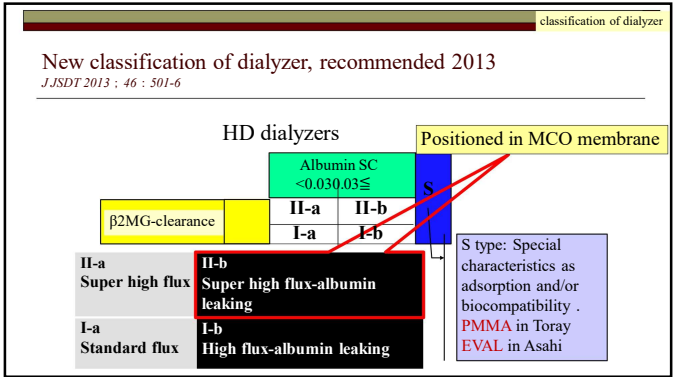
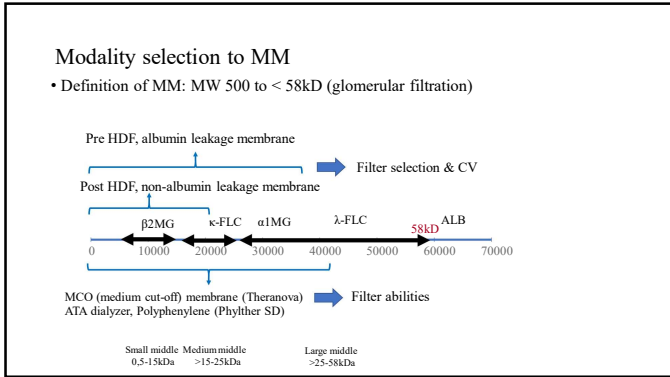
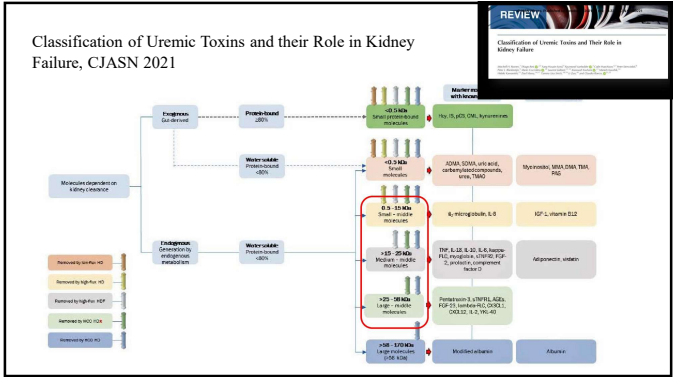
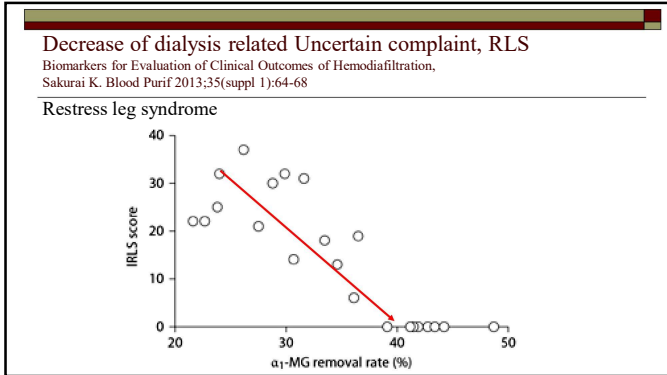


Hemodiafiltration, Expanded Hemodialysis & High flux HD

A Look Towards the Future

Hideki Kawanishi
Tsuchiya General Hospital, Hiroshima, JAPAN





Function of alpha1MG hypothesis, by Kim ST

In serum, the ratio of free and IgA bound form alphaMG is almost same, and the removal rate per HDF is limited to 60% (controversial by Dr Tomo)

Physiological function :

- Disadvantage : Cell toxicity
- Benefit : Antioxidant action (Heme Scavenger)

Dialysis patients: the serum alphaMG is more than ten times higher than normal, and most of them are deteriorated (oxidized) alphaMG.

Removing the deteriorated alphaMG -> produce new alphaMG from the liver -> recovery of antioxidant effect

Dr Tomo T
IgA bound / free %
Healthy < HD-free ↑(deteriorated)
=>Increase cell toxicity

Clinical effects of alpha1MG removal : Radical scavenging action

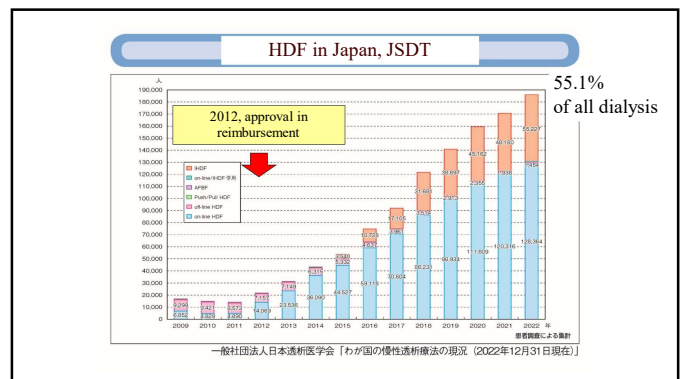
Kim ST 金成泰, High Performance Membrane 23.腎と透析Vol96, 2024

Hypothesis of spinal cord dorsal horn :

- Restress Leg Syndrome (RLS), Pain, Itching
- Spinal cord dorsal horn Sinapis
 - alpha1MG deteriorate => Microglia, Astrocyte => Radical
 - Synaps stimulus => Pain/itching

alpha1MG removal => Newly alpha1MG-Radical scavenging action

- Protection against hemolysis (Heme scavenge)
- Pigmentation suppression



EU vs Japan

Pre dilution online HDF, albumin leakage membrane

EU-Post dilution online HDF, Non-albumin leakage membrane

- Higher blood flow 300-350mL/min,
- Higher convection volume (CV) 20-24L
- Target solute < small-medium middle (<20kDa)

β 2MG: 10000 (Small middle 0.5-15kDa)
 α 1MG: 20000 (Medium middle >15-25kDa)
 ALB: 60000 (Large middle >25-58kDa)

Japan-Pre dilution online HDF, Albumin leakage membrane

- Low blood flow 200-300mL/min,
- Higher convection volume (CV) 48-72L
- Target solute < large middle (<35kDa)

Global trends in HDF

Canaud B, et al. Nephrol Dial Transplant (2020) 35: 398-407

Survival

Results of CONVINC

Blankestijn PJ et al., N Engl J Med. 2023 Jun 16. doi: 10.1056/NEJMoa2304820

- 2018 to 2021, Total 1360, High-dose HDF (CV>23L) 683, High-flux HD 677,
- Medial follow up 30m, mean CV 25.3L
- Primarily outcome: all-cause mortality, Second outcome: cause-specific mortality, CVD, infection

A Overall Survival

All-cause mortality
HDF 118 patients (17.3%) vs HD 148 (21.9%)
(hazard ratio, 0.77; 95% confidence interval, 0.65 to 0.93).

	0	1	2	3
No. at Risk				
High-dose hemodiafiltration	683	625	519	384
High-flux hemodialysis	677	622	501	370
No. of Events				
High-dose hemodiafiltration	0	44	92	150
High-flux hemodialysis	0	54	100	140

ORIGINAL ARTICLE
Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

Improvement of patient's survival : pre-online HDF

JRDR: propensity score matching, Kidney International (2019) 95, 929-938

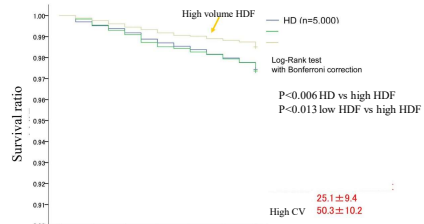
Survival ratio

25.1 ± 9.4
50.3 ± 10.2

P<0.001 HD vs high HDF
P<0.001 low HDF vs high HDF

Improvement of patient's survival : pre-online HDF

JRDR: propensity score matching, *Kidney International* (2019) 95, 929-938

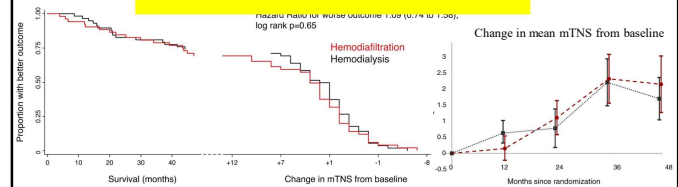


Effect of Hemodiafiltration on the Progression of Neuropathy, FINESSE study

Kang A, et al., *CJASN* 2021; 16: 1365-1375



- RCT in Australia, HFHD vs Post on-line HDF (CV 24.7 (22.4-26.5))
- Age 66 (13)yo, Vintage 3.2 (1.9-5.2)yr, 5hr/session x 3times/wk
- Outcome: total neuropathy score (mTNS), survival



Conclusion


- Dialysis modality should be determined on Middle molecules classification
- The evidence of Protein bound substances in HD is not sufficient
- Online HDF & HDx (MCO) are higher removal capacity of MM
- The survival effect of HDF is now on study and discuses.
- Removal α 1MG: Possibility for recovery of Antioxidant effect
- On-line HDF possible to effect to HD patients

CKD-MBD mineral and bone disorder

Hideki Kawanishi

Tsuchiya General Hospital, Hiroshima JAPAN

Terminology



ROD (Renal osteodystrophy): Bone fracture

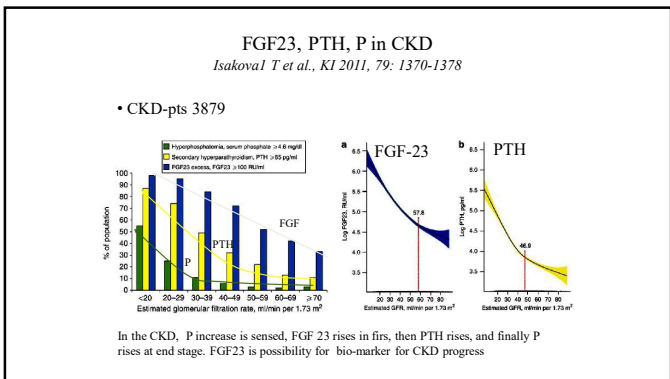
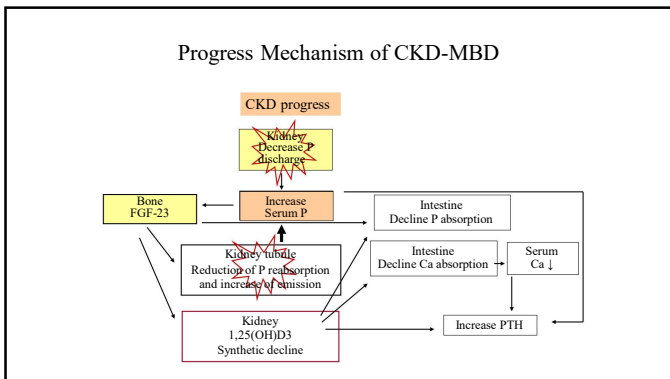
↓

CKD-MBD (mineral and bone disorder)
: Vascular Calcification

Need for the balance of Bone vs calcification

Important factors for CKD-MBD

- P, Ca
- Fibroblast growth factor-23 (FGF-23)
- 1,25 (OH)₂-D₃
- PTH
- Vascular Calcification
- Bone



Calciprotein particles (CPPs) Vascular calcification

Pasch A et al. JASN 2012;23:1744-1752

- Ca + P ⇒ crystalline hydroxyapatite [Ca₁₀(PO₄)₆(OH)₂]
- Ca + P + Serum ⇒ soluble colloidal particles
- Primary CPPs (radius 75 nm)
- Secondary CPPs (radius 120 nm)

Ca + Phos

Water 0 min. 1 min. 400 min.

CPPs develop

TEM

TEM

Fetuin A-CPPs Vascular calcification

Jahnen-Dechent W et al. Circulation Research 2011;108:1494-1509

Hydroxyapatite Fetuin A positive charge

negative charge

1st CPPs 2nd CPPs

Calcification
Cell injury
Inflammation

Calciprotein particles (CPPs) Vascular calcification

Pasch A et al. JASN 2012;23:1744-1752

light scatter [RNU]

time

Enhancer

Inhibitor

phosphate
calcium
lack of inhibitors
low pH

primary CPP <100 nm

secondary CPP >100 nm

more / bigger CPPs

fewer / smaller CPPs

500 nm

500 nm

T₅₀

FGF23 related to CVD mortality Vascular calcification

FGF-23 & risk of Death, CV event, initiation of dialysis

Kendrick J et al., JASN 2011, doi: 10.1681/ASN.2010121224

■ CKD-4&5, Mean GFR 18mL/min

■ FGF-23: <216, 217-380, 381-945, >946 RU/mL

Faul C, et al., JCI. 2011

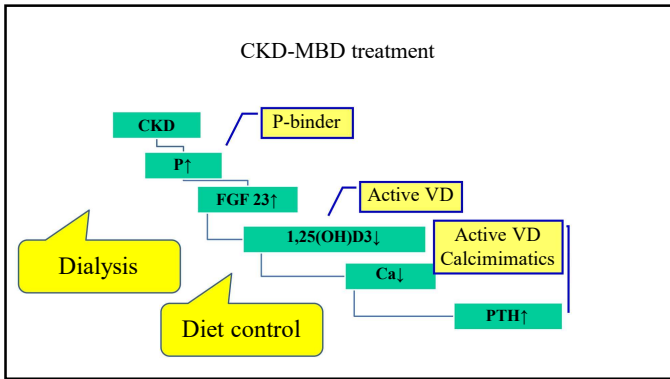
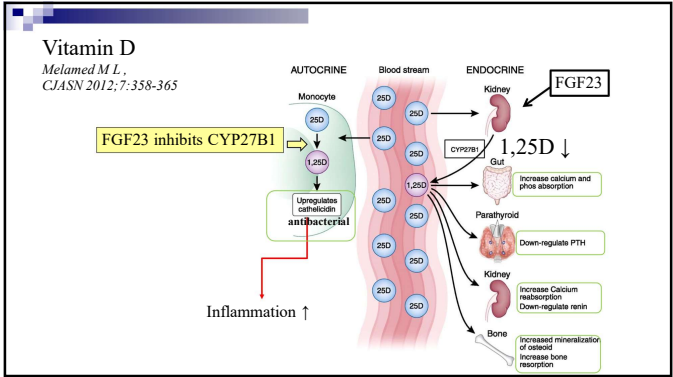
All cause

CV event

Functions of VD

25 (OH)D3 \Rightarrow 1,25(OH)₂D₃

- Intestine P, Ca absorption $\uparrow \Rightarrow$ S-Ca, P \uparrow
- Kidney: Ca reabsorption $\uparrow \Rightarrow$ S-Ca \uparrow
- Parathyroid: PTH secretion \downarrow
- Bone: mineralization \uparrow
- Monocyte: antibacterial action \uparrow



International GL for CKD-MBD

GL	Year	P, mg/dL	Ca, mg/dL	PTH, Pg/mL
EDTA	2000	2.4-4.6	8.8-11.0	85-170
K/DOQI	2003	3.5-5.5	8.4-9.5	150-300
JSDT	2008	3.5-6.0	8.4-10.0	60-180
KDIGO	2009	Normal	Normal	2-9 times upper Normal (Around 130 - 585pg/ml)
JSDT	2012	3.5-6.0	8.4-10.0	60-240
New KDIGO	2017	Normal	Normal	2-9 times upper Normal (Around 130 - 585pg/ml)

Calcimimetics: Cinacalcet-HCL

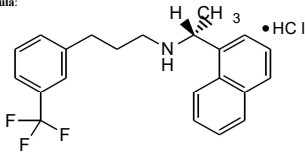
Common name : Cinacalcet Hydrochloride

Chemical name: *N*-[(1*R*)-1-(Naphthalen-1-yl)ethyl]-3-[3-(trifluoromethyl)phenyl]propan-1-amine monohydrochloride

Molecular formula: C₂₂H₂₃F₃N · HCl

Molecular weight: 393.87

Structural formula:



Comparison of Drugs for CKD-MBD Treatment

Drugs		Blood level	PTH	Ca	P	FGF23
Phosphate Binder	Ca		↓	↑	↓	⇨
	Polymer		⇨	⇨	↓	↓
	Lanthanum		⇨	⇨	↓	↓
	Iron		⇨	⇨	↓	↓
Vitamin D			↓	↑	↑	↑
Calcimimetics			↓	↓	↓	↓

↓ : Decrease ↑ : Increase ⇨ : No Individual action

Naraino, N et al. PHARM STAGE 16. 60.66. 2019