투석 치료의 적절도

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  - Present
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투석 치료의 목표

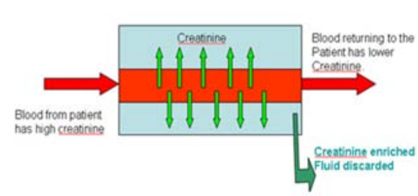
- 요독을 제거함으로써 요독 증상의 완화, 삶의 질 개선, 중요 장기의 기능 부전을 최소화 하여 생존률을 향상시키는 것이다.
- 더 광의적 개념으로는 환자 개인이 받아들일 만한 건강상태를 유지하는 것이다. 즉 환자의 주관적인 참살이 (well being) 및 요독 증세로부터 해방이며,
- 객관적으로는 적정 체액상태, 정상 혈압, 빈혈 해소 및 생화학 검사의 합리적 수치의 유지 등이다
- 객관적인 지표 필요

투석 치료 모니터링을 위한 객관적인 지표

Parameters	Criteria
spKt/V	> 1.2
Hematocrit	> 33%
Serum albumin	> 4.0 g/dL
Caclium	8.4 - 9.5 mg/dL
Phosphorus	3.5 – 5.5 mg/dL
iPTH	
Predialysis BP	< 140/90 mmHg
Preservation of residual renal function	?
Dry body weight (Fluid status)	?
Nutritional status	nPCR 1.0-1.2 g/kg/day
Vascular access	?
Health-related quality of life	SF-36, KDQOL

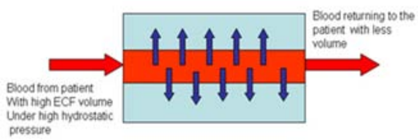
Solute transport

- Diffusion
  - Movement of solutes from greater to lower concentration
  - Urea, creatinine, uric acid, and electrolytes
    - move from the blood to the dialysate
    - the net effect of lowering their concentration in the blood

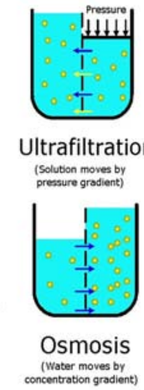


Solute transport

- Convection
  - The process of solute transfer associated with flow of water
    - Solvent drag
  - Hemodialysis
    - the amount of low–molecular weight solute (*eg*, urea) removed by convection is negligible
  - Continuous renal replacement therapies (Hemofiltration)
    - this is a major mechanism for solute transport



Ultrafiltration



Dialysis adequacy index

- Urea reduction ratio
- Kt/V
- Protein catabolic rate (nPCR), Albumin
- Solute removal index
- Time averaged concentration of urea

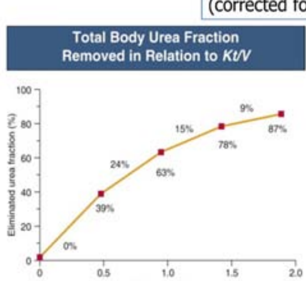
Dialysis adequacy: Urea reduction ratio

- URR = (Pre BUN – Post BUN) / Post BUN ×100 (%)
- 2006년 NKF-DOQI guideline9)에서는 잔여신기능과 무관하게 요소 감소율은 최소 65% 이상, 목표치를 70% 이상 유지하도록 제시.
- 단, 혈액 투석을 처음 시작하는 만성 신질환 환자의 경우에는 disequilibrium syndrome을 막기위해 URR <30%로 혈액 투석 효율을 낮춰야 한다
  - 투석 시간을 짧게, 혈류 속도는 낮게
  (dialysis initiation: time = 2 hrs, blood flow <120 mL/min)

Dialysis adequacy: Kt/V

Kt/V

투석막의 요소 청소율 x 투석시간 / 요소 분포용적 = total body water, (corrected for volume lost during UF)

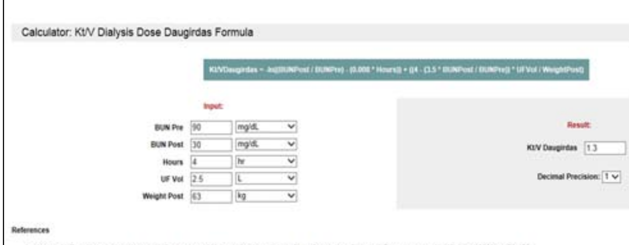


Dialysis adequacy: Kt/V in HD

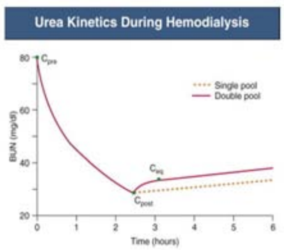
- Single pool (non-equilibrated) Kt/V

= -ln (R - 0.03) + [(4 - 3.5R) x (UF ÷ W)]

(UF = ultrafiltration volume in liters, W =postdialysis weight in kg, and R = the ratio of the postdialysis (종료 2분전 BUN) to predialysis BUN)

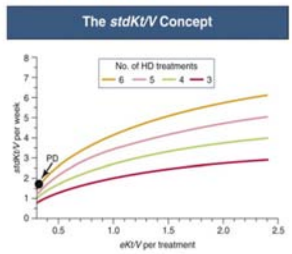


Kt/V in HD
double pool, weekly stdKt/V



Single pool: Urea generation 만 생각

Double pool: Urea generation
+ intercompartmental urea redistribution

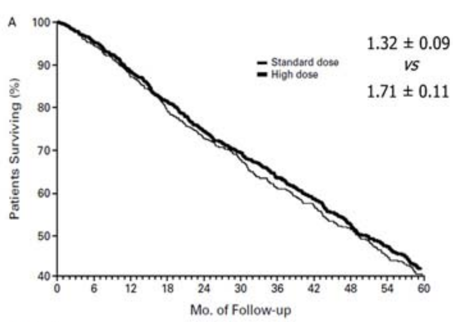


1주일간의 extracorporeal urea clearance
X 10.080 (minutes/week) /V
Directly compatible with PD weekly Kt/V
and with native residual renal Kt/V.
Minimum target std-Kt/V of 2.0/week
= spKt/V of 1.2 or eKt/V of 1.0
in anuric patients

Dialysis adequacy: Kt/V in HD

- The equilibrated, double-pool Kt/V
  - The equilibration of urea from the extravascular compartment into the vascular space can take up to 30 minutes after dialysis ends (투석 종료 30분 후 BUN).
  - Since the urea concentration measured with the equilibrated sample is higher than that observed in the non-equilibrated sample.
  - 0.21 for the usual range of delivered doses of hemodialysis.
- Target of Kt/V
  - US KDOQI: sp Kt/V> 1.2 (dialysis one session, minimum level)
    - Urea reduction ratio = 65%
  - European Best Practice guideline: equilibrated kt/V > 1.2
    - Sp Kt/V > 1.4

HEMO study



No. at Risk

Standard dose	854	759	630	524	451	382	315	253	197	149
High dose	857	753	637	538	470	399	327	266	219	166

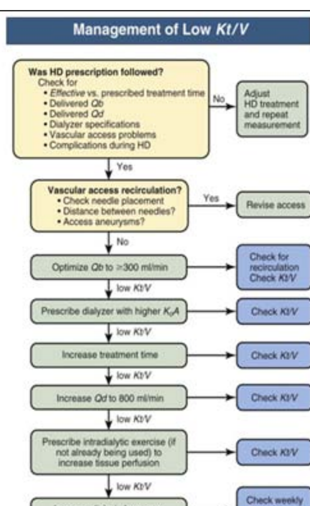
NEJM, 2000

The causes of low kt/V in HD

Kt/V

투석막의 요소 청소율 x 투석시간 / 요소 분포용적= total body water,

- 40%
  - a lower than prescribed blood flow or time of dialysis.
  - Inadequate needle placement and patient-initiated time constraints, respectively.
- 25%
  - significant access recirculation
- The others
  - Increased body mass, impaired sodium removal, and poor dialysate flow rate; blood tubing effects; and needle gauge size, dialysis using a central venous catheter



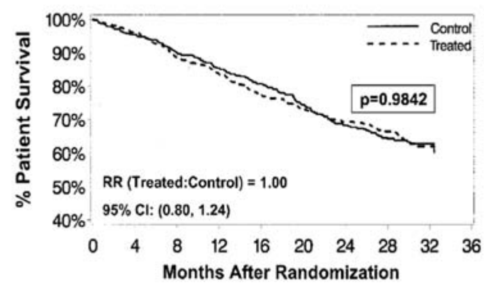
Optimizing Low kt/V in HD

- Fistula integrity
  - Access problems are common causes of inadequate dialysis.
- Treatment duration
  - a late-arriving patient, the late initiation of dialysis by staff, early termination because of patient request, and events during the treatment that cause the temporary cessation of dialysis (such as hypotension, a blood leak, needle difficulties, excessive triggering of machine alarms related to high venous pressures).
- Method of obtaining blood urea nitrogen (BUN) samples
- Dialysis machine and patient-specific variables
  - Inadequate machine calibration, low blood flow rates, and overestimation of dialyzer clearance all may result in low Kt/V.

Dialysis adequacy: weekly Kt/V in PD

- The daily Kt/Vurea is calculated from the daily urea clearance
  - the daily urea clearance (Kt): sum of the all 24 hrs drain volumes (peritoneal + urine) and the ratio of the urea concentration in the pooled drained dialysate or urine to the plasma (D/P urea).
  - Kt is normalized to total body water: the volume of distribution of urea (V).
- 2006 K/DOQI work group recommend the following
  - For patients with residual renal function (urine volume >100 mL/day), : Kt/Vurea ≥1.7/week.
  - For patients without RRF (urine volume <100 mL/day), : Kt/Vurea of ≥1.7/week.
  - We suggest that the minimal dose of Kt/Vurea should be 1.7/week for those undergoing APD.

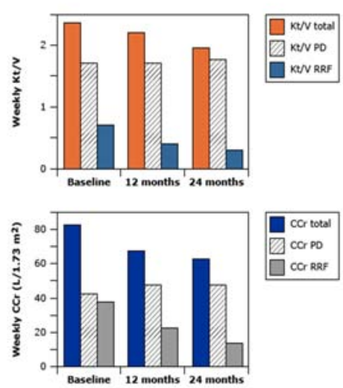
ADEMEX study



1.80 ± 0.02
vs
2.27 ± 0.02

JASN, 2002

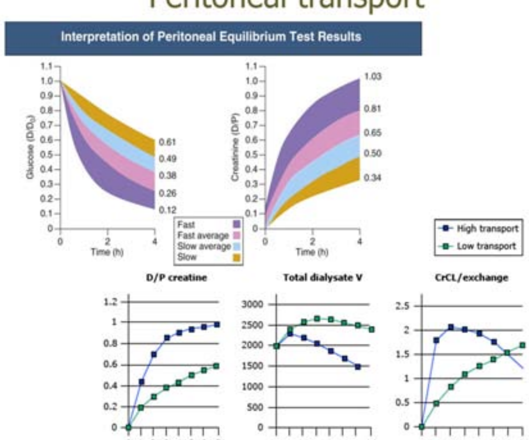
Dialysis adequacy: weekly Kt/V in PD



The causes of low kt/V in PD

- Dialysate solute concentration and volume이 결정적!
- Poor compliance
- Hypercatabolism
- Loss of residual renal clearance
- Decreased peritoneal transport
- Increased peritoneal transport

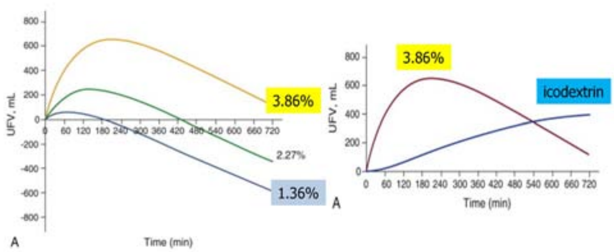
Peritoneal transport



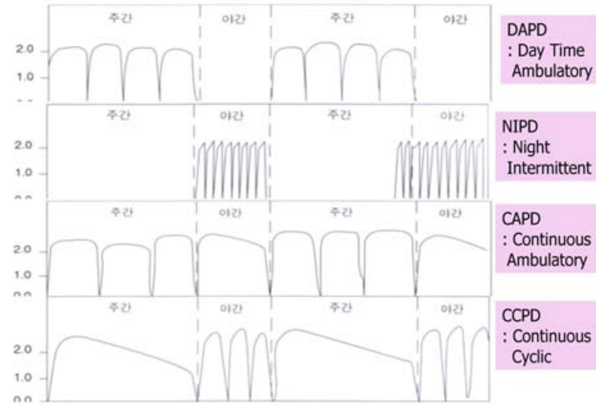
Optimizing low kt/V in PD

- These causes can be distinguished in part by PET
- Low peritoneal transport
  - increasing the volume of inflow dialysate per exchange and possibly the number of exchanges/day.
  - Among patients on automated peritoneal dialysis (APD) such as continuous cycler peritoneal dialysis (CCPD) who are not performing a midday exchange, adding a midday exchange.
- Impaired peritoneal ultrafiltration
  - High peritoneal transport, acute episode of peritonitis
  - Shortening the dwell time of each exchange, or by using more frequent hypertonic exchanges.
  - the use of diuretics in patients with residual renal function.
  - Icodextrin dialysate
  - APD

Ultrafiltration volume
time and concentration



Mode of dialysis



PD adequacy

Criteria for Peritoneal Dialysis Adequacy	
Clinical	Patient feels well and has stable lean body mass No symptoms of anorexia, asthenia, nausea, emesis, insomnia Stable nerve conductance velocity
Small-solute clearance	Weekly *Kt/V* urea >1.7 (renal + peritoneal) Weekly creatinine clearance >50 l/1.73 m ^{2}
Large-solute clearance	Albumin clearance <0.15 ml/min
Fluid balance	No edema No hypertension No postural hypotension
Electrolyte balance	Serum potassium <5 mmol/l
Acid-base balance	Serum bicarbonate >24 mmol/l
Nutrition	Daily protein intake ≥1.2 g/kg Daily calorie intake >35 kcal/kg/day Serum albumin >3.5 g/l BMI 20-30 kg/m ^{2} Stable midarm muscle circumference

Limitations of Kt/V

Kt/V

투석막의 요소 청소율 x 투석시간 / 요소 분포용적 = total body water, (corrected for volume lost during UF)

- OVERESTIMATE
  - A high Kt/V may indicate either high Kt (clearance x time) or low V (volume).
  - Low volume may reflect reduced skeletal muscle mass and malnutrition.
  - Kt/V tends to overestimate delivered dialysis among small-sized or malnourished patients.
  - Such patients may be under-dialyzed if their dialysis time is shortened because of high Kt/V.
- Urea clearance determined by any method may not represent the kinetic behavior of other potentially toxic molecules (other small solutes, middle molecules, protein-bound solutes, phosphate, etc).

Dialysis adequacy
normalized Protein Catabolic Rate (nPCR)

- 투석간 요소 생성률로 단백질 섭취량을 결정하고 이에 따라 환자의 영양 상태를 판단하는 단백질 이화속도 (PCR)로 모니터링.

Hemodialysis

- G=[(C2V2-C0V0)+Uurea]/Tid (g/minute)
  : PCR (or PNA)=9.35G+0.294V (g/day)
  : nPCR=PCR/DW (g/kg/day)

Peritoneal dialysis

- nPCR =[(UUN+DUN)×6.25]/weight (kg)

G: 요소 생성율 (urea generation rate)
C2: 투석 직전 BUN
V2: 투석 직전 total body water
C0: 이전 투석 종료시 BUN
V0: 이전 투석 종료시 total body water
Uurea: 투석간 소변에서 측정한 요소의 양
Tid: interdialytic interval (minutes)
V: volume of urea distribution
DW: Dry weight
UUN: 24시간 소변 BUN농도
DUN: 24시간 dialysate에서의 BUN농도

- Target
  - HD > 1.0 g/kg (ideal body Weight)/일
  - PD > 1.2 g/Kg

New paradigms in dialysis adequacy

- Uremic toxins
  - Range from very small metabolite-Na, P-to peptide, proteins.
- Assessing and managing more effectively fluid status
  - Monitoring a more adequate dry body weight
  - The patient remains normotensive, without antihypertensive medication, until next dialysis session.
- Assessing and correcting underlying chronic inflammation
  - In, CKD-5D, chronic inflammation is independently associated with malnutrition and anemia, leading to accelerated atherowclesosis, cardiovascular complications, and mortality.

Hemodialysis vs Hemodiafiltration

Table 1. Summary of Findings From 4 Meta-analyses on the Efficacy of Convective Therapies for the Treatment of Chronic Kidney Failure

	Rabindranath et al (2006)	Susantitaphong et al (2013)	Wang et al (2014)	Nistor et al (2014)
Population	ESRD	ESRD	ESRD	ESRD
Methods				
Data sources	MEDLINE (1966-2006), EMBASE (1980-2006), Cochrane Central Register of Controlled Trials (2006), CINAHL (1872-2006).	MEDLINE (inception-December 2012), Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, ASN scientific abstracts (2003-2012 meetings)	Cochrane Register of Controlled Trials (Central), MEDLINE (1946-February 2013), EMBASE (1980-February 2013).	MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, ASN Database, CINAHL, Cochrane Renal Group's specialized register (through February 2013)
Intervention	Hemodiafiltration, hemofiltration, acetate-free biofiltration	Hemodiafiltration, hemofiltration, acetate-free biofiltration, high-flux/super high-flux HD	Hemodiafiltration, acetate-free biofiltration, hemofiltration	Hemodiafiltration, hemofiltration, acetate-free biofiltration
Comparator	Low-flux or high-flux HD	Low-flux HD	Low-flux or high-flux HD	Low-flux or high-flux HD
No. of RCTs (sample size) study design, and publication types	20 (657 patients): 8 crossover and 12 parallel-arm trials; 20 published articles	65 (12,182 patients): 29 crossover and 36 parallel-arm trials; 64 published articles and 1 published abstract	16 (3,220 patients): 2 crossover and 14 parallel-arm trials; 16 published articles	35 (4,039 patients): 17 crossover and 18 parallel-arm trials; 25 published articles and 10 published abstracts
Analytical approach	Random-effects models	Random-effects models	Random-effects models	Random effects models
Results				
All-cause mortality	RR, 1.68 (95% CI, 0.23 to 12.13); I^2 index, 61%	RR, 0.88 (95% CI, 0.76 to 1.02); I^2 index, 18%	RR, 0.83 (95% CI, 0.65 to 1.05); I^2 index, 59%	RR, 0.87 (95% CI, 0.70 to 1.07); I^2 index, 34%
Cardiovascular mortality	NR	RR, 0.84 (95% CI, 0.71 to 0.98); I^2, 0%	RR, 0.85 (95% CI, 0.66 to 1.10); I^2 index, 42%	RR, 0.75 (95% CI, 0.58 to 0.97); I^2 index, 0%
Therapy-related hypotension	MD,[a] −5.4 (95% CI, −23.7 to 12.9); I^2, 0%	RR, 0.55 (95% CI, 0.35 to 0.87); I^2 index, 99%	RR, 0.49 (95% CI, 0.30 to 0.81); I^2 index, 78%	RR, 0.72 (95% CI, 0.66 to 0.80)
β_2-Microglobulin clearance (mL/min)	MD, 23.0 (95% CI, 20.2 to 25.8); I^2 index, 0%	MD, 64.8 (95% CI, 46.8 to 82.8); I^2 index, 99%	NR	NR
Pre-treatment β_2-Microglobulin level (mg/L)	MD, −12.2 (95% CI, −26.1 to 1.7); I^2 index, 91%	MD, −9.9 (95% CI, −12.4 to −7.5); I^2 index, 88%	[b]MD, −5.9 (95% CI, −10.3 to −1.6); I^2 index, 96%	MD, −5.6 (95% CI, −9.1 to −2.0); I^2 index, 94%

SUMMARY

- Target spKt/V
  - Although minimal level are well defined, there are no optimal targets to be achieved.
  - HD > 1.2
  - PD > 1.7
- nPCR
  - 1.0 – 1.2 g/kg/day
- 투석의 적절도는 다양한 생화학적 지표와 함께, 환자가 느끼는 삶의 질 까지 고려해야 한다.