XXX Corso Nazionale di Aggiornamento

17 - 18 - 19 aprile Sala Congressi Hotel Mediterraneo Riccione
Piazzale Roma, 3, 47838 Riccione RN

Corso Nazionale Ante 2023

Ante

Provider N° 354 E.C.M. Educazione Continua in Medicina
Programma Nazionale per la Formazione degli operatori della Sanità

Evento N. 370906 edizione N. 1
Crediti assegnati 9,8

Direttore Scientifico Paolo Fabbrini

Presidente Ante Paolo Besati

Dialisi e Tecnologia
"Presente e futuro della Nefrologia Italiana"

La Dose Dialitica nel paziente con AKI-D

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No Conflict of interests to declare

STADIAZIONE AKI

RIFLE		AKIN		KDIGO		Urine output (common to all)
Class	sCr or eGFR	Stage	sCr	Stage	sCr	
Risk	Increase sCr × 1.5 or eGFR decrease > 25%	1	≥ 0.3 mg/dl or ≥ 1.5- to 2-fold from baseline	1	≥ 0.3 mg/dl (≤ 48 hours) or 1.5–1.9 × baseline (≤ 7 days)	< 0.5 ml/kg/h (≥ 6 hours)
Injury	Increase sCr × 2 or eGFR decrease > 50%	2	> 2- to 3-fold from baseline	2	2.0–2.9 × baseline	< 0.5 ml/kg/h (≥ 12 hours)
Failure	Increase sCr × 3 or ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl or eGFR decrease > 75%	3	> 3-fold from baseline or ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl or Initiation of RRT	3	3.0 × baseline or ≥ 4.0 mg/dl or Initiation of RRT	< 0.3 ml/kg/h (≥ 24 hours) or Anuria (≥ 12 hours)
Loss	Persistent ARF > 4 weeks					
ESRD	ESRD > 3 months					

Terapia dialitica in AKI

Obiettivi	Strumenti
Bilancio di fluidi	Ultrafiltrazione netta
Adeguatezza e Dose	Clearance/Modalità
Acido-Base	Soluzioni e Tampone
Elettroliti	Dialisato/Reinfusione
Timing	Tipo di tecnica
Modalità	Macchine
Operatività	Parametri

Inizio del trattamento

Quali criteri utilizzare per iniziare la RRT?
Quanto presto dobbiamo iniziare?
Quanto aggressivi dobbiamo essere?

Rischi collegati alla malattia

Rischi collegati al trattamento

Abbiamo oggi dei criteri fissi per decretare l'inizio?

Sappiamo oggi quale tecnica depurativa è da preferire?

Inizio precoce della RRT in AKI

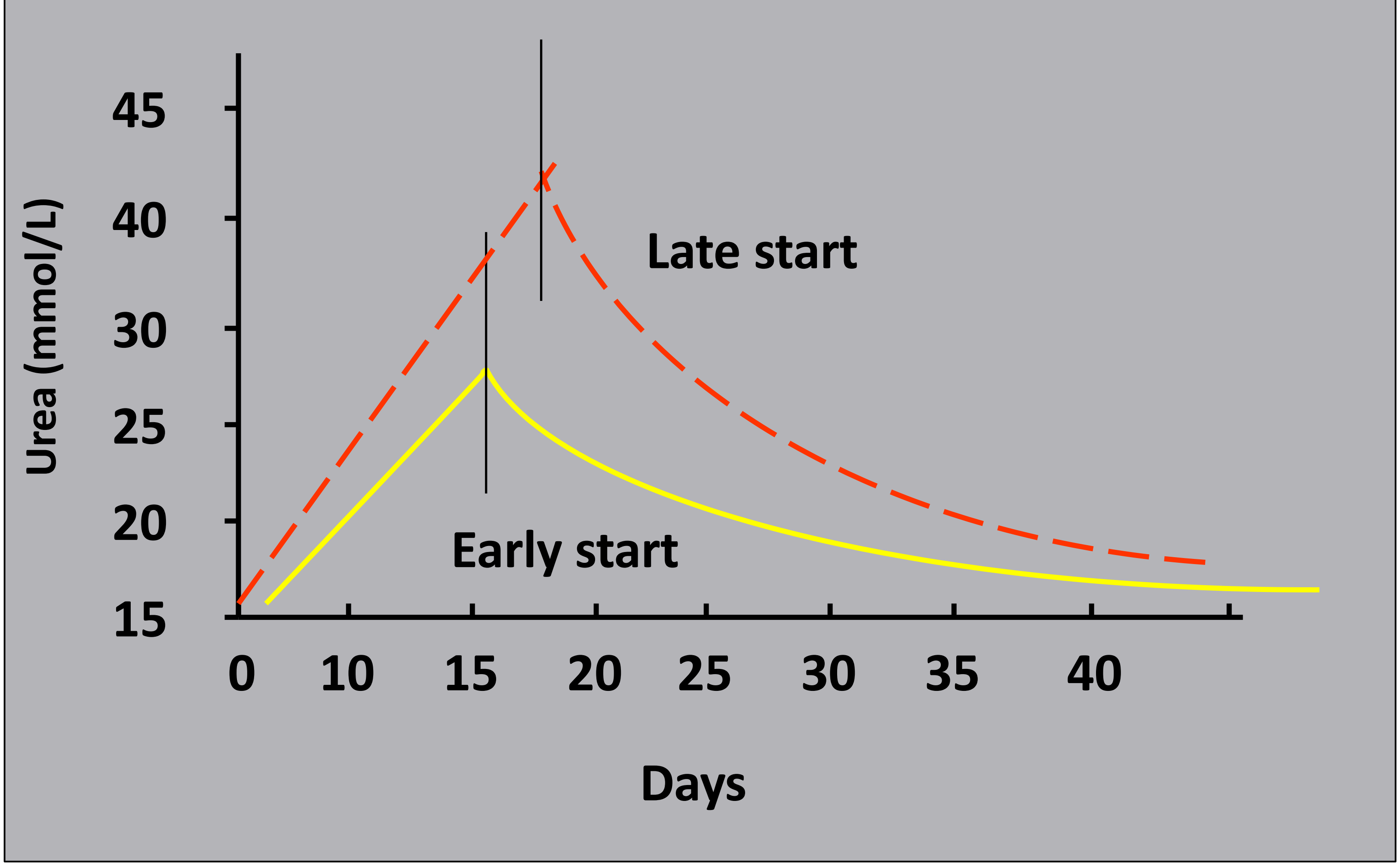
Attese:

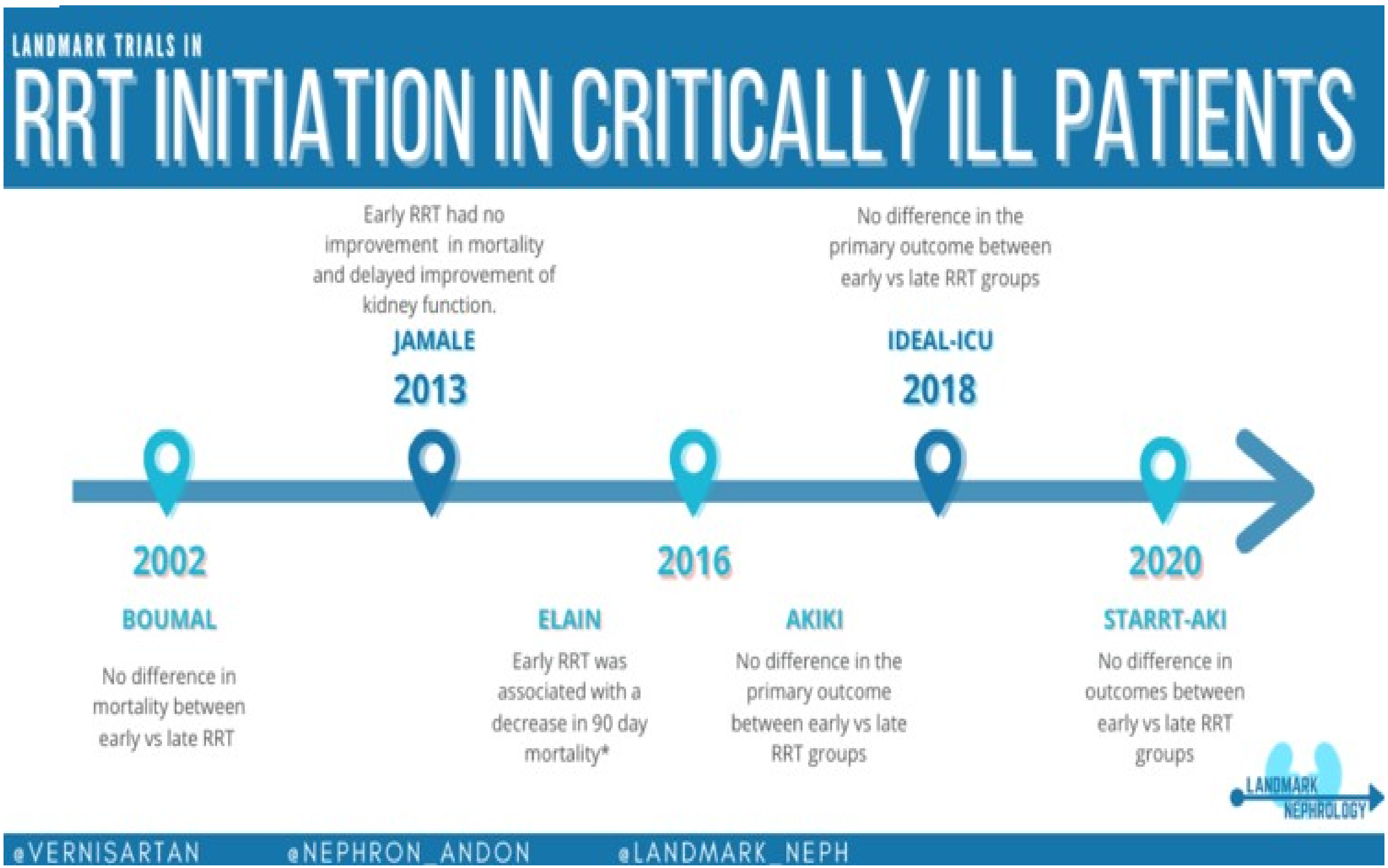
- Razionale biologico
- Consistenza dei risultati negli studi clinici per
  - Migliore sopravvivenza
  - Migliore ripresa funzionale del rene
  - Maggiore brevità della terapia sostitutiva
  - Ridotta lunghezza di permanenza in ICU

Vantaggi teorici:

- Controllo dell'uremia
- Controllo del volume
- Omeostasi acido-base
- Funzione di altri organi
- Mitigazione dell'infiammazione
- Migliori outcomes clinici

In teoria un migliore controllo uremico




LANDMARK TRIALS IN
RRT INITIATION IN CRITICALLY ILL PATIENTS
Early RRT had no improvement in mortality and delayed improvement of kidney function.
JAMALE
2013
No difference in the primary outcome between early vs late RRT groups
IDEAL-ICU
2018
2002
BOUMAL
No difference in mortality between early vs late RRT
ELAIN
Early RRT was associated with a decrease in 90 day mortality*
2016
AKIKI
No difference in the primary outcome between early vs late RRT groups
2020
STARRT-AKI
No difference in outcomes between early vs late RRT groups
LANDMARK NEPHROLOGY
@VERNISARTAN
@NEPHRON_ANDON
@LANDMARK_NEPH

Quale tecnica di RRT dobbiamo privilegiare in AKI-D?

Fluid shift mechanism	Ultrafiltration	Ultrafiltration	Ultrafiltration
Solute shift mechanism	Diffusion	Diffusion, convection, or both	Diffusion
Blood flow rate	≥ 200 ml/min	< 200 ml/min	200 ml/min
Dialysate flow rate	≥ 500 ml/min	17-34 ml/min	300 ml/min
Duration	3-4 hours	24 hours/day	6-12 hours
Advantages/special uses			
• Rapid fluid removal	✓		
• Rapid solute clearance	✓		
• Severe hyperkalemia	✓		
• Hemodynamic instability		✓	✓
• Better fluid control		✓	✓
• High nutritional support		✓	?
• Removal of middle-molecular weight solutes		✓	

Gaudry *et al. Critical Care* (2022) 26:93
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Critical Care

RESEARCH Open Access

Continuous renal replacement therapy *versus* intermittent hemodialysis as first modality for renal replacement therapy in severe acute kidney injury: a secondary analysis of AKIKI and IDEAL-ICU studies

Stéphane Gaudry[1,2,3,4*], François Grolleau[5], Saber Barbar[6], Laurent Martin-Lefevre[7], Bertrand Pons[8], Éric Boulet[9], Alexandre Boyer[10], Guillaume Chevrel[11], Florent Montini[12], Julien Bohe[13], Julio Badie[14], Jean-Philippe Rigaud[15], Christophe Vinsonneau[16], Raphaël Porcher[5], Jean-Pierre Quenot[17,18,19†] and Didier Dreyfuss[3,20†]

Abstract

Background: Intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT) are the two main RRT modalities in patients with severe acute kidney injury (AKI). Meta-analyses conducted more than 10 years ago did not show survival difference between these two modalities. As the quality of RRT delivery has improved since then, we aimed to reassess whether the choice of IHD or CRRT as first modality affects survival of patients with severe AKI.

Methods: This is a secondary analysis of two multicenter randomized controlled trials (AKIKI and IDEAL-ICU) that compared an early RRT initiation strategy with a delayed one. We included patients allocated to the early strategy in order to emulate a trial where patients would have been randomized to receive either IHD or CRRT within twelve hours after the documentation of severe AKI. We determined each patient's modality group as the first RRT modality they received. The primary outcome was 60-day overall survival. We used two propensity score methods to balance the differences in baseline characteristics between groups and the primary analysis relied on inverse probability of treatment weighting.

Results: A total of 543 patients were included. Continuous RRT was the first modality in 269 patients and IHD in 274. Patients receiving CRRT had higher cardiovascular and total-SOFA scores. Inverse probability weighting allowed to adequately balance groups on all predefined confounders. The weighted Kaplan–Meier death rate at day 60 was 54·4% in the CRRT group and 46·5% in the IHD group (weighted HR 1·26, 95% CI 1·01–1·60). In a complementary analysis of less severely ill patients (SOFA score: 3–10), receiving IHD was associated with better day 60 survival compared to CRRT (weighted HR 1.82, 95% CI 1·01–3·28; $p < 0.01$). We found no evidence of a survival difference between the two RRT modalities in more severe patients.

Conclusion: Compared to IHD, CRRT as first modality seemed to convey no benefit in terms of survival or of kidney recovery and might even have been associated with less favorable outcome in patients with lesser severity of disease. A prospective randomized non-inferiority trial should be implemented to solve the persistent conundrum of the optimal RRT technique.

Keywords: Renal replacement therapy, Acute kidney injury, Critical care

RESEARCH Open Access

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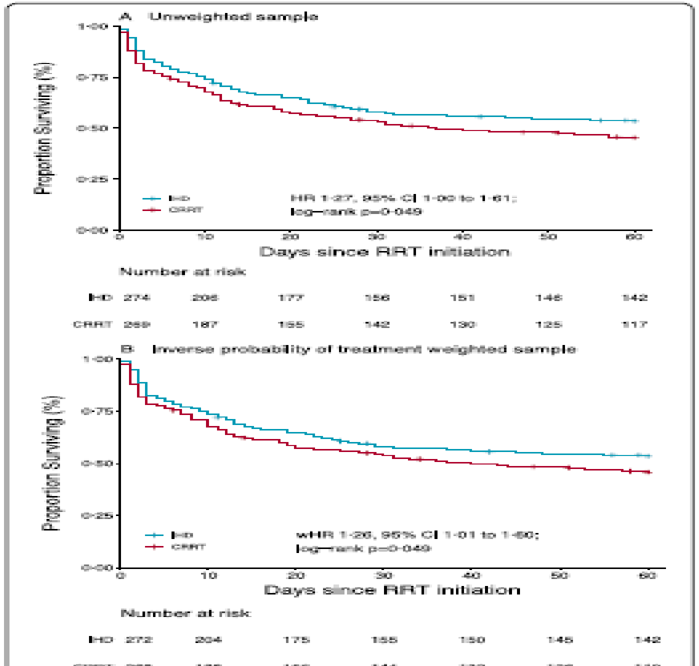


Fig. 2 Primary outcome: probability of survival in the unweighted sample (**A**) and in the IPTW sample (**B**). *HR* hazard ratio, *IHD* intermittent hemodialysis, *CRRT* continuous renal replacement therapy

In conclusione

- Non vi è consenso su quando iniziare
- Non vi sono dimostrazioni solide a favore di una tecnica in confronto ad un'altra
- Si può usare RIFLE come surrogato di parametri di inizio
- Il processo di scelta della tecnica da utilizzare è legato alle indicazioni che hanno portato al trattamento:

Necessità depurative → tecniche classiche HD, HDF, CRRT

Sovraccarico liquidi → ultrafiltrazione

Sepsi → tecniche speciali

Che cosa è la dose?

La dose del trattamento può essere definita:

Efficienza	=	Inst. Clearance (K)
Intensità	=	Clearance x tempo (Kt)
Frequenza	=	Giorni/Settimana-Continua
Efficacia	=	Kt/Vsp – Kt/Veq – StdKt/V

Il K_OA per una membrana

$$KoA = \left[Q_B \Big/ \left(1 - \frac{Q_B}{Q_D}\right) \right] \ln \left[\frac{1 - \frac{C_X}{Q_D}}{1 - \frac{C_X}{Q_B}} \right]$$

Dove:

C_X = Clearance del soluto

X Q_B = Flusso sangue

Q_D = Flusso dialisato

ln = logaritmo naturale

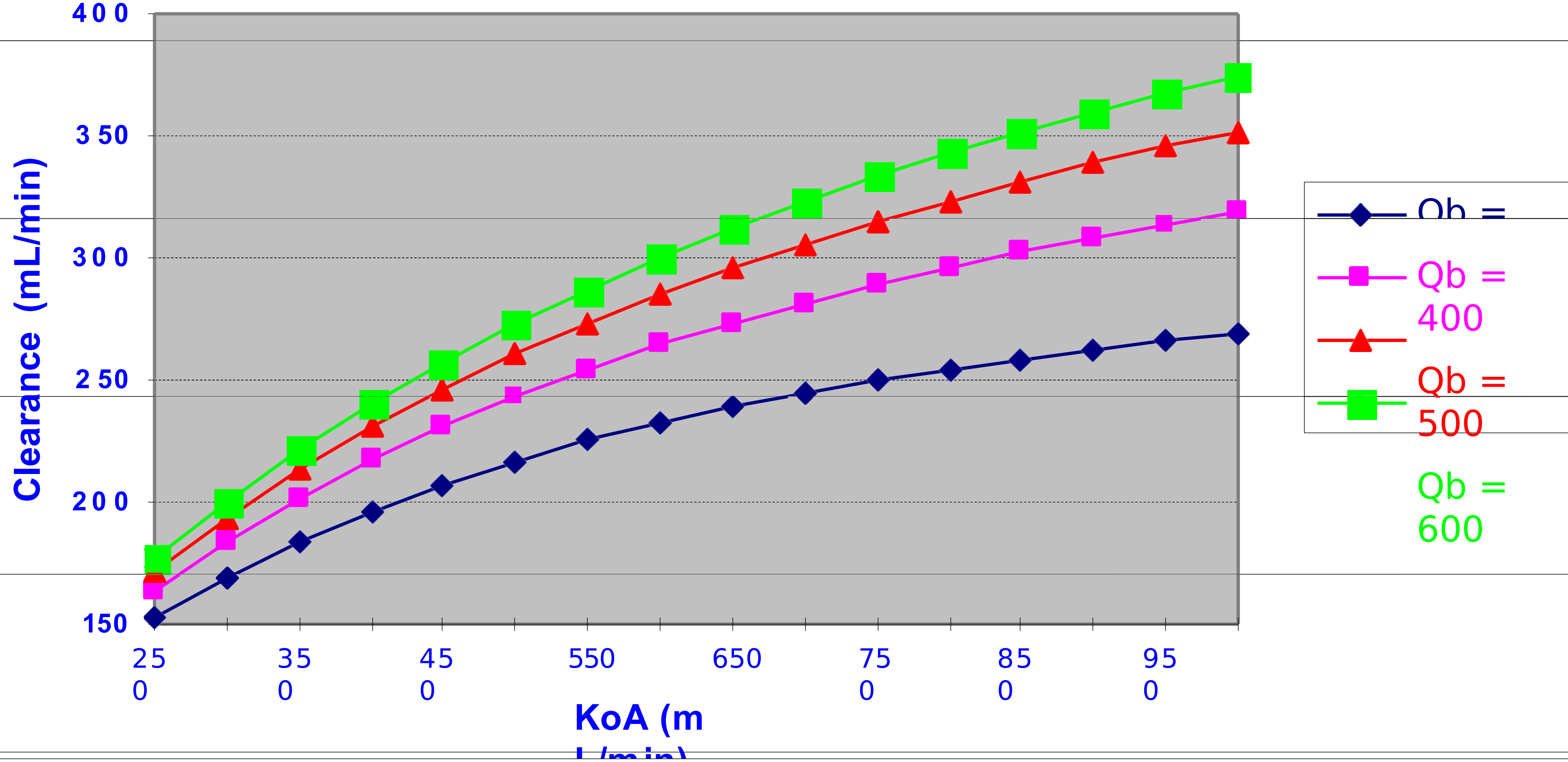
e = 2.718281828......

Calcolare la clearance urea usando KoA

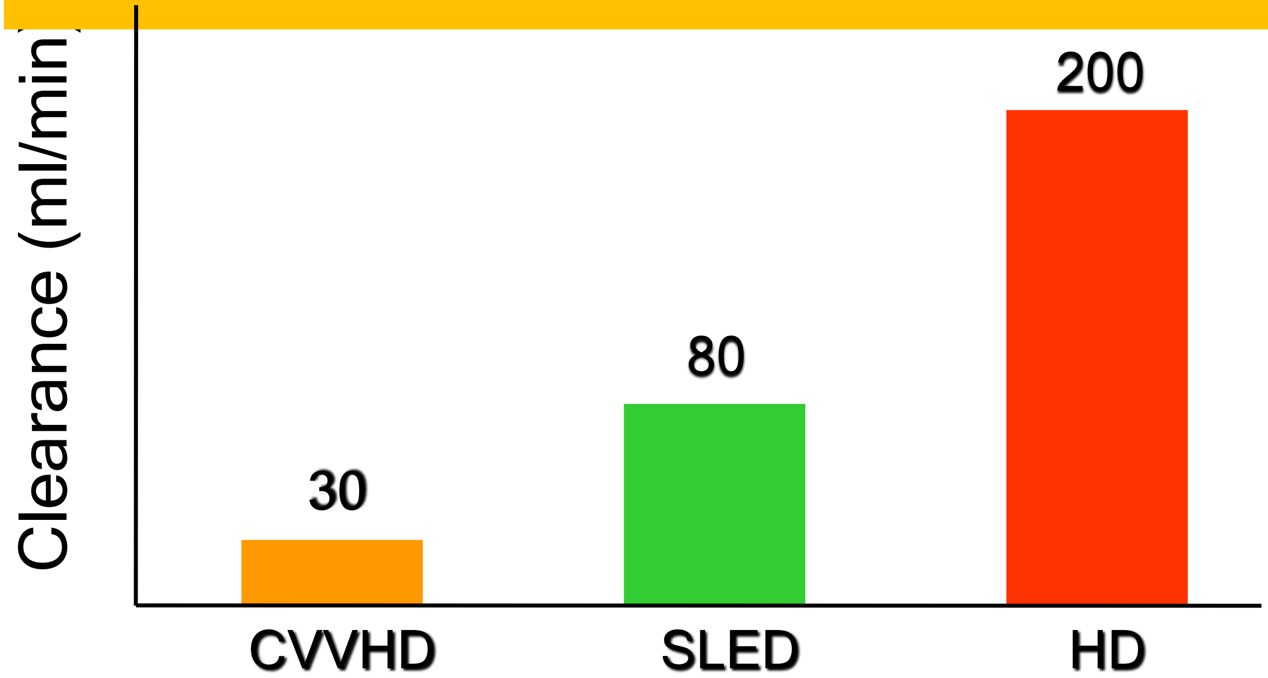
$$C_{BUN} = \frac{Q_B\left(e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-1\right)}{e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-\frac{Q_B}{Q_D}}$$

Q_B = Flusso sangue
Q_D = Flusso dialisato
KoA = Coefficiente di clearance
e = 2.718281828....

Clearance vs. KoA
(Qd = 600 mL/min)



Efficienza (K) (Instant. Clearance)
ml/min



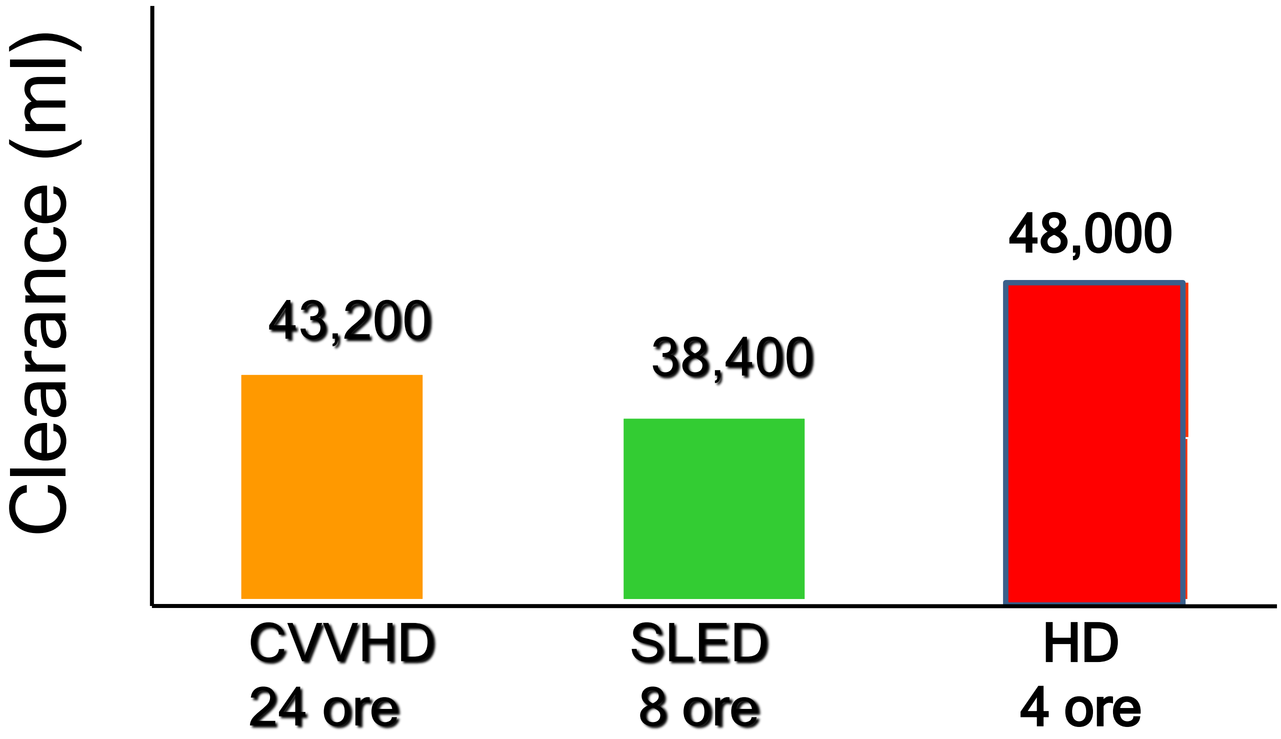
Qb= 300 ml/min,

Qd = 600 ml/min

KoA =400 ml/min

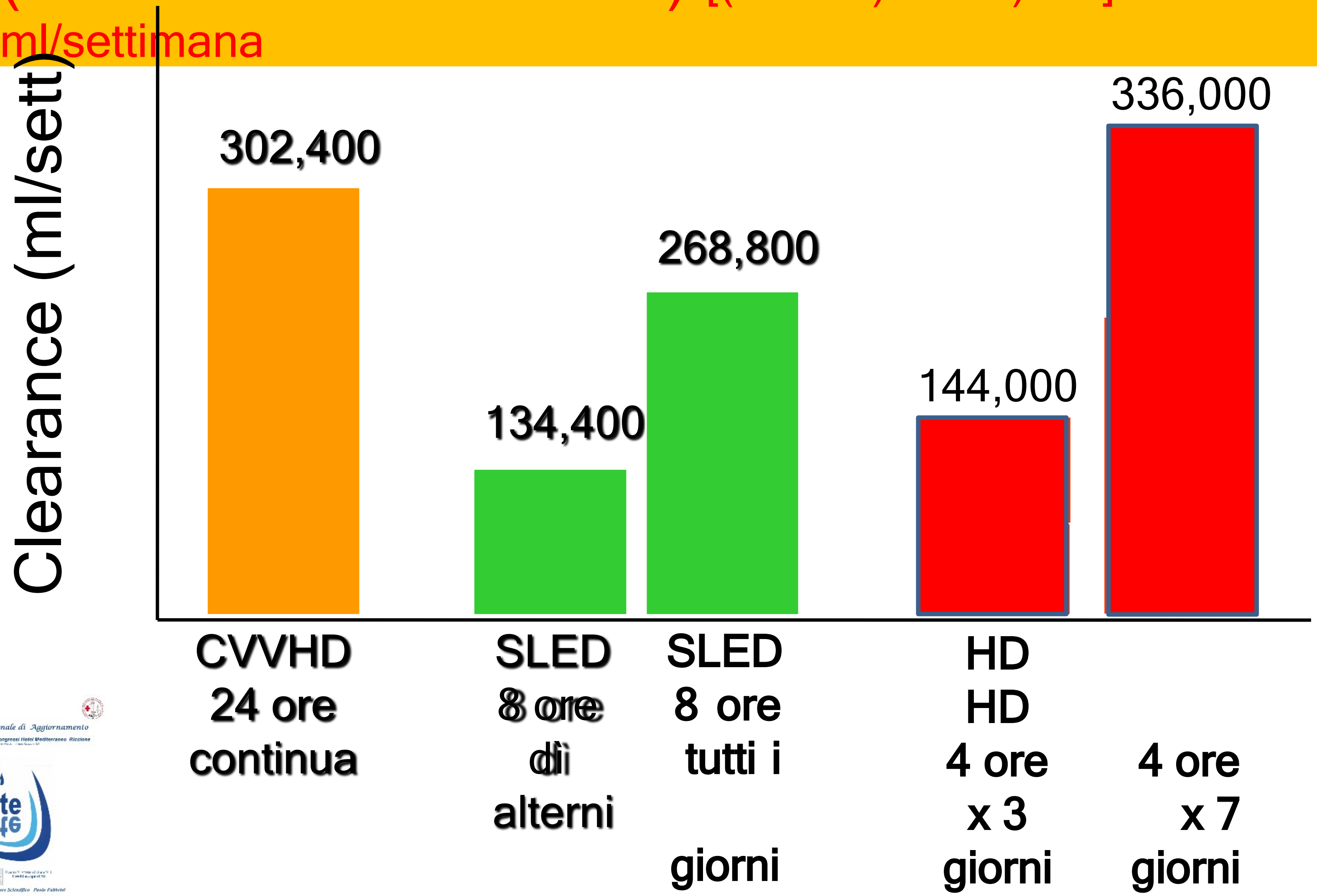
Intensità (K x t) (Clearance giornaliera)

[(ml/min) x min)] = ml

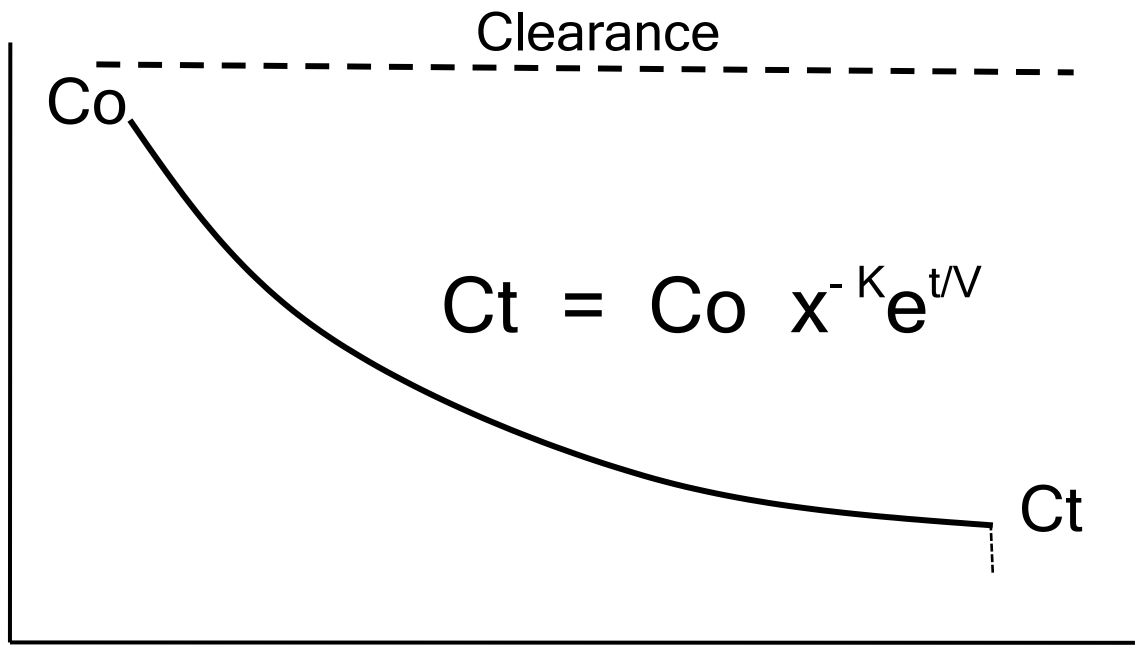


Intensità x Frequenza (K x t x d/w)

(Clearance settimanale) [(ml/min) x min) x d] = ml/settimana



Efficacia: Clearance Frazionale (K x t / V)

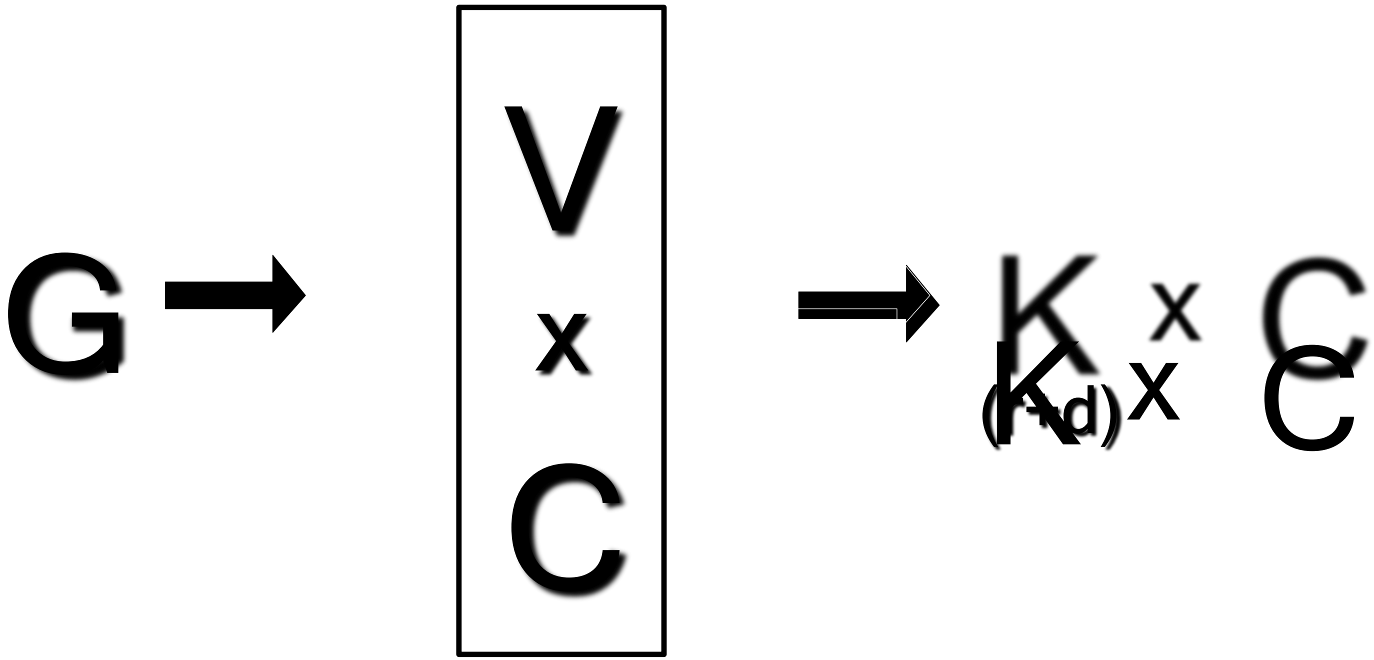


K = Clearance media durante trattamento

t = tempo

V = Volume di distribuzione dell’urea(TBW)

SOLUTE MASS BALANCE
(Single Pool Model)



$$d(V \times C) / dt = G - KC$$

Efficacia corretta per generazione di urea

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

C = Urea plasmatica (mg/mL)

C_0 = Urea plasmatica pre-dialisi (mg/mL)

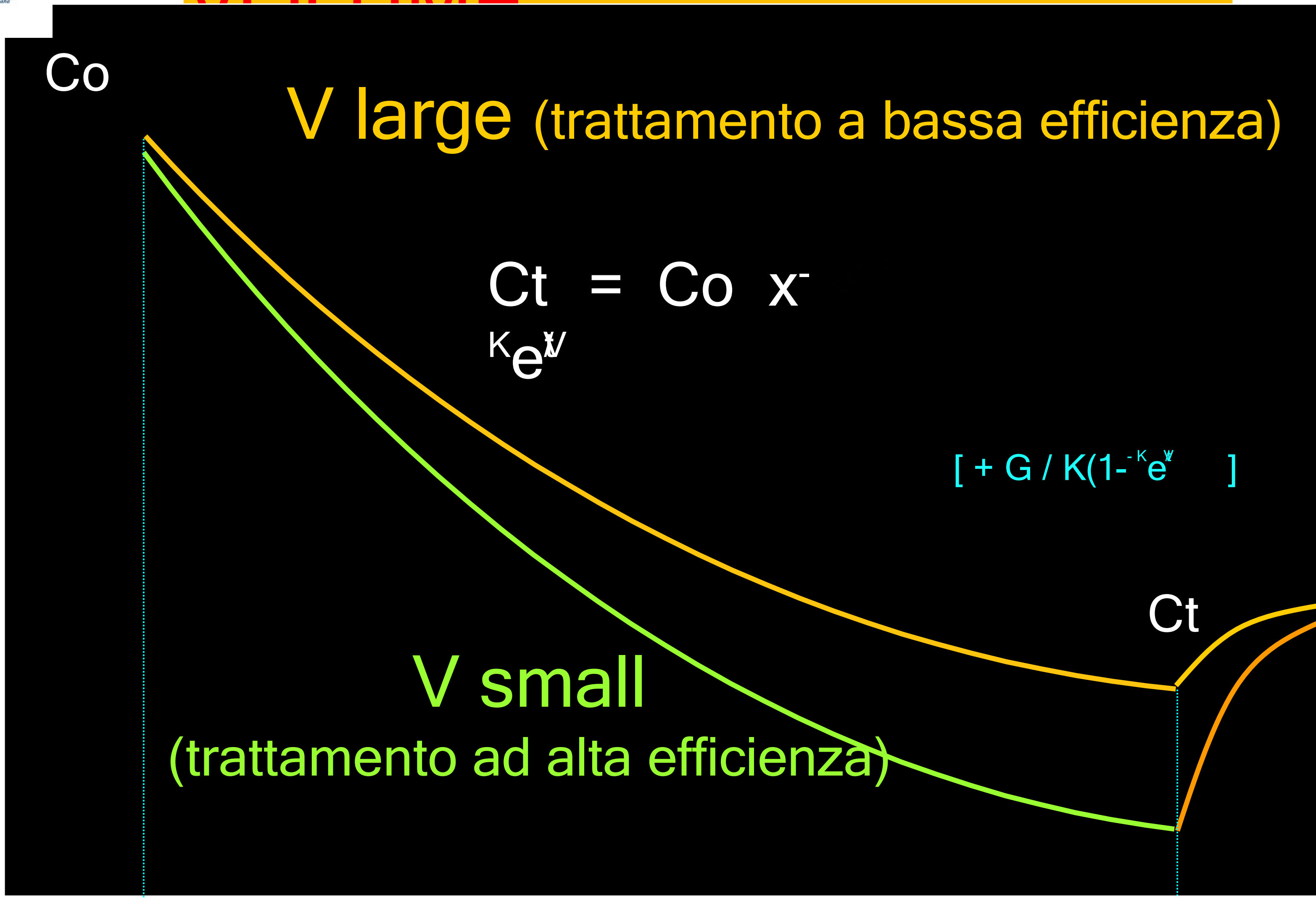
K = Clearance istantanea (mL/min)

t = tempo (minuti)

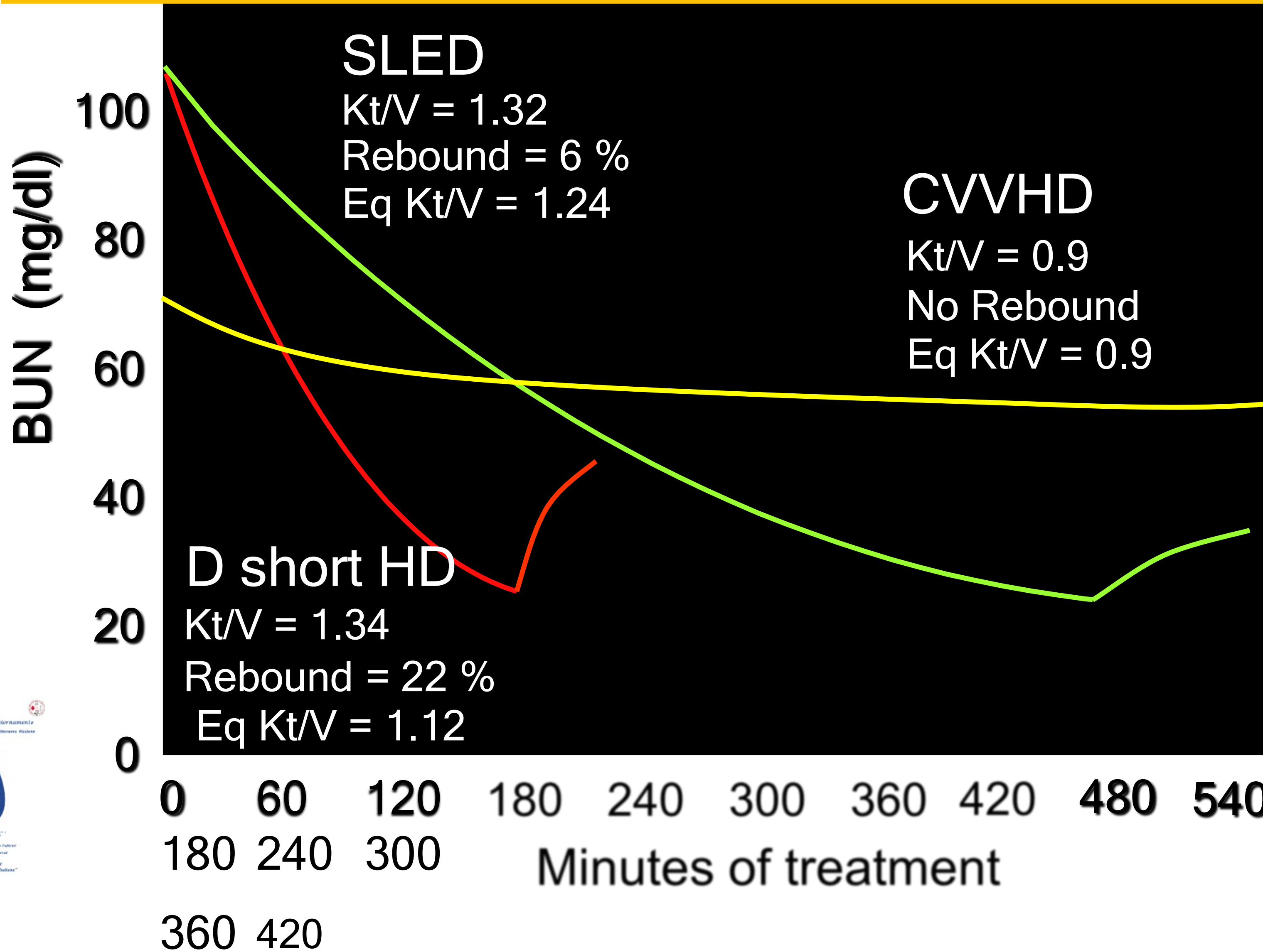
V = Volume di distribuzione del pz. (mL)

G = Generazione urea (mg/min)

CINETICA UREA e VOLUME



REBOUND POSTDIALITICO UREA



Calcolo quantitativo di depurazione ematica

Esempio

D short HD	D Ext. HD	CVVHD
K = 200 ml/min	K = 80 ml/min	K = 30 ml/min
Urea [C]o = 110 mg/dl	Urea [C]o = 110 mg/dl	Urea [C]o = 70 mg/dl
Urea [C]t = 30 mg/dl	Urea [C]t = 30 mg/dl	Urea [C]t = 65 mg/dl
Tx time = 180 mins	Tx time = 480 mins	Tx time = 1440 mins
Kt/V = 1.12	Kt/V = 1.24	Kt/V = 0.9
Tot. Clear. = 36 L	Tot. Clear. = 38.4 L	Tot. Clear. = 43.2 L
Urea rimossa = 18 g	Urea rimossa = 27 g	Urea rimossa = 33.6 g
Rebound = 22 %	Rebound = 6 %	No Rebound

ADEGUATEZZA / DOSE

Fissa: Standard = 2 L/h High Vol. = > 3 L/h

Personalized: Standard = 30-35 ml/h/Kg b.w. High Vol.

In CVVH = ml/min or L / 24 h

45 ml/h/Kg

Perché la Uf = Dose in CVVH ?

V Clearance rene umano (K) = [U] x ... / P]

Clearance del filtro (K) = [Uf] x ... / [P]

Dove: [Uf]/[P] = Sieving Coefficient (S)

Costante?

$$\text{Urea K} = \frac{[Uf] \ \times \ Uf}{[P]} = \frac{80 \ \times \ 35}{80} = 35 \text{ ml/min}$$

Paziente X.Y. = Peso corporeo 65 Kg

Sovraccarico di fluidi stimato = 5 Kg

Ultrafiltrazione precoce → Target B.W. = 60 Kg

V stimato = 36 Liters

48 L/24h = Kt/V : 1.3

Target : 2L/h or 33 ml/min

Target 2L/h or 33 ml/min

CVVH = Ultrafiltrazione equivale a clearance (post-dil.)

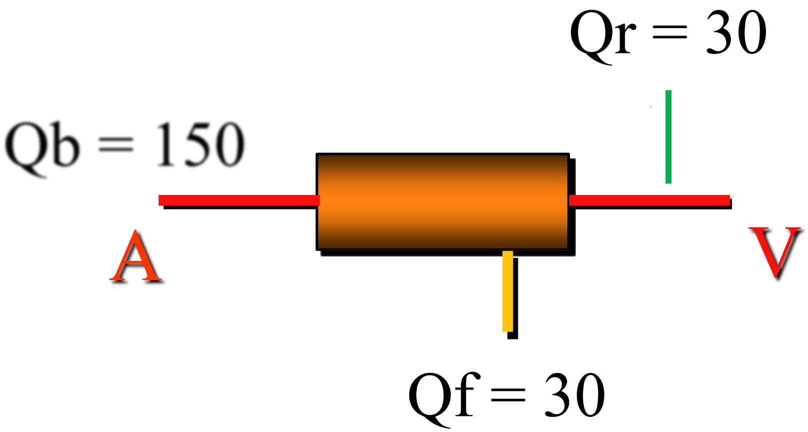
CVVHD = l’effluente equivale alla clearance solo se c’è una saturazione del 100% (dipende dal filtro e dai flussi)

CVVHDF = La clearance dipende dalla ultrafiltrazione, dal sito di reinfusione, dal flusso del dialisato e dalla sua saturazione (filtro e flussi)

Pre- e post- diluizione sono uguali?

K = Qf x S where S = UF/A

CREATININE

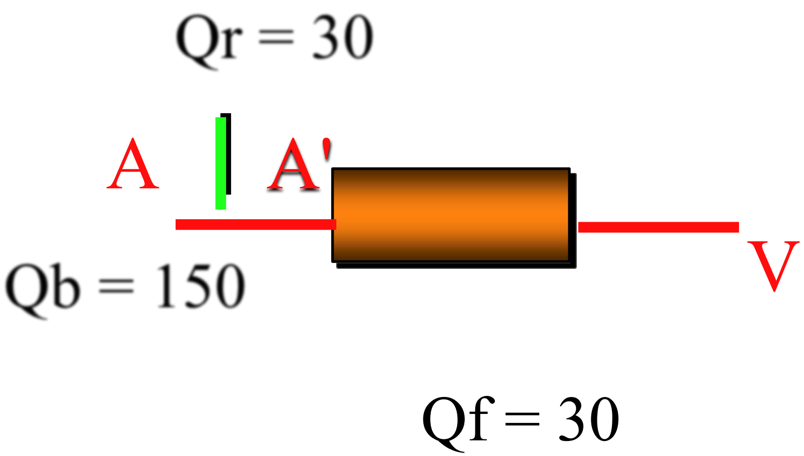


Qf = 30 ml/min

A = 10 mg/dl

Uf = 10 mg/dl

K = 30 ml/min



Qf = 30 ml/min

A = 10 mg/dl

A' = 8.0 mg/dl

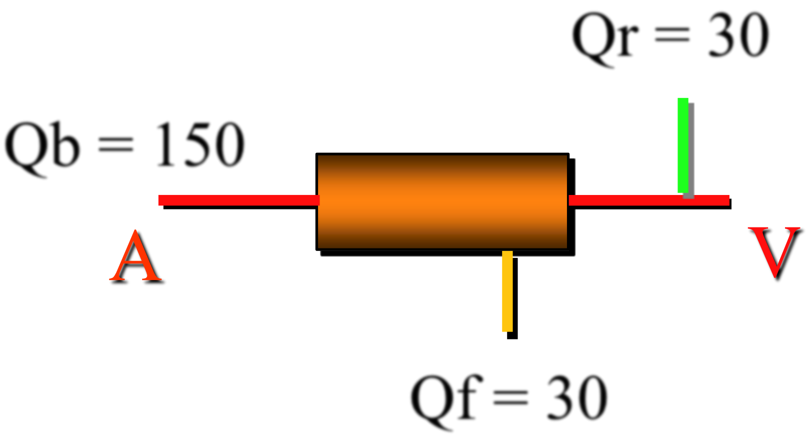
Uf = 8.0 mg/dl

K = 24 ml/min

Pre- e post- diluizione sono uguali?

CREATININE

K = Qf x S   where S = UF/A

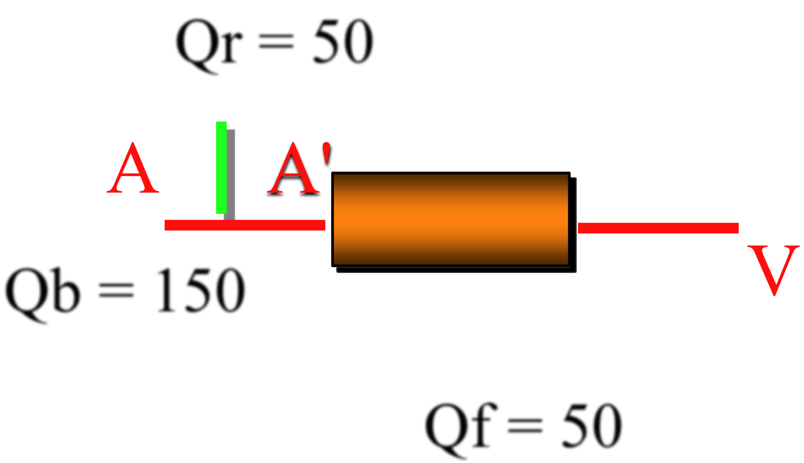


Qf = 30 ml/min

A = 10 mg/dl

Uf = 10 mg/dl

K = 30 ml/min



Qf = 50 ml/min

A = 10 mg/dl

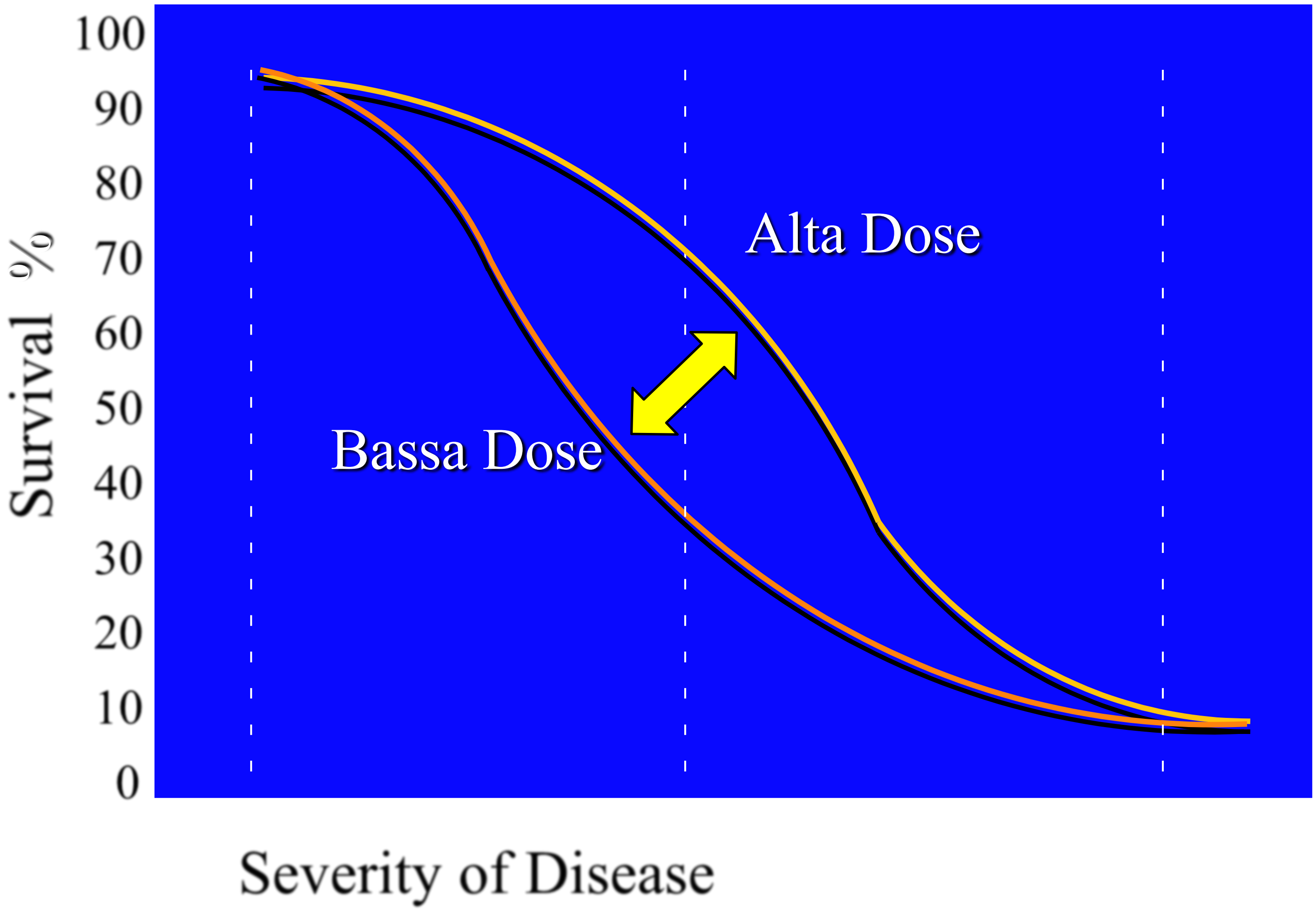
A' = 6.6 mg/dl

Uf = 6.6 mg/dl

K = 33 ml/min

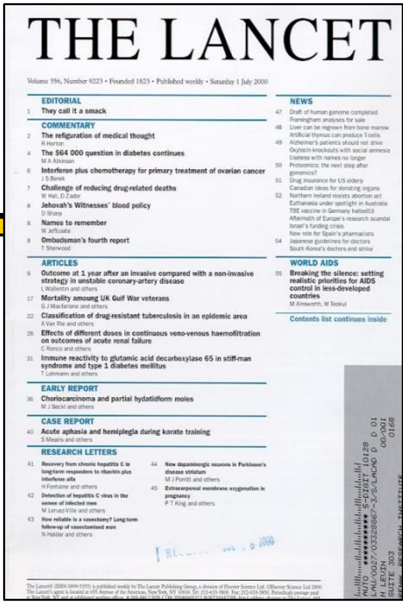
CRRT: Impatto sull’outcome

The Cleveland Clinic Observation



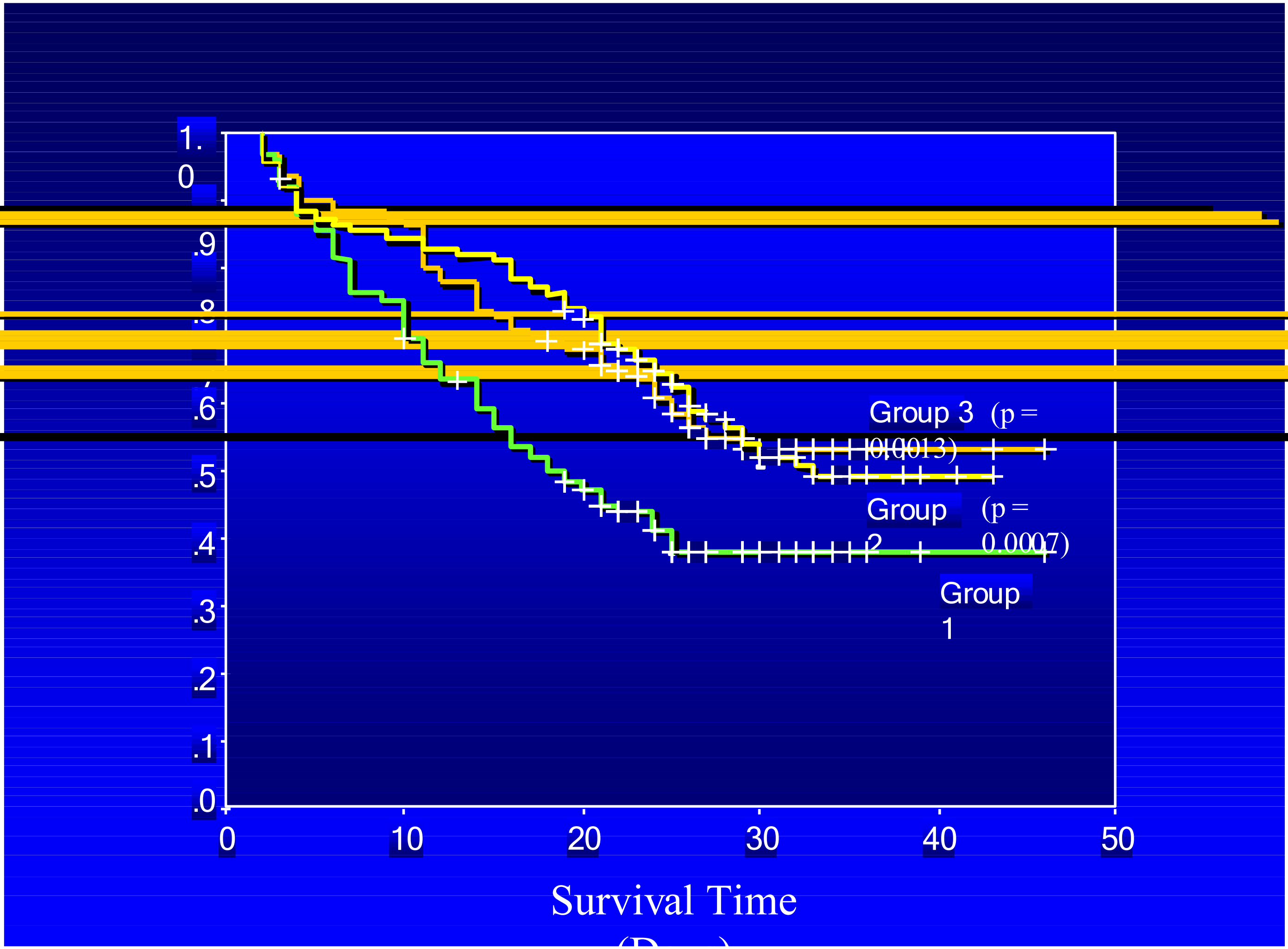
Ronco C, Bellomo R, Brendolan A, Dan M, Piccinni P, La Greca G. Effect of different doses in continuous veno venous hemofiltration on outcomes of acute renal failure.

The Lancet 2000



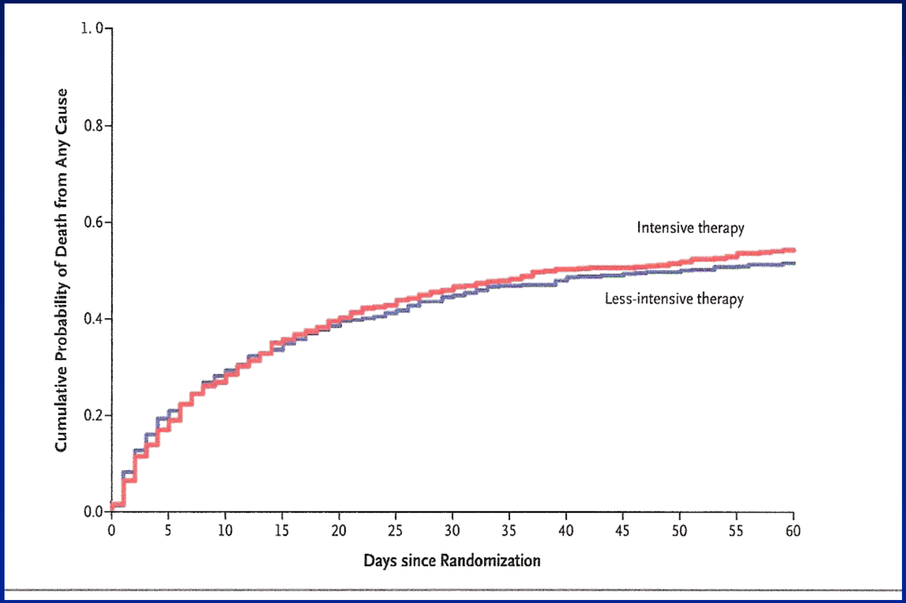
THE LANCET

Volume 356, Number 9223 • Founded 1823 • Published weekly • Saturday 1 July 2000

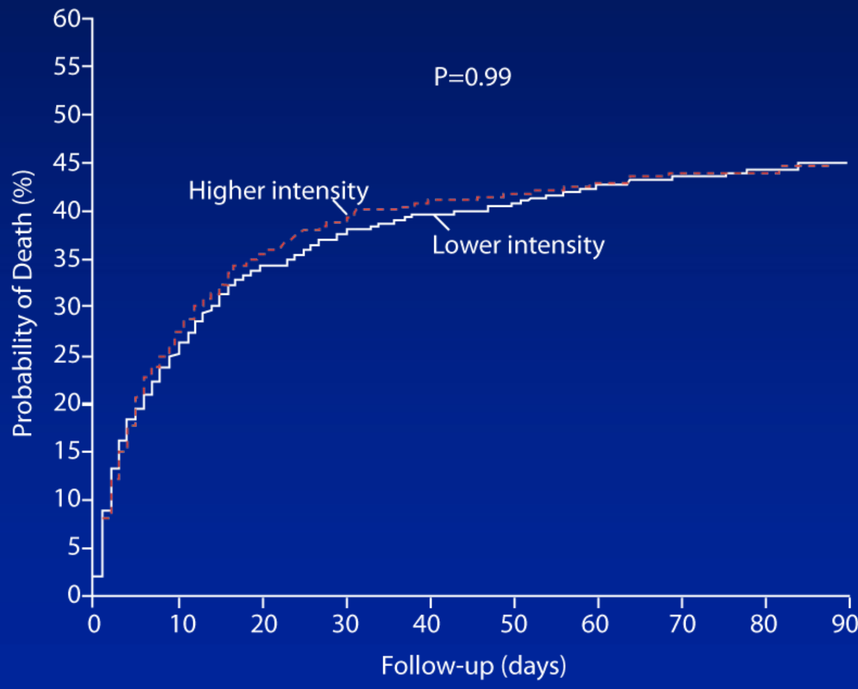


ATN Study: Primary Outcome

VA/NIH Trial Group, NEJM 2008

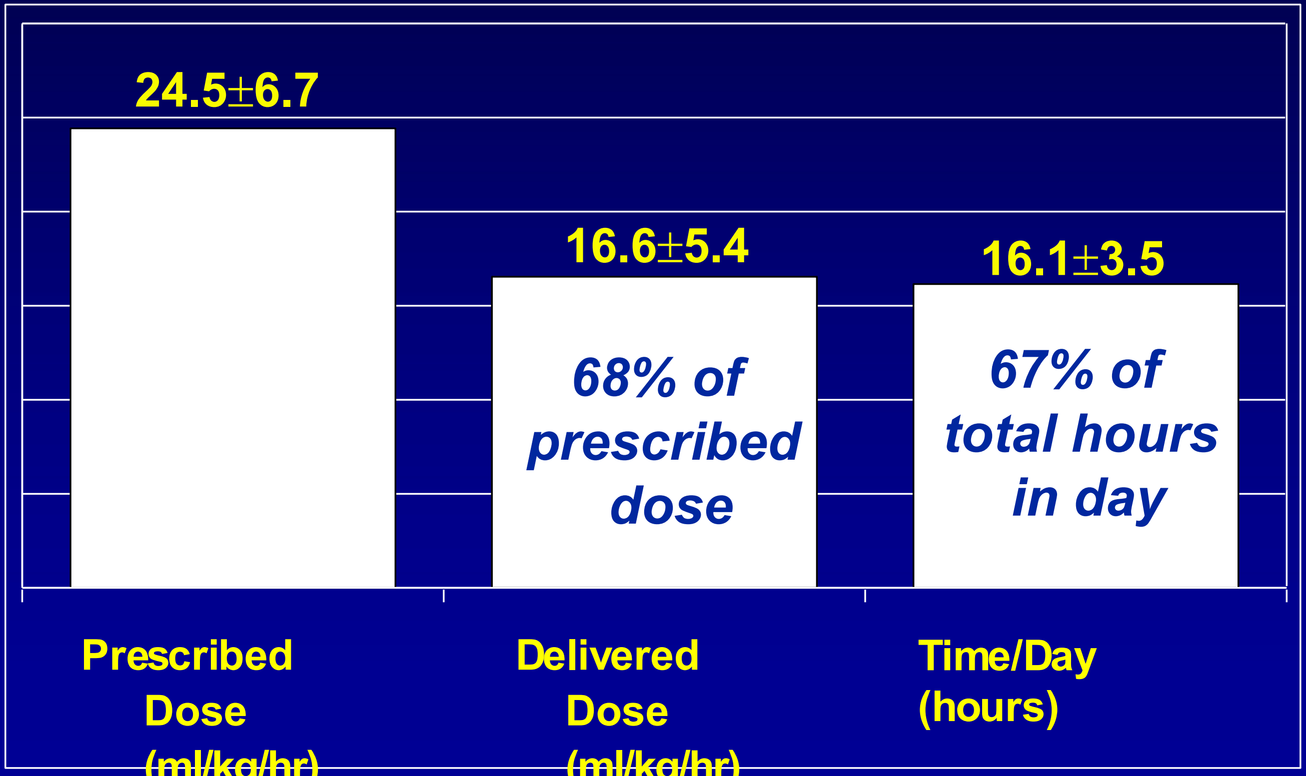


Mortality Outcomes in RENAL



CRRT: Somministrazione vera verso prescrizione

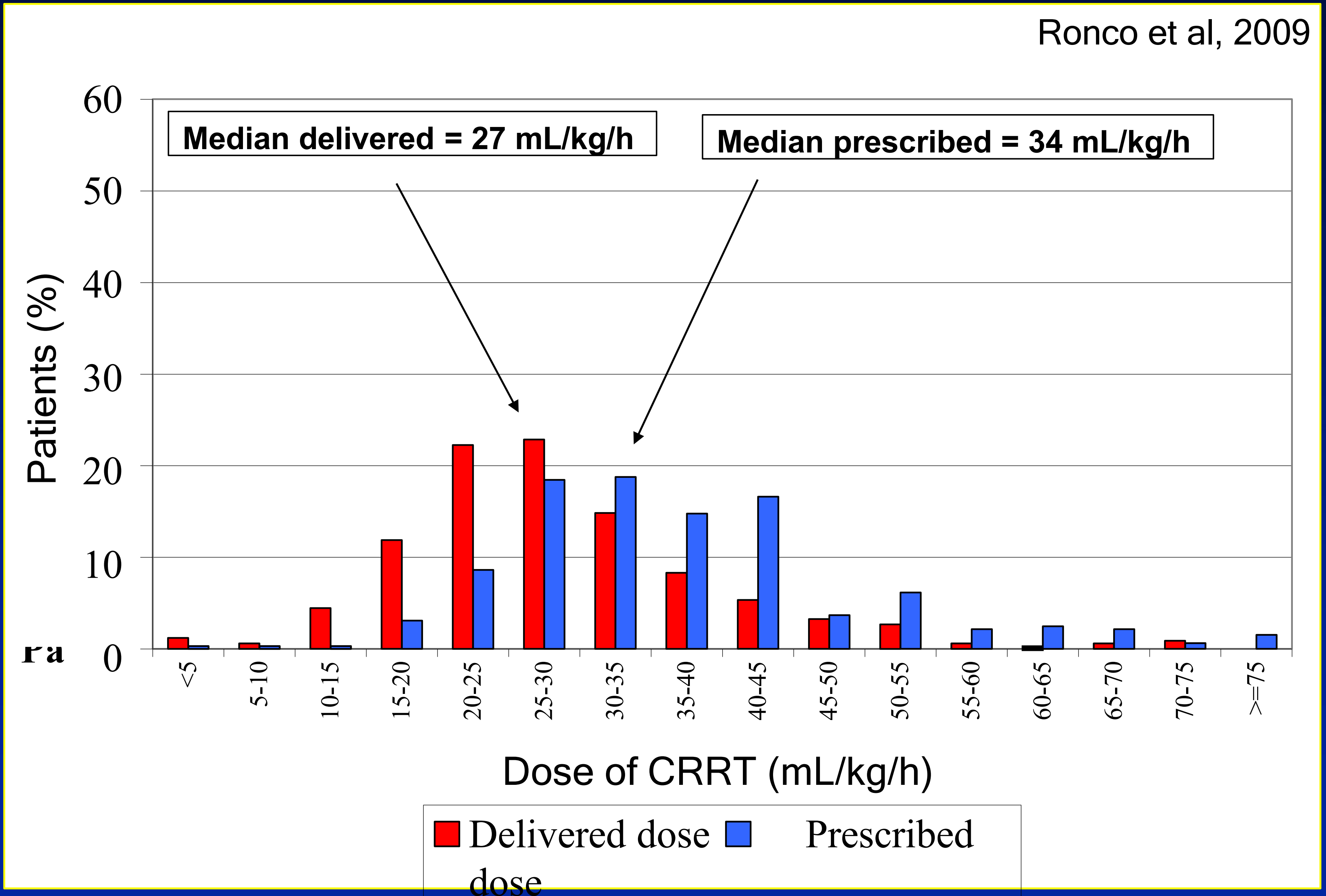
Venkataraman et al, J Crit Care, 2002



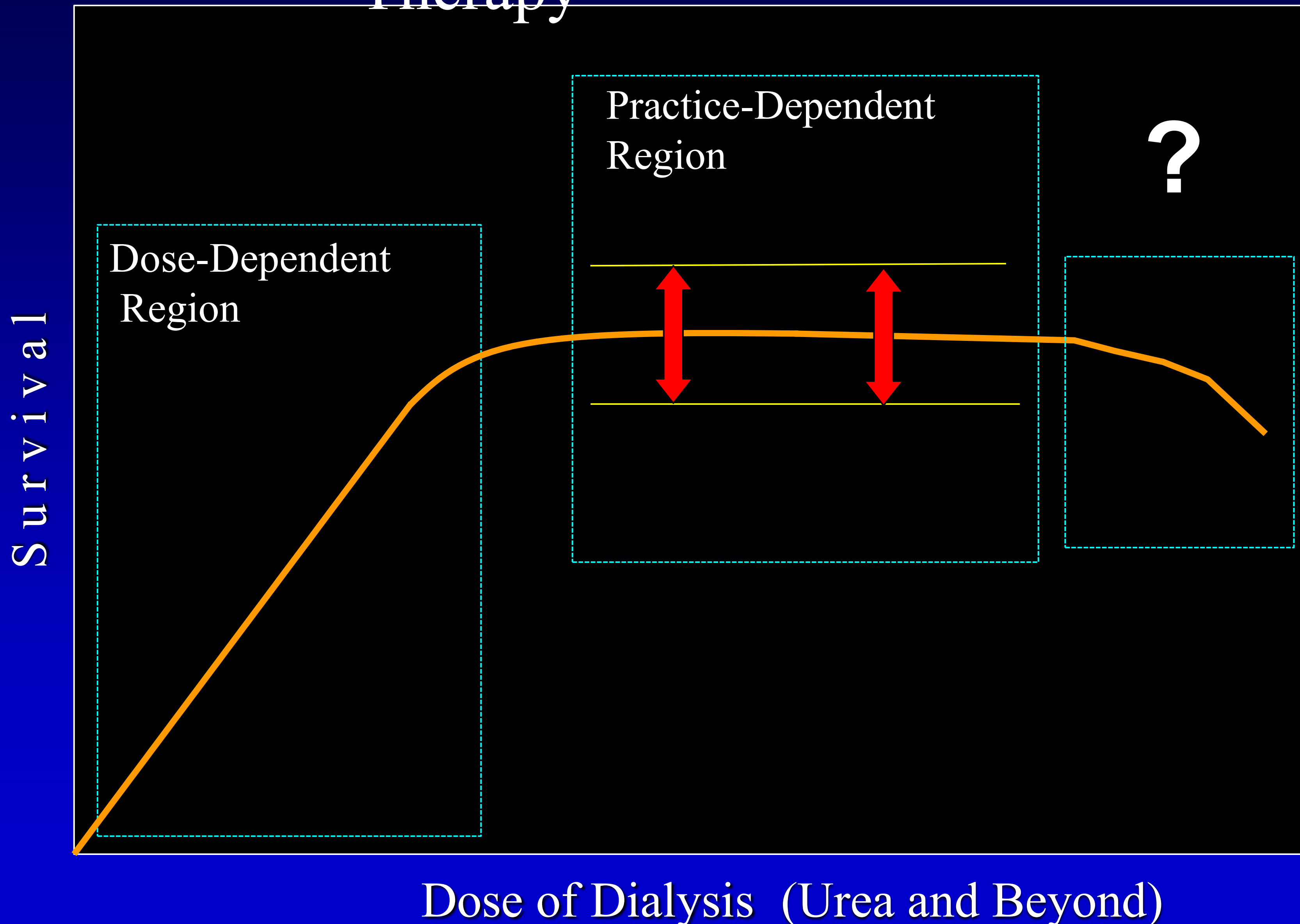
Clearance prescritta e somministrata effettivamente Fattori che influenzano la discrepanza

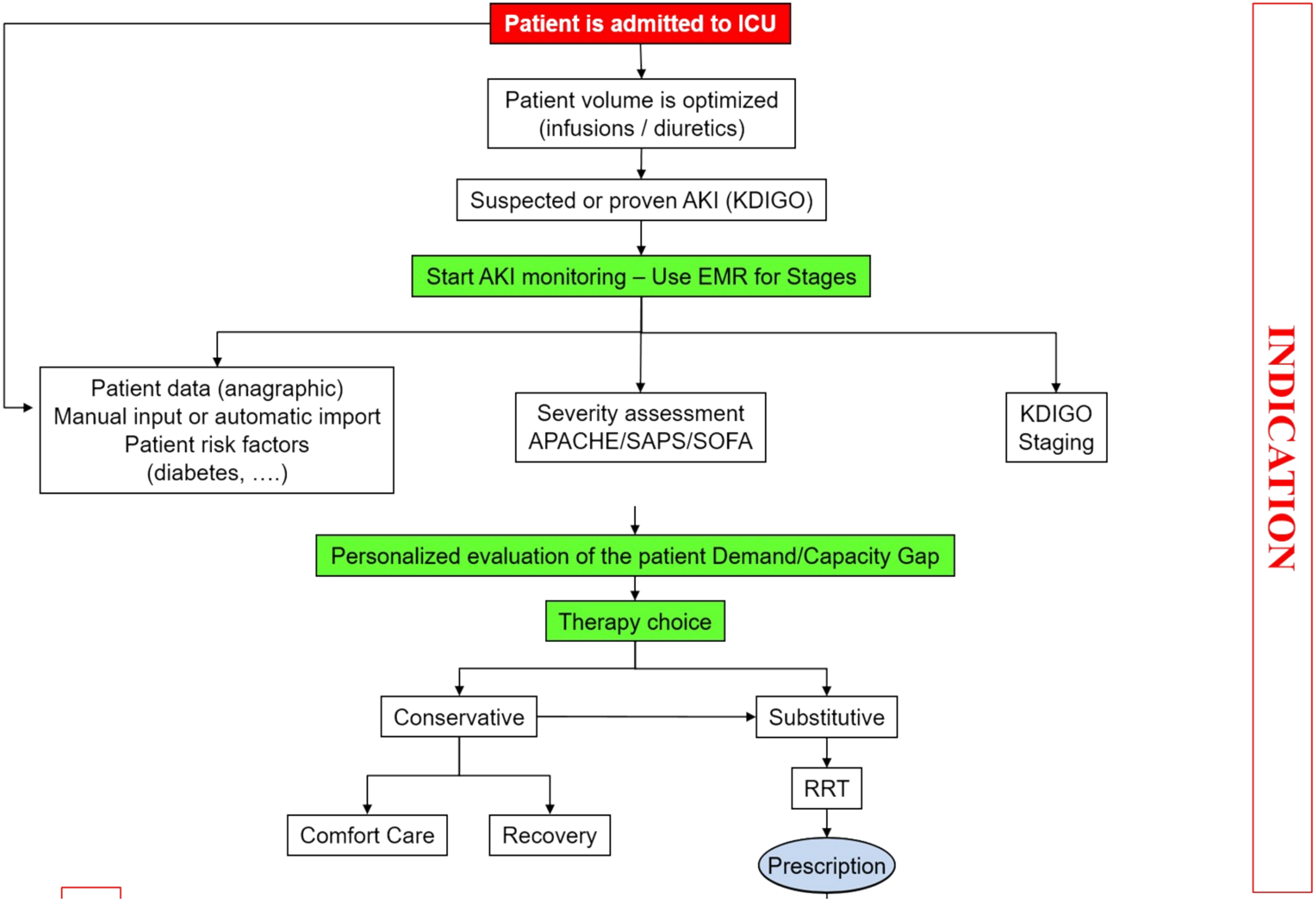
- Flusso sangue più basso del programmato e di quello dichiarato dalla macchina di dialisi, Accesso vascolare inadeguata
- Flusso dialisato/filtrato più basso del programmato o di quello dichiarato dalla macchina. Eccessiva frazione di filtrazione
- Inadeguata performance del filtro/dializzatore
    - Priming incorretto
    - Perdita di superficie (coaguli, aria)
    - Perdita di permeabilità (clogging della membrana)
    - Alta viscosità ematica o ematocrito
    - Frazione di filtrazione eccessiva

DoReMi Database (N=865)

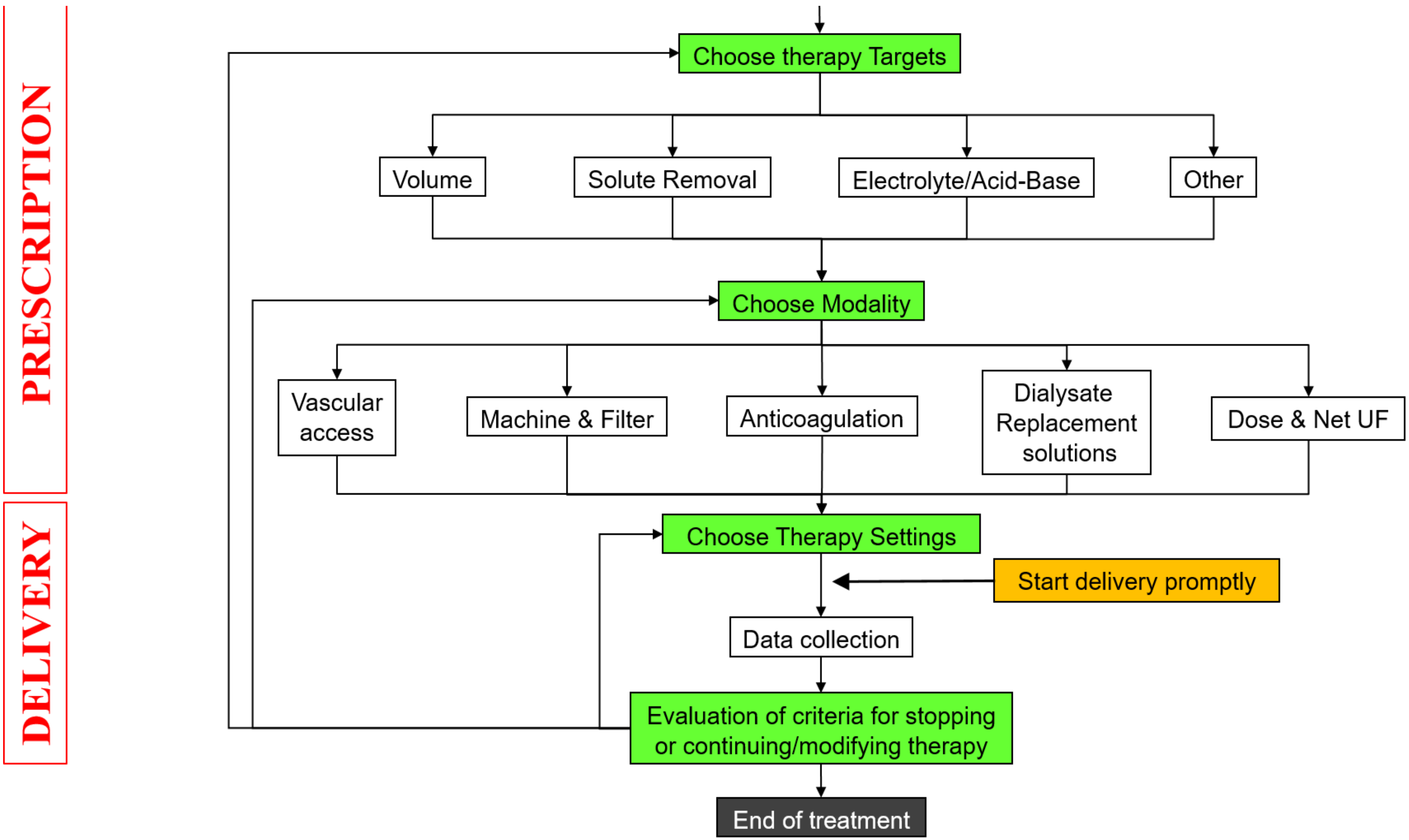


Renal Replacement Therapy





Patient is admitted to ICU
Patient volume is optimized (infusions / diuretics)
Suspected or proven AKI (KDIGO)
Start AKI monitoring – Use EMR for Stages
Patient data (anagraphic)
Manual input or automatic import
Patient risk factors
(diabetes, ….)
Severity assessment
APACHE/SAPS/SOFA
KDIGO
Staging
Personalized evaluation of the patient Demand/Capacity Gap
Therapy choice
Conservative
Substitutive
Comfort Care
Recovery
RRT
Prescription
INDICATION


PRESCRIPTION
DELIVERY
Choose therapy Targets
Volume
Solute Removal
Electrolyte/Acid-Base
Other
Choose Modality
Vascular access
Machine & Filter
Anticoagulation
Dialysate Replacement solutions
Dose & Net UF
Choose Therapy Settings
Start delivery promptly
Data collection
Evaluation of criteria for stopping or continuing/modifying therapy
End of treatment