There are no shortcuts to Dialysis Outcomes

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Wednesday, March 21st, 2018 (3:10 pm – 4:10 pm)

Quality in Hemodialysis

"Quality Health Care is the degree to which health services increases the likelihood of desired health outcomes.. and is consistent with current professional knowledge."

Lohr, 1992

The National Cooperative Dialysis Study - (NCDS)

- Followed 151 Patients
- In 9 Different Centers
- For 5 Years (1974-1979)
- Seeking correlation with Patient Morbidity and Mortality

Published in New England Journal of Medicine 1981; 305:1176-1181

National Cooperative Study Analysis

Patient Group	Treatment Hours	Midweek BUN	KT/V Index
I	4.5	72 mg/dL	1.16
II	4.5	90 mg/dL	0.61
III	3.0	72 mg/dL	0.95
IV	3.0	90 mg/dL	0.55

Patient Group	% withdrawn for medical reasons	Hospitalizations: Actual vs. Expected
I	9.7%	0.31
II	34.3%	1.62
III	4.9%	0.95
IV	48.6%	0.55

Conclusion: KT/V <0.9= Inadequate Dialysis

NCDS Findings

- Urea Levels Correlated Most Closely to Patient Morbidity
- Emphasized importance of Adequate Dietary Protein Intake
- Defined a Maintenance BUN Level for Adequate Dialysis
- Created an Index for Individual Measure of Adequate Treatment using Urea Levels:

$$K\,(t) = V$$

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 1.1 – Timing of Hemodialysis Initiation
  - Patients who reach CKD stage 4 (GFR , 30 mL/min/1.73 m2) or have imminent need
- Guideline 1.2 – Timing of Hemodialysis Initiation
  - The decision to initiate maintenance dialysis in patients should be based primarily upon:
    - An assessment of signs and/or symptoms associated with uremia
    - Evidence of protein-energy wasting
    - Have the ability to safely manage metabolic abnormalities and/or volume overload with medical therapy

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 2.1 - Frequent Hemodialysis
  - In-center HD - Suggest that patients with end-stage kidney disease be offered in-center short frequent hemodialysis
  - In center HD - Consideration given to individual patient preferences, quality of life, and the risks of these therapies.
- Guideline 2.2 - Frequent Hemodialysis
  - In-center HD - Patients considering incenter short frequent hemodialysis be informed about the risks of this therapy, including a possible increase in vascular access procedures and the potential for hypotension during dialysis.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 2.3 – Home Long Duration HD
  - Consider home long hemodialysis (6-8hours, 3 to 6 nights per week) for patients with end-stage kidney disease who prefer this therapy for lifestyle considerations.
- Guideline 2.4 – Home Long Duration HD
  - We recommend that patients considering home long frequent hemodialysis be informed about the risks of this therapy, including possible increase in vascular access complications, potential for increased caregiver burden, and possible accelerated decline in residual kidney function.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 3: Measurement of Dialysis—Urea Kinetics
- Guideline 3.1 - We recommend a target single pool Kt/V (spKt/V) of 1.4 per hemodialysis session for patients treated thrice weekly, with a minimum delivered spKt/V of 1.2.
- Guideline 3.2 - In patients with significant residual native kidney function (Kru), the dose of hemodialysis may be reduced provided Kru is measured periodically to avoid inadequate dialysis.
- Guideline 3.3 - For hemodialysis schedules other than thrice weekly, we suggest a target standard Kt/V of 2.3 volumes per week with a minimum delivered dose of 2.1 using a method of calculation that includes the contributions of ultrafiltration and residual kidney function.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 4 – Treatment Time
  - Guideline 4.1- Recommend that patients with low residual kidney function (< 2 mL/min) undergoing thrice weekly hemodialysis be prescribed a bare minimum of 3 hours per session.
- Guideline 4.1.1- Consider additional hemodialysis sessions or longer hemodialysis treatment times for patients with:
  - Patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, and poor metabolic control

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

NKF-DOQI Guidelines - Hemodialysis Adequacy

- Guideline 4 – Volume and Blood Pressure Control
- Guideline 4.2 - We recommend both reducing dietary sodium intake as well as adequate sodium/water removal with hemodialysis to manage hypertension, hypervolemia, and left ventricular hypertrophy.
- Guideline 4.2.1 - Prescribe an ultrafiltration rate for each hemodialysis session that allows for an optimal balance among achieving euvolemia, adequate blood pressure control and solute clearance, while minimizing hemodynamic instability and intradialytic symptoms.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.

Urea Reduction Ratio (URR)

- The standard used to measure the dose of dialysis given an ESRD patient
- Determined by measuring the BUN of the patient pre and post treatment
- The equation:
- URR = $[(C_{PRE} - C_{POST}) / C_{PRE}] \times 100\%$

Urea Reduction Ratio
Advantages

- Accepted by K-DOQI as easiest to use
- Accepted by K-DOQI as satisfactory predictor of mortality
- Can be completed with two blood draws in a single day

Urea Reduction Ratio Disadvantages

- Kt/V is considered the Gold Standard
- Cannot provide PCR information
- Cannot assess UF contribution
- Error rate 10% (40% in high and low ranges)
- Dependent on a consistent protocol
- Is a snapshot of a single treatment

Defining Kt/V

- Kt/V = a calculated estimate of the dose of dialysis given a patient
- K = dialyzer clearance, t = time of treatment, V = patient volume
- spKt/V = single pool Kt/V Assumes the body is a single pool of fluid from which the urea will be extracted. It’s value is calculated from the urea reduction ratio based on pre and post treatment blood tests
- eKt/V = equilibrated Kt/V Similar to spKt/V except the Post urea blood test is taken 30 – 60 minutes after the treatment
- Since there will be a urea rebound, the urea reduction ratio will be lower, and eKt/V will be less than spKt/V

spKt/V Equation for 3X week Dialysis

- A linear equation has been developed and been shown to give reliable results for spKt/V when applied to HD administered 3 times per week:
- $spKt/V = -\ln(R – 0.008 \times t) + (4 - 3.5 \times R) \times 0.55 \times UF/V$
- $eKt/V = -\ln(R_{eq} – 0.008 \times t) + (4 - 3.5 \times R_{eq}) \times 0.55 \times UF/V$
  - R is the ratio of postdialysis to predialysis BUN
  - R_{eq} is the ratio of rebounded postdialysis to predialysis BUN
  - V is body water volume
  - Weight loss is expressed in the same units
  - T is treatment time in hours.

The Clearance Equation for Dialyzers

$$C_X = \frac{Q_B\left(e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-1\right)}{e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-\frac{Q_B}{Q_D}}$$

Where: **C_X = Clearance of solute, X**

Q_B = Blood flowrate

Q_D = Dialysate flowrate

In = Natural logarithm = e

e = 2.718281828..

KoA = clearance coefficient for x

BUN of Venous Blood based on Dialyzer KoA

Q_B = 300 mL/min Q_D = 600 mL/min

KoA (mL/min)	Clearance (mL/min)	Arterial Blood BUN Values (mg/dL) 70	80	90	100	110
500	217	19.4	22.1	24.9	27.7	30.4
600	232	15.9	18.1	20.4	22.7	24.9
700	245	12.8	14.7	16.5	18.3	20.2
800	254	10.7	12.3	13.8	15.3	16.9
900	262	8.9	10.1	11.4	12.7	13.9
1000	269	7.2	8.3	9.3	10.3	11.4
1100	274	6.1	6.9	7.8	8.7	9.5
1200	278	5.1	5.9	6.6	7.3	8.1

Residual Kidney Function (K_{ru})

- For Stage 5, K_{ru} is 15 mL/min
- K_{ru} works continuously. 1 week = 10,080 min.
- K_{ru} x t = (15) x (10,080) = 151,200 mL
- Assume patient V = 38,500 mL
- $K_{ru}t/V$ =151,200 mL/38,500 mL = 3.93
- 3 treatments/week = 3.93/3 = 1.31

Determining a Patient's Fluid Volume

- Body Weight: Male = 55%, Female = 50%
- Calculated from Body Parameters (Watson equation)
  - Male V = 0.1074(H) + 0.3362(W) – 0.09516(A) + 2.447
  - Female V = 0.1069(H) + 0.2466(W) – 2.097

    H = Height in centimeters (172) W = Weight in kilograms (70) A = Age in years (50)
    V = Volume in liters
  - For a Patient of 70 kilograms:
    - Body weight: Male = 38.5 liters, Female = 35.0 liters
    - Female V = 0.1069(172) + 0.2466(70) – 2.097 = 33.6 liters
    - Male V = 0.1074(172) + 0.3362(70) – 0.09516(50) + 2.447 = 39.7 liters

Length of Treatment

$$Kt/V = 1.4$$

K = Dialyzer Clearance (mL/min)

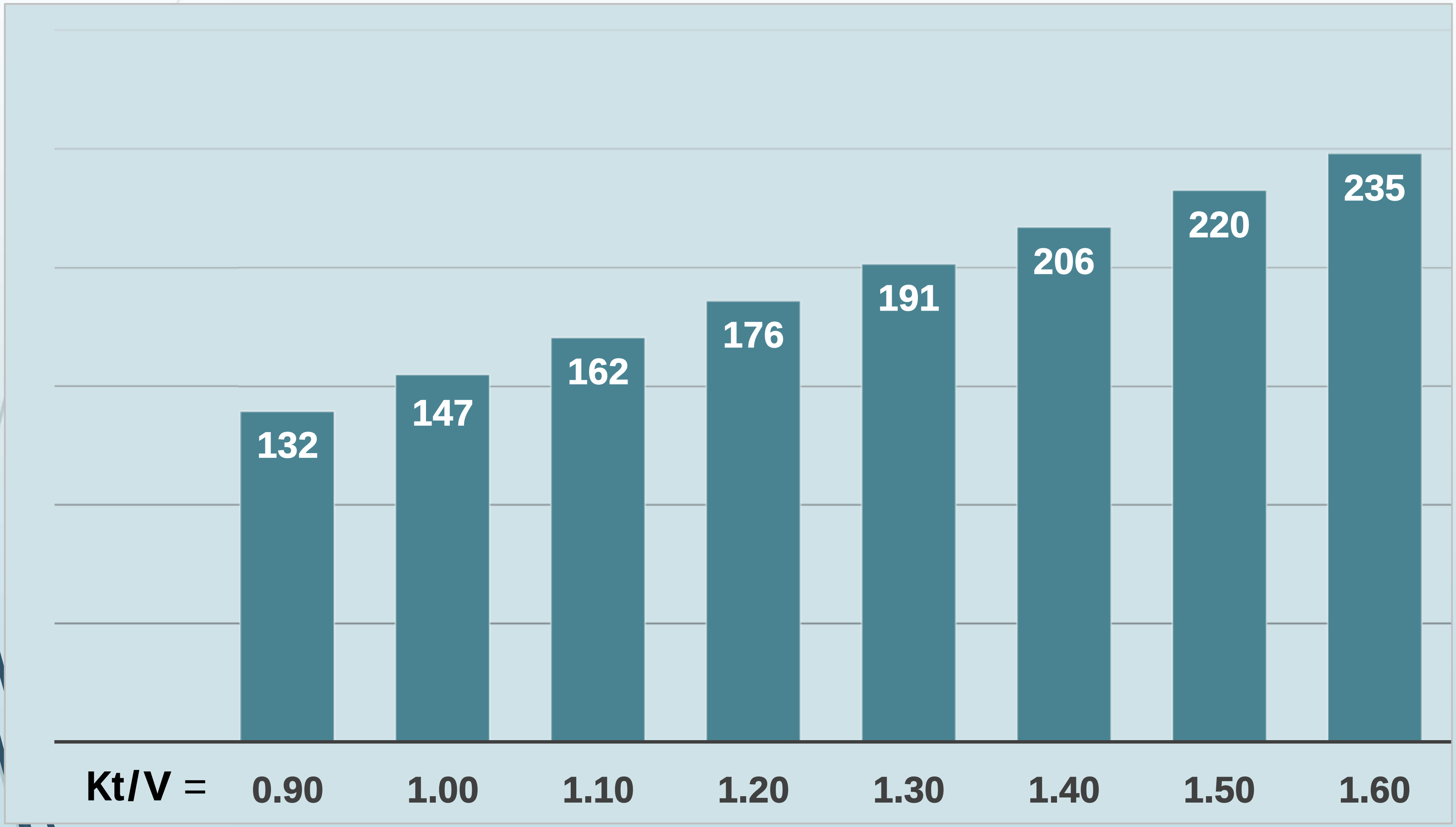
t = Time of Treatment (min)

V = Patient’s volume (mL)

$$t = (1.4 \times V)/K$$

Treatment Time (minutes) vs. Kt/V

(Patient V= 38.5 L, C_x = 262 mL/min)



Patient BUN Gain/Day (mg/dL)

PCR g/kg/day	Patient Weight (kg)						
	50.0	60.0	70.0	80.0	90.0	100.0	110.0
0.80	15.38	16.36	17.05	17.58	17.99	18.31	18.58
0.90	18.04	19.01	19.71	20.23	20.64	20.97	21.23
1.00	20.69	21.67	22.37	22.89	23.30	23.62	23.89
1.10	23.35	24.32	25.02	25.54	25.95	26.28	26.54
1.20	26.00	26.98	27.68	28.20	28.61	28.93	29.20
1.30	28.66	29.63	30.33	30.86	31.26	31.59	31.85
1.40	31.31	32.29	32.99	33.51	33.92	34.24	34.51

Urea Reduction during Treatment

$$C = C_0\, e^{-Kt/V} + G/K\,(1 - e^{-Kt/V})$$

C = Plasma BUN Concentration (mg/mL)*

C_0 = Predialysis BUN Concentration (mg/mL)*

K = Dialyzer Clearance (mL/min)

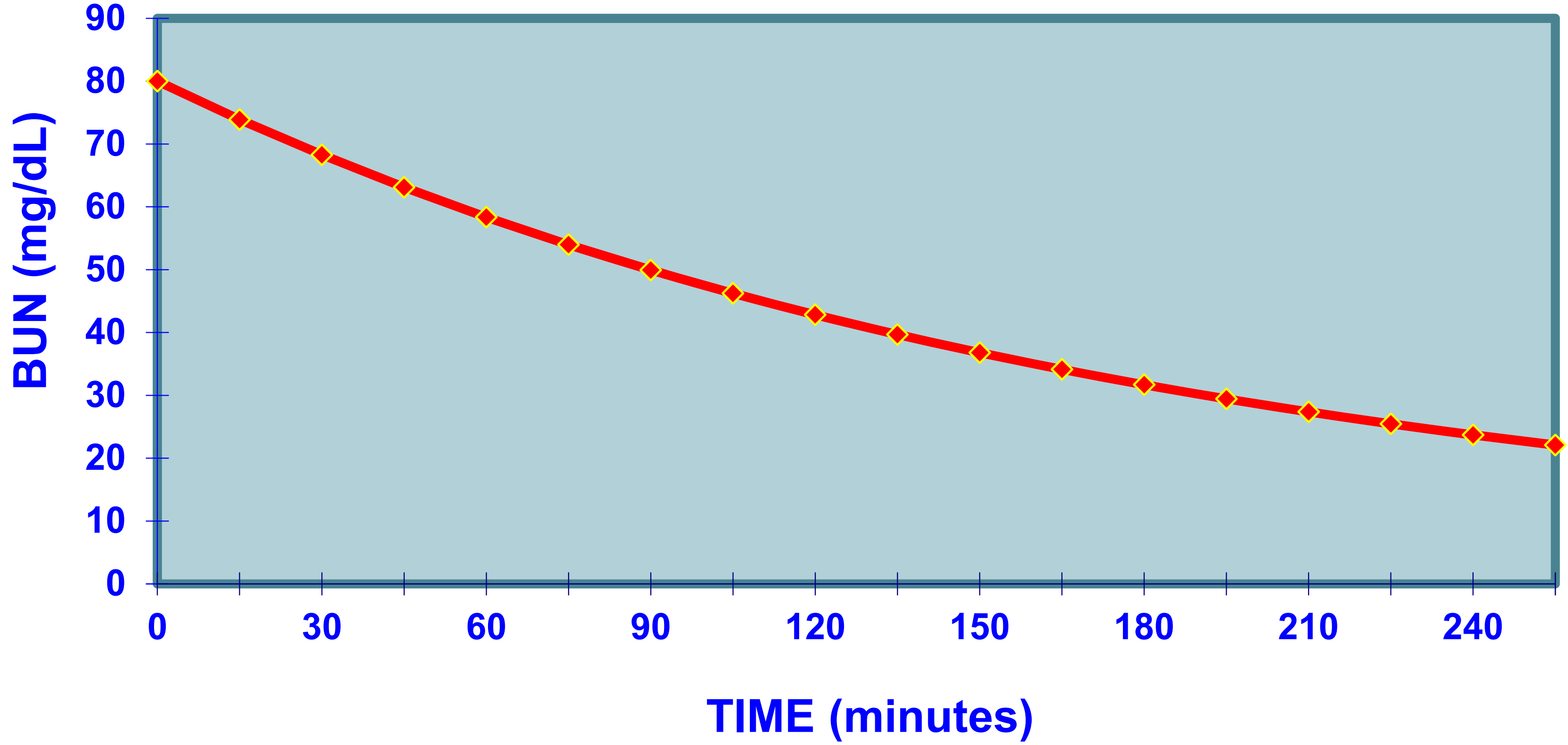
t = time (minutes)

V = Patient Volume (mL)

G = Generation of urea (mg/min)

* mg/mL equals mg/dL divided by 100.

Patient's Mid-week Urea Reduction



UF Effect on Kt/V

$$Kt/V = 2.2 - 3.3(R - 0.03 - UF/W)$$

$R = C_{POST} / C_{PRE}$ UF = Fluid Removed   W = Post Weight = 70 kg

Column 3 = Post BUN effective reduction due to UF (mg/dL)

Column 4 = Needed dialyzer clearance with no UFR for reduction in column 3

T_x UF (kg)	R = 0.30	Column 3	Column 4
0.0	1.31	24	221
1.0	1.36	22.8	230
2.0	1.40	21.8	236
3.0	1.45	20.6	245
4.0	1.50	19.4	253
5.0	1.54	18.4	260

Handbook of Dialysis – John T. Daugirdas, Peter G. Blake, Todd S. Ing - 4nd Edition

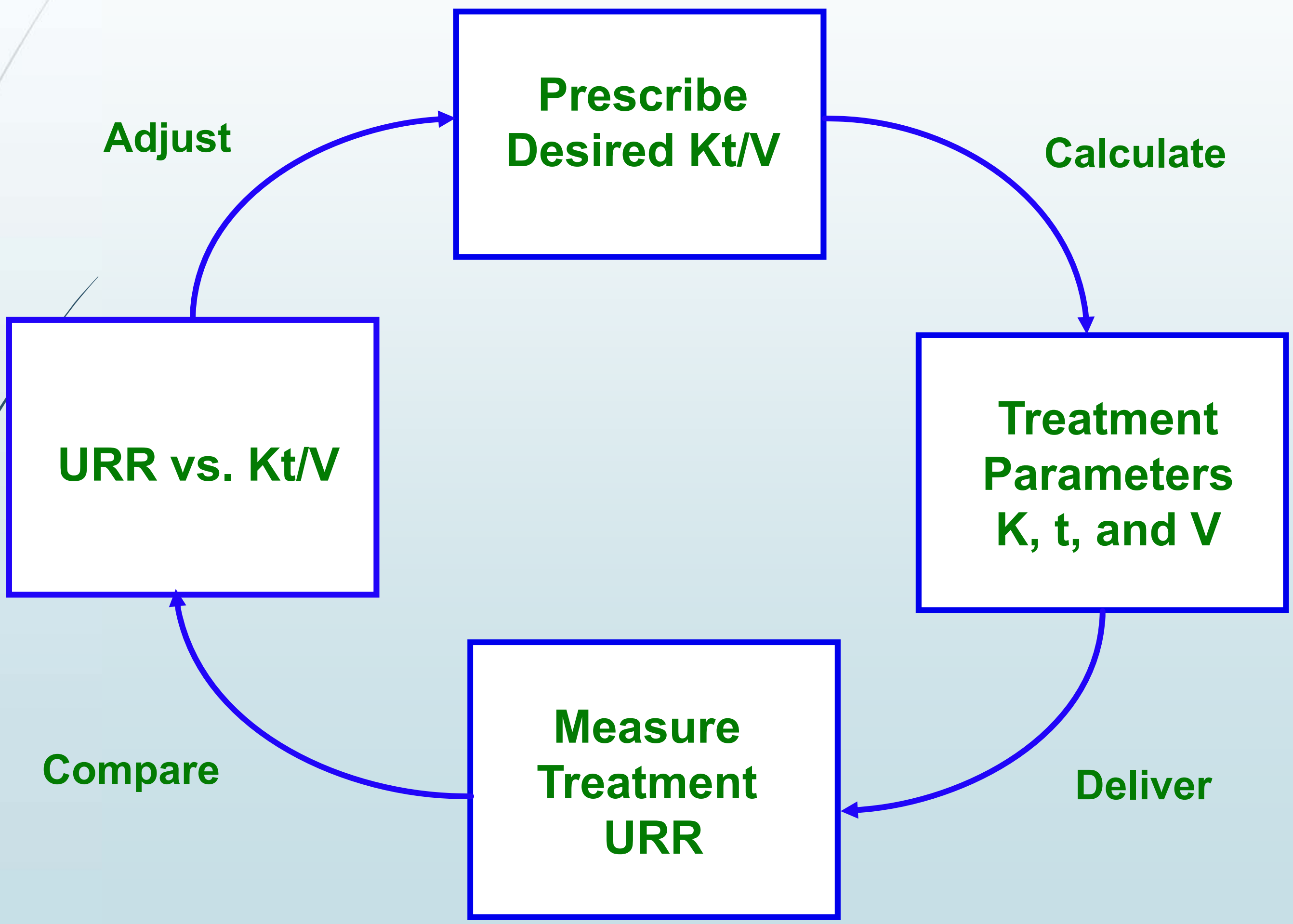
What takes so long?

- A patient has a fluid volume of 38,500 mL @ 80 mg/dL
- Blood Flowrate = 400 mL/min
- Dialyzer urea reduction is 90% (80 in, 8 out) KoA would be about 1000
- Time to process 38,500 mL = 38,500/400 = 96 min.
- Patient's final urea would be 8 mg/dL

Dialysis reality

- The example requires that all the patient's blood be removed, cleaned, and then returned.
- In reality the blood cleaned by the dialyzer is returned to the patient and diluted by all the blood still at a urea of 80 mg/dL
- After 1st minute 38,100 mL will still be at 80 mg/dL and 400 mL will be at 8 mg/dL
- Dilution results in the total blood volume being reduced to 79.25 mg/dL in one minute
- As the treatment continues the urea concentration entering the dialyzer will be reduced and as a result the amount of urea being removed will be reduced

Achieving Quality Therapy



What if $Kt/V_{DESIRED} < Kt/V_{ACTUAL}$?

DOQI Clinical Practice Guidelines for Hemodialysis Adequacy– Appendix E

- Dialyzer Clearance
  - Effective Dialyzer Clearance
  - Errors in Blood Flow Rate
  - Errors in Dialysate Flow Rate
- Treatment Time
  - Inadequate measurement method
  - Numerous treatment Interruptions
  - Early termination of treatment
  - Elective shortening of treatment
- Errors in BUN Concentration
  - Pre-dialysis BUN sample high or low
  - Post-dialysis BUN sample high or low

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In-vitro vs. In-vivo

Leading Nephrologists Recognize Clinical Significance

"In conclusion, prescribing dialysis treatments using manufacturer *in vitro* generated clearances can lead to marked under dialysis of patients. We recommend measuring Kt/V and adjusting dialysis prescription accordingly. When initially prescribing dialysis, if possible, *in vivo* data should be used. If this is not possible, then the K value should be taken approximately 20% less than the in vitro generated values."

Saha, L. K. & Van Stone, J.C. Differences between Kt/V measured during dialysis and Kt/V predicted from manufacturer clearance data. The International Journal of Artificial Organs (1992): 15 (8).

URR and Kt/V

- URR = Urea Reduction Ratio

  $URR = (C_{PRE} - C_{POST}) / C_{PRE}$

  Patient = (80 – 24)/80 = 0.70

- Kt/V = Dialysis Treatment Index

  Kt/V = Clearance x T_X time ÷ Patient V

  Patient (in vitro) = 262 x 240 ÷ 38,500 = 1.63

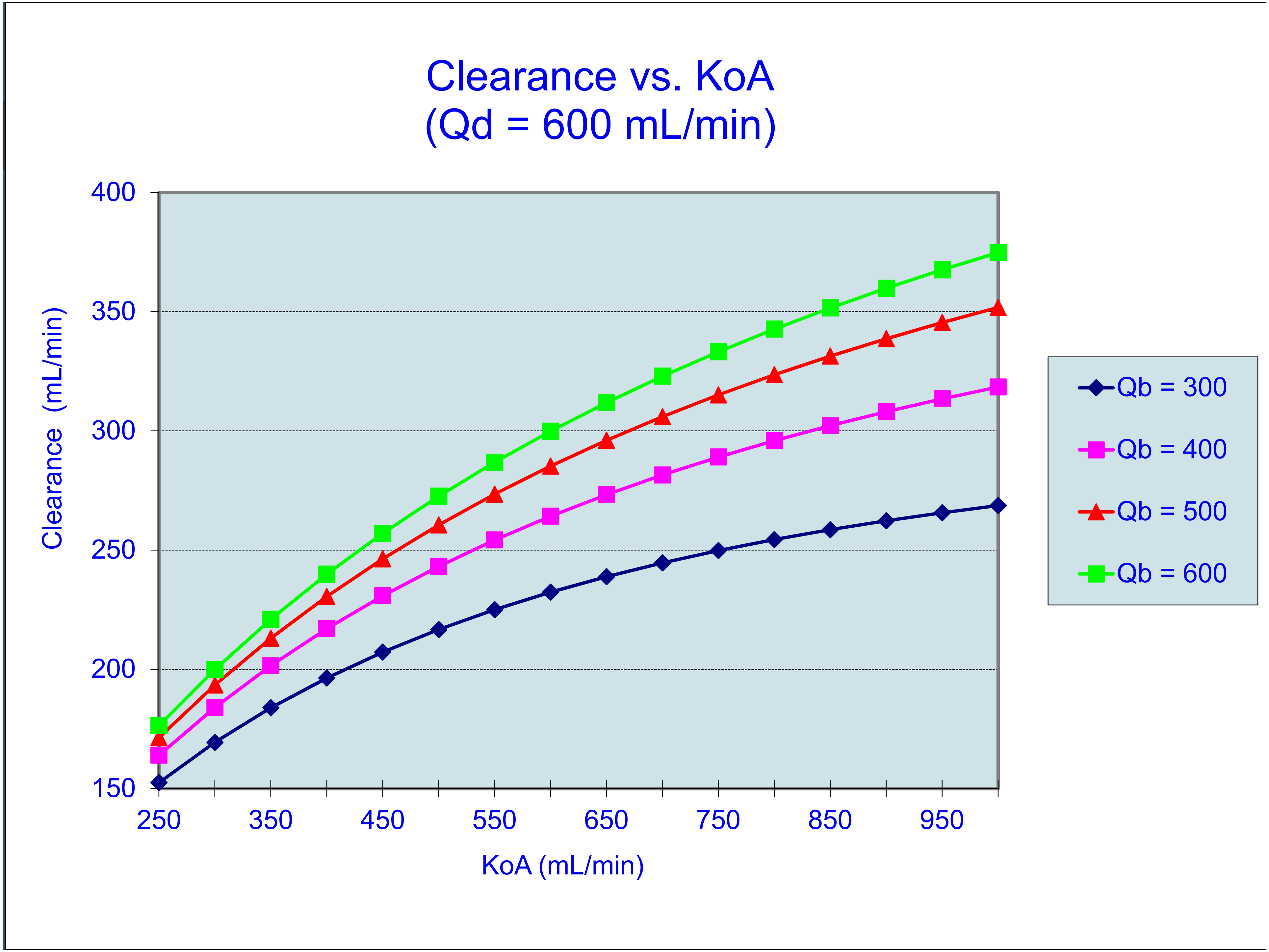
  Patient (in vivo) = 80% of In Vitro = 1.30

Saha, L. K. & Van Stone, J.C. Differences between Kt/V measured during dialysis and Kt/V predicted from manufacturer clearance data. The International Journal of Artificial Organs (1992): 15 (8).

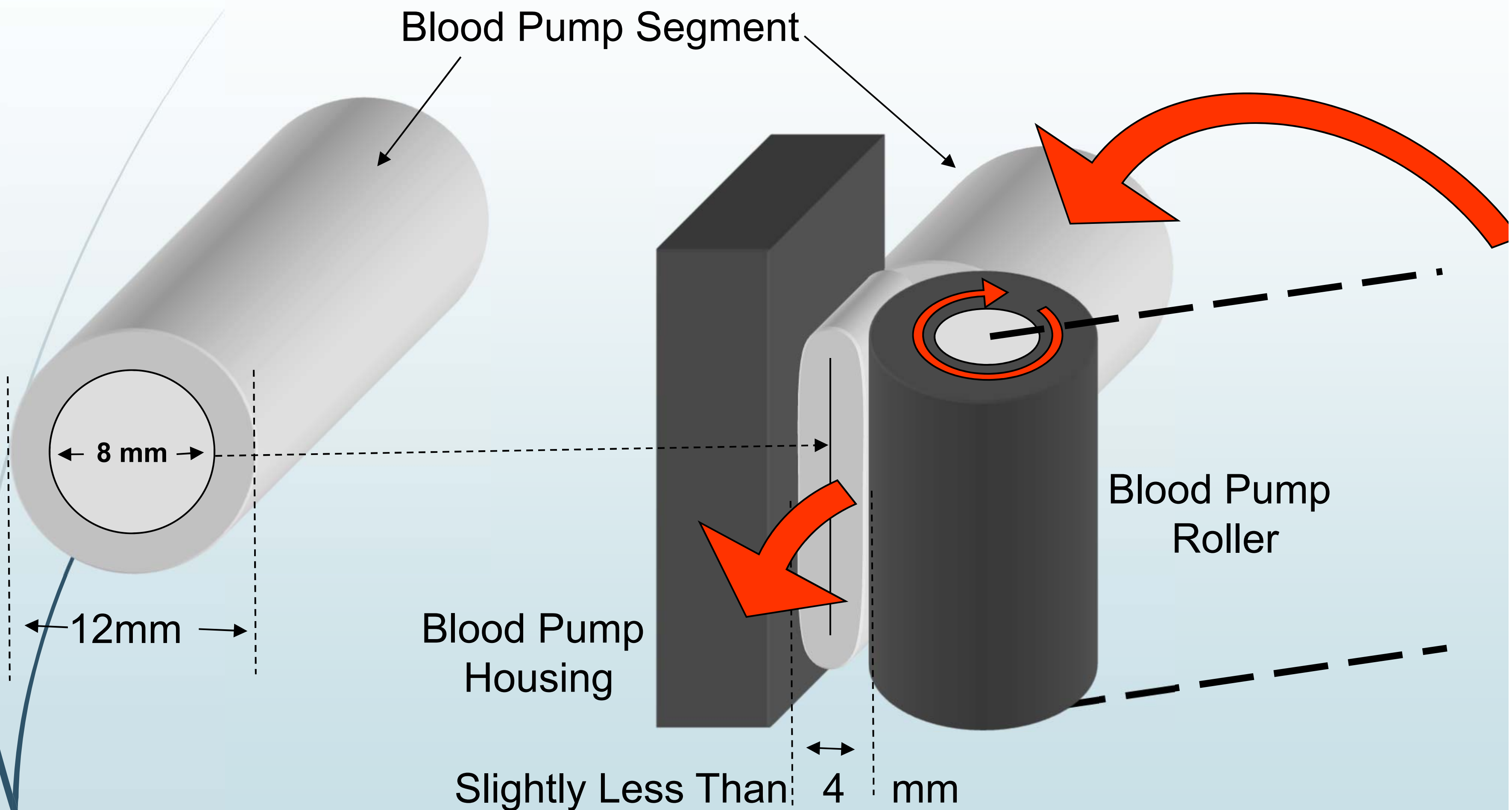
Renal Physicians Association Working Committee on Clinical Practice Guidelines. Clinical Practice Guideline on Adequacy of Hemodialysis. Clinical Practice Guideline, Number 1. Washington, D.C. December 1993.

Blood Flow Rate

- **Suboptimal Flow Rate**
  - **Insufficient extracorporeal blood flow is defined as a failure to attain and maintain an extracorporeal flow sufficient to perform hemodialysis without significantly lengthening the hemodialysis treatment**
    - **Opinion DOQI Guideline 23**


Clearance vs. KoA
(Qd = 600 mL/min)
Clearance (mL/min)
400
350
300
250
200
150
250
350
450
550
650
750
850
950
KoA (mL/min)
Qb = 300
Qb = 400
Qb = 500
Qb = 600

Blood Tubing Occlusion



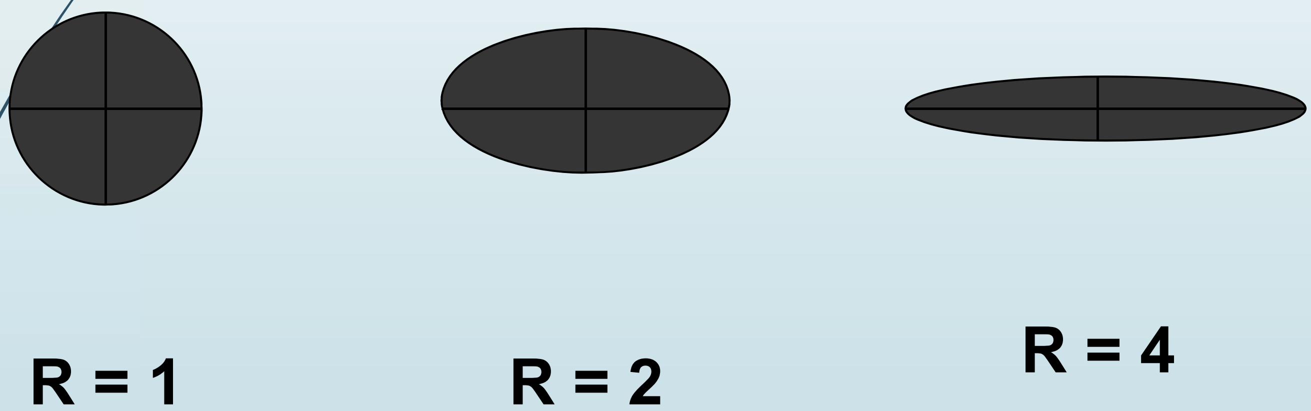
Blood Tubing Occlusion

- In order for a blood pump to deliver expected blood flow, it is necessary for the blood tubing segment to be properly occluded.
- Occlusion setting and testing procedures are found in the manufacturer's service manuals.
- In general, occlusion tests are performed using air pressure. Both rollers are tested at a minimum of two points
- Blood volumes are confirmed by measuring pump output into a graduated cylinder. Generally over a three minute time interval.

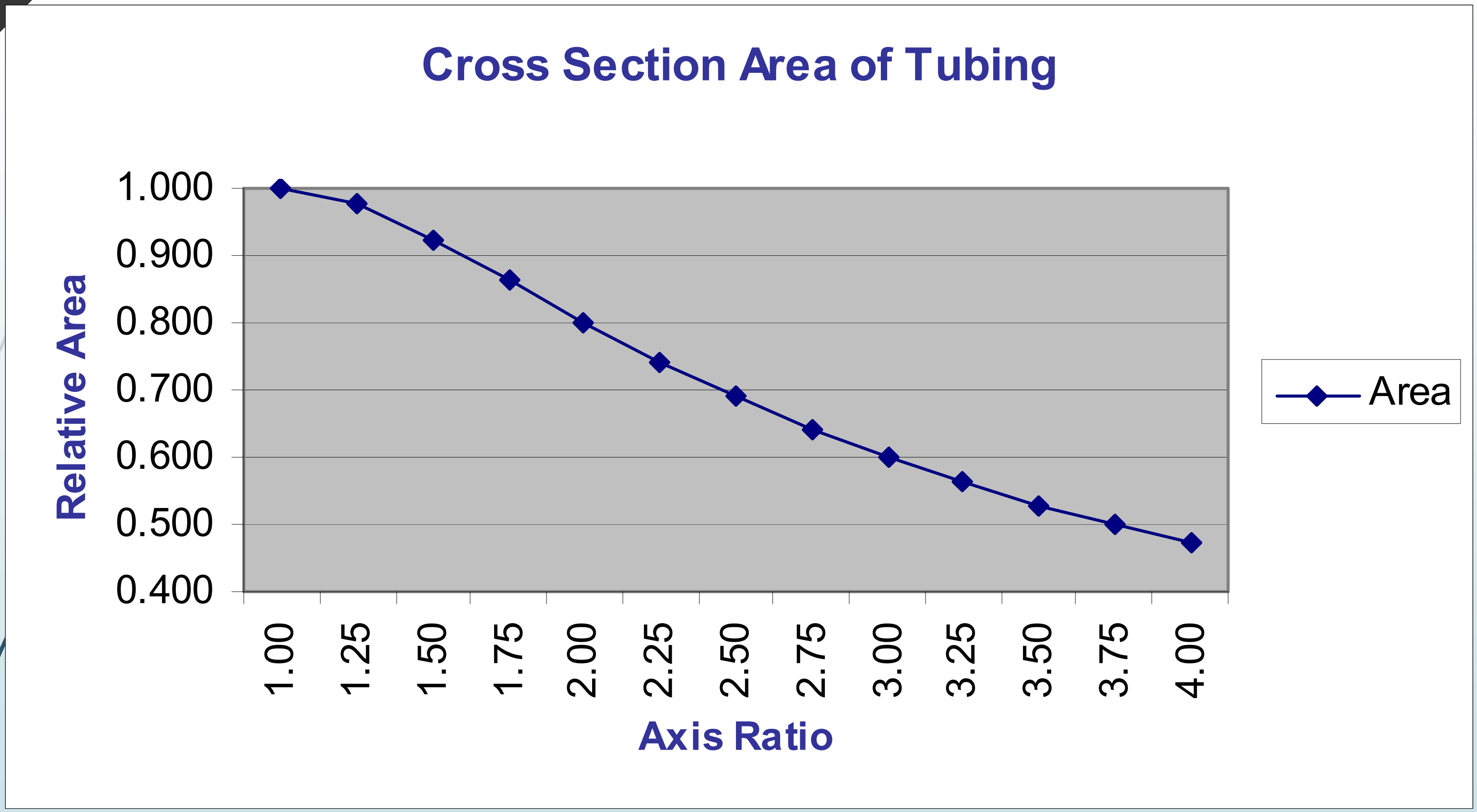
Collapsing Tubing

Cross sectional area = $2R/(1 + R^2)$

R = Ratio of Axis Length = Major/Minor



Pressure Effects on Hemodialysis Blood Flow, Thomas Depner, M.D., Syed Rizwan, M.D., Terri A. Stasi, ASAIO Manuscript, 1991



Pressure Effects on Hemodialysis Blood Flow, Thomas Depner, M.D., Syed Rizwan, M.D., Terri A. Stasi, ASAIO Manuscript, 1991

Pressure Effects on Roller Pump Blood Flow During Hemodialysis

- Study done by Thomas A. Depner, M. D., Syed Rizwan, M. D., and Terri A. Stasi
- Conducted at the University of California, Davis
- Measured Quantities:
  - Pump Inlet Pressure: - 50 to - 400 mmHg
  - Pump Outlet Pressure: 50 to 300 mmHg
  - Hematocrit: 0, 21, 38%
  - Blood Flowrates: 200, 400, 600 mL/min
- Tubing used:
  - 8 mm Polyvinyl Chloride

Pressure Effects on Hemodialysis Blood Flow, Thomas Depner, M.D., Syed Rizwan, M.D., Terri A. Stasi, ASAIO Manuscript, 1991

Pressure Effects on Roller Pump Blood Flow

Study Results:

Blood Flow rate was unaffected by:

Hematocrit level

Post-pump pressure

Pre-pump pressure of – 50 mmHg

Blood Flow rate was reduced by:

8.5% +/- 1.3% at a pre-pump pressure of – 200 mmHg

33% +/- 1.9% at a pre-pump pressure of – 400 mmHg

Pressure Effects on Hemodialysis Blood Flow, Thomas Depner, M.D., Syed Rizwan, M.D., Terri A. Stasi, ASAIO Manuscript, 1991

Blood Flow Reduction vs. Treatment Time

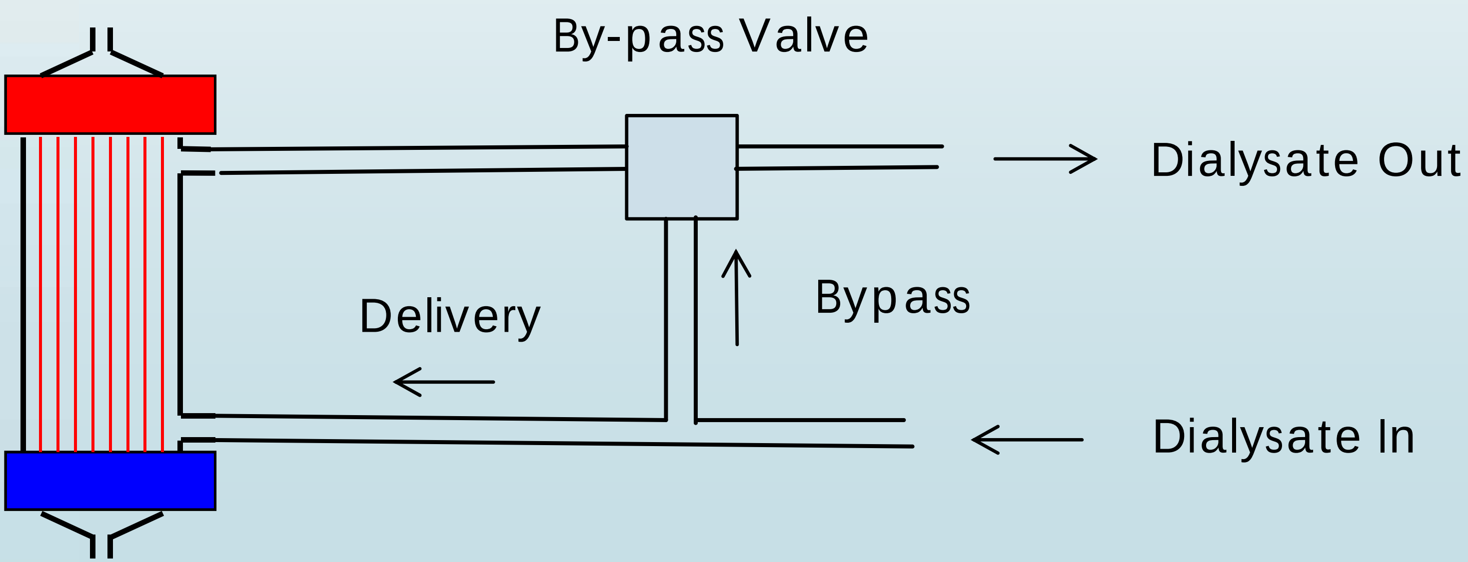
Blood Flow mL/min	Clearance mL/min	Kt/V	Time Correction
300	262	1.40	217 minutes
274 (-8.5%)	240	1.40	236 minutes
201 (-33%)	176	1.40	322 minutes
400	350	1.40	162 minutes
366 (-8.5%)	320	1.40	178 minutes
268 (-33%)	234	1.40	242 minutes

Causes of Reduced Blood Flow Rate

- Belief that machine displayed blood flow rate is correct
- Reduction done due to blood pressure alarm then not reset to proper speed
- Pressure alarm corrected by pushing the “reset” switch to silence the alarm
- Switch tubing suppliers? Blood segment the same?

Dialysate Flowrate Errors

- Is the machine calibrated correctly?
- Quick Disconnects OK?
- Does the bypass valve leak?



Clearance vs. Blood and Dialysate Flowrates

BLOOD FLOW	DIALYSATE FLOW (ml/min)				
(mL/min)	400	500	600	700	800
200	175	179	181	183	184
300	217	226	232	237	240
400	240	255	264	271	276
500	255	273	285	294	301

URR Protocol

Stop Pump (Post-Dialysis) Technique

- "Pre" Sample: Draw from dry arterial line after cannulation and before heparinization, saline or initiation of dialysis.
- "Post" Sample: At end of treatment, reduce ultrafiltration to minimum and reduce or stop Dialysate Flow. Slow BFR to 100 ml/min for 15 seconds.
- Turn off blood pump
- Clamp both blood lines and arterial needle tubing.
- Draw off blood for sample with clean syringe from arterial sample port or directly from arterial needle.
- Discontinue treatment according to unit protocol
- Send serum of both specimens for BUN

Formula: [(Pre - Post)/Pre] X 100 = URR

Adequacy of Dialysis Dose isn't the Whole Story

- "The ultimate goal of treatment for patients with CKD stage 5 is improvement in quality of life, with prolongation of life often an additional goal. This requires more than the dialysis treatment itself."
  - Management of anemia
  - Nutrition
  - Metabolic bone disease
  - Diabetes
  - Cardio Vascular disease

KDOQI References beyond Hemo Adequacy

- National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease in adults. Am J Kidney Dis. 2006;47(5) (suppl 3):S16-S85.
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- NKF Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification – Andrew S. Levey, MD, et al, Annals of Internal Medicine, Volume 139, No. 2, July 2003
- Hemodialysis for Nurses and Dialysis Personnel – Judith Z. Kallenbach, MSN, RN, CNN, 8th Edition, ©2012, Elsevier/Mosby Inc., ISBN 978-0-323-07702-6
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