Slide 1:

Measuring Residual Renal Function

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Slide 2:

Why bother with RRF ?

Kt/Vurea for all

Slide 3:
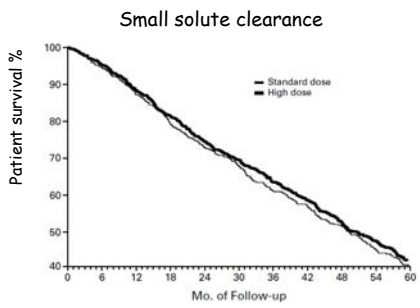
HEMO study

randomised prospective trial

Small solute clearance

Eknoyan et al NEnglJMed 2002

Residual renal function

KRU 6 months after start of HD (ml/min)
<1
≥1

Vilar et al NDT 2009
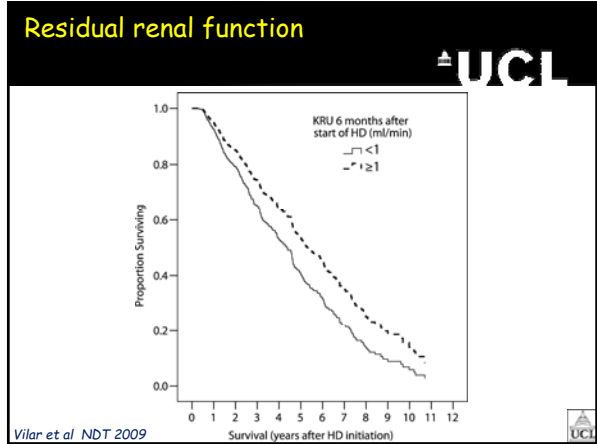
Uraemic Toxins (EuTox) [uraemic/normal] conc

20 solutes scoring ≥15		19 solutes scoring <2.5	
Guanidinosuccinic acid	216.67	Retinol-binding protein	2.40[a]
Methylguanidine	106.00[a]	Methylglyoxal	2.34
Indoxyl sulfate	88.33	Cholecystokinin	2.30[a]
Indole-3-acetic acid	50.00	3-deoxyglucosone	2.27
Hippuric acid	49.40[a]	Degranulation inhibiting	
1-methylinosine	45.96	protein I	2.21
p-cresol	33.50	κ-Ig light chain	2.20
Clara cell protein (CC16)	33.00[a]	Methionine-enkephalin	1.76[a]
β₂-microglobulin	27.50[a]	Kinurenine	1.76[a]
N²,N²-dimethylguanosine	26.27	ADMA	1.75
Pseudouridine	26.20	ß-endorphin	1.74[a]
Arab(in)itol	25.00[a]	Hyaluronic acid	1.73[a]
Parathyroid hormone	20.00[a]	Guanidinoacetic acid	1.73
Mannitol	20.00[a]	Dimethylglycine	1.51[a]
Interleukin-6	19.50	Cytidine	1.46[a]
α-N-acetylarginine	18.14	Hypoxanthine	1.33
Pentosidine	17.36	Uric acid	1.24[a]
Orotidine	16.83	β-Lipotropin	1.13[a]
Oxalate	16.33	Argininic acid	1.05[a]
Quinolinic acid	15.00	Neuropeptide Y	0.81[a]

Toxicity for protein bound solutes

Cardiovascular risk
- cell culture
- animal models
- dialysis patients

Low IS group

High IS group

Log-Rank P < 0.001

Cao et al CJASN 2015
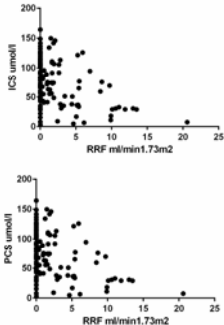
Role of residual renal function

Why measure residual renal function

Residual renal function

o preservation

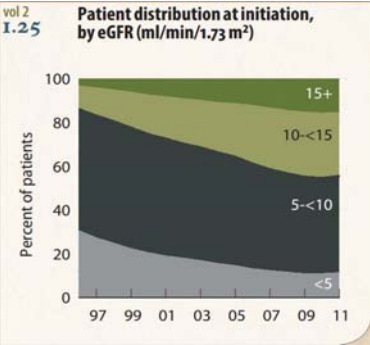 ❖ improved survival
    ❖ clearance protein bound toxins

Background USRDS data

Residual Renal Function

Yoshitsugu et al AmJKidDis 2016
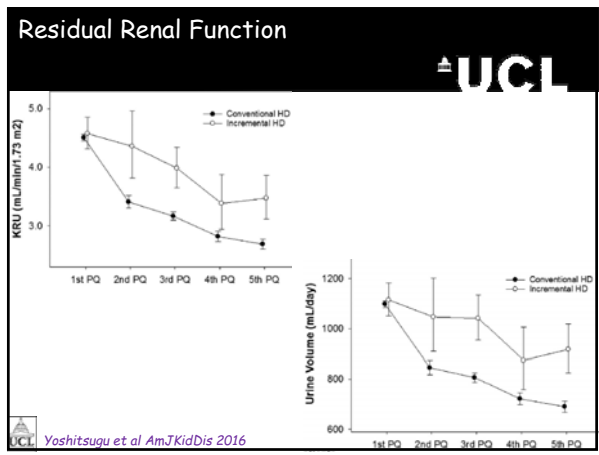
Incremental dialysis approach

Patient orientated treatment

o Individualised dialysis

  ❖ Prescription

    ✓ adjusted

      ▪ residual renal function

all well and good ….

But …..

o problems

  ❖ measure residual renal function
  ❖ adjust for residual renal function
    ▪ serial measurements
    ▪ serial adjustments

Measuring glomerular filtration

UCL

Research

o Clearance studies

  ❖ inulin infusion
  ❖ isotope/radiocontrast
    ▪ Cr-EDTA
    ▪ iothalamate
    ▪ iohexol

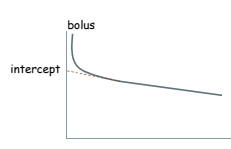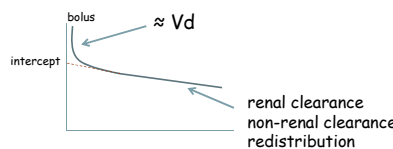
Measuring glomerular filtration

UCL

bolus

intercept

Measuring glomerular filtration

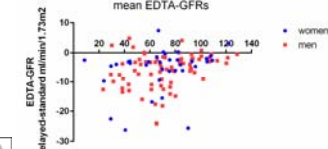**UCL**

bolus ≈ Vd

intercept

renal clearance
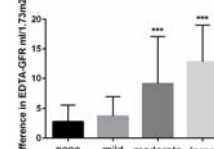non-renal clearance
redistribution

mean EDTA-GFRs

EDTA-GFR delayed-standard ml/min/1.73m2

20 40 60 80 100 120 140

women
men

difference in EDTA-GFR ml/1.73m2

none   mild   moderate   large
ascites grade
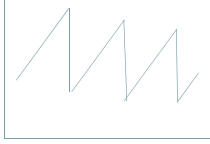
Measuring glomerular filtration

In clinical practice

o Urine collections

❖ duration of collection
- 24 hour
- inter-dialytic
❖ Timing of collection
- start of dialysis week
- middle of dialysis week
- end of dialysis week

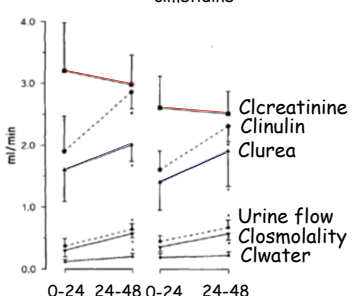## Measuring glomerular filtration

cimetidine

Clcreatinine
Clinulin
Clurea

Urine flow
Closmolality
Clwater

0-24 24-48 0-24 24-48

Van Olden et al NDT 1995 Inter-dialytic interval

Measuring residual renal function

In clinical practice

o Urine collections

❖ Urea clearance
- KRU
❖ Combined urea & creatinine clearance
- PD

Measuring creatinine

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platforms	1	2	3	4	5
LCMSMS	59	60	84	86	122
H917enzymatic	59	59	79	84	120
H917 Jaffe R/B with offset	62	65	85	89	126
Advia 2400 with offset	52	54	73	80	112
Olympus 5400 with offset	61	62	82	86	123
Vitros 950	65	67	83	88	124
Integra 700 with offset	49	52	72	78	111
Dimension RxL	60	61	78	90	139
Beckman LX20	64	61	81	89	126
Abbott 8200	72	74	91	99	126

Creatinine measurements

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assessing renal function in end stage kidney failure

❖ creatinine methods
- ○ Jaffe
- ○ modified Jaffe
- ○ enzymatic

1) O'Leary modified Jaffe -potassium ferricyanide oxidizes bilirubin to biliverdin (pre-step). An increase in absorbance was measured at 505nm and blanking at 570nm.

2) Compensated (rate blanked) kinetic Jaffe measures increase in absorbance at 505nm with blanking at 570nm.

3) Enzymatic creatinine(ECr): creatininase/creatinase/sarcosine oxidase system with detection at 546nm and absorbance blanking at 700nm.
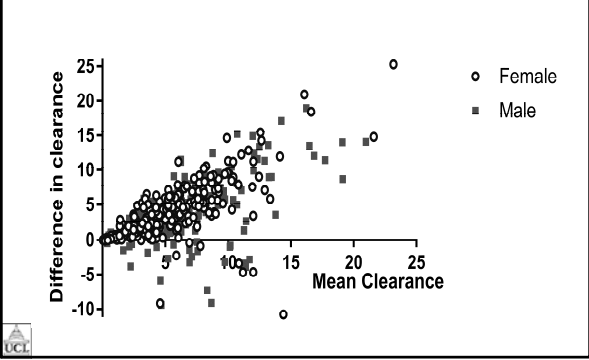
Creatinine or urea clearance
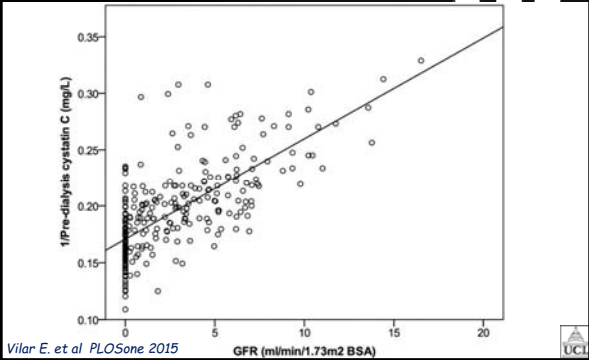
⏚UCL

Cystatin C

Vilar E. et al PLOSone 2015

Cystatin C

Vilar E. et al CJASN 2014

Alternative methods

β2 microglobulin

Vilar E. et al PLOSone 2015

Comparison

Vilar E. et al PLOSone 2015
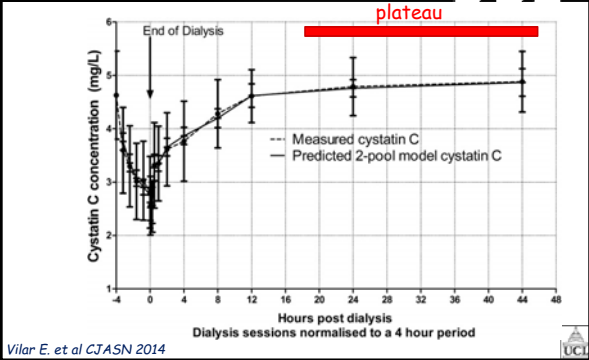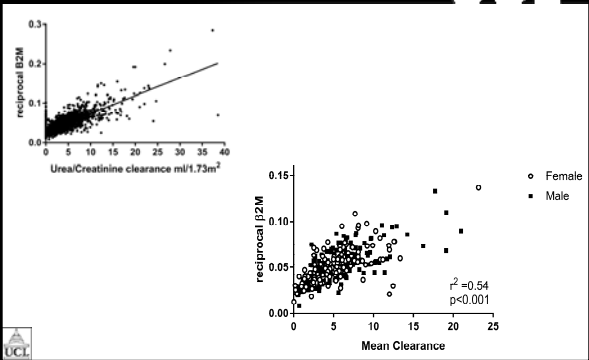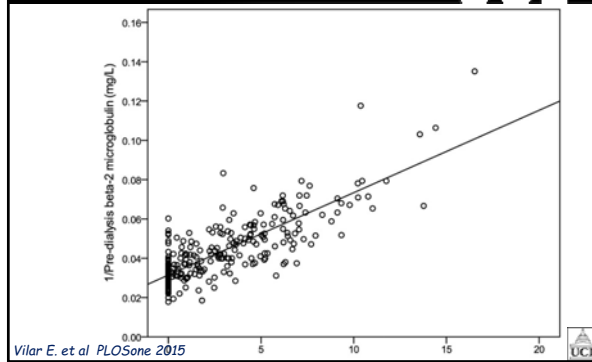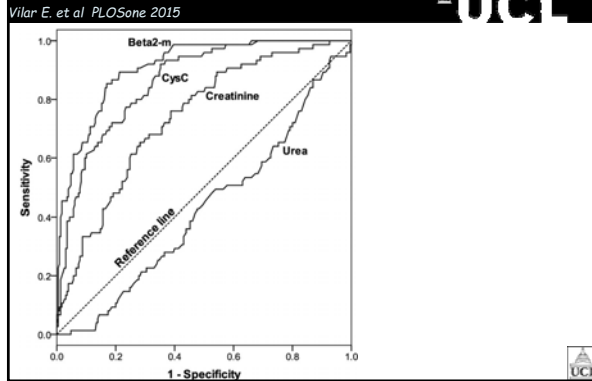
β2 microglobulin

MHC class 1

❖ increased
- ✓ Acute inflammation
- ✓ Chronic inflammation
- ✓ Cancer

Dialysis patient
- ✓ myeloma
- ✓ lymphoma
- ✓ chronic hepatitis
- ✓ SLE

Dialysis clearance

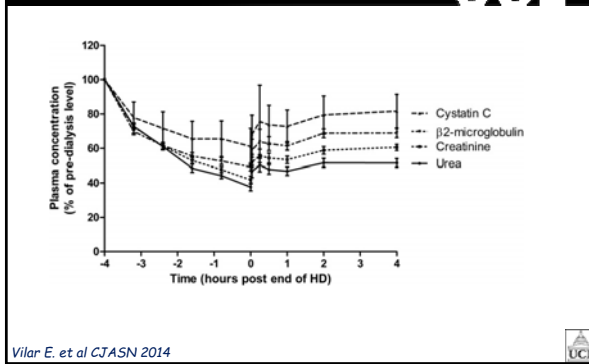Vilar E. et al CJASN 2014

Dialysis clearance

Vilar E. et al CJASN 2014

βTP estimated GFR

Filler et al ClinBichem 2014

Effect of Residual renal function
Gerhardt et al NDT 2007

Effect of Residual renal function
Shafi et al CJASN 2016

Dialysis clearance
Gerhardt et al NDT 2007

Measuring residual renal function

UCL
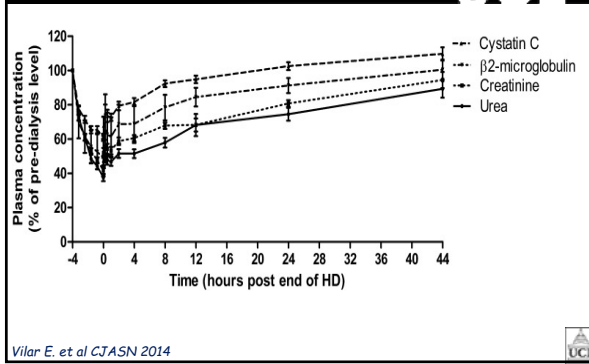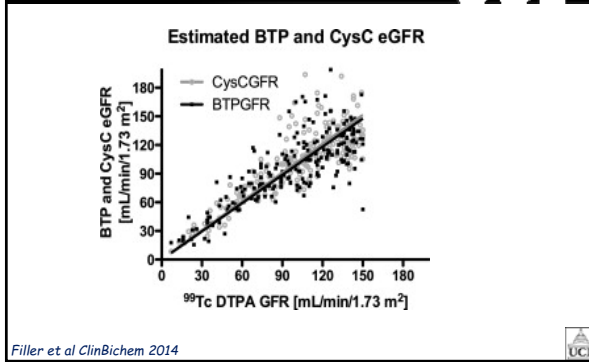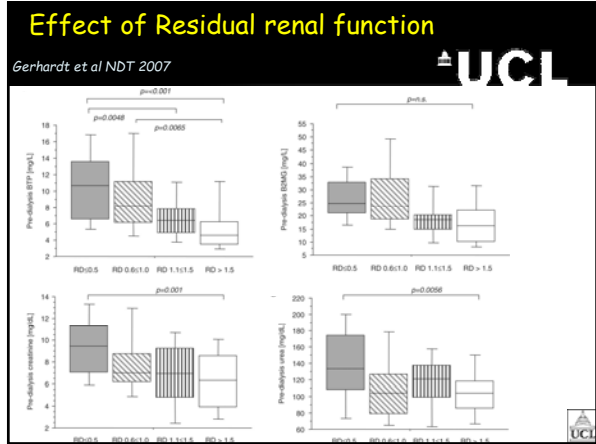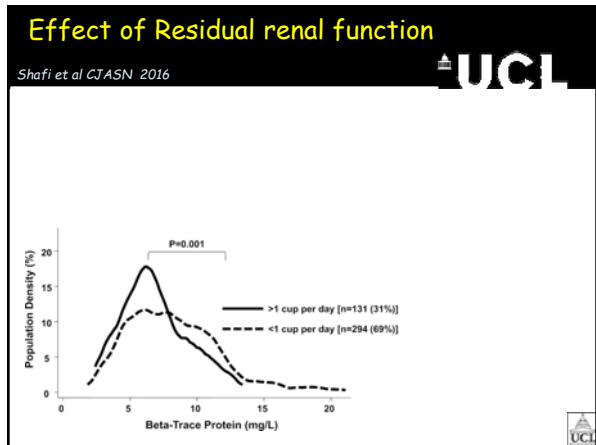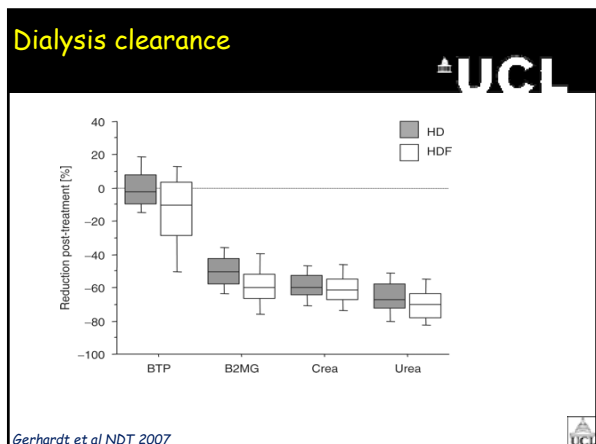
What is most important ?

o glomerular filtration rate
  o combined urea and creatinine clearance
  o βtrace protein
  o β2 microglobulin
o renal tubular function
  o PAH
  o IS
o both
  o creatinine clearance

How can we add residual renal function ?

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residual renal function ≠ dialyzer urea clearance

Estimating sessional dialysis target

UCL

twice weekly dialysis schedule

— KRrurea 2 ml/min
- - KRurea 4 ml/min

adequacy line

inadequacy line

EKRc ml/min

Sessional Kt/Vurea

Casino-Lopez NDT 1999
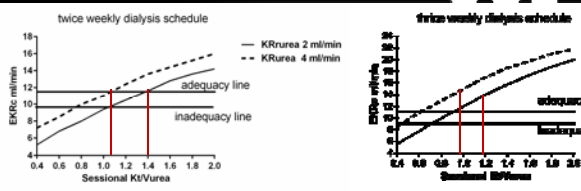
Estimating sessional dialysis target

Casino-Lopez & Basile NDT 2017
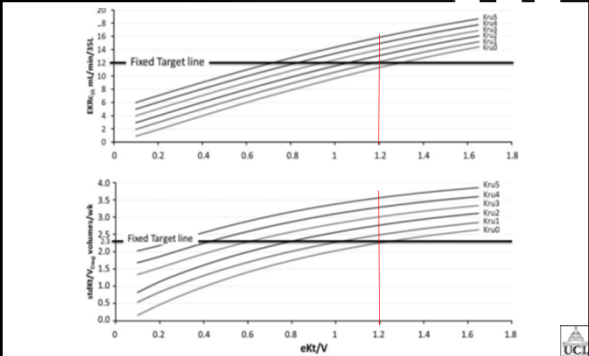
Estimating residual renal function

current
- urine collections
  - inter-dialytic
    - urea clearance
    - urea & creatinine

- validation equations
  - containing
    - $\beta 2$ microglobulin
    - β trace protein

thank you for your attention !