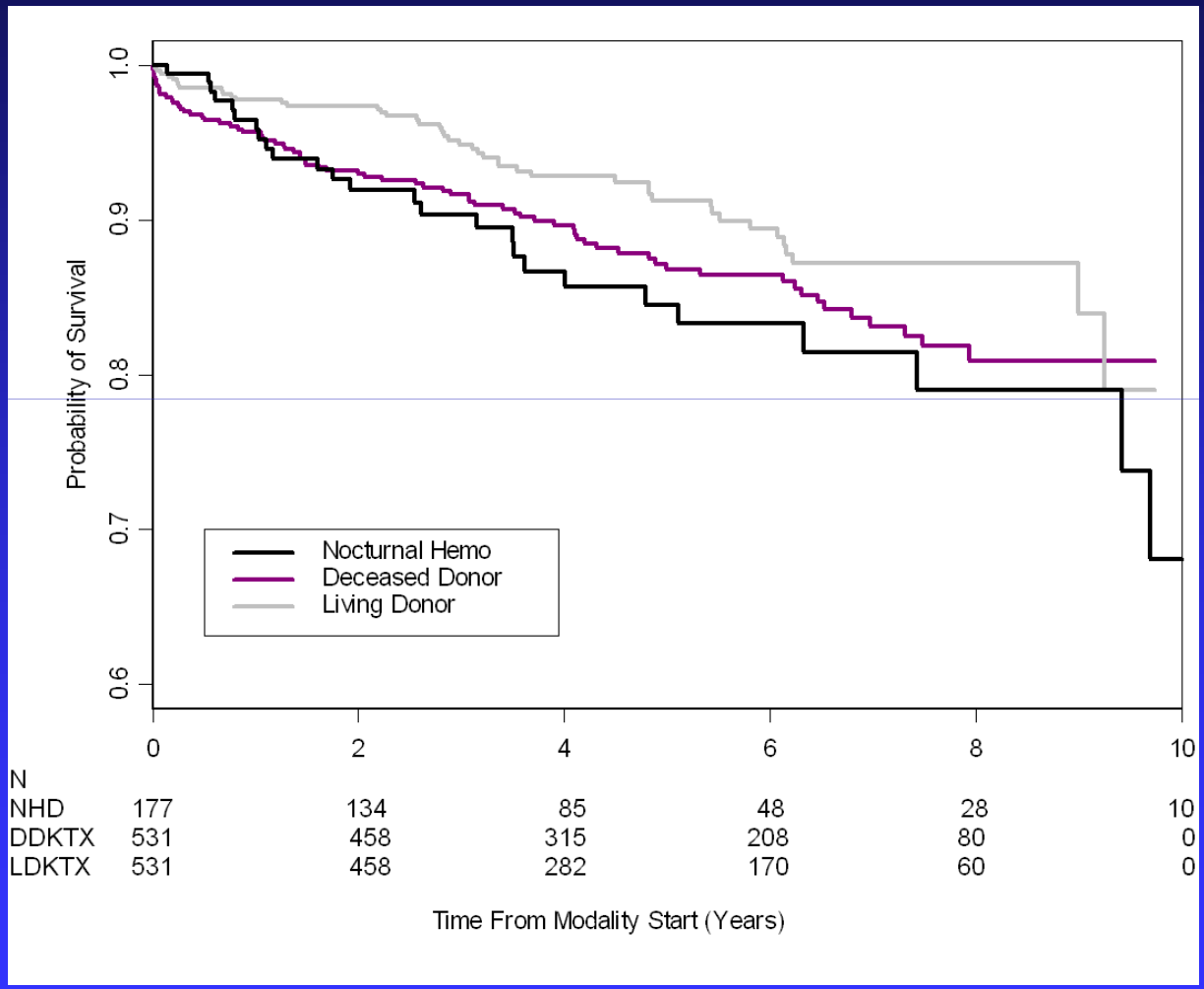
Survival Benefits?

SDHD survival



Kjellstrand et al – NDT 2008

No difference in survival between patients treated with deceased donor transplantation and nocturnal hemodialysis.



Pauly et al. NDT 2009.

Survival and hospitalization among patients using nocturnal and short daily compared to conventional hemodialysis: a USRDS study

Kirsten L. Johansen[1,2], Rebecca Zhang[1], Yijian Huang[1], Shu-Cheng Chen[3], Christopher R. Blagg[4], Alexander S. Goldfarb-Rumyantzev[5], Chistopher D. Hoy[6], Robert S. Lockridge Jr[7], Brent W. Miller[8], Paul W. Eggers[9] and Nancy G. Kutner[1]

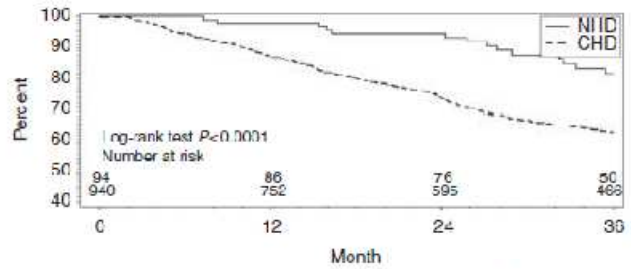


Figure 1 | Kaplan–Meier analysis of nocturnal hemodialysis (NHD) therapy patient and conventional hemodialysis (CHD) control survival from baseline. Patient survival was analyzed as time until death; observations were censored at the end of follow-up or transplantation.

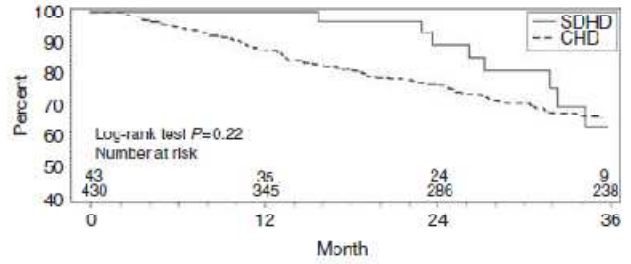


Figure 2 | Kaplan–Meier analysis of short-duration daily hemodialysis (SDHD) therapy patient and conventional hemodialysis (CHD) control survival from baseline. Patient survival was analyzed as time until death; observations were censored at the end of follow-up or transplantation.

	All cause mortality	Mortality + AMI + Stroke
NHD	0.36 (0.22,0.61)*	0.56 (0.35,0.81)*
SDHD	0.64 (0.31,1.31)	0.83 (0.42,1.85)

Johansen et al (KI epub ahead of print)

Why aren't people doing frequent HD?

Barriers to self-care dialysis

- Fear of failure to perform dialysis adequately
- Fear of social isolation
- Lack of confidence / knowledge

Effects of Quotidian HD

Variables	NHD	SDHD
BP control	+++ Reduction in TPR	++ Reduction in ECFV
LVH	+++ ⇓ Afterload	++ ⇓ preload
LV systolic function	+++ ⇓ Afterload	Not shown
Arterial compliance	+++	Not shown
Sleep Apnea	Correction	Not shown
Cardiac ANS abnormalities	Restoration	Not shown
Phosphate	Correction	Depends on duration

Effects of Quotidian HD (cont)

Variables	NHD	SDHD
Inflammation	Dec CRP, IL6	Dec CRP
Anemia	EPO resistance dec. ++	EPO resistance dec. +
QOL / Cognition	++/+	+/?

Future Challenges

- Need for RCT to validate NHD prospectively
  - NIH sponsored FHN study
    - Results (2010)
  - ACTIVE
- Need for International Collaboration
- Need to better understand patient selection / criteria
- Improvement in technology
- Resource allocation

Acknowledgment

- Home hemodialysis units -UHN
- Human Cardiovascular Physiology Group
  - JS Floras
- Stem Cell Group
  - S Verma
  - H Messner
- Genomics
  - Peter Liu
- E-Health Group
  - A Jadad, P Rossos, J Granton, R Owens, A Easty, P Milgrim
- CIHR, HSFO, BUL – Medicine, PSI, Baxter Extramural Grant Program
- NIDDK