

Advancing Dialysis

Individual Patient Data Meta-Analysis of the Frequent Hemodialysis Network Trials: Comparing Diurnal and Nocturnal Hemodialysis

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Background

- The two Frequent Hemodialysis Network (FHN) trials tested the effects of intensive hemodialysis (HD).

Daily Trial	Nocturnal Trial
6 short, diurnal sessions	6 long, nocturnal sessions
vs. 3 conventional sessions	vs. 3 conventional sessions †
	† Relatively long

FHN Trials

Features of Interventions

	Daily Trial		Nocturnal Trial	
	Conventional Hemodialysis (N = 120)	Frequent Hemodialysis (N = 125)	Conventional Hemodialysis (N = 42)	Frequent Hemodialysis (N = 45)
Treatments per week	2.88 ± 0.39	5.17 ± 1.11	2.91 ± 0.21	5.06 ± 0.80
Time per dialysis session (min)	213 ± 28	154 ± 25	256 ± 65	379 ± 62
Weekly standard Kt/V	2.57 ± 0.26	3.60 ± 0.57	2.91 ± 0.86	5.03 ± 1.23

FHN Trials

Baseline Characteristics

	Daily Trial		Nocturnal Trial	
	Conventional Hemodialysis (N = 120)	Frequent Hemodialysis (N = 125)	Conventional Hemodialysis (N = 42)	Frequent Hemodialysis (N = 45)
Age	52.0 ± 14.1	48.9 ± 13.6	54.0 ± 12.9	51.7 ± 14.4
Race				
White	38.3%	34.4%	50.0%	60.0%
Black	44.2%	39.2%	26.2%	26.7%
Other	17.5%	26.4%	23.8%	13.3%
Duration of ESRD				
<2 years	16.7%	16.0%	71.4%	62.2%
2-5 years	42.5%	35.2%	11.9%	17.8%
>5 years	40.8%	48.8%	16.7%	20.0%
Residual kidney function				
Anuria	60.0%	72.0%	26.2%	28.9%
>0 ml/min	40.0%	28.0%	73.7%	71.2%

FHN Trials

Significant Effects ($P < 0.05$) on Secondary Outcomes

- The conventional wisdom is that the Daily Trial was positive, whereas the Nocturnal Trial was negative.

	Daily Trial	Nocturnal Trial
Left ventricular mass index	<input type="checkbox"/>	
Predialysis SBP	<input type="checkbox"/>	<input type="checkbox"/>
Predialysis phosphorus	<input type="checkbox"/>	<input type="checkbox"/>
Physical-health composite score	<input type="checkbox"/>	
Beck Depression Inventory		
Predialysis albumin		

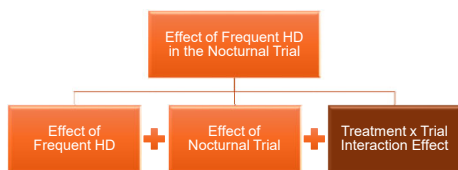
What Happened Here?

- Differences in HD intensity
 - At 6 treatments per week, different effects of diurnal (short) and nocturnal (long) HD (?)
 - Differences in "conventional" HD *between* trials
- Differences in patient populations
 - Between trials
 - Within trials
- Low precision in the FHN Nocturnal Trial

Objective

- Pool data from both FHN trials to assess whether treatment effects of frequent versus conventional HD differed significantly.

Conceptual Model



Methods

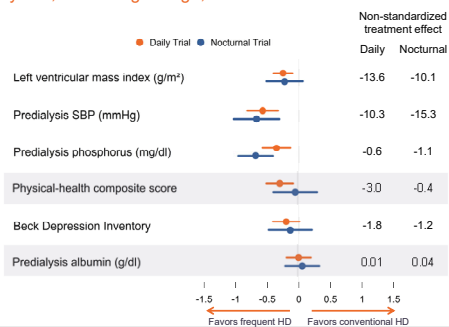
- We analyzed pooled individual patient data from both FHN trials.
- We applied mixed-effects models of the change in secondary outcomes to estimate the interaction between assigned treatment (frequent vs. conventional) and study (Nocturnal vs. Daily), with adjustment for baseline outcome value, age, sex, diabetes, and residual renal function (RRF).

Results

- The pooled cohort included 332 patients.
 - 162 patients assigned to conventional HD
 - 170 patients assigned to frequent HD
- The conventional HD group included 83 (51%) patients with no residual renal function (RRF).
- The frequent HD group included 103 (61%) patients with no RRF.

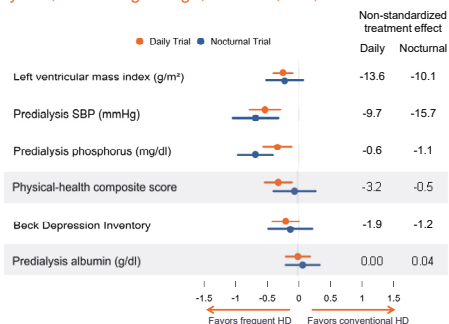
Standardized Treatment Effects

By trial, controlling for age, diabetes

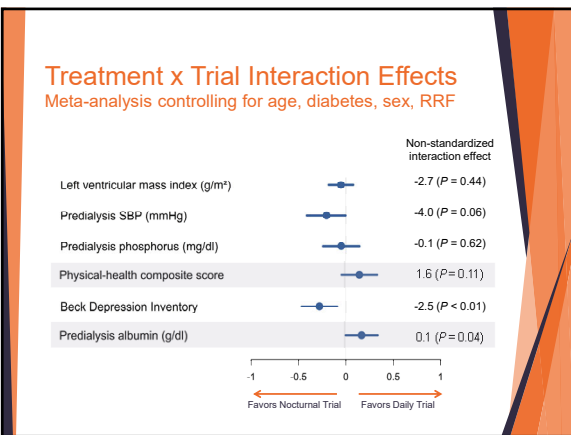


Standardized Treatment Effects

By trial, controlling for age, diabetes, sex, RRF



Individual Patient Data Meta-Analysis: Key Results



Results

- These findings were unchanged in a sensitivity analysis that included only patients without RRF at baseline.

Conclusions
Physiology

- The effects of frequent HD on left ventricular mass, systolic blood pressure, and serum phosphorus were **not statistically different** with diurnal versus nocturnal treatment.
 - Numerically larger effects on left ventricular mass and systolic blood pressure with nocturnal treatment

Conclusions
Quality of life

- The effect of frequent HD on physical health was **larger with diurnal treatment**.
 - Not significant ($P = 0.11$)
- The effect of frequent HD on depressive symptoms was **larger with nocturnal treatment**.
 - Significant ($P = 0.004$)

In context

- Higher treatment frequency decreases interdialytic fluid load.
- Frequent nocturnal HD sharply lowers ultrafiltration intensity.
 - Less intradialytic hypotension
 - Less organ (e.g., cardiac) stunning
 - Decline in total peripheral resistance

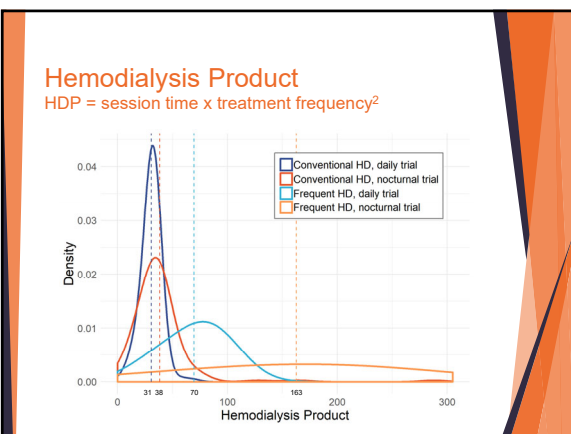
Hemodialysis Product

HDP = session time x treatment frequency²

TABLE I. Various values of the Hemodialysis Product (HDP), as well as the corresponding expected clinical findings.

Hours per Dialysis Session	Dialysis Sessions per Week	HDP*	Clinical Results
3	3	27	Totally inadequate. Severe malnutrition
4	3	36	Inadequate. A high percent of the U.S. dialysis population is malnourished.
5	3	45	Borderline. Some malnutrition, BP control difficult. ^{8,12}
8	3	72	Only 3 days/wk schedule has proven to be adequate. ^{8,12}
5	4	80	No data yet available.
3	5	75	No data available. BP control should be easy.
2-3	6	72-108	Preliminary data: Good well-being. BP control possible if sodium intake is limited.
8	6	288	Best so far because PO ₂ is normalized. BP control very easy. ^{14,17}

*Hemodialysis Product = (hours/dialysis session) x (dialysis sessions/week)²



Implications

- Quality of life on nocturnal HD
 - Slower dialysis, less recovery time
 - Poor sleep quality while dialyzing?
- Frequent diurnal and nocturnal HD may be clinically differentiated modalities, but there is limited RCT evidence supporting this claim.

Parting Thought

- Is the FHN Nocturnal Trial a negative trial, like so many others in nephrology?
- Does the FHN Nocturnal Trial instead demonstrate non-inferiority of frequent nocturnal HD, relative to frequent diurnal HD?
