



HOME THERAPIES (HOME HD & PD) PRESCRIPTIONS AS THEY RELATE TO BLOOD PRESSURE AND VOLUME

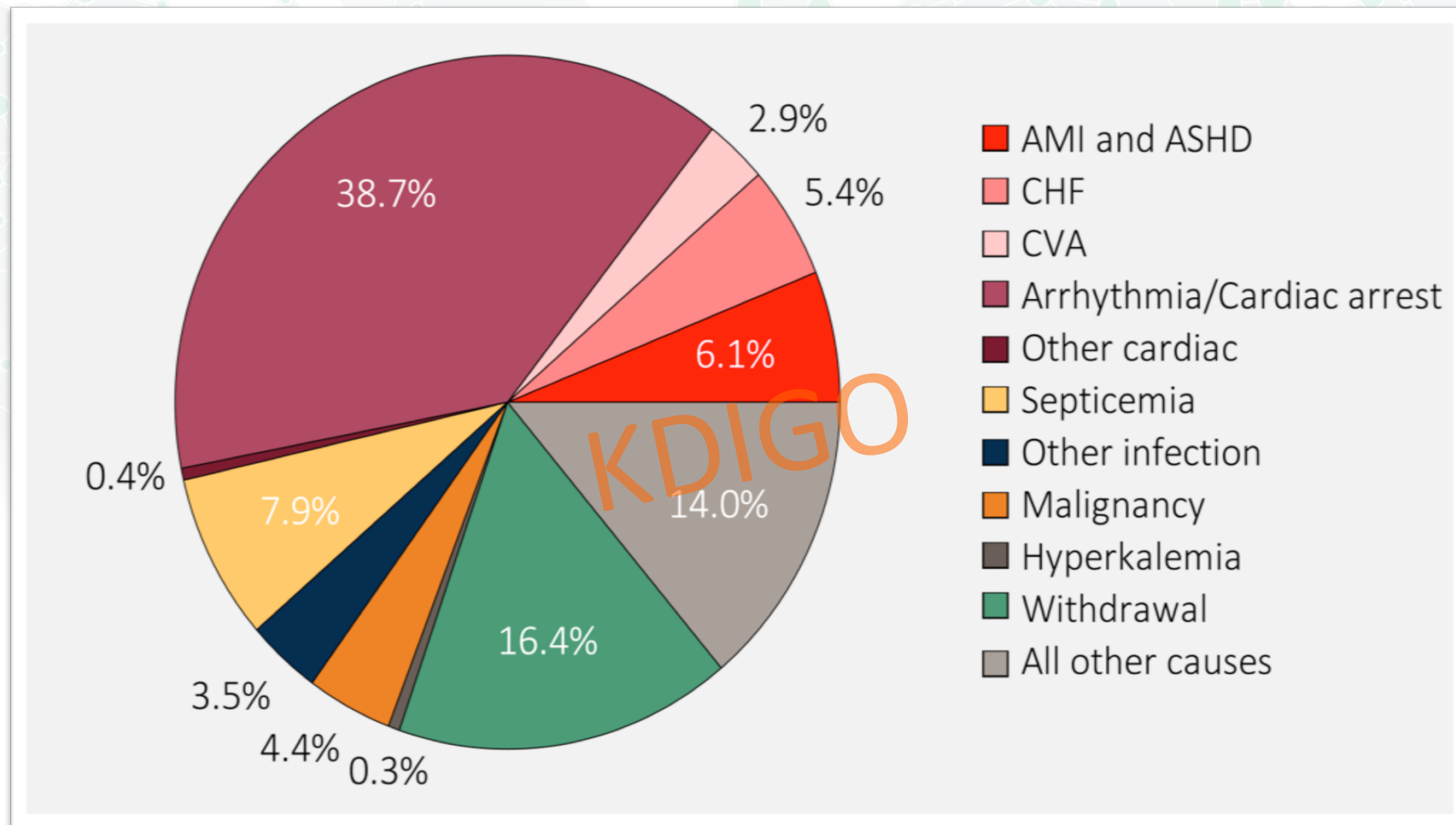
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Professor of Medicine – University of Toronto
R Fraser Elliott Chair in Home Dialysis
Director – Division of Nephrology – University Health Network
Deputy Physician in Chief – University Health Network

DISCLOSURES

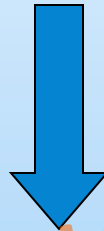
- I have consulted for Baxter, Medtronic and NxStage Inc.
- I have received extramural grant support from Baxter EMG and Medtronic ERP programs

KDIGO

Causes of death in ESRD patients, 2012-2014

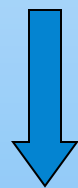


$$\text{MAP} = \text{C.O.} \times \text{T.P.R}$$

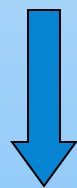


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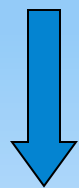
$$\text{SV} \times \text{HR}$$



MAP →



CO, TPR or both



SV, HR
preload



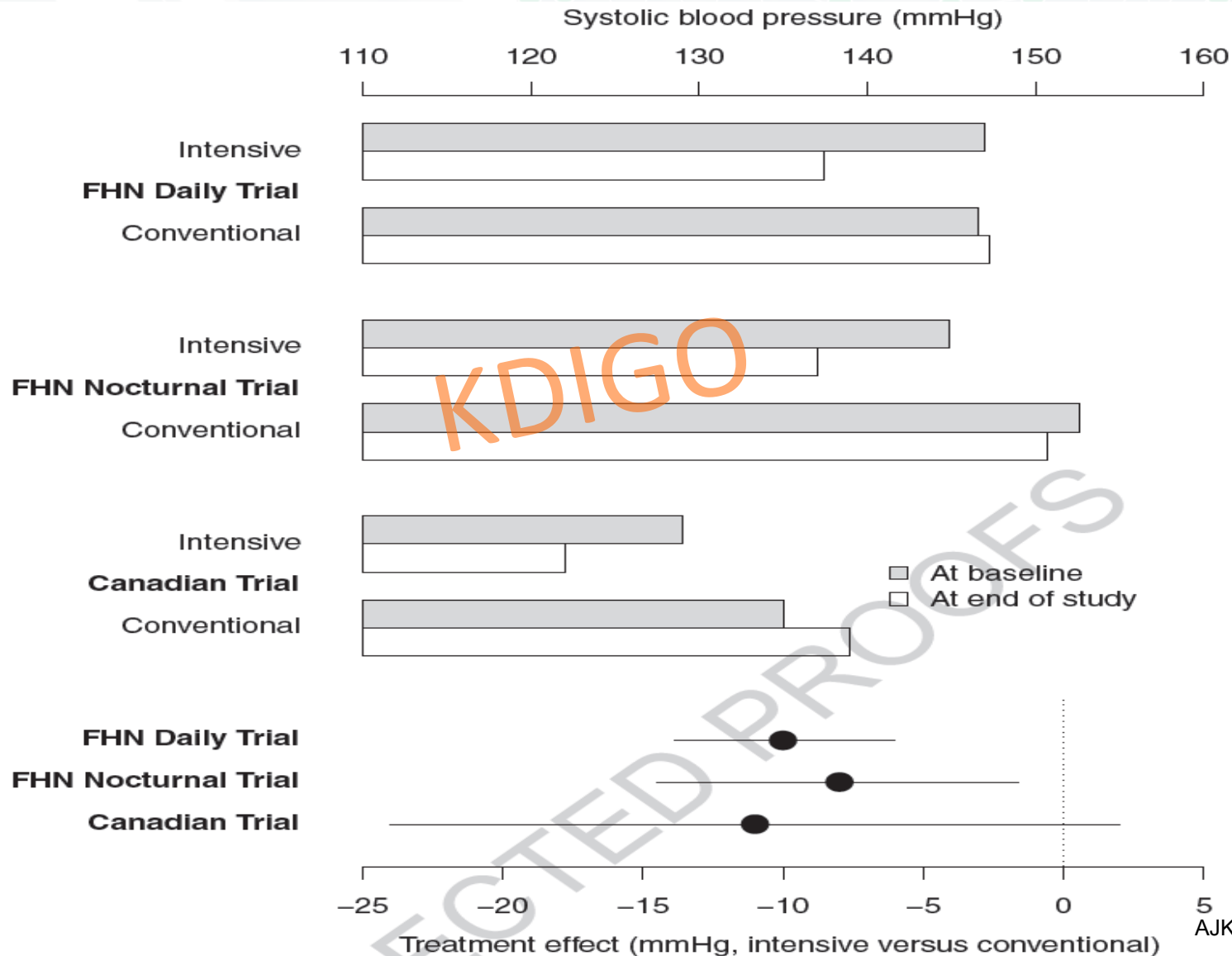
SNS, endo/paracrine
Endothelial vasoconstriction

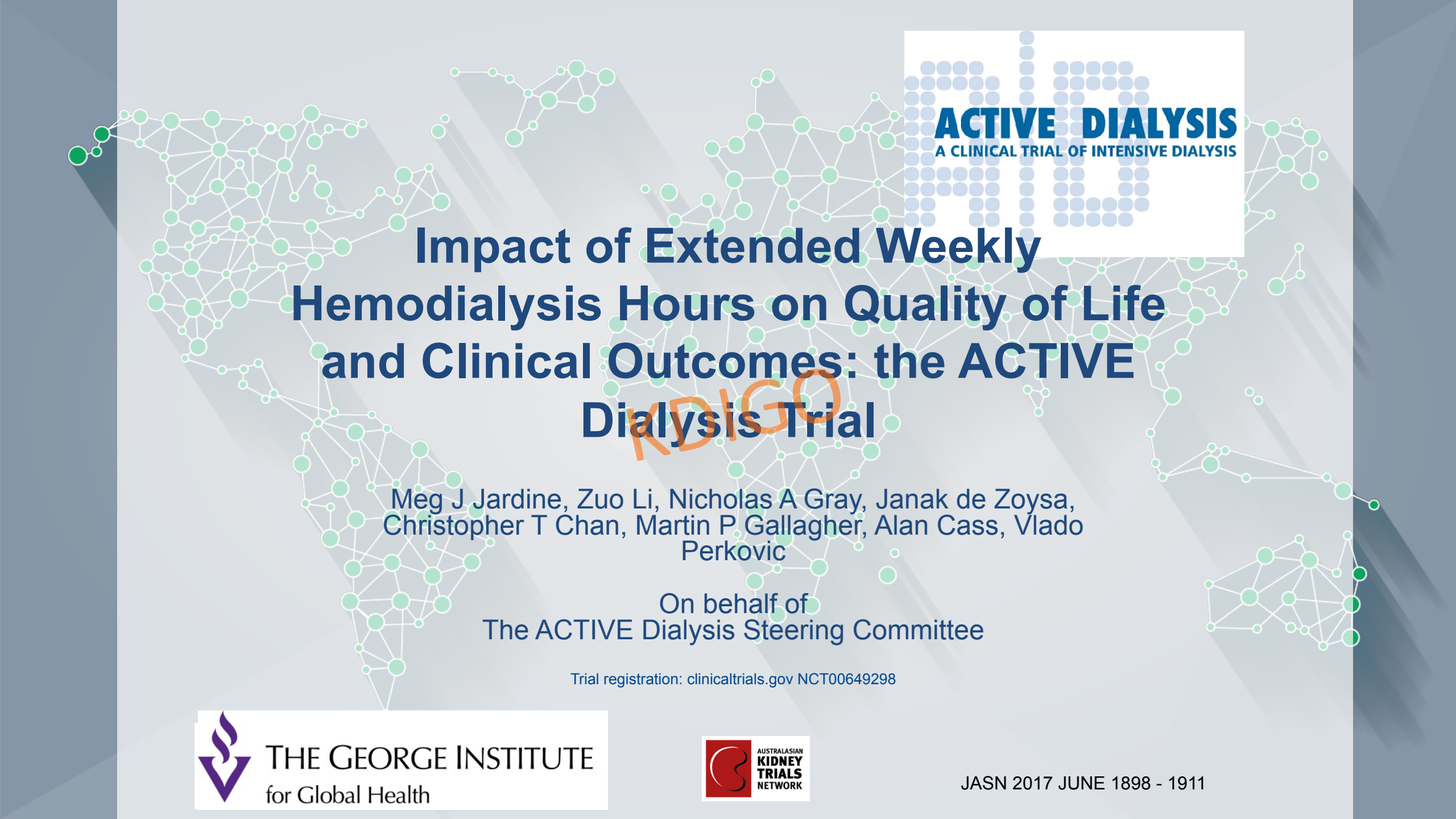
Better Cardiovascular Outcomes with Home HD / PD?

- Blood Pressure
 - LVH regression
 - Hemodynamics
 - Solute(s) Removal
- ECF volume overload
 - Sleep Apnea
- Sudden Cardiac Death
 - Sympathetic overactivity
- ? Hospitalization

KDIGO

BP / anti-BP meds and frequent HD





ACTIVE DIALYSIS
A CLINICAL TRIAL OF INTENSIVE DIALYSIS

Impact of Extended Weekly Hemodialysis Hours on Quality of Life and Clinical Outcomes: the ACTIVE Dialysis Trial

Meg J Jardine, Zuo Li, Nicholas A Gray, Janak de Zoysa,
Christopher T Chan, Martin P Gallagher, Alan Cass, Vlado
Perkovic

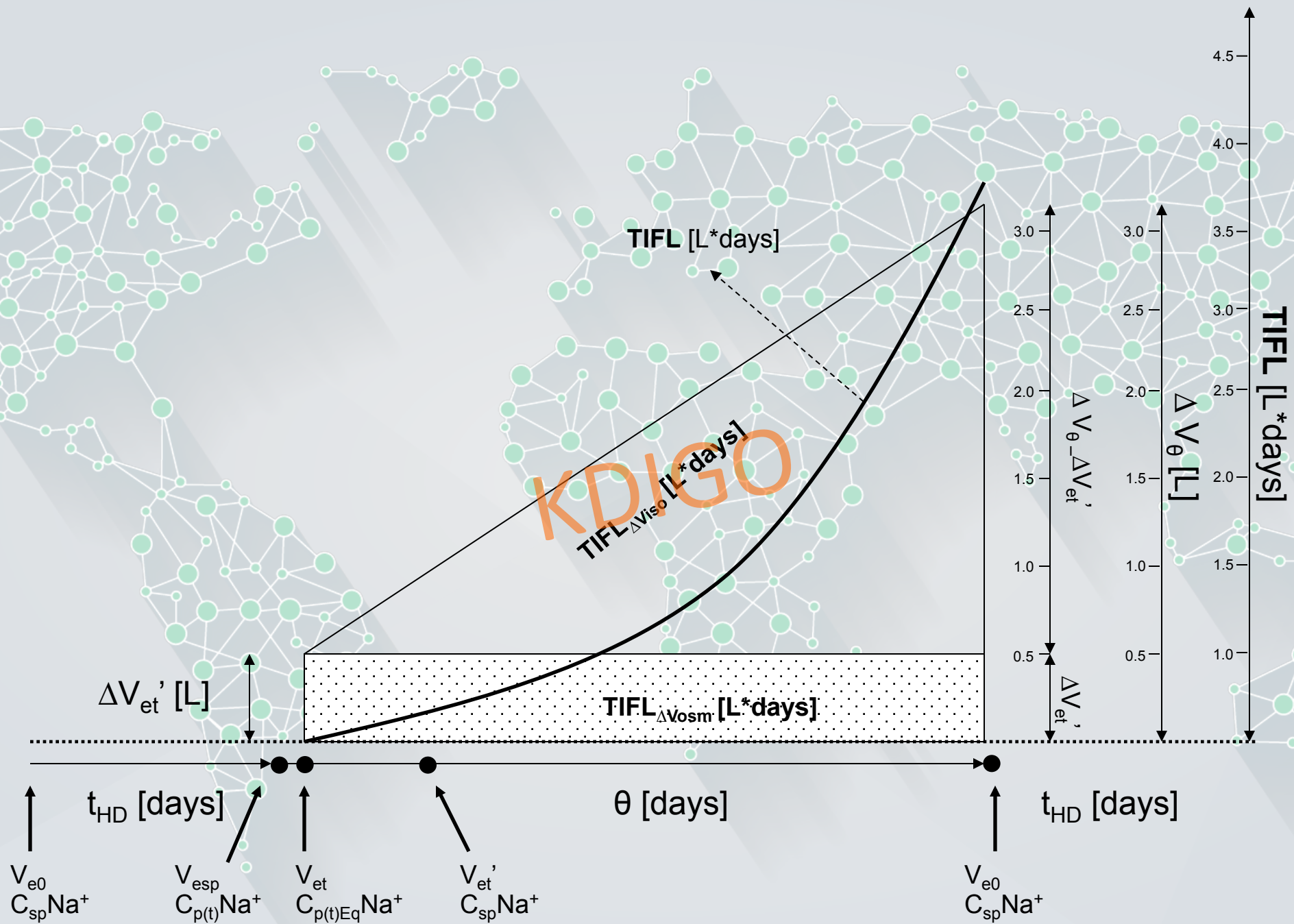
On behalf of
The ACTIVE Dialysis Steering Committee

Trial registration: clinicaltrials.gov NCT00649298

		Average intervention effect Mean difference (95%CI)	p-value
Electrolytes and Mineral Metabolism	Potassium (meq/L)	-0.35 (-0.50, -0.20)	<.0001
	Phosphate (mg/dL)	-0.77 (-1.08, -0.46)	<.0001
	PTH (pg/mL)	-11 (-131, 108)	0.85
	Phosphate binders (tablets)	-0.83 (-1.61, -0.04)	0.04
	Corrected calcium (mg/dl)	0.2 (0.04, 0.36)	0.01
Haematinics	Haemoglobin (g/dl)	0.52 (0.18, 0.86)	<0.01
	ESA dose (EPO units)	-250 (-1480, 970)	0.68
Body habitus and nutrition	Weight (pounds)	2.56 (0.46, 4.63)	0.02
	Waist:hip ratio (cm:cm)	-0.00 (-0.01, 0.01)	0.60
	Albumin (g/dL)	-0.07 (-0.16, 0.02)	0.14
Blood pressure control	Systolic Blood Pressure	-2.88 (-6.83, 1.06)	0.15
	Diastolic Blood Pressure	-1.64 (-3.89, 0.61)	0.15
	BP lowering agents (classes)	-0.29 (-0.53, -0.06)	0.01

Vascular Effects of NHD

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



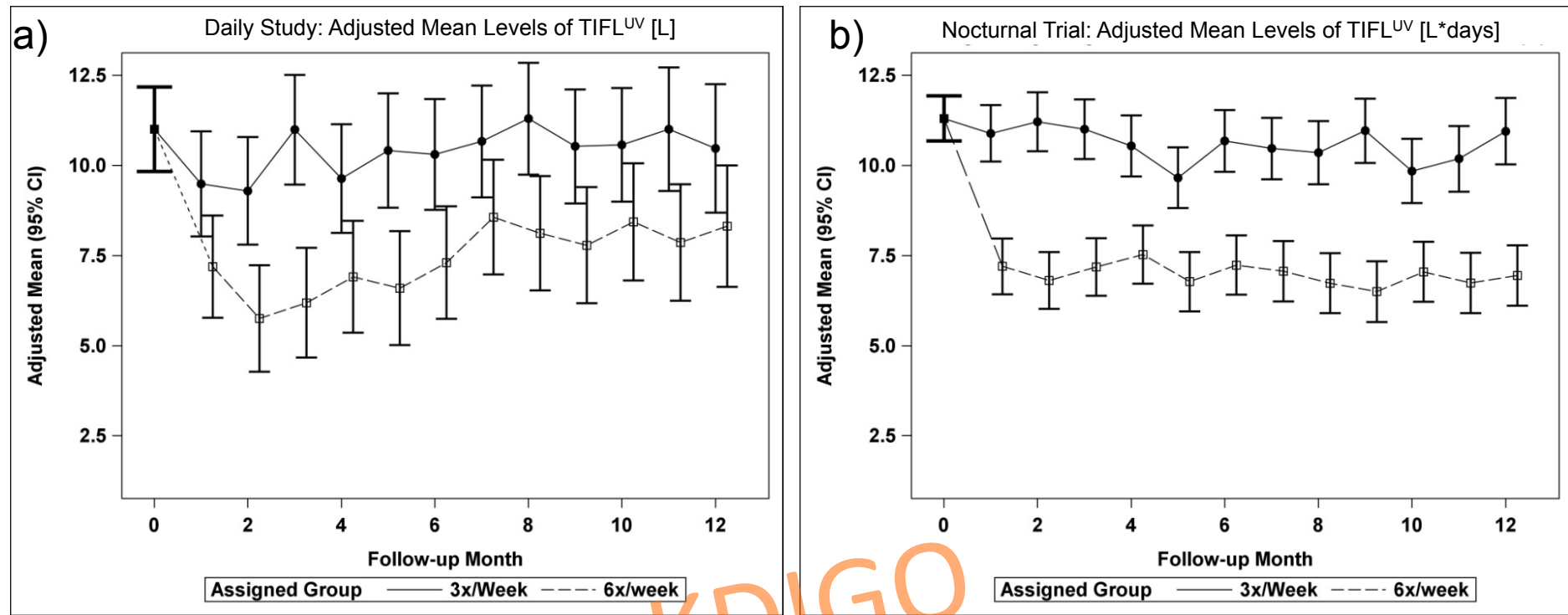


Figure 4, Blood Purification 2016

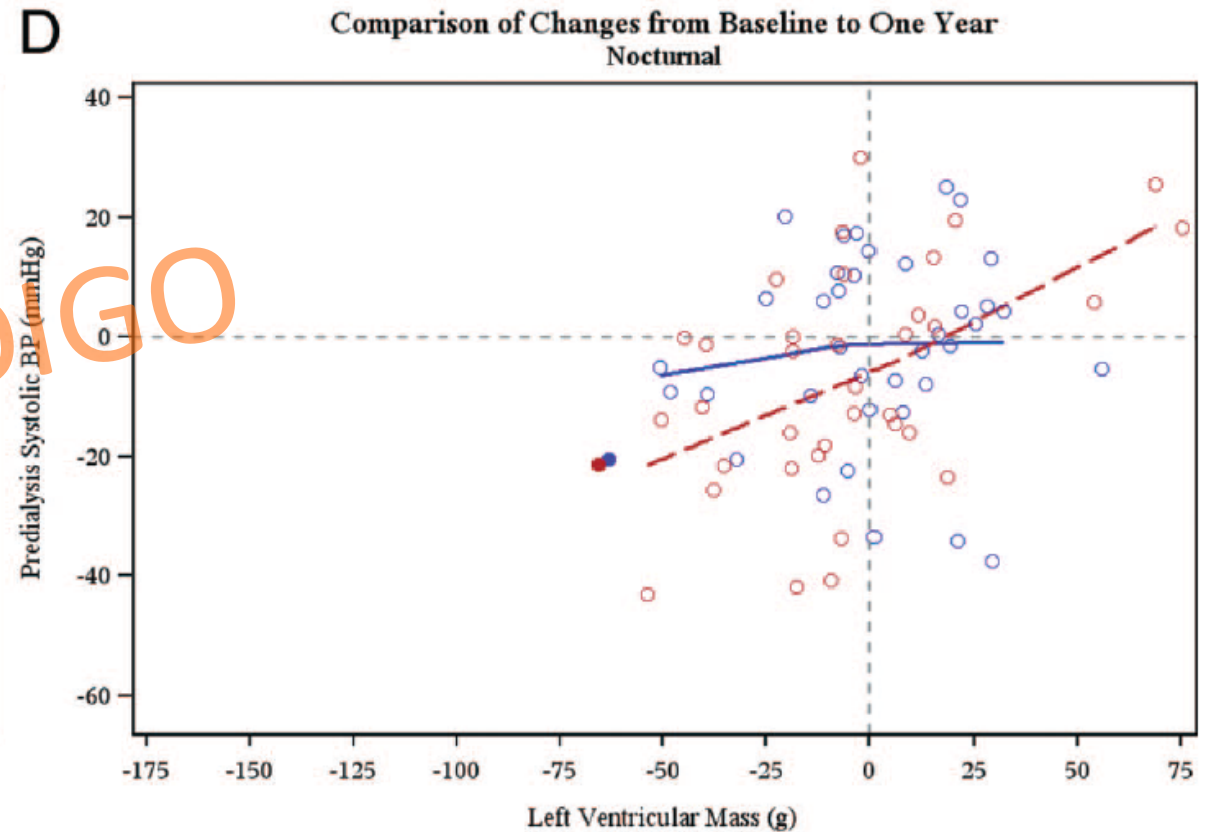
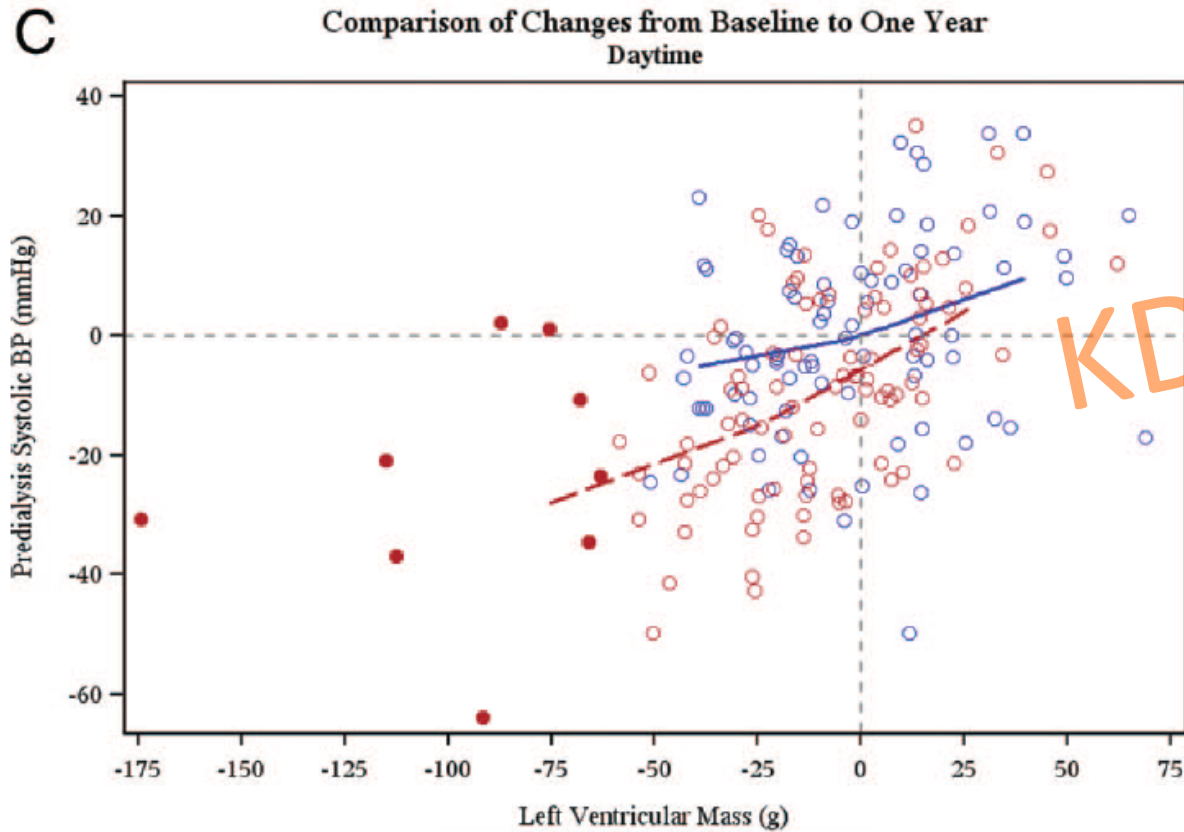
Table 3. Randomized trials comparing the effect of icodextrin versus glucose-containing dialysate solutions on BP in patients on peritoneal dialysis

Author	Year	N	Patient Characteristics	Design	Follow-Up, mo	Intervention	Effect on Body Weight	Effect on UF Volume	Effect on BP
Woodrow <i>et al.</i> (47)	2000	14	Patients on APD	Crossover	1	Icodextrin versus 2.27% glucose dialysate in daytime dwell	↓	↓	Icodextrin lowered BP by 19.5/6.0 mm Hg, despite the parallel reduction in antihypertensive drugs in six out of 14 participants
Plum <i>et al.</i> (46)	2002	39	Patients on APD	Parallel	3	Icodextrin versus 2.27% glucose dialysate in daytime dwell	↓	↓	No difference
Konings <i>et al.</i> (44)	2003	40	Patients on CAPD or APD	Parallel	4	Icodextrin versus standard dialysate glucose during the long dwell	↓	↓	No difference
Davies <i>et al.</i> (43)	2003	50	Hypertensive patients on CAPD or APD	Parallel	6	Icodextrin versus 2.27% glucose dialysate during the long dwell	↓	↓	No difference in BP levels, but icodextrin-treated participants required fewer antihypertensive medications during follow-up
Paniagua <i>et al.</i> (45)	2008	59	Diabetic patients on CAPD	Parallel	12	Icodextrin versus 2.27% glucose dialysate during the long night-time dwell	↓	↓	Icodextrin lowered BP by 10.4/6.2 mm Hg versus 2.27% glucose dialysate ($P<0.01$)

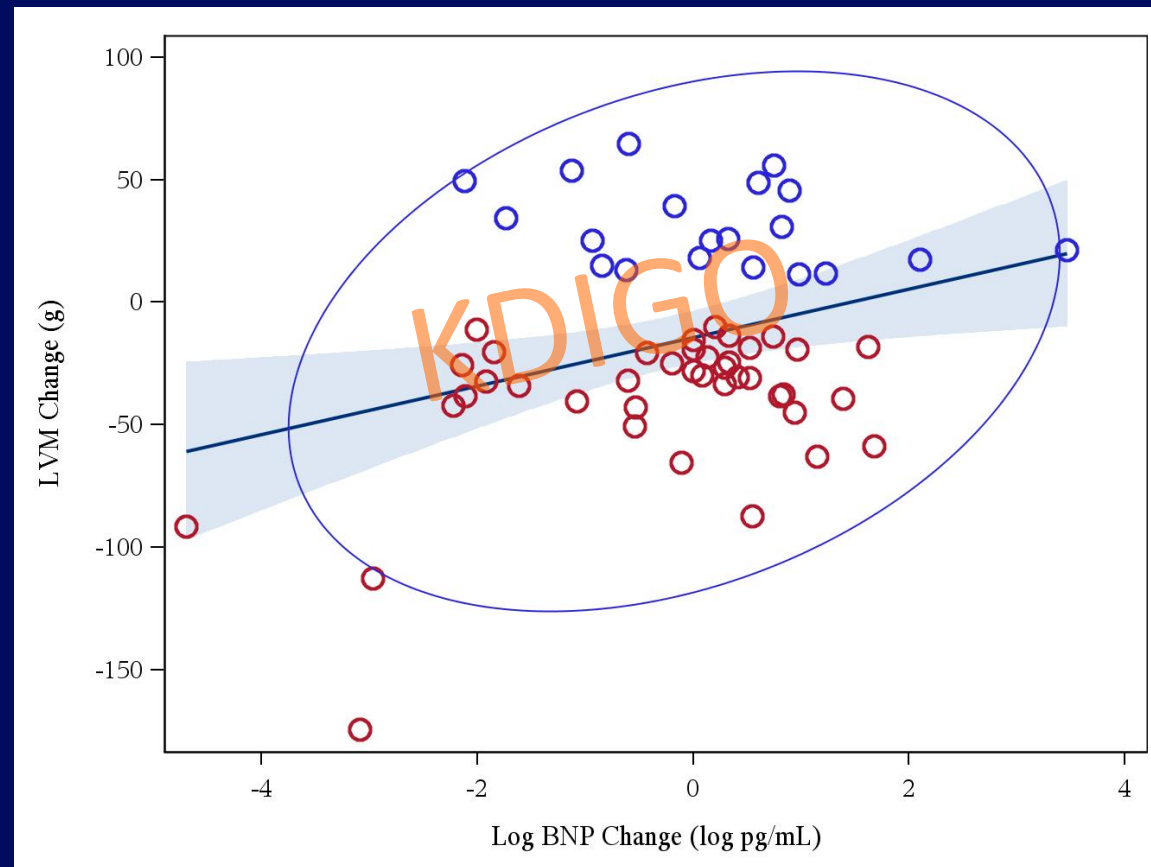
UF, ultrafiltration; APD, automated peritoneal dialysis; ↓, significant reduction in icodextrin groups relative to control group; CAPD, continuous ambulatory peritoneal dialysis.

	Mean Δ, Adjusted for Baseline Value, Age, Diabetes, Center	Unadjusted Mean Δ	HR for Rank Based Analysis Including Death
LVM (g)	-13.1 (-21.3, -5.0) [0.002]	-13.9 (-23.1, -4.8) [0.003]	0.61* (0.46, 0.82) [<0.001]
LVM / Baseline BSA (g/m²)	-6.9 (-11.3, -2.4) [0.003]	-7.1 (-12.0, -2.2) [0.005]	0.65 (0.49, 0.87) [0.003]
% Change in Geometric Mean of LVM	-7.0 (-12.6, -1.0) [0.02]	-7.5 (-13.2, -1.5) [0.02]	0.64 (0.48, 0.85) [0.002]

Relationship between LVM and BP changes in FHN

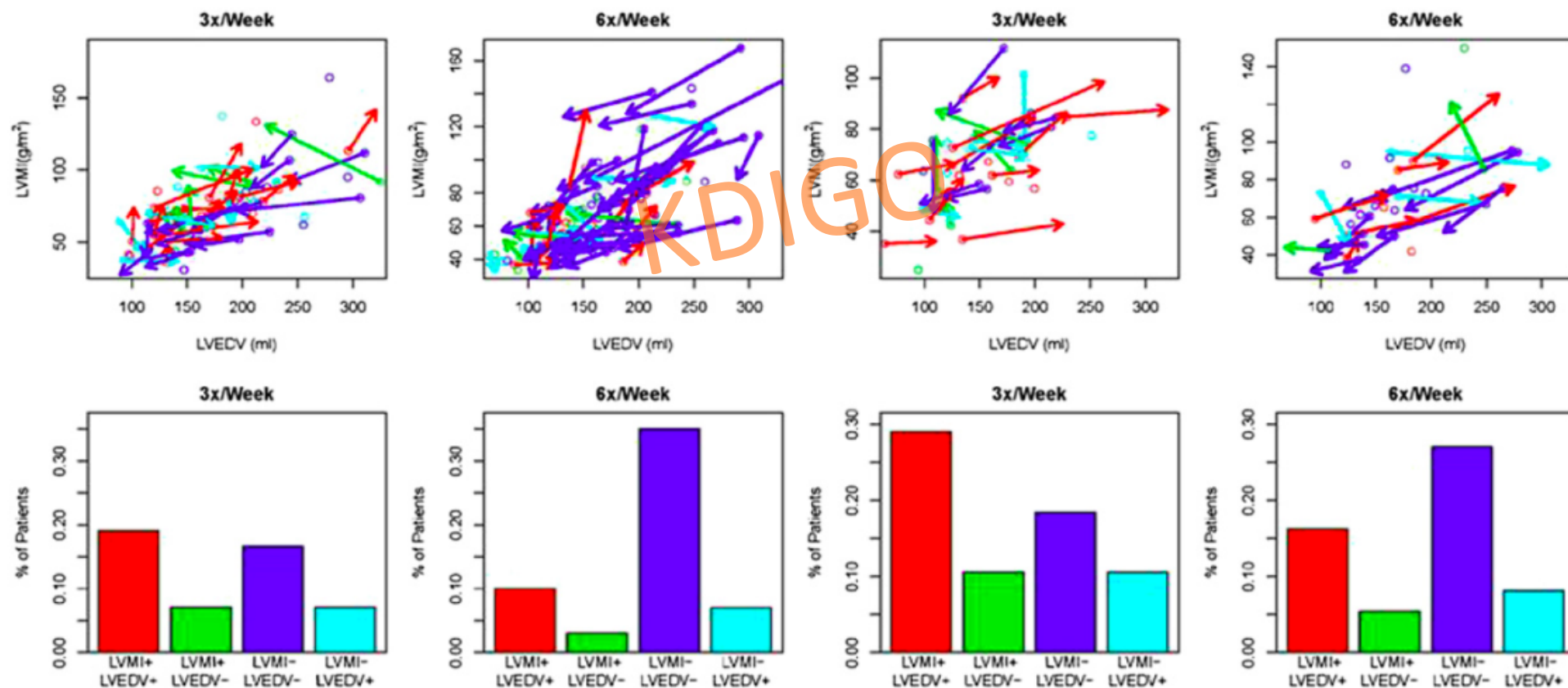


BNP vs LVM Change



Effects of Frequent Hemodialysis on Ventricular Volumes and Left Ventricular Remodeling

Christopher T. Chan,^{*} Tom Greene,[†] Glenn M. Chertow,[‡] Alan S. Klinger,[§] John B. Stokes,^{||} Gerald J. Beck,[¶] John T. Daugirdas,^{**} Peter Kotanko,^{††} Brett Larive,[¶] Nathan W. Levin,^{††} Ravindra L. Mehta,^{‡‡} Michael Rocco,^{§§} Javier Sanz,^{|||} Phillip C. Yang,[‡] Sanjay Rajagopalan,^{¶¶} and the Frequent Hemodialysis Network Trial Group



Association between conversion to in-center nocturnal hemodialysis and right ventricular remodeling

Gauri R. Karur¹, Ron Wald^{2,3}, Marc B. Goldstein^{2,3}, Rachel Wald^{3,4}, Laura Jimenez-Juan^{3,5}, Mercedesh Kiaii⁶, Jonathon Leipsic⁷, Anish Kirpalani^{1,3}, Olugbenga Bello⁸, Ashita Barthur¹, Ming-Yen Ng⁹, Djeven P. Deva^{1,3} and Andrew T. Yan^{3,8}

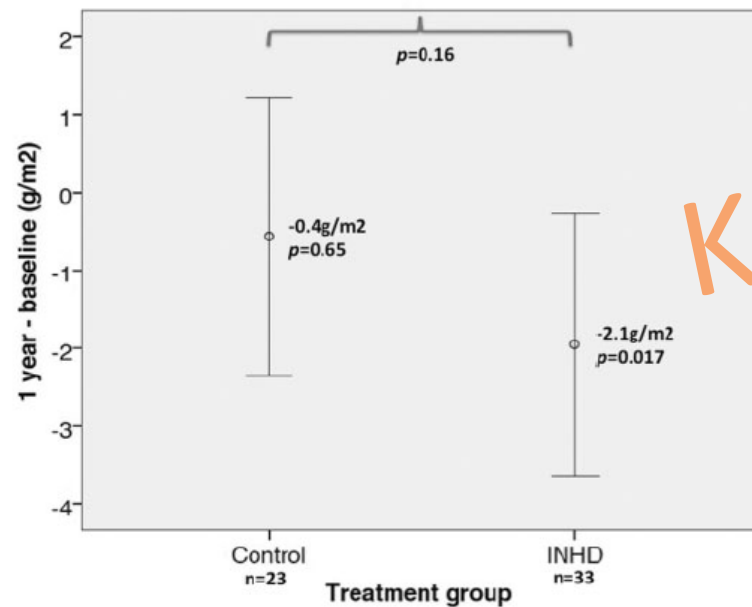


FIGURE 1: Mean changes in RV mass index over 1 year in the INHD versus CHD (control) group.

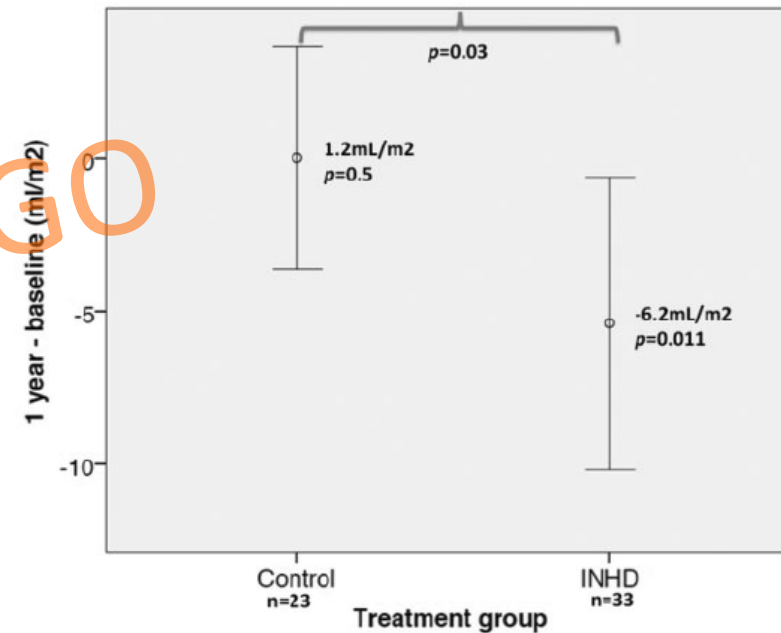


FIGURE 4: Mean change in the RVESVI over 1 year in the INHD versus CHD (control) group.

Impact of Frequent Nocturnal Hemodialysis on Myocardial Mechanics and Cardiomyocyte Gene Expression

Christopher T. Chan, MD; Sara Arab, PhD; Shemy Carasso, MD; Gil Moravsky, MD;
Guo Hua Li, PhD; Peter P. Liu, MD*; Harry Rakowski, MD*

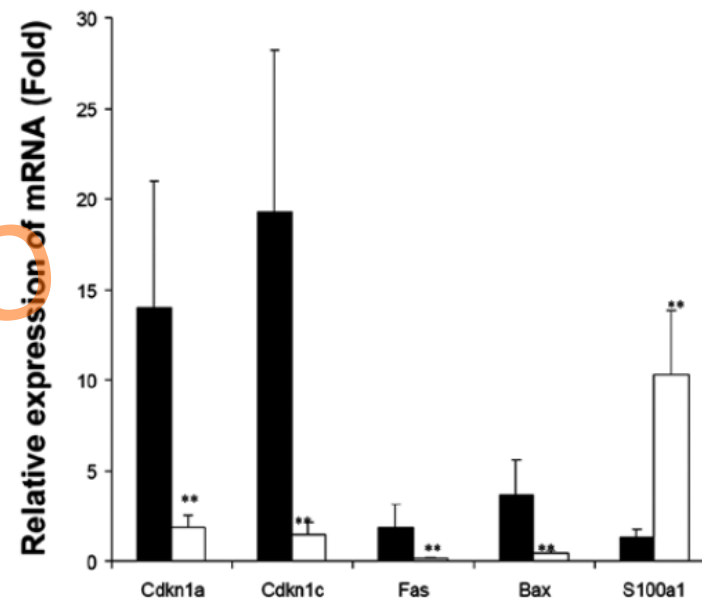
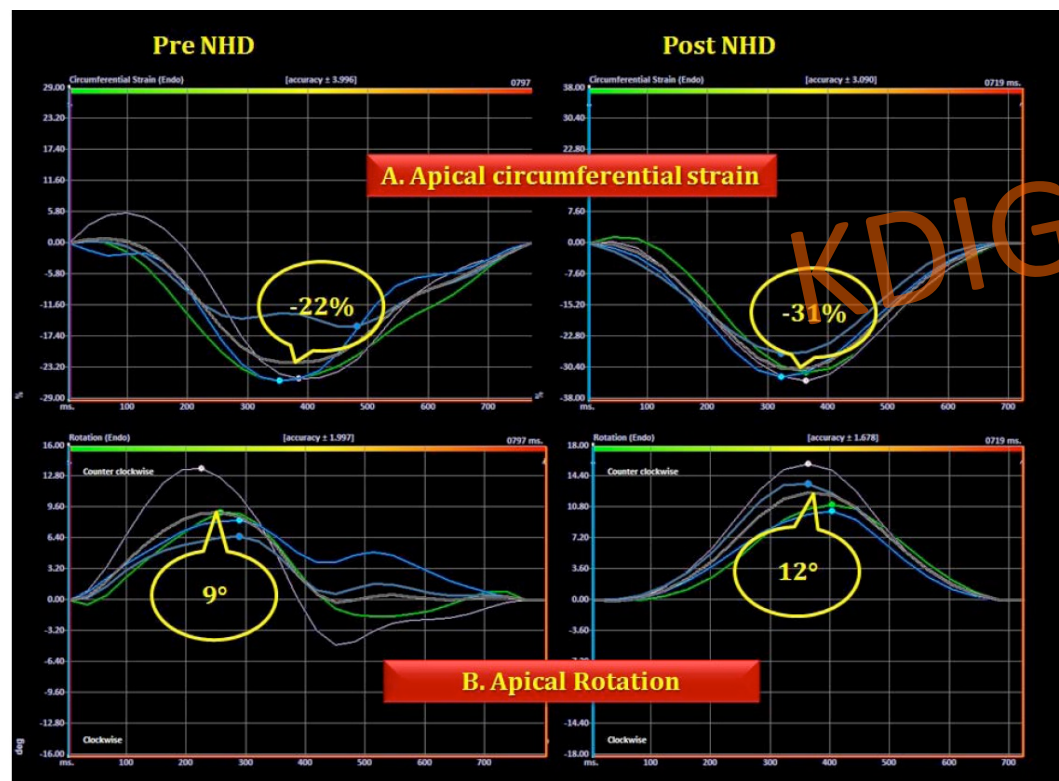
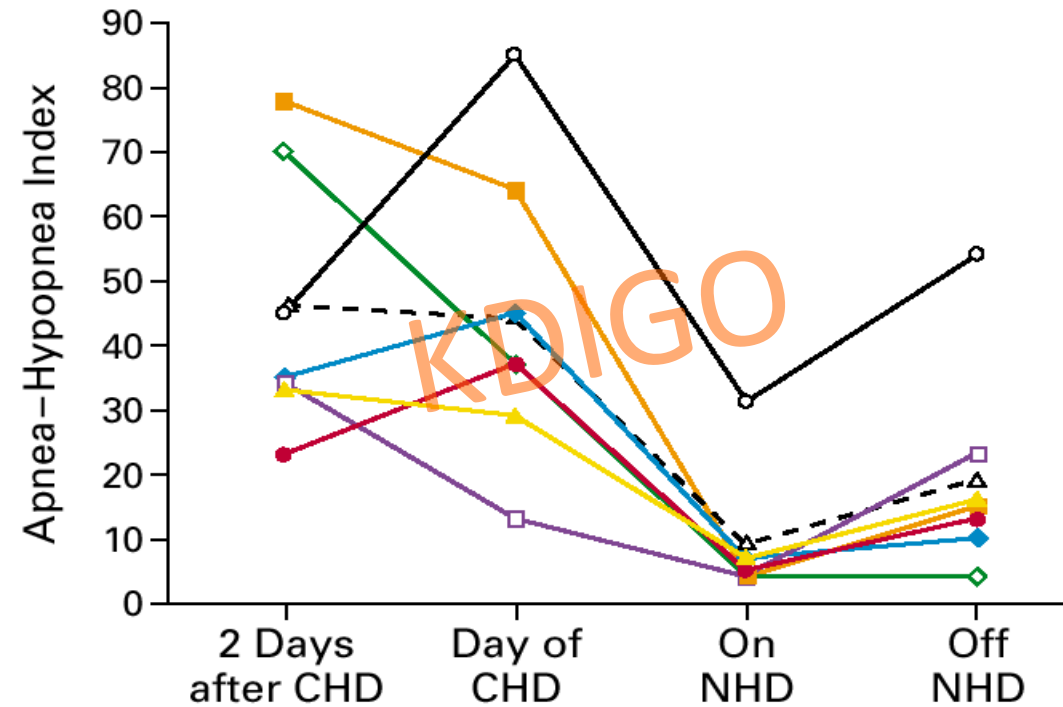


Figure 2. Real-time quantitative polymerase chain reaction confirmation of cardiomyocyte gene signature before and after conversion from conventional to nocturnal hemodialysis. Black bar indicates conventional hemodialysis. White bar indicates nocturnal hemodialysis. ** $P < 0.05$ between conventional hemodialysis and nocturnal hemodialysis. *Cdkn1a* indicates cyclin-dependent kinase inhibitor 1A; *Cdkn1c*, cyclin-dependent kinase inhibitor 1C; *Bax*, Bcl2-associated X protein; *S100a1*, S 100 calcium binding protein A1.

Correction of Sleep Apnea with NHD

Hanly P, Pierratos A. NEJM 2001

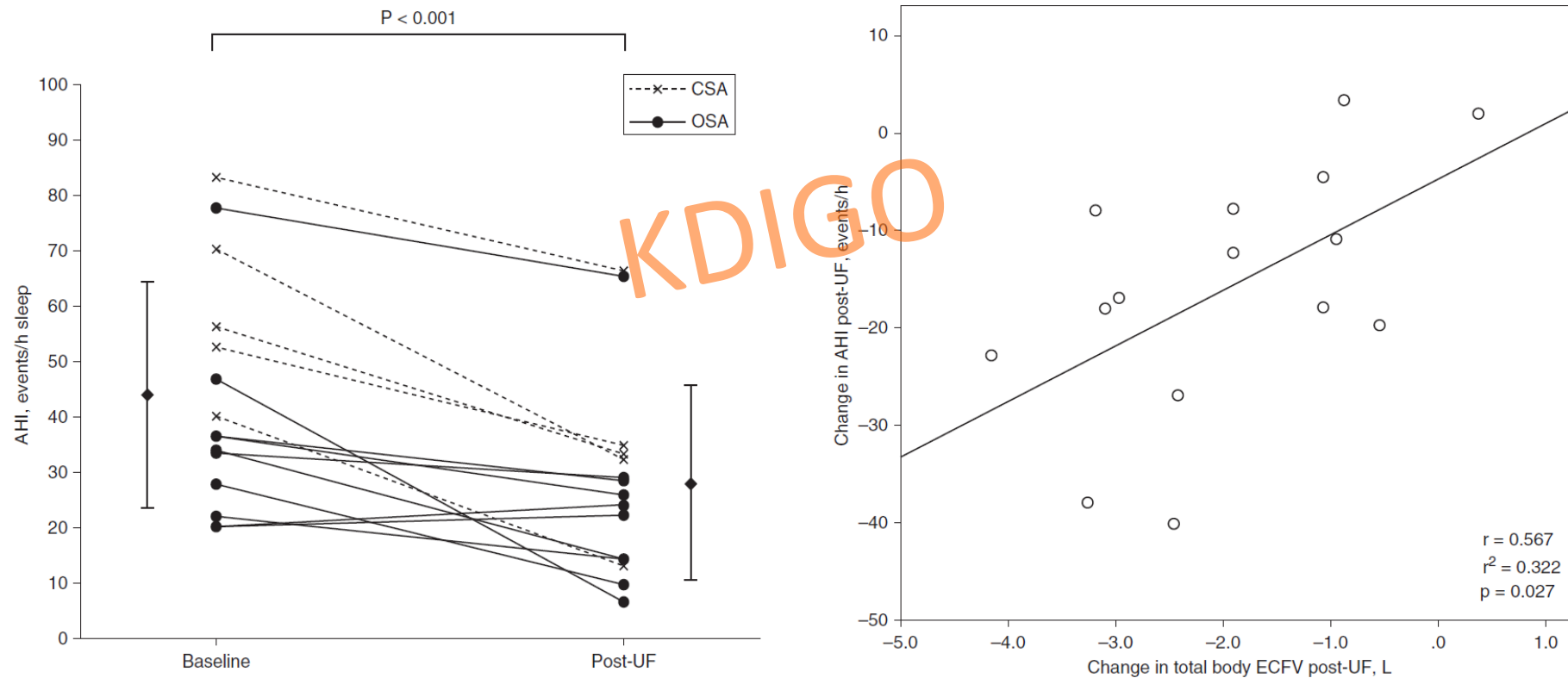


AHI decreased from 46 ± 19 to 9 ± 9 episodes/hour, $p = 0.006$

Effect of Ultrafiltration on Sleep Apnea and Sleep Structure in Patients with End-Stage Renal Disease

Owen D. Lyons^{1,2}, Christopher T. Chan³, Azadeh Yadollahi^{1,2}, and T. Douglas Bradley^{1,2,3}

¹Sleep Research Laboratory, University Health Network Toronto Rehabilitation Institute, Toronto, Canada; ²Centre for Sleep Medicine and Circadian Biology, University of Toronto, Toronto, Canada; and ³Department of Medicine, University Health Network Toronto General Hospital, Toronto, Canada



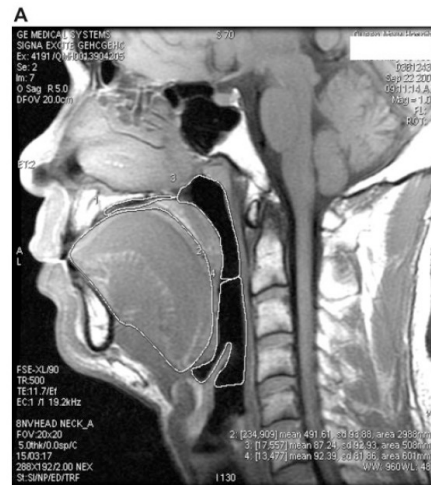
Improvement in Sleep Apnea during Nocturnal Peritoneal Dialysis Is Associated with Reduced Airway Congestion and Better Uremic Clearance

Sydney C. W. Tang,^{*} Bing Lam,[†] Andrew S. H. Lai,[‡] Clara B. Y. Pang,[‡] Wai Kuen Tso,[‡] Pek Lan Khong,[‡] Mary S. M. Ip,[†] and Kar Neng Lai^{*}

^{*}Division of Nephrology and [†]Division of Respiratory Medicine, Department of Medicine, The University of Hong Kong and Queen Mary Hospital; and [‡]Department of Diagnostic Radiology, Queen Mary Hospital, Hong Kong, China

Table 2. Polysomnographic data while on NPD or CAPD ($n = 38$)

	On NPD	On CAPD	<i>P</i>
Total sleep time (h)	5.0 $\pm$ 1.60	5.55 $\pm$ 1.41	NS
Sleep efficiency ^a	57.4 $\pm$ 14.4	62.8 $\pm$ 12.7	NS
Stage of sleep (% of total sleep time)			
rapid eye movement	18.2 $\pm$ 10.5	16.7 $\pm$ 8.6	NS
stage 1, 2	78.8 $\pm$ 22.1	79.3 $\pm$ 20.0	NS
slow wave (stage 3, 4)	1.9 $\pm$ 3.2	4.0 $\pm$ 3.6	NS
AHI (no./h)	9.6 $\pm$ 2.74	21.5 $\pm$ 4.15	<0.001



MR Venogram of Internal Jugular Vein

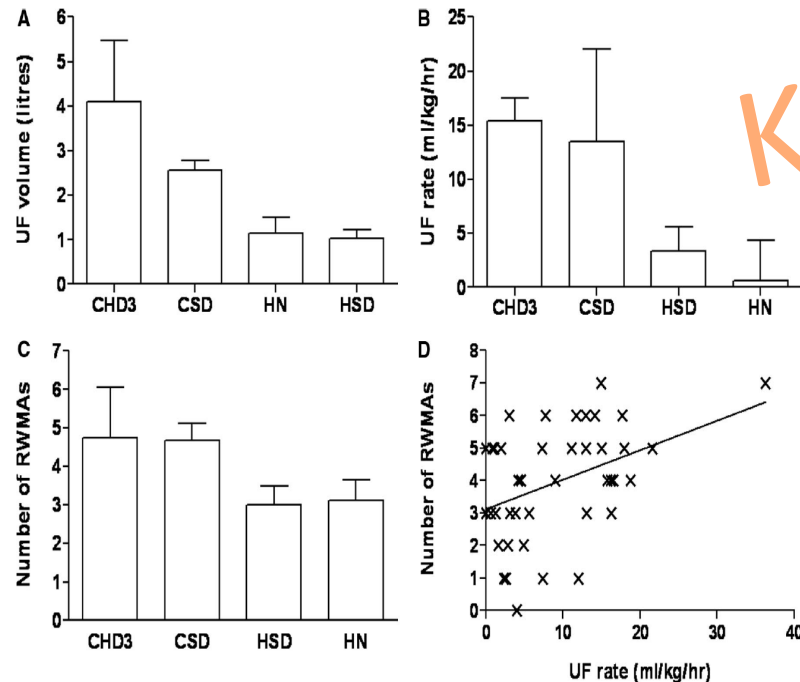


NHD → Alleviate Upper Airway Mucosal Edema

Myocardial Stunning

Frequent Hemodialysis Schedules Are Associated with Reduced Levels of Dialysis-induced Cardiac Injury (Myocardial Stunning)

Helen J. Jefferies,* Bhupinder Virk,** Brigitte Schiller,** John Moran,** and Christopher W. McIntyre*§



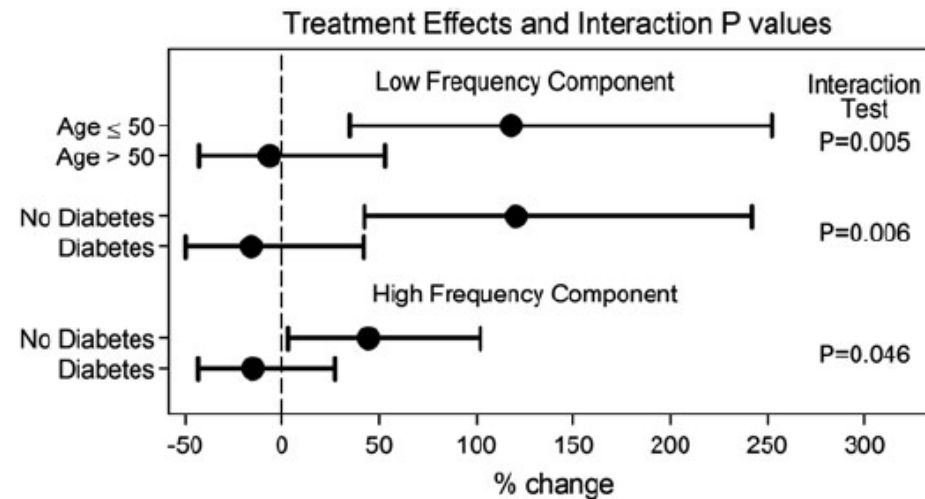
- PD is not associated with myocardial stunning
- 10 PD patients
- Very low frequency of RWMA

Effects of daily hemodialysis on heart rate variability: results from the Frequent Hemodialysis Network (FHN) Daily Trial

Frequent HD is associated with:

LF component of HRV

Reduction of LVM → increased vagal modulation of heart rate (HF)



CVS Hospitalization: Frequent HD versus Conventional HD

Table 2. Pooled HRs of Type-Specific Hospital Admissions for Daily Home Hemodialysis Patients in Intention-to-Treat and On-Treatment Analysis

	Intention-to-Treat		On-Treatment	
	HR (95% CI)	% ^a	HR (95% CI)	% ^a
Cardiovascular disease				
Arrhythmia	0.97 (0.84-1.12)	10.4	1.00 (0.86-1.17)	11.2
Cerebrovascular disease	0.85 (0.71-1.02)	5.8	0.75 (0.60-0.93)	5.9
Heart failure, fluid overload, and cardiomyopathy	0.69 (0.62-0.77)	20.4	0.59 (0.52-0.68)	18.5
Hypertensive disease	0.88 (0.80-0.96)	24.0	0.84 (0.75-0.93)	24.4
Ischemic heart disease	0.94 (0.84-1.05)	16.6	0.91 (0.80-1.03)	16.1
Peripheral artery disease	1.06 (0.95-1.18)	16.8	1.02 (0.90-1.15)	17.5
Other cardiovascular disease	1.18 (0.98-1.41)	5.9	1.19 (0.97-1.45)	6.3

Discussion

- Frequent HD lowers BP

- Longer and more frequent HD is associated with changes in vascular resistance
- Overall volume control is better with frequent HD
 - UF rate
 - Total overall control of volume
 - Impact on sleep apnea, LV mass and hospitalization
 - RV and pulmonary impact?

- PD is tightly associated with volume + BP control

- Overall volume control (depends on urine + PD removal)

- Na/volume regulation requires more investigation in frequent HD + PD

KDIGO