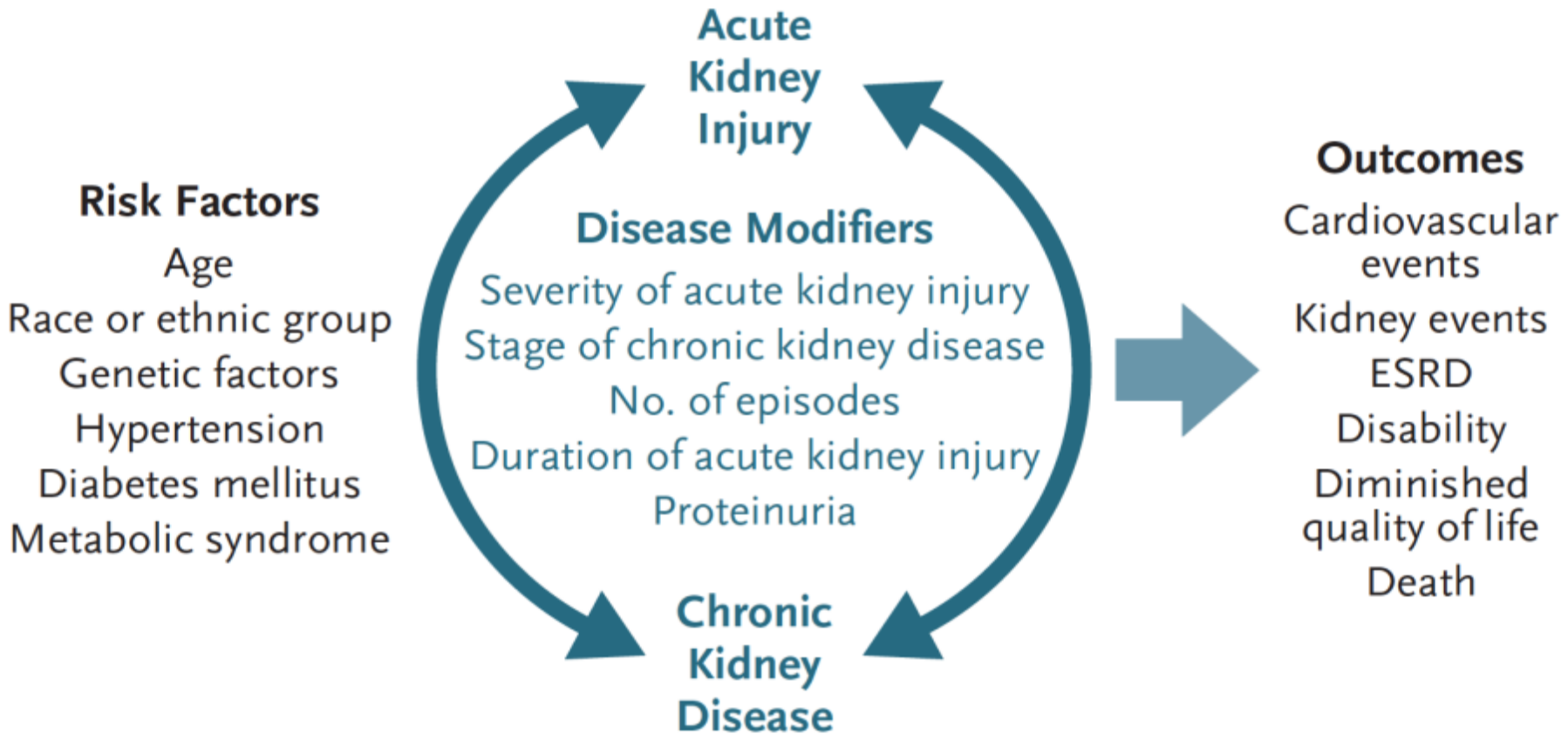
HELLENIC SOCIETY OF NEPHROLOGY
ΕΛΛΗΝΙΚΗ ΝΕΦΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ

Acute Kidney Injury as a continuum

IRRIV
International Renal Research Institute Vicenza

Claudio Ronco, MD

The continuum of acute and chronic kidney disease



AKI issues in 2024

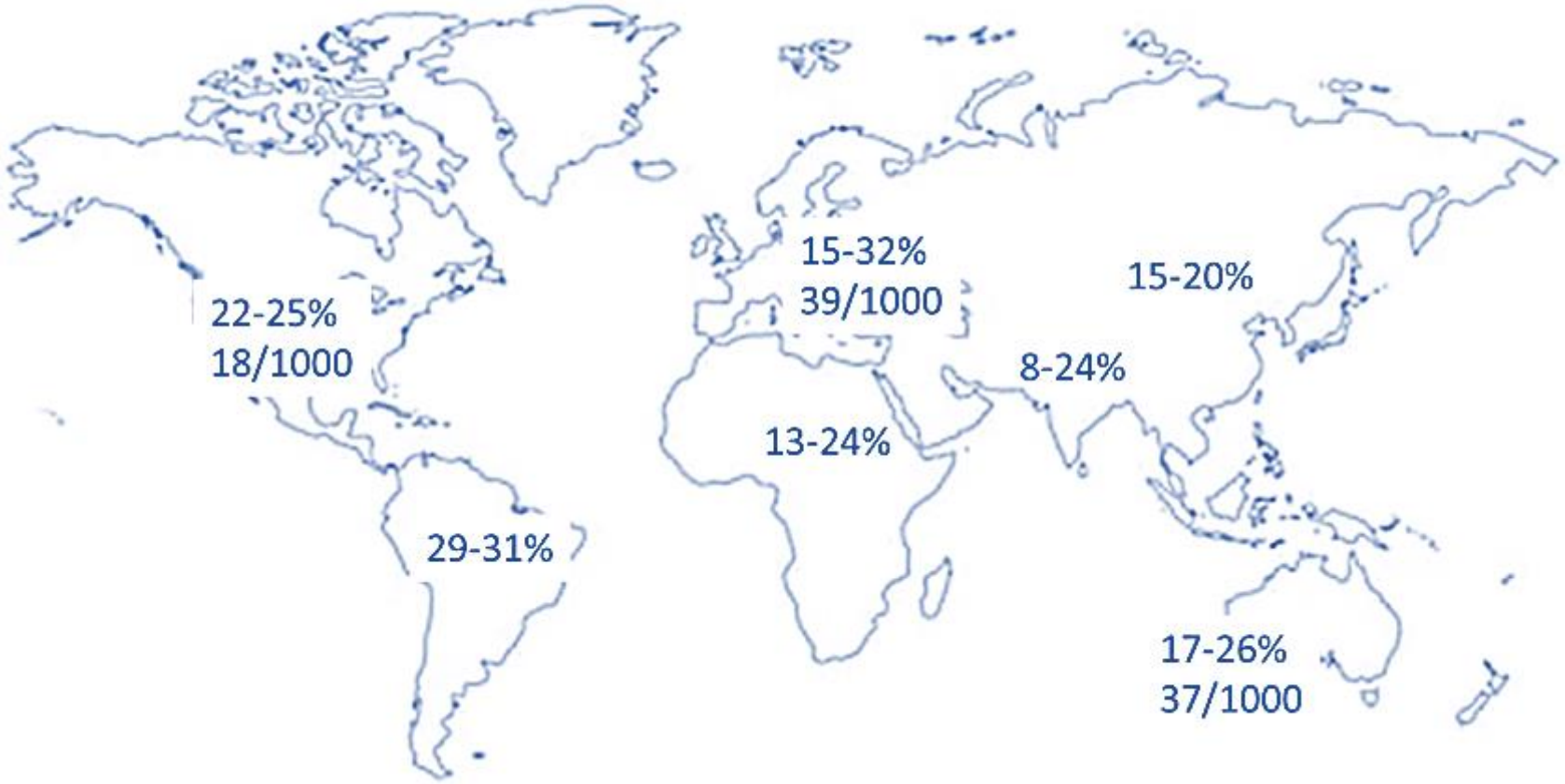
- Community awareness
- Recognition & diagnosis
- Prevention & Protection
- Management of AKI-AKD
- Management of recovery
- Transition to CKD

Observational Study > Lancet. 2016 May 14;387(10032):2017-25.
doi: 10.1016/S0140-6736(16)30240-9. Epub 2016 Apr 13.

Recognition and management of acute kidney injury in the International Society of Nephrology 0by25 Global Snapshot: a multinational cross-sectional study

Ravindra L Mehta [1], Emmanuel A Burdmann [2], Jorge Cerdá [3], John Feehally [4], Fredric Finkelstein [5], Guillermo García-García [6], Melanie Godin [7], Vivekanand Jha [8], Norbert H Lameire [9], Nathan W Levin [10], Andrew Lewington [11], Raúl Lombardi [12], Etienne Macedo [2], Michael Rocco [13], Eliah Aronoff-Spencer [14], Marcello Tonelli [15], Jing Zhang [14], Giuseppe Remuzzi [16]

AKI is common across the continents



Seminar

THE LANCET
Volume 379 · Number 9714 · Pages 1–68 · July 3–9, 2010 www.thelancet.com

Year 2012

Acute kidney injury

Rinaldo Bellomo, John A Kellum, Claudio Ronco

Lancet 2012; 380: 756–66
Published Online
May 21, 2012
http://dx.doi.org/10.1016/
S0140-6736(11)61454-2

Acute kidney injury (formerly known as
kidney's excretory function and is typicall
(urea and creatinine) or decreased urine ou
the kidney acutely. Acute kidney injury is
these patients, it is most often seconda

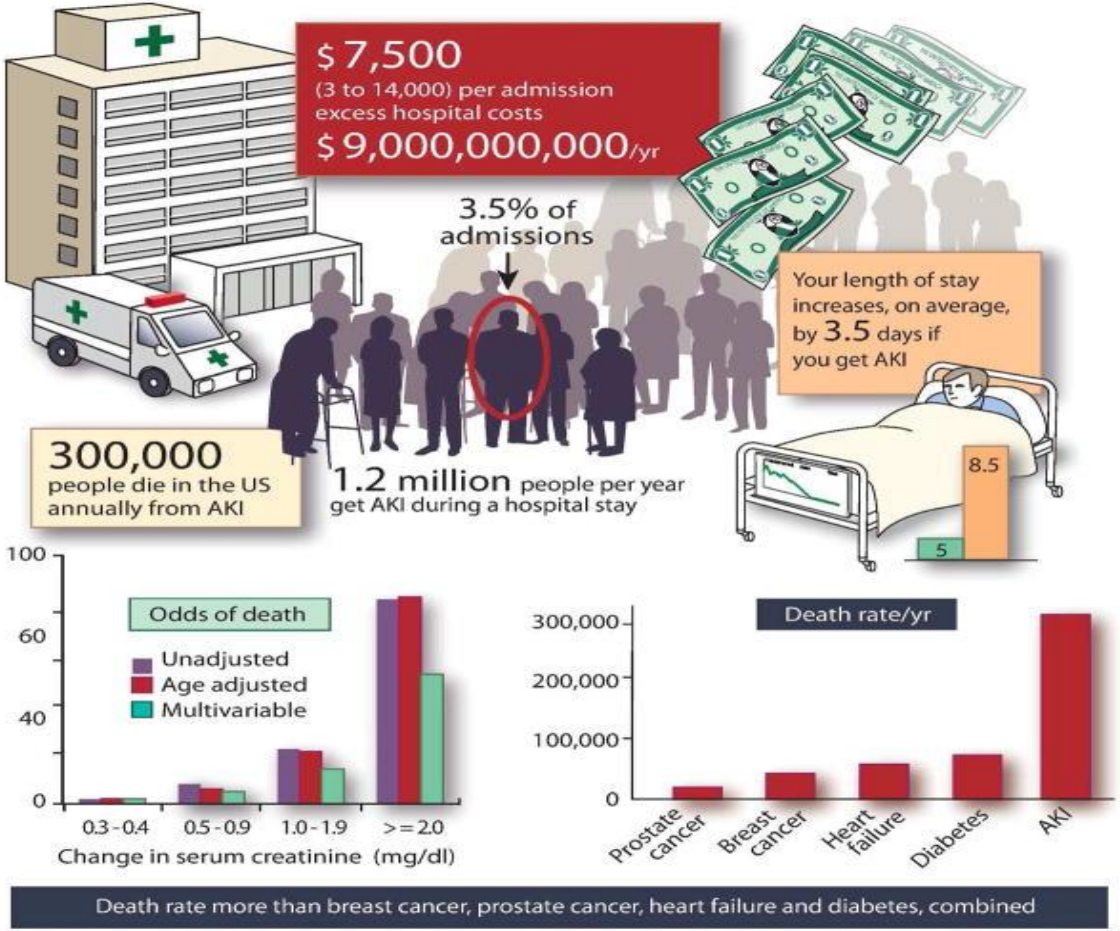
Year 2020

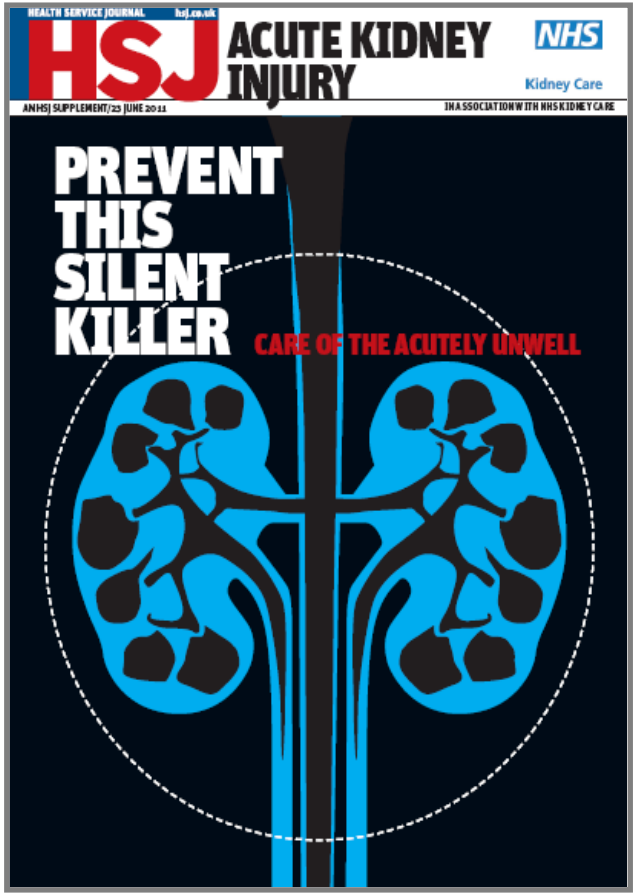
Acute kidney injury

Claudio Ronco, Rinaldo Bellomo, John A Kellum

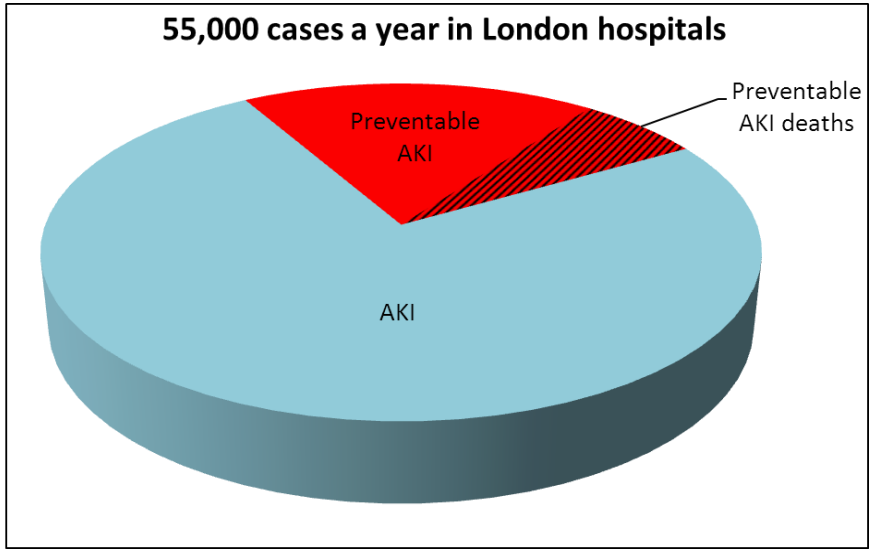
Acute kidney injury (AKI) is defined by a rapid increas
occurs in approximately 10–15% of patients admitted to
in more than 50% of patients. Kidney dysfunction or dam
with acute and chronic kidney disease. Biomarkers of kid
possibly guide therapy. AKI is not a single disease bu

Are the societal costs of the AKI epidemic known?

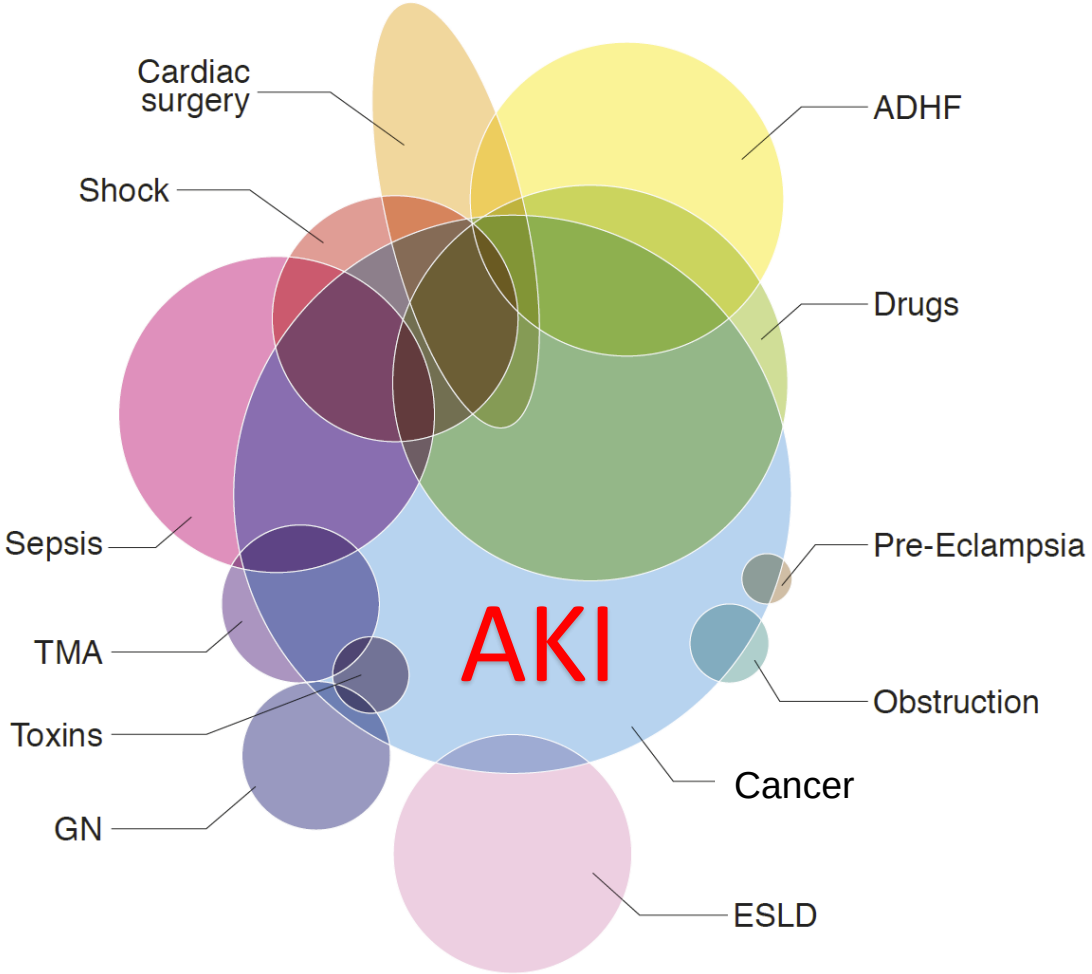




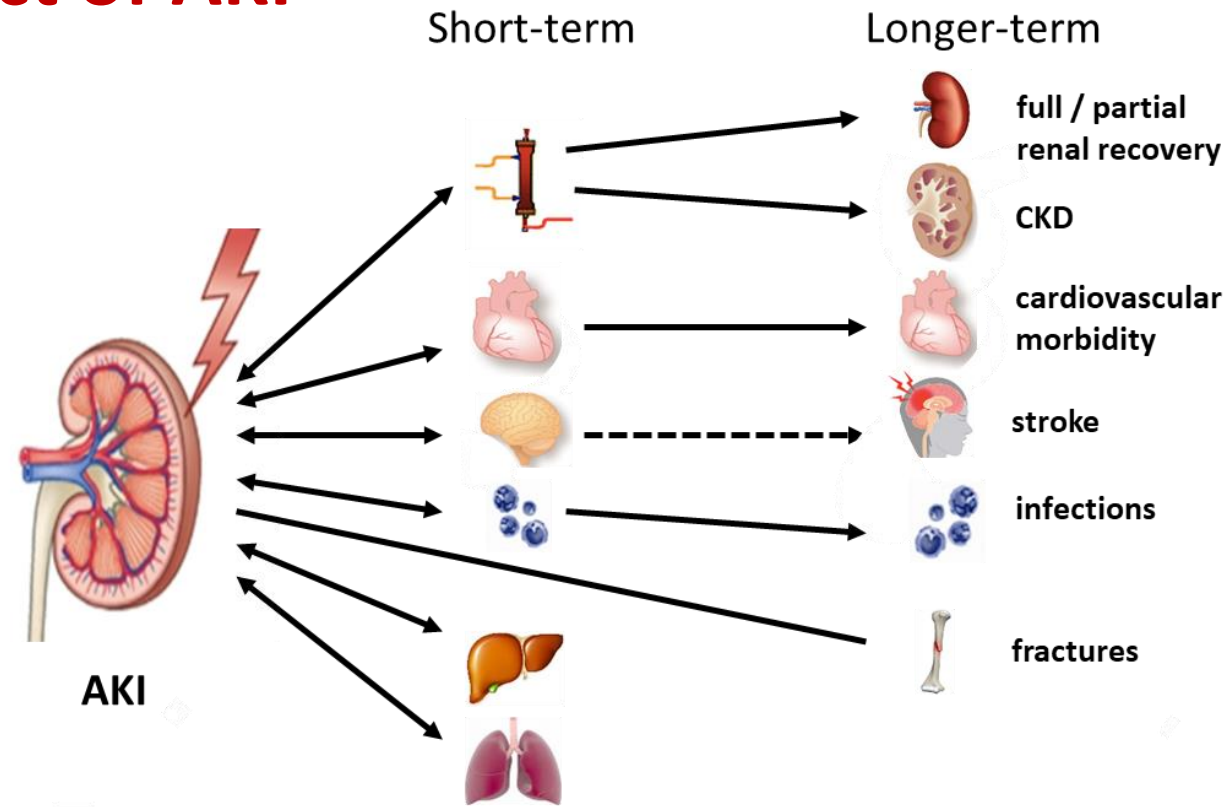
UK data:
20% - 30% of AKI is considered preventable



- 11,000 - 16,000 preventable cases of AKI in London hospitals each year
- 3,000 - 4,000 preventable AKI-related deaths each year


Cardiac surgery
ADHF
Shock
Drugs
Sepsis
Pre-Eclampsia
AKI
TMA
Obstruction
Toxins
Cancer
GN
ESLD

Impact of AKI



Recognition & Diagnosis

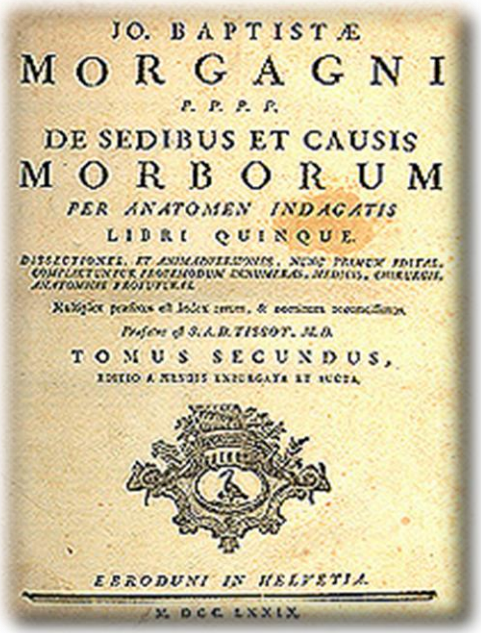
Medicine in Bisantium

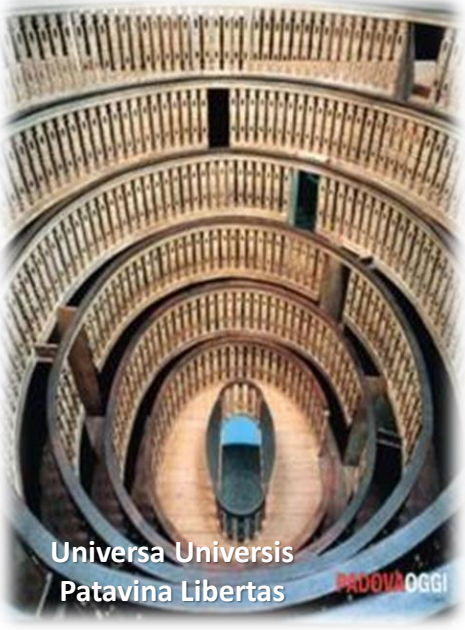
(Book «de pestilentia» VIII century)

Salerno Urinoscopy

(Instrument «Matula» VIII century)

Medicine of the Renaissance





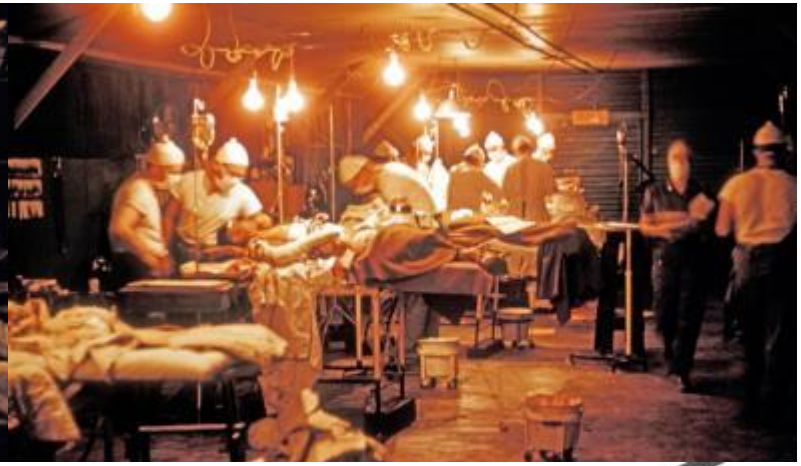
G. Morgagni nel 1760 became famous for the anatomical models of diseases that he proposed based on the autoptic eveluation and the pathology examination.

ARF=ATN: autoptic diagnosis

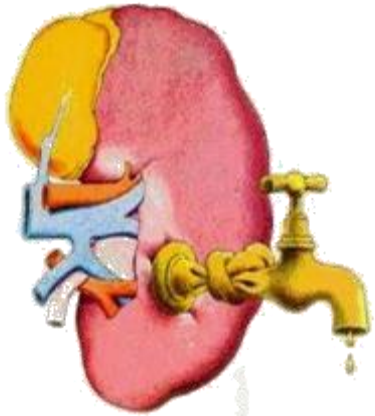
During the bombing of London in world war II, in 1941 Bywaters described cases of acute loss of kidney function in severely injured crush victims. Histological evidence for patchy necrosis of renal tubules at autopsy, suggested him to use the term Acute Tubular Necrosis (ATN) for this clinical entity. The diagnosis was made by autopsy.

The concept of «functional & reversible» ARF

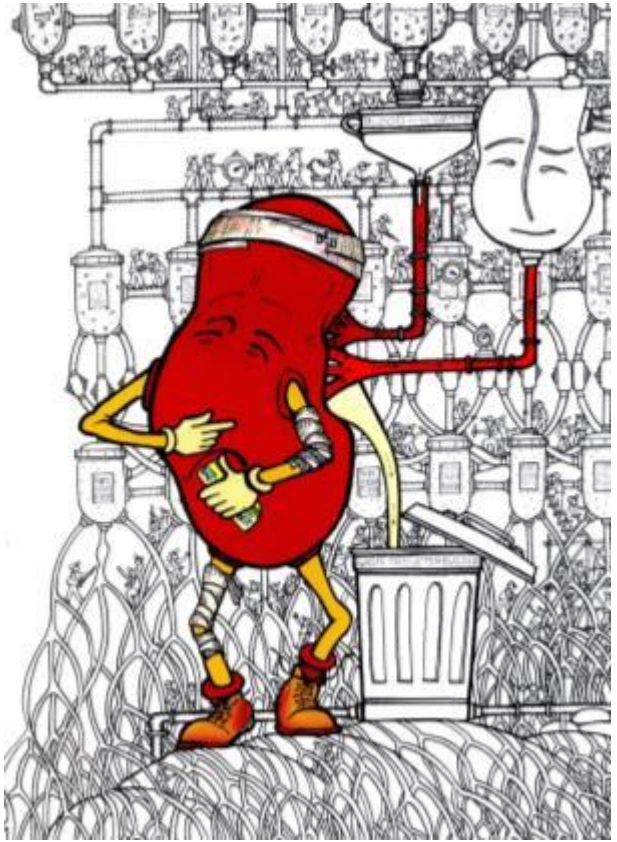





ARF in 1900: the clinical diagnosis



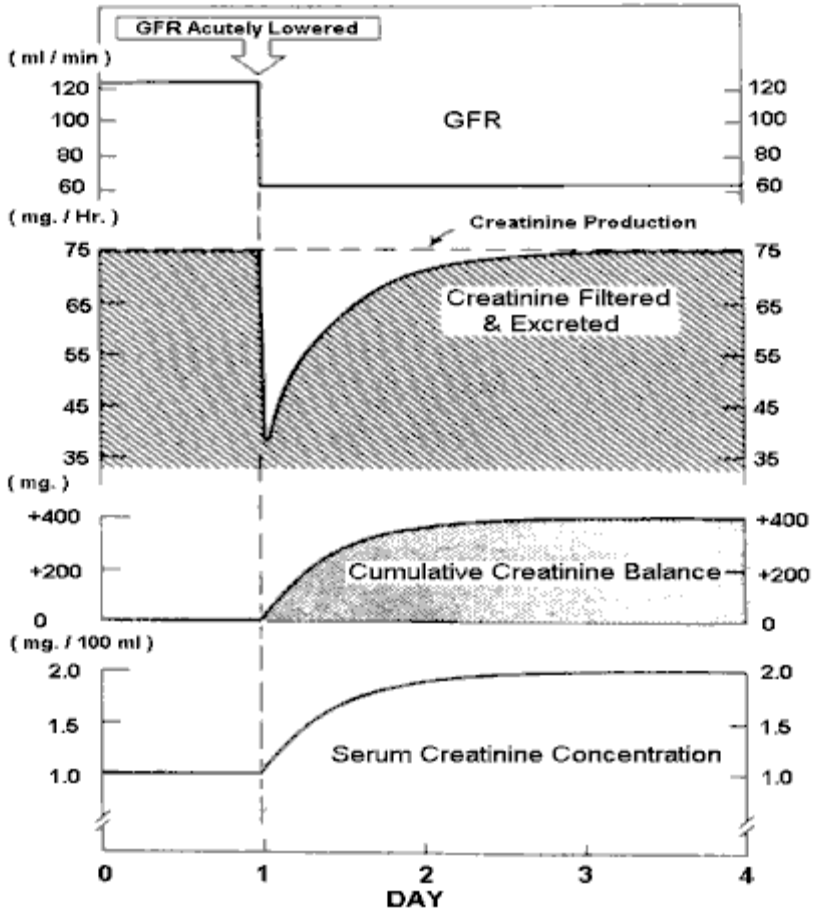
ARF was diagnosed from signs and symptoms such as oliguria, fatigue, vomiting, GI bleeding.
«Disorders of the Renal Glands»



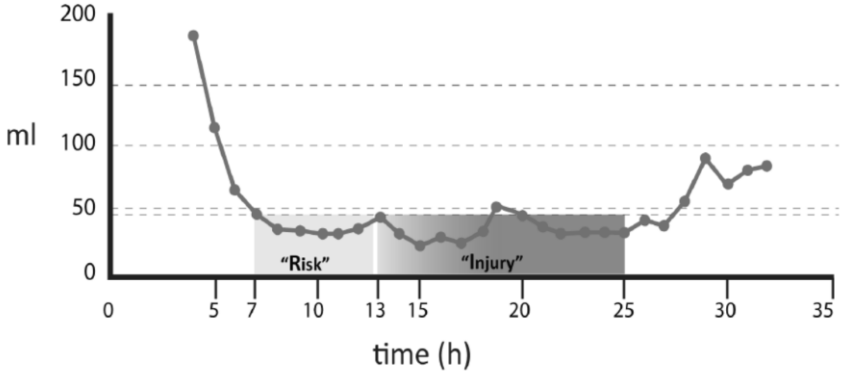
Dimitrios Petras

From a purely clinical diagnosis to the use of clinical chemistry and laboratory medicine

Creatinine Kinetics



Urine Output

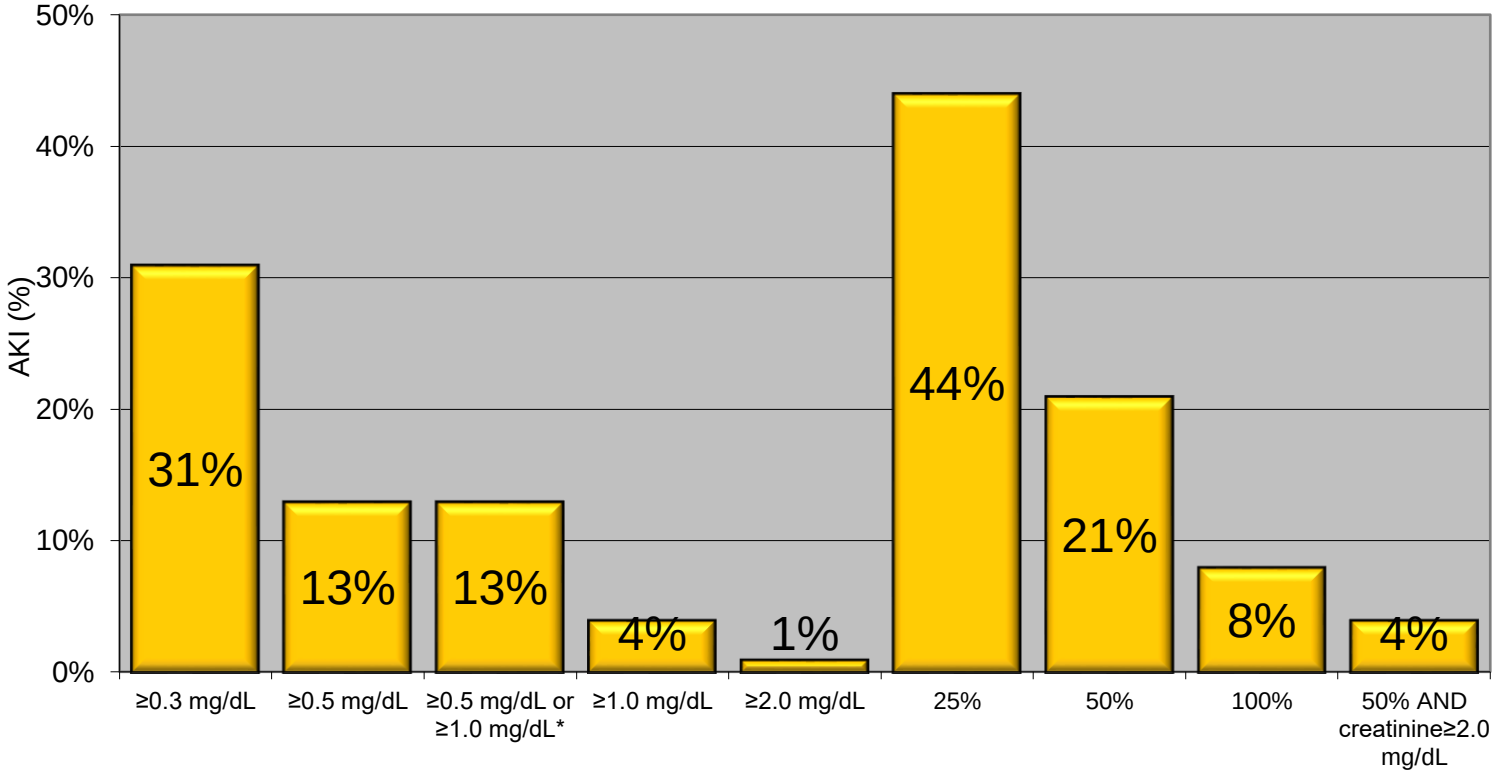


Over 30 definitions of ARF existed in the literature

1. Creat Δ 0.1 mg/dL
2. Creat increase >0.5 mg/dL
3. Creat>= 0.5 mg/dL
4. Creat >= 1.7 mg/dL
5. Creat >= 1.5 mg/dL
6. Creat >= 2 mg/dL
7. Creat>= 2.1 mg/dL and x 2
8. Creat >= 177µmol/L Δ>62µmol/L
9. Creat > 200µmol/L (2.36 mg/dL)
10. Creat> 3.2 mg/dL or x 2
11. Creat>5 mg/dL or K > 5.5
12. RIFLE
13. Creat increase >= 25%
14. Creat increase >= 50%
15. Creat increase >= 100%
16. ΔCr72h >0µmol/L
17. ΔCr72h >25µmol/L
18. ΔCr72h >44µmol/L
19. ΔCr72h >50µmol/L
20. ΔCr72h >100µmol/L
21. Cockcroft-Gault Cr Cl < 30 mL/min
22. Cockcroft-Gault Cr Cl 30–60 mL/min
23. ΔCockcroft-Gault72hr <0%
24. ΔCockcroft-Gault72hr <-15%
25. ΔCockcroft-Gault72hr <-25%
26. ΔCockcroft-Gault72hr <-50%
27. MDRD: 50% change in GFR
28. UO <100 q 8hr
29. U α1-microglob
30. U β2- microglobulin
31. U N-acetyl- β-D-glucosaminidase
32. U gluthation transferase-π
33. U gluthation transferase- α
34. NGAL
35. RRT

Incidence of AKI

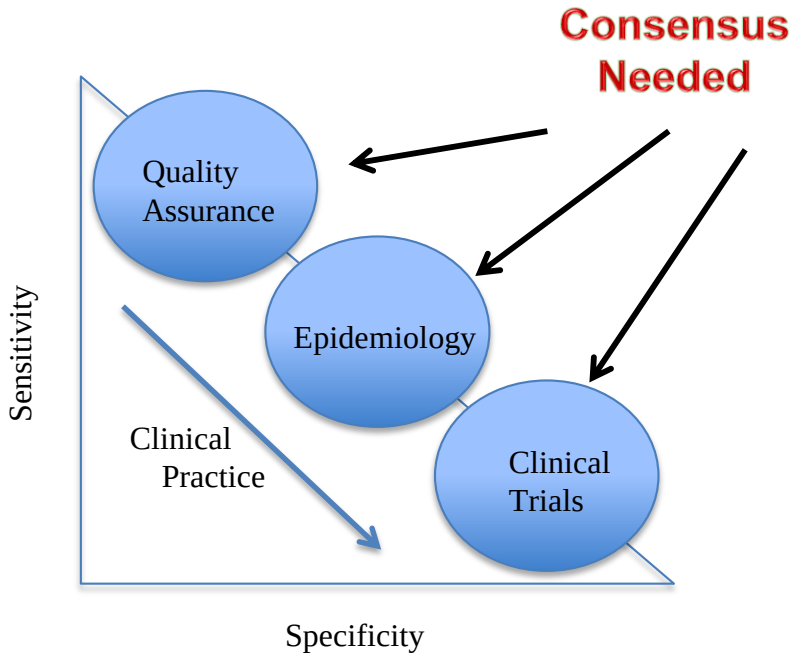
(Definition/Reporting Issues)



ADQI

ADQI, May 10-12, 2002 Vicenza

AKI Definition

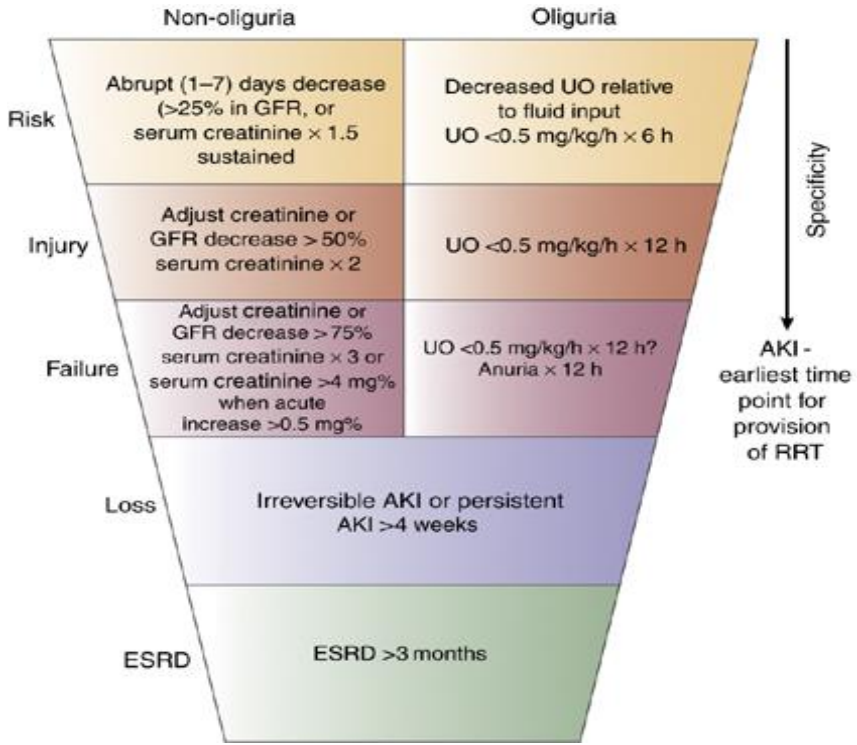


From lab results to an organic classification

RIFLE, AKIN, KDIGO

Over 30 definitions of AKI/ ARF in the literature

1. Creat Δ 0.1 mg/dL
2. Creat increase >0.5 mg/dL
3. Creat>= 0.5 mg/dL
4. Creat >= 1.7 mg/dL
5. Creat >= 1.5 mg/dL
6. Creat >= 2 mg/dL
7. Creat>= 2.1 mg/dL and x 2
8. Creat >= 177µmol/L Δ>62µmol/L
9. Creat > 200µmol/L (2.36 mg/dL)
10. Creat> 3.2 mg/dL or x 2
11. Creat>5 mg/dL or K > 5.5
12. RIFLE
13. Creat increase >= 25%
14. Creat increase >= 50%
15. Creat increase >= 100%
16. ΔCr72h >0µmol/L
17. ΔCr72h >25µmol/L
18. ΔCr72h >44µmol/L
19. ΔCr72h >50µmol/L
20. ΔCr72h >100µmol/L
21. Cockcroft-Gault Cr Cl < 30 mL/min
22. Cockcroft-Gault Cr Cl 30–60 mL/min
23. ΔCockcroft-Gault72hr <0%
24. ΔCockcroft-Gault72hr <-15%
25. ΔCockcroft-Gault72hr <-25%
26. ΔCockcroft-Gault72hr <-50%
27. MDRD: 50% change in GFR
28. UO <100 q 8hr
29. U α1-microglob
30. U β2- microglobulin
31. U N-acetyl- β-D-glucosaminidase
32. U gluthation transferase-π
33. U gluthation transferase- α
34. NGAL
35. RRT
36. ….

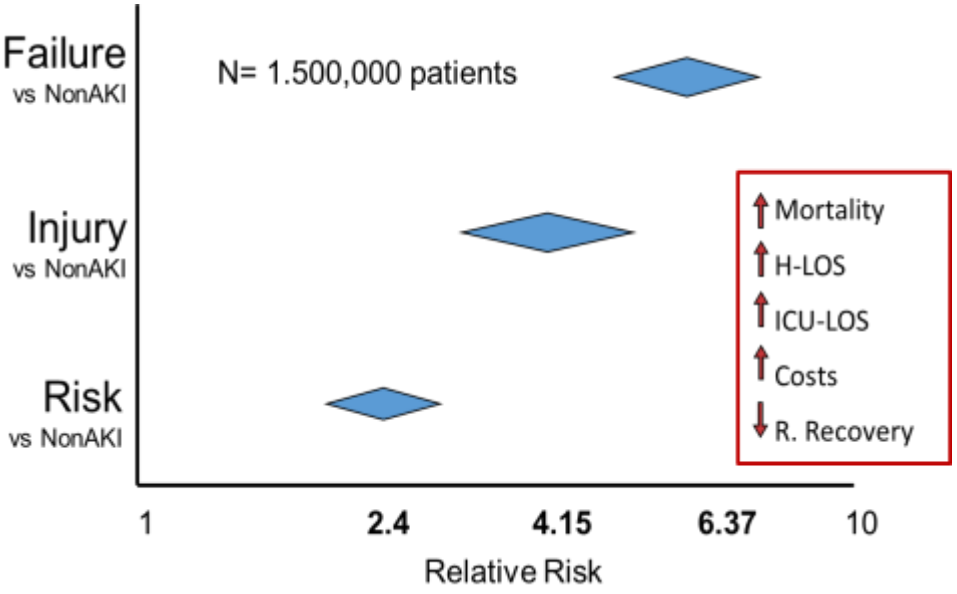


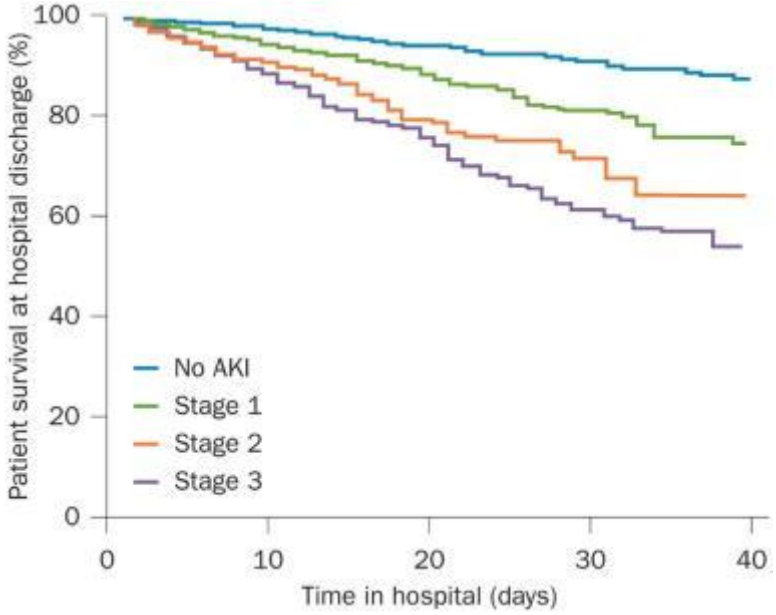
The RIFLE criteria and mortality in acute kidney injury: A systematic review

Z Ricci[1], D Cruz[2,3] and C Ronco[2,3]

[1]Department of Pediatric Cardiosurgery, Bambino Gesù Hospital, Rome, Italy; [2]Department of Nephrology, Dialysis and Transplantation, S Bortolo Hospital, Vicenza, Italy and [3]International Renal Research Institute Vicenza (IRRIV), Vicenza, Italy

Increase in All-Cause Mortality with worse RIFLE Class





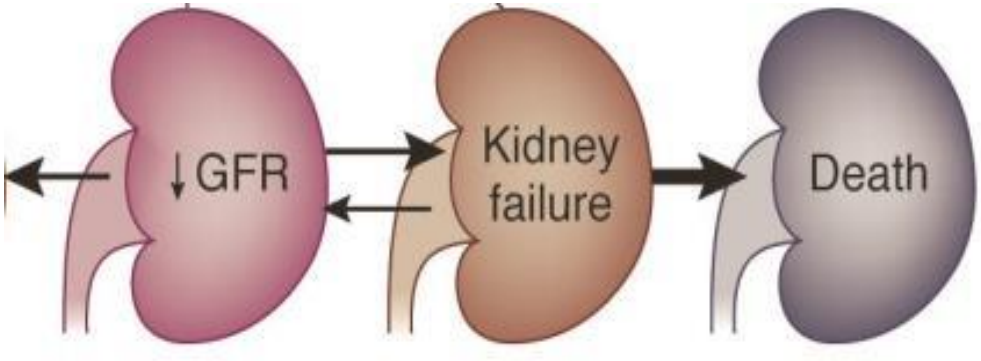
IRRIV.COM

Limitations of Creatinine as a Marker

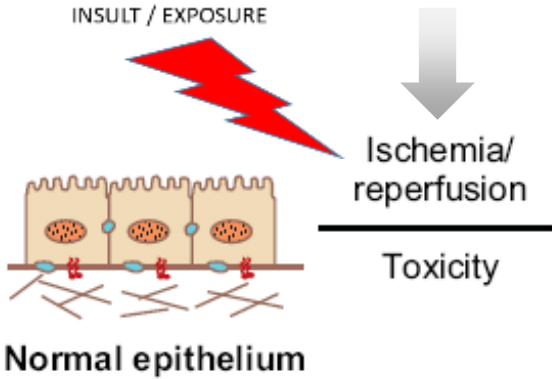
- Mainly a marker of glomerular function and not damage
- Generation is highly variable (age, sex, muscle mass and diet)
- 10-40% cleared by tubular secretion (hiding decline in GFR)
- Increases only when at least 50% of nephron mass is lost
- Drugs may impair secretion (i.e. trimethoprim, cimetidine).
- Actual levels do not depict real-time changes in GFR (leading to possible delay in diagnosis)

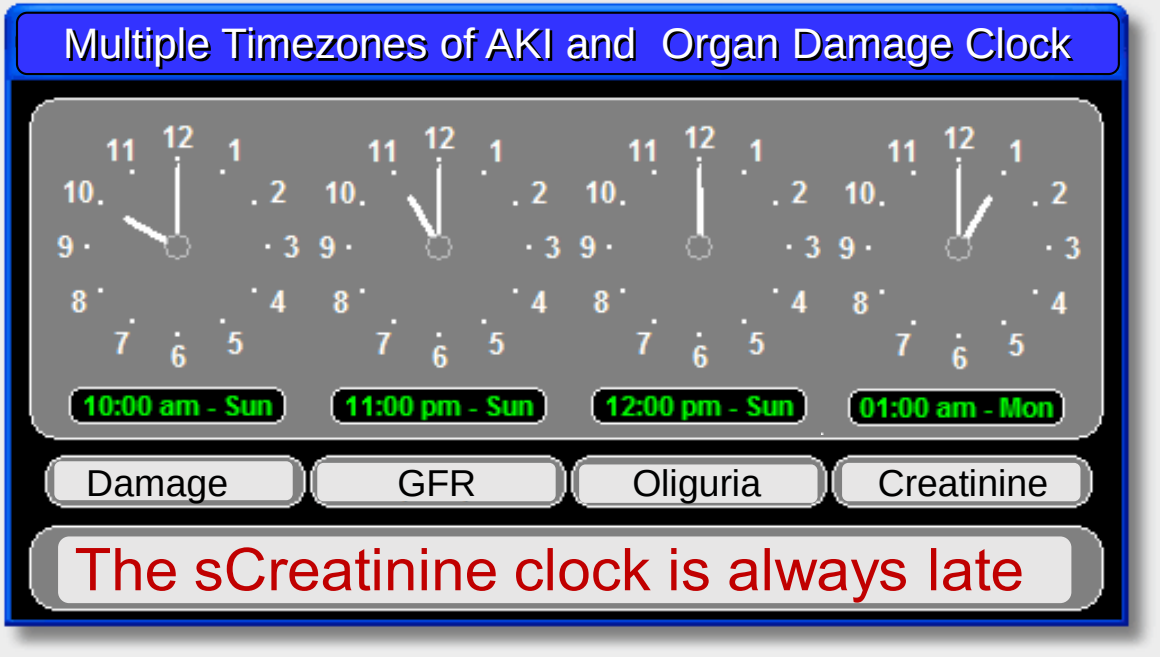
KDIGO Definition of AKI

?

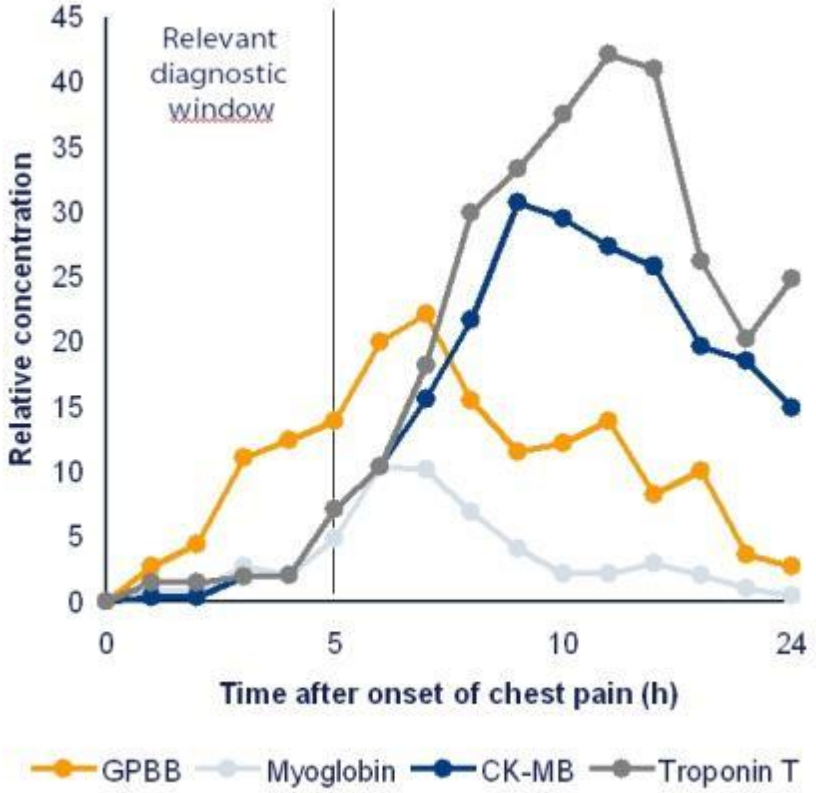


Stage 1	Stage 2	Stage 3
Δ sCr > 0.3 mg/dL	sCr x 2	sCr x 3

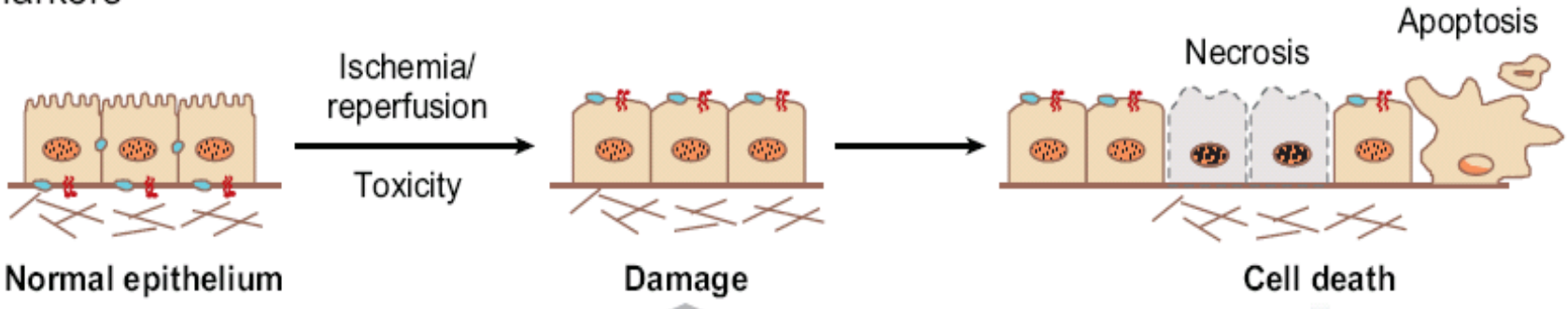

INSULT / EXPOSURE
Ischemia/
reperfusion
Toxicity
Normal epithelium

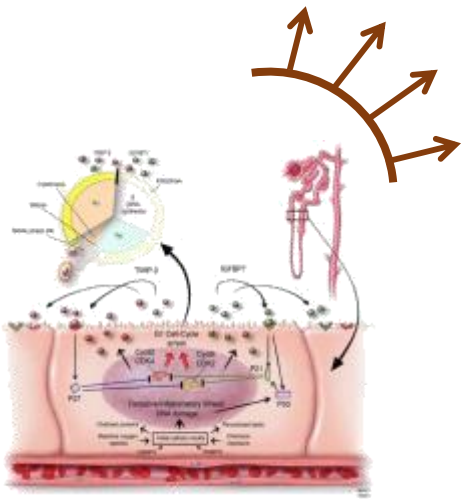

Multiple Timezones of AKI and Organ Damage Clock
10:00 am - Sun
11:00 pm - Sun
12:00 pm - Sun
01:00 am - Mon
Damage
GFR
Oliguria
Creatinine
The sCreatinine clock is always late

Why not learning from Cardiology?



Biomarkers





TIMP-2 - IGFBP7

Potential urinary biomarkers for early diagnosis of AKI

NAG	NGAL
β_2M	CYR-61
α_1M	IL-18
RBP	OPN
Cystatin C	FABP
KIM-1	NHE3
Clusterin	Fetuin A
Microalbumin	

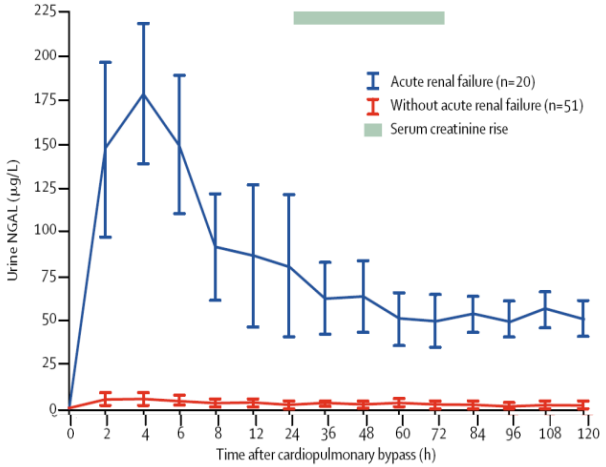
↓GFR

Delayed biomarkers for kidney injury

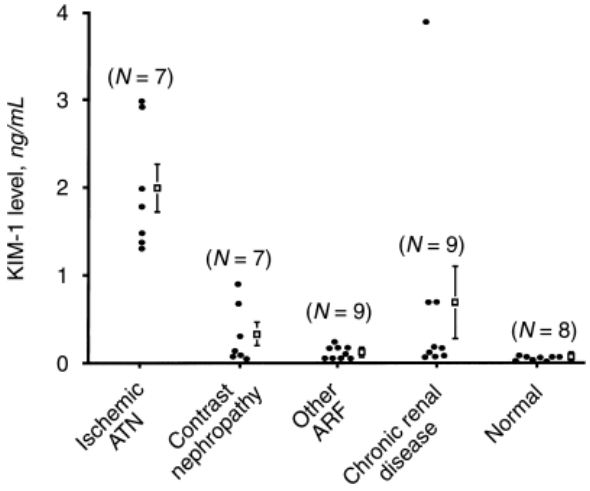
- ↑ Serum creatinine
- ↑ Blood urea nitrogen

AKI Biomarkers

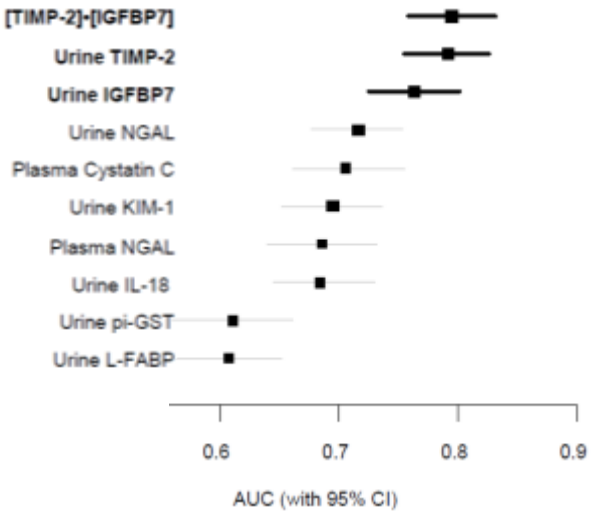
NGAL



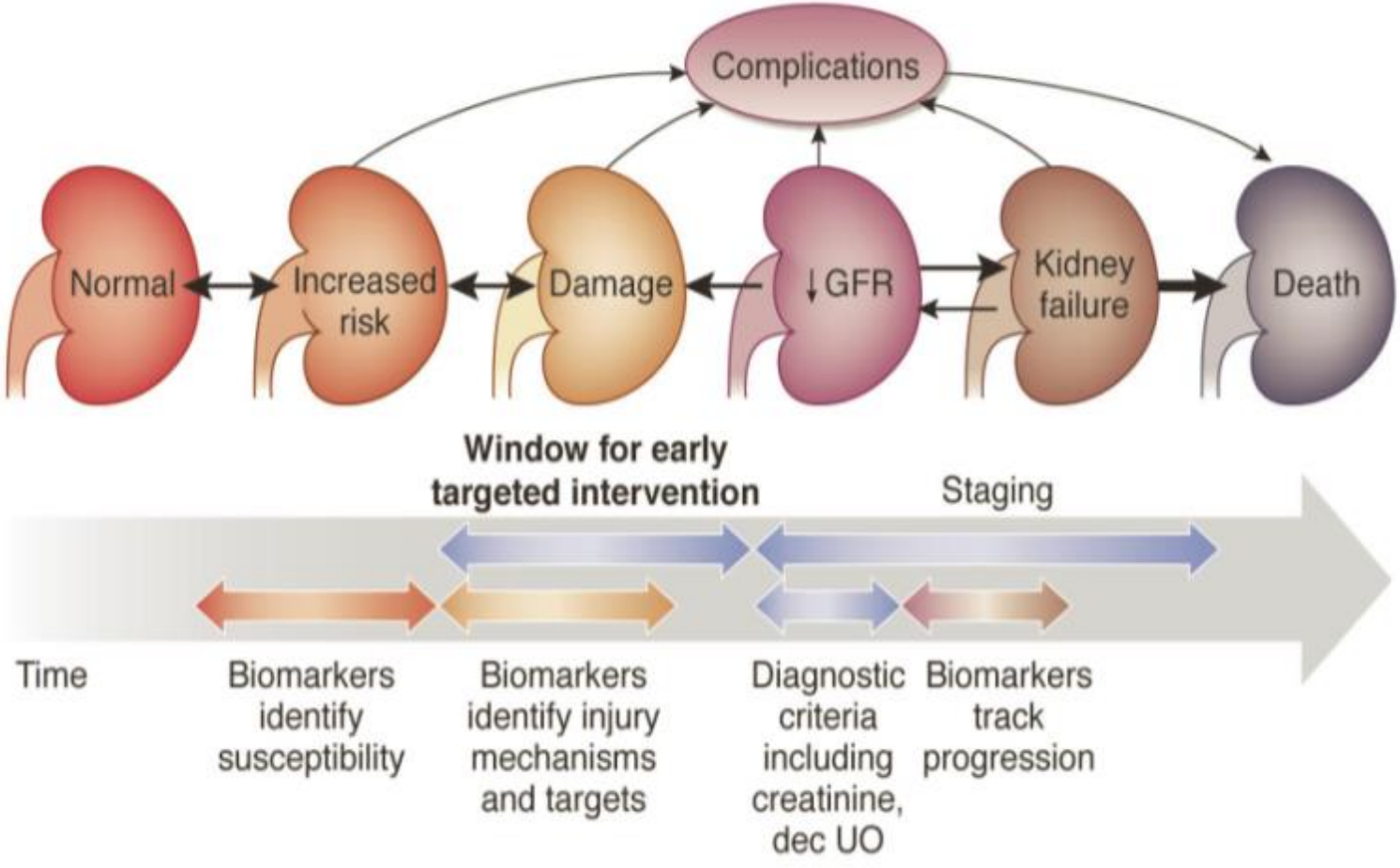
KIM - 1



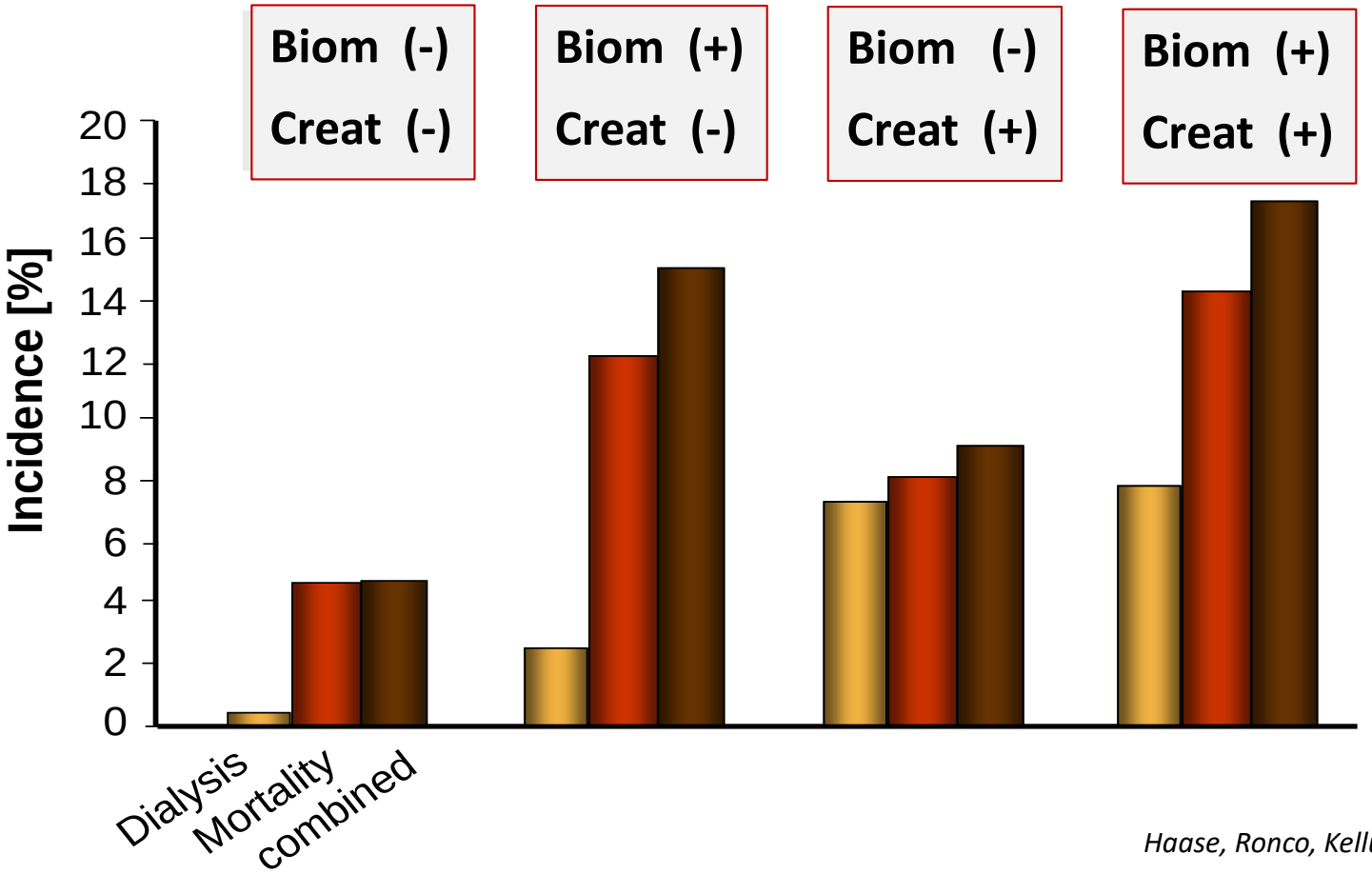
Nephrocheck



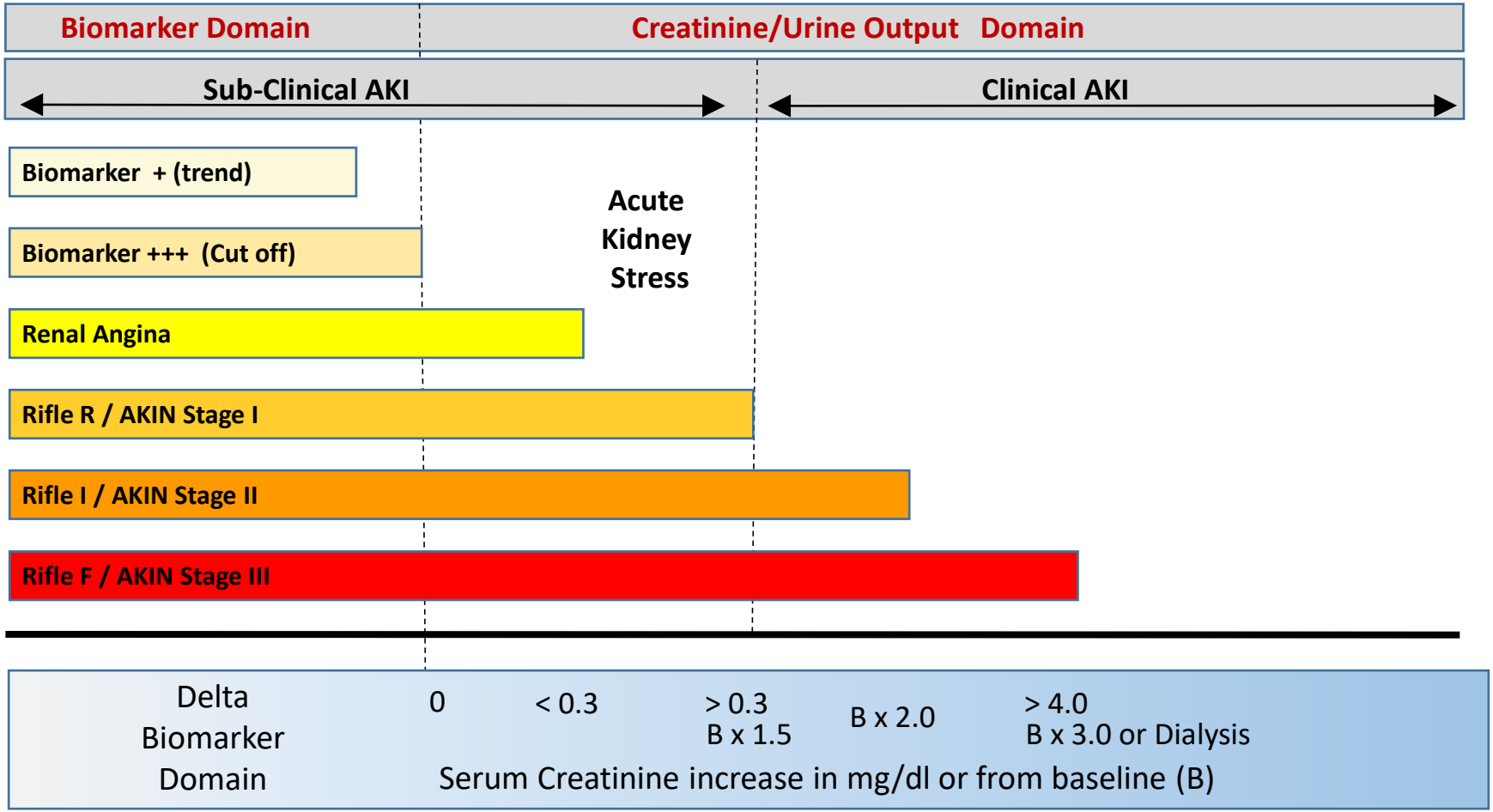
The Rise of AKI Biomarkers



Creatinine, Biomarkers and AKI outcomes



Haase, Ronco, Kellum: JACC 2012


Biomarker Domain
Creatinine/Urine Output Domain
Sub-Clinical AKI
Clinical AKI
Biomarker + (trend)
Biomarker +++ (Cut off)
Renal Angina
Rifle R / AKIN Stage I
Rifle I / AKIN Stage II
Rifle F / AKIN Stage III
Acute Kidney Stress
Delta Biomarker Domain
0
< 0.3
> 0.3 B x 1.5
B x 2.0
> 4.0 B x 3.0 or Dialysis
Serum Creatinine increase in mg/dl or from baseline (B)

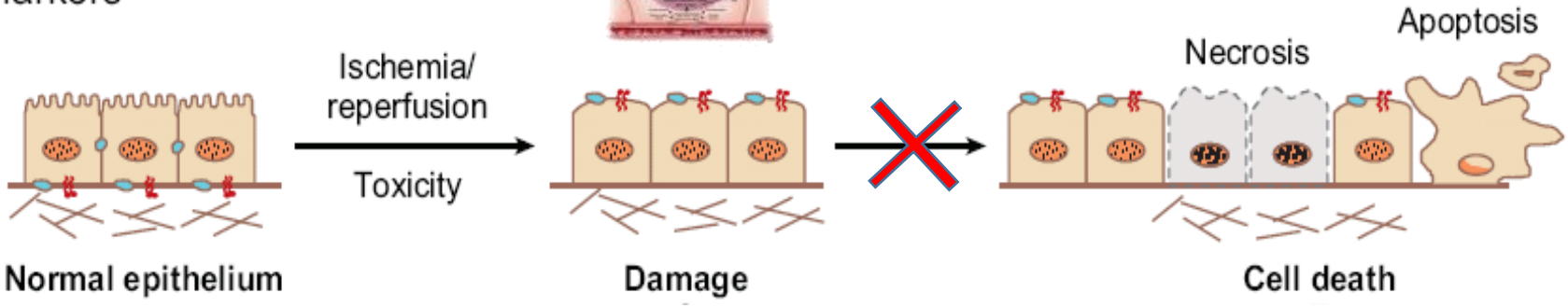
JAMA Network | Open.

Consensus Statement | Critical Care Medicine

Recommendations on Acute Kidney Injury Biomarkers From the Acute Disease Quality Initiative Consensus Conference
A Consensus Statement

Functional criteria	Stage	Damage criteria
No change or sCr level increase <0.3 mg/dL and no UO criteria	1S	Biomarker positive
Increase of sCr level by ≥0.3 mg/dL for ≤48 h or ≥150% for ≤7 days and/or UO <0.5 mL/kg/h for >6 h	1A	Biomarker negative
	1B	Biomarker positive
Increase of sCr level by >200% and/or UO <0.5 mL/kg/h for >12 h	2A	Biomarker negative
	2B	Biomarker positive
Increase of sCr level by >300% (≥4.0 mg/dL with an acute increase of ≥0.5 mg/dL) and/or UO <0.3 mL/kg/h for >24 h or anuria for >12 h and/or acute KRT	3A	Biomarker negative
	3B	Biomarker positive

Biomarkers



ACUTE KIDNEY INJURY

AKI: the myth of inevitability is finally shattered

John A. Kellum

Acute kidney injury continues to challenge physicians, researchers and patients. To date, there is no efficient treatment for acute kidney injury and its occurrence in many critically ill patients seems inevitable. However, a new study might just change the way we approach this seemingly intractable problem.

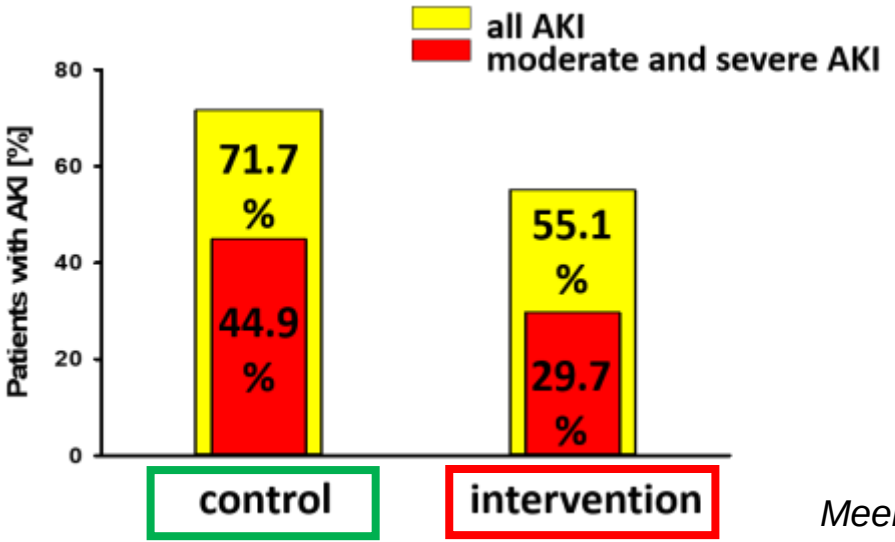
PREVAKI

Measuring [TIMP2]*[IGFBP7] 4h after cardiac surgery: if [TIMP2]*[IGFBP7] is ≥ 0.3

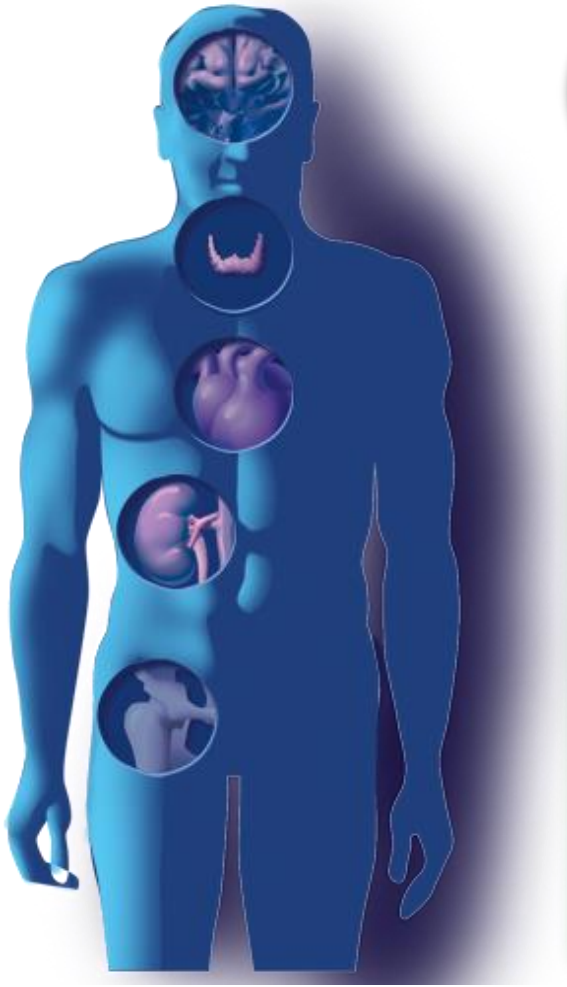
↓

Randomization

Control group (Standard) | Intervention group (KDIGO)



Meersch M, ICM 2017



The Biomarker Alliance and the Nephrology Rapid Response Team

Our Pathway to Adoption of Biomarkers

2014 Clincal Prediction Model

2015 Additional Value of BM

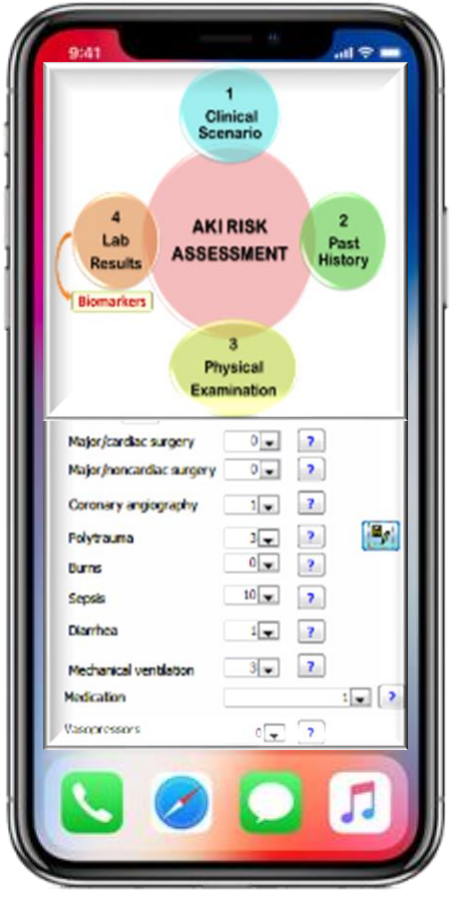
2016 BM + intervention (NRRT)

2017 Routine Adoption (analysis)


IRRIV
Ospedale San Bortolo – Vicenza
Laboratorio
di Analisi Cliniche e Microbiologiche
NEPHROLOGY RAPID RESPONSE TEAM
Paziente: Franco Pavan
Reparto: Terapia Intensiva
Letto: 11/b
Diagnosi: Politrauma
Nephrocheck
Alarm
0.1
17 Settembre 2016 Ore: 06.45


IRRIV
Ospedale San Bortolo – Vicenza
Laboratorio
di Analisi Cliniche e Microbiologiche
NEPHROLOGY RAPID RESPONSE TEAM
Paziente: Giovanni Rossi
Reparto: Cardiochirurgia
Letto: 17/a
Diagnosi: Bypass Coronarico
Nephrocheck
Alarm
4.7
17 Settembre 2016 Ore: 07.26


9:41
Tuesday
12
Mail
Calendar
Photos
Camera
Maps
Clock
Weather
News
Home
Notes
Stocks
Reminders
TV
App Store
iTunes Store
iBooks
Health
Wallet
Settings



F1 Clinical Scenario | F2 Past History | F3 Physical Examination | F4 Laboratory

F1 Clinical Scenario

Codice 0

Major/cardiac surgery	0	?
Major/noncardiac surgery	0	?
Coronary angiography	1	?
Polytrauma	3	?
Burns	0	?
Sepsis	10	?
Diarrhea	1	?
Mechanical ventilation	3	?
Medication	1	?
Vasopressors	0	?
Contrast media	0	?

Pazients | F1 Clinical Scenario | F2 Past History | F3 Physical Examination | F4 Laboratory

F2 Clinical History

id 0

Age >65	1		Previous AKI	5	
Low income country	1		Heart failure	0	?
Black race	0		Liver disease	0	?
BMI =>30 kg/m2	0		lung disease	5	?
Diabetes	0	?	Cancer	0	? e
Hypertension	0		Medications and or Nephrotoxins	0	?
CKD	0	?			

ents | F1 Clinical Scenario | F2 Past History | F3 Physical Examination

F3 Physical Examination

Codice 0

Hemodynamic instability	0	?
HR	0	?
MAP	0	?
Dehydration	0	?
Peripheral edema .... Ascites Rales	0	?
Urinary output <=0,5 ml/kg/h for 6-12 hours	0	

ents | F1 Clinical Scenario | F2 Past History | F3 Physical Examination | F4 Laboratory

F4 Clinical Chemistry & Biomarkers

Codice 0

Serum creatinine or Urine	0	?
e GFR <60 ml/m'	0	
Anemia (HB <11 g/dl)	0	
Proteinuria >300 G/+	0	
Hematuria	0	
CPK U/l	0	
+AKI biomarkers	0	?

Report

Score

28

AKI Risk Assessment

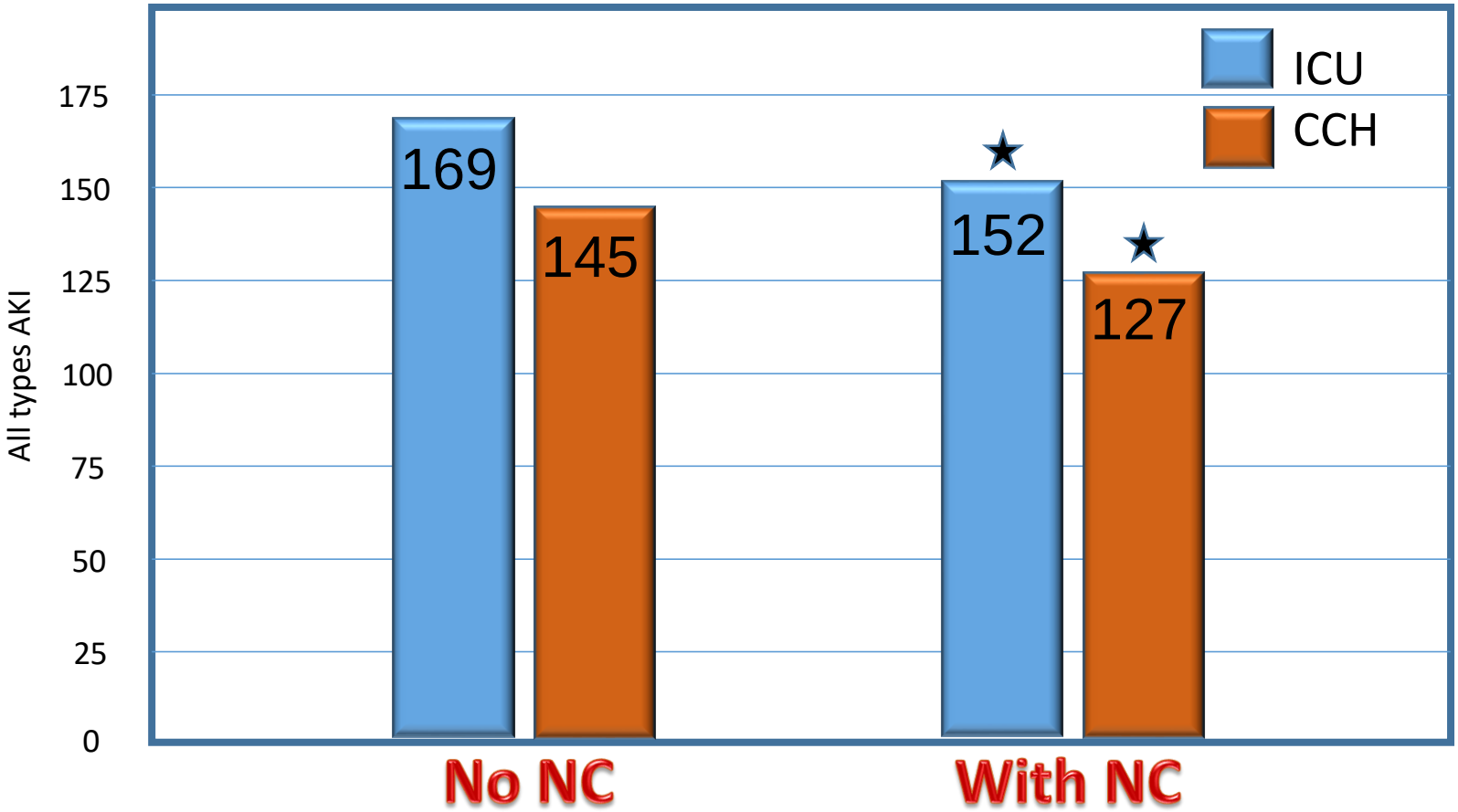
ARA Moderate

INPUT

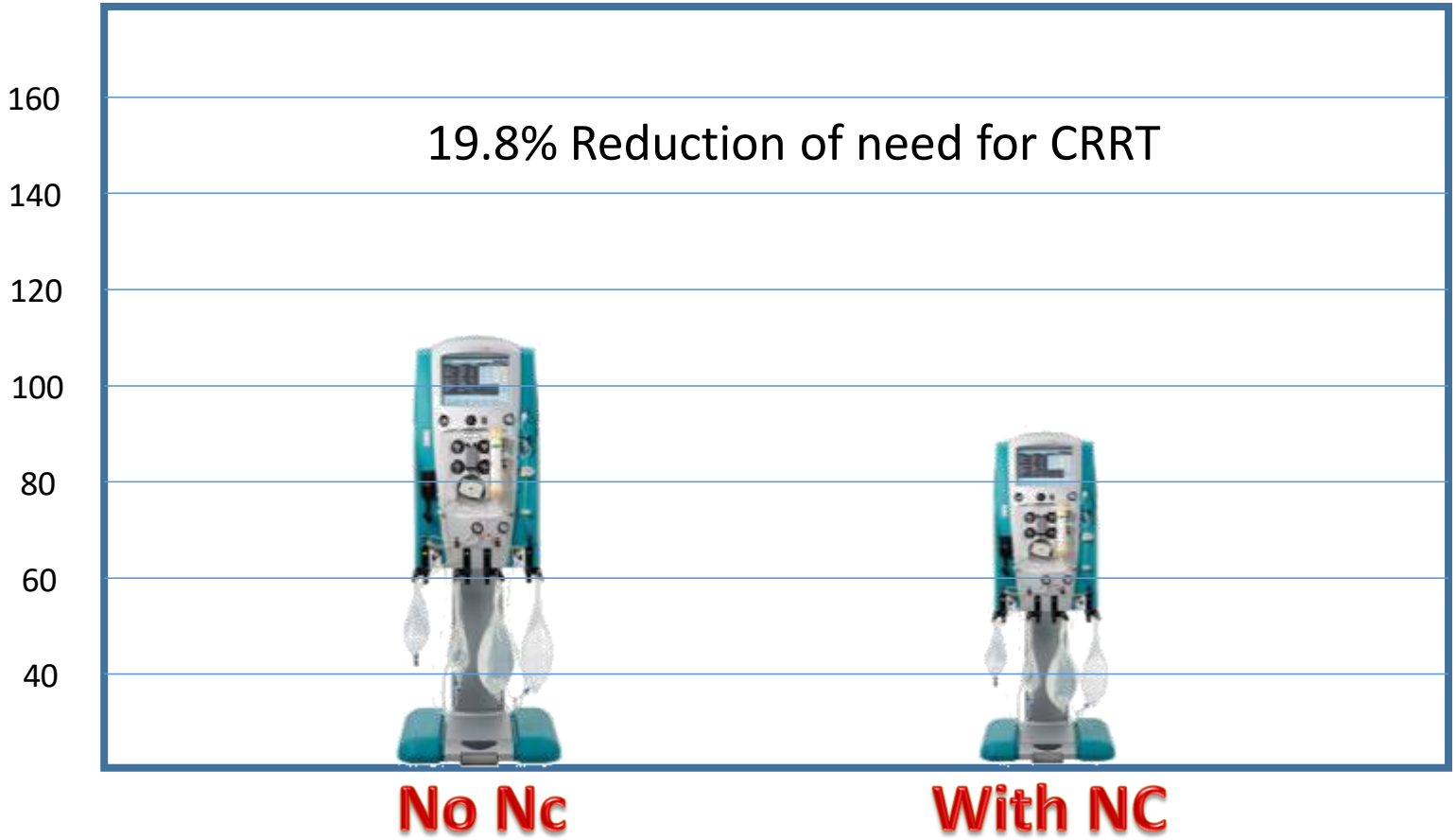
Checklist

Bundle

Vicenza NRRT Study



Number of Patients requiring CRRT



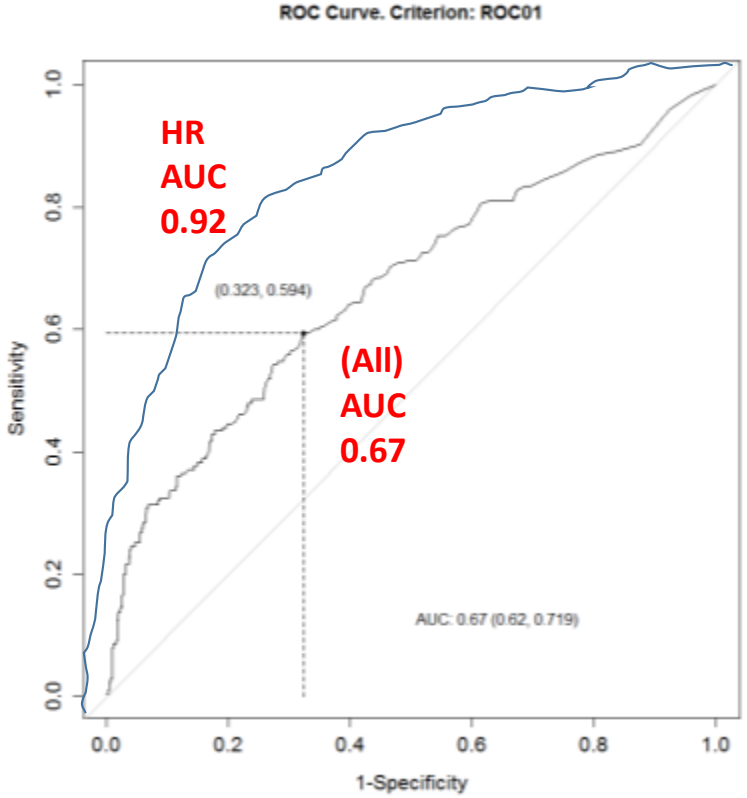
ROC

(All patients admitted to ICU versus high risk patients)

- Number of optimal cutoffs: 1

	Estimate	95% CI lower limit	95% CI upper limit
cutoff	0.5900000	-	-
Se	0.5942857	0.5175908	0.6677304
Sp	0.6770833	0.6332154	0.7187528
PPV	0.4015444	0.3558555	0.4793100
NPV	0.8207071	0.7702682	0.8480037
DLR.Positive	1.8403687	1.5399260	2.1994282
DLR.Negative	0.5992088	0.4956900	0.7243462
FP	155.0000000	-	-
FN	71.0000000	-	-
Optimal criterion	0.2688793	-	-

Optimal NC Cut-off value for All patients is 0.59



CardioRenal Medicine

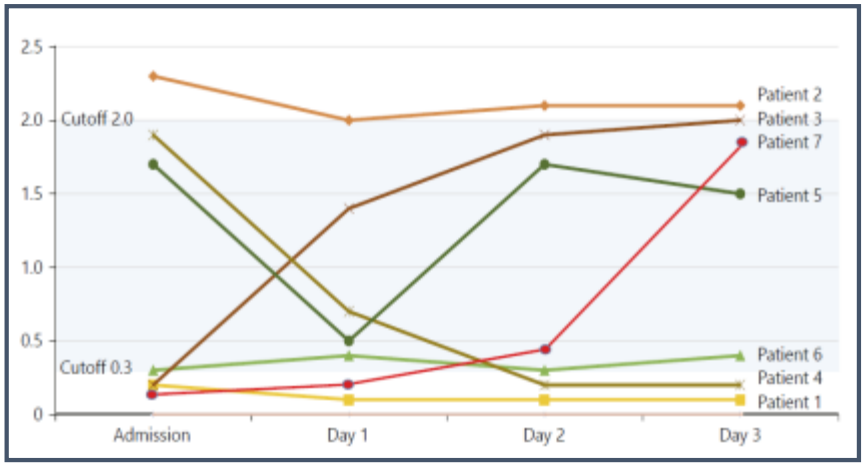
Cardiorenal Med
DOI: 10.1159/000503443
Received: September 16, 2019
Accepted: September 16, 2019
Published online: October 16, 2019

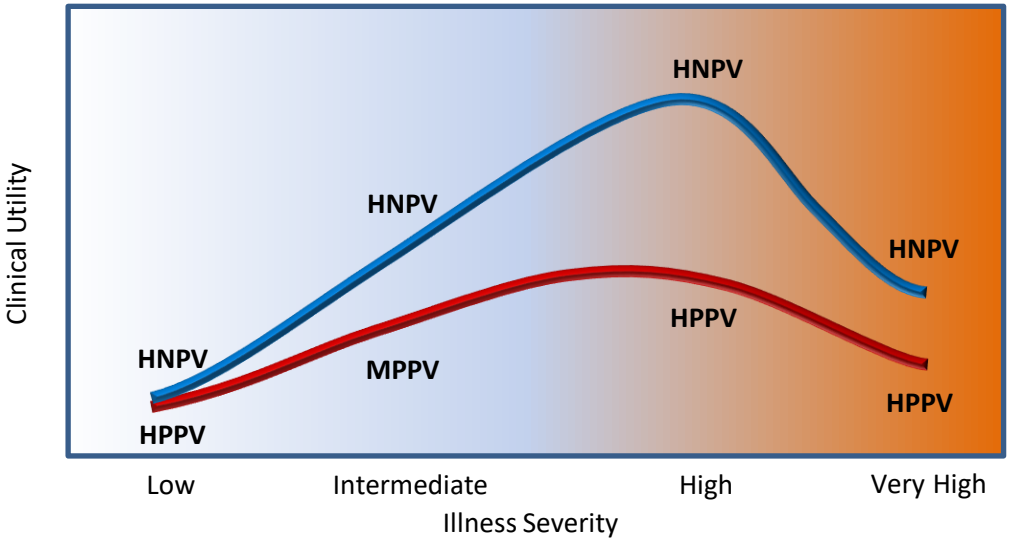
Editorial

Acute Kidney Injury Biomarkers: Are We Ready for the Biomarker Curve?

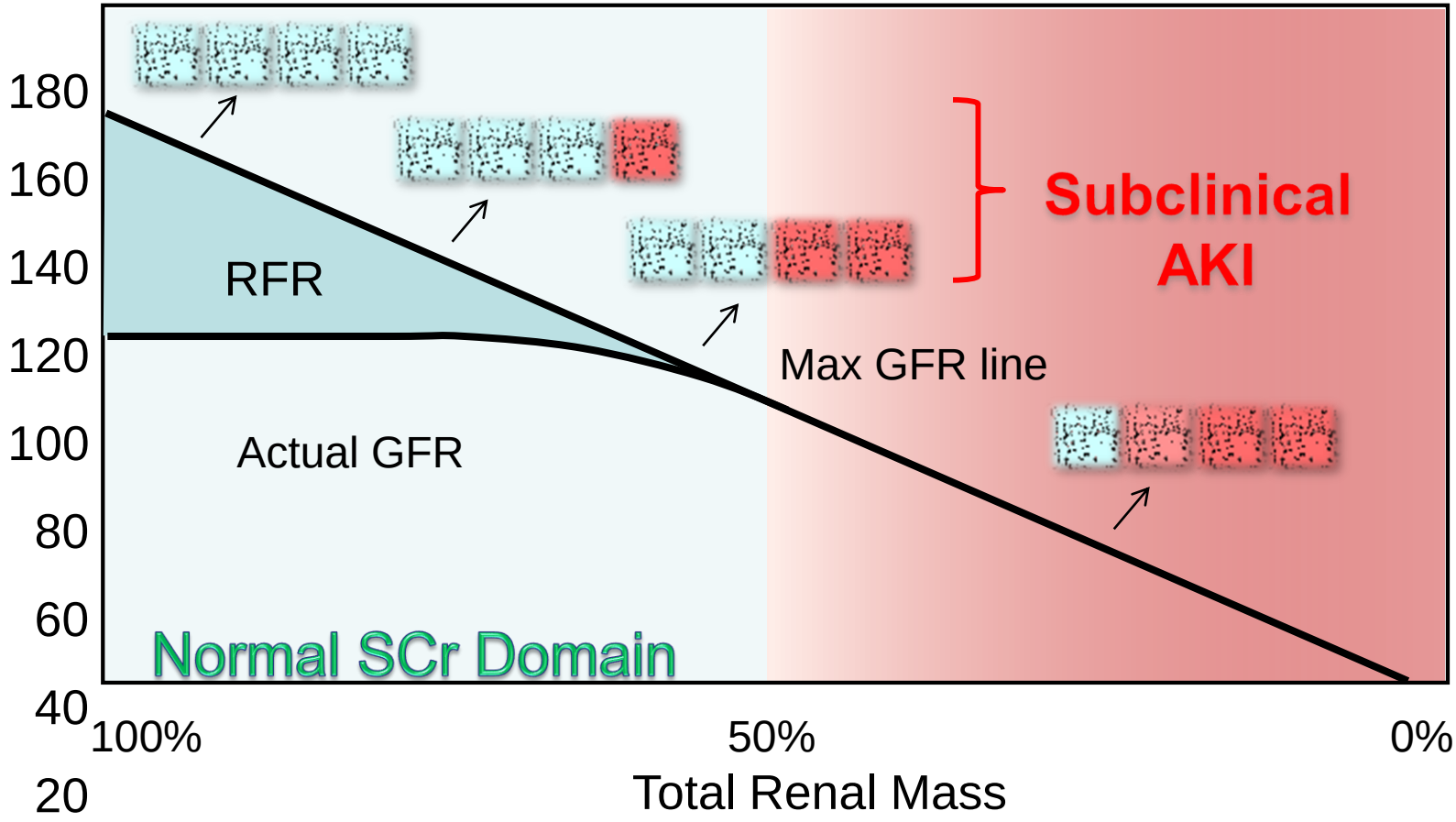
Claudio Ronco

Department of Medicine, University of Padua, San Bortolo Hospital, Vicenza, Italy

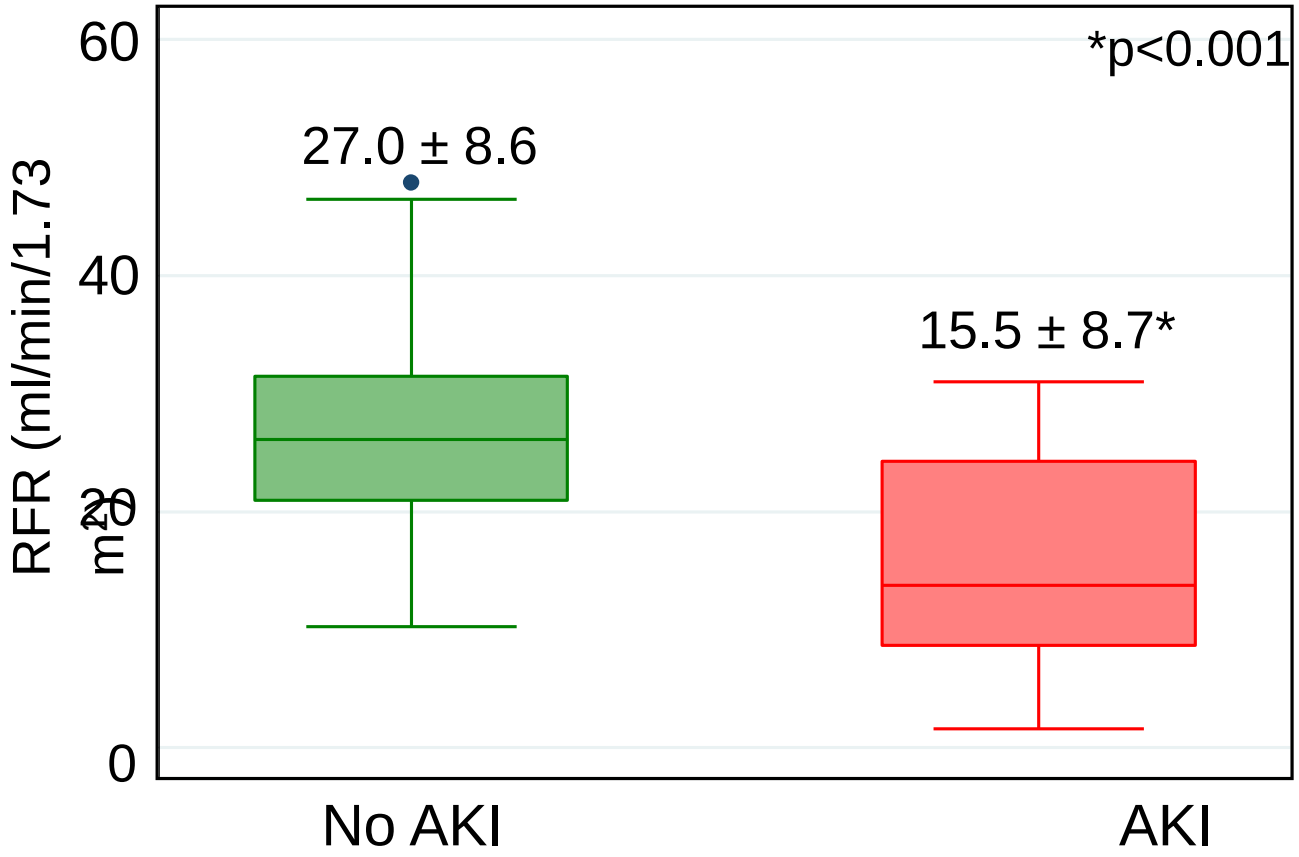




Creatinine and GFR



Preoperative RFR in patients without AKI versus AKI

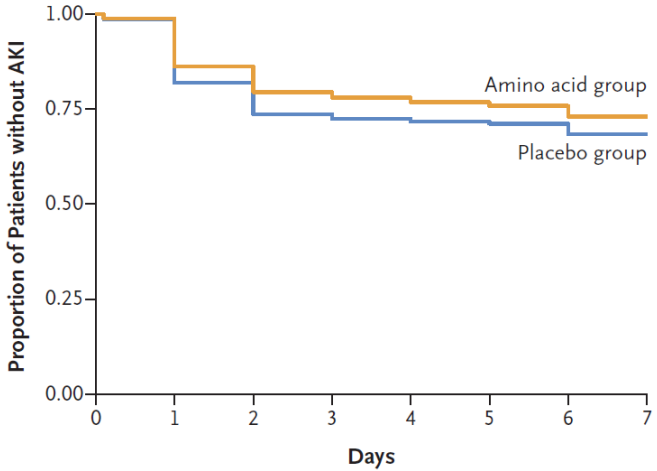


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Intravenous Amino Acids for Kidney Protection

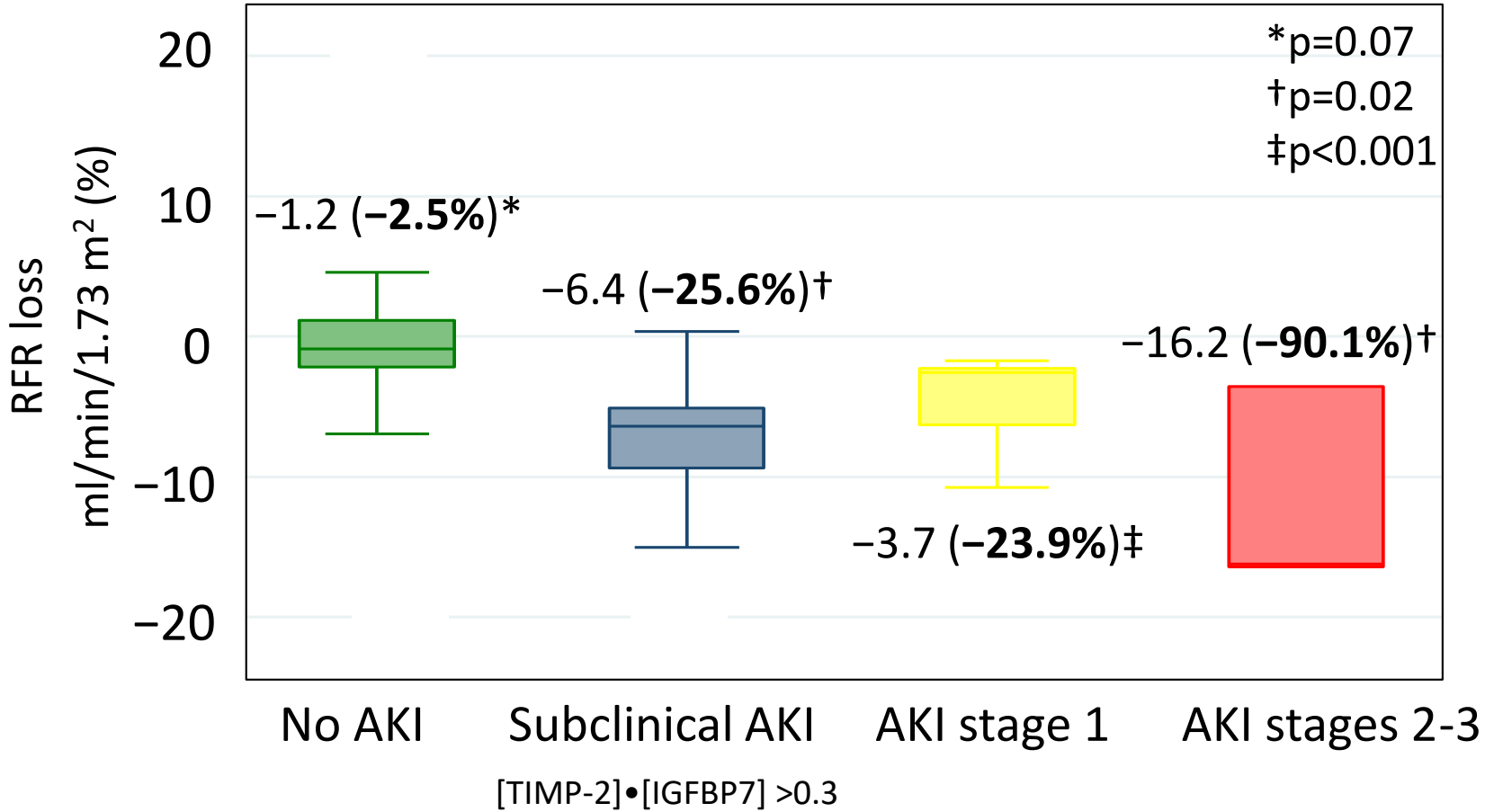
G. Landoni, F. Monaco, L.K. Ti, M. Baiardo Redaelli, N. Bradic, M. Comis,

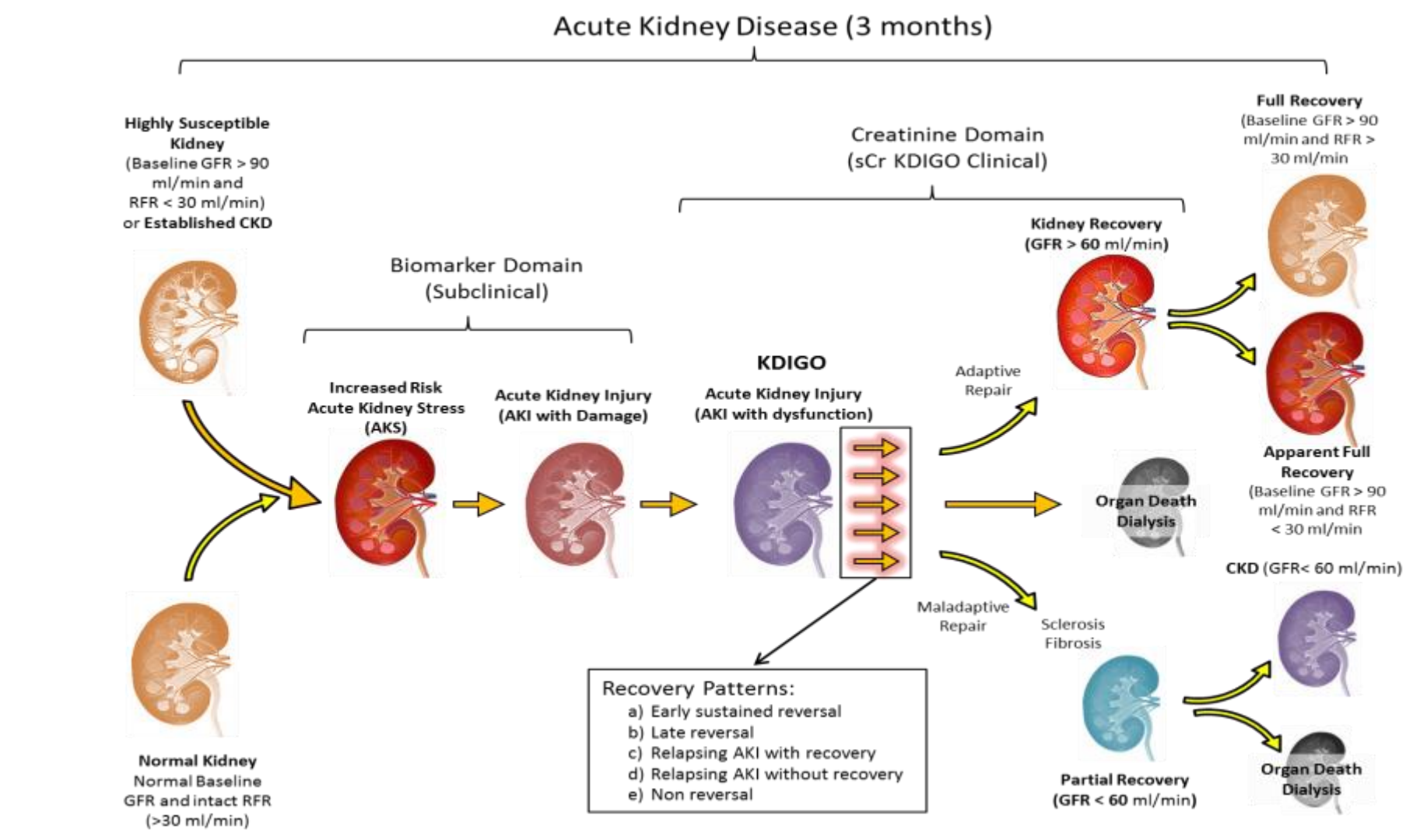


Among adult patients undergoing cardiac surgery, infusion of amino acids reduced the occurrence of AKI.

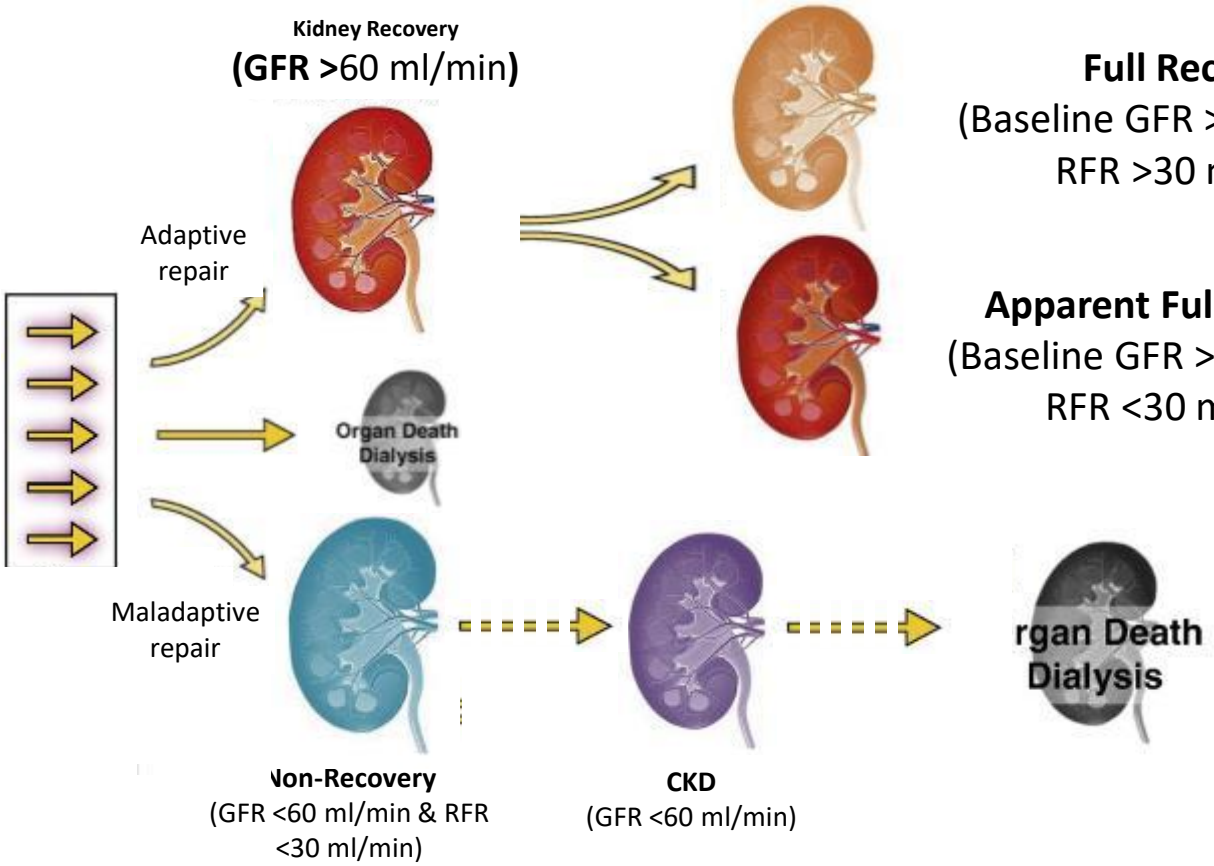
(PROTECTION ClinicalTrials.gov number, NCT03709264.)

RFR loss in patients with AKI and subclinical AKI (3 months follow up)




Acute Kidney Disease (3 months)
Highly Susceptible Kidney
(Baseline GFR > 90 ml/min and RFR < 30 ml/min) or Established CKD
Biomarker Domain
(Subclinical)
Creatinine Domain
(sCr KDIGO Clinical)
Increased Risk Acute Kidney Stress (AKS)
Acute Kidney Injury (AKI with Damage)
KDIGO
Acute Kidney Injury (AKI with dysfunction)
Kidney Recovery (GFR > 60 ml/min)
Full Recovery
(Baseline GFR > 90 ml/min and RFR > 30 ml/min
Adaptive Repair
Organ Death Dialysis
Apparent Full Recovery
(Baseline GFR > 90 ml/min and RFR < 30 ml/min
CKD (GFR< 60 ml/min)
Maladaptive Repair
Sclerosis Fibrosis
Partial Recovery
(GFR < 60 ml/min)
Organ Death Dialysis
Recovery Patterns:
a) Early sustained reversal
b) Late reversal
c) Relapsing AKI with recovery
d) Relapsing AKI without recovery
e) Non reversal
Normal Kidney
Normal Baseline GFR and intact RFR (>30 ml/min)

Renal Recovery

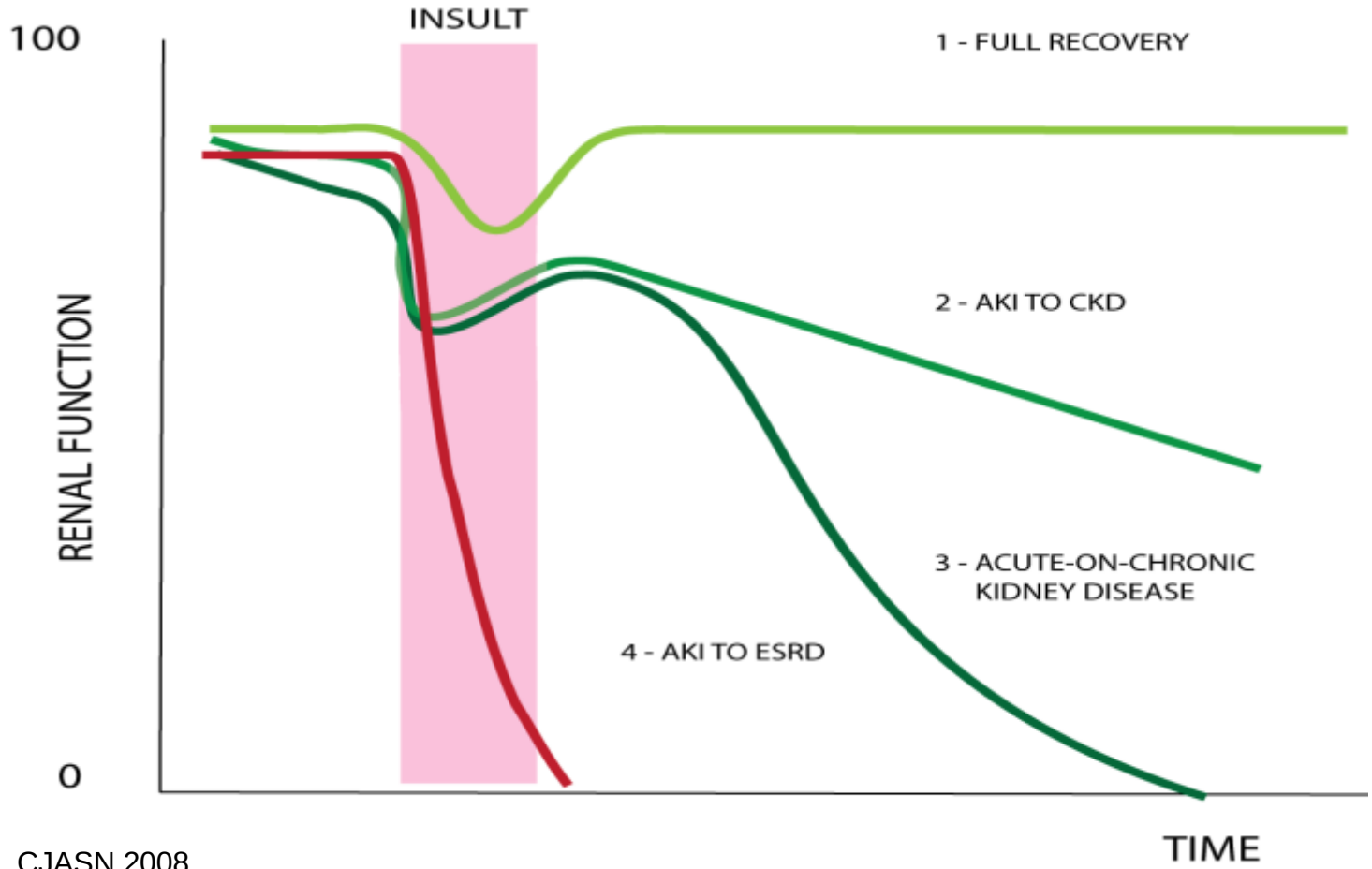


Full Recovery
(Baseline GFR >90 ml/min & RFR >30 ml/min)

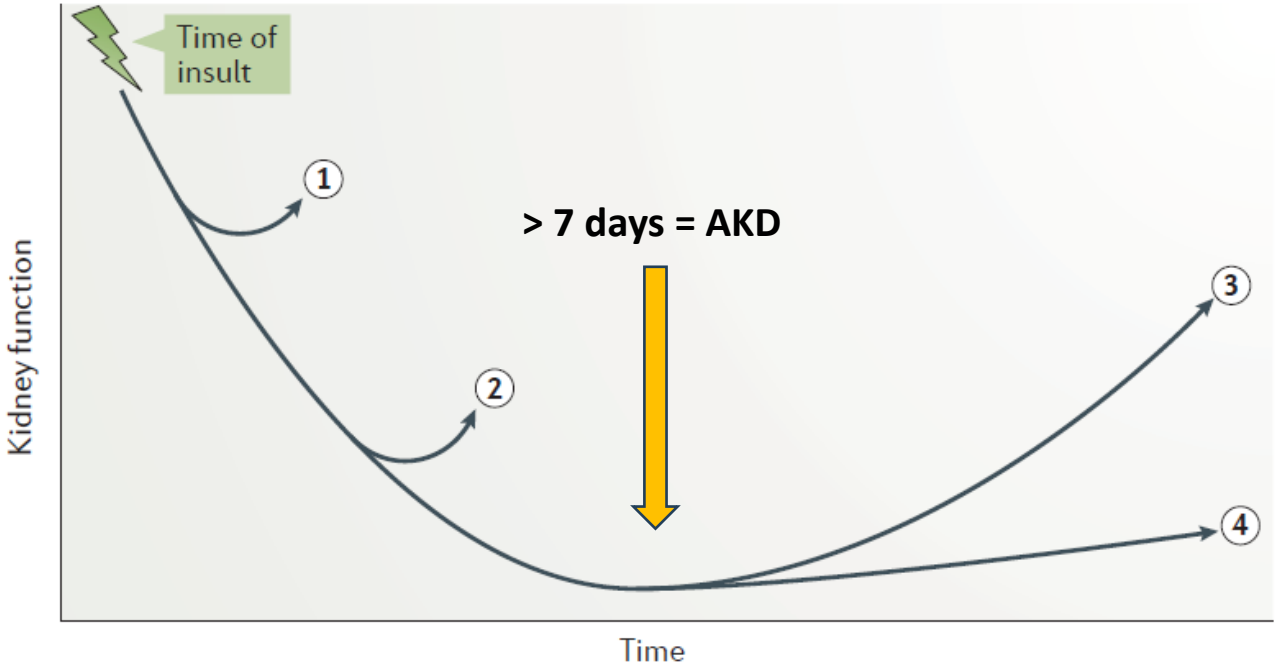
Apparent Full Recovery
(Baseline GFR >90 ml/min & RFR <30 ml/min)

Ronco C et al. Am J Respir Crit Care Med 2017

Natural History of AKI



Cerda et al, CJASN 2008



Biomarker, GFR and imaging assessments throughout the clinical course

- Individualized risk based adjustment
- Adjust renally excreted medications, avoid or withdraw nephrotoxic medications
- Withdraw drugs with active metabolites
- Introduce or re-introduce medications
- Consider drugs with renoprotective properties

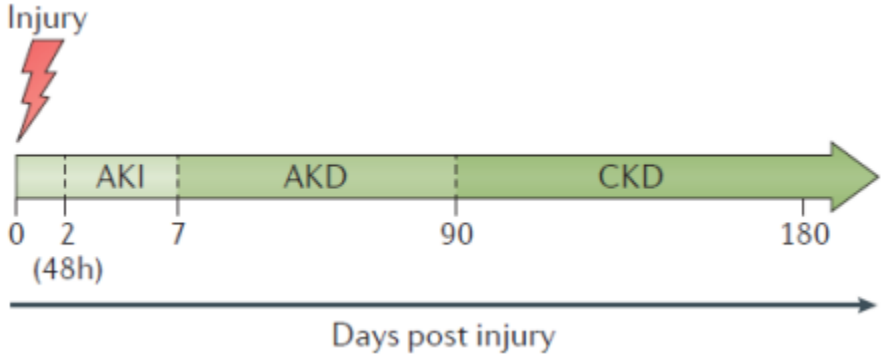
Renal Recovery

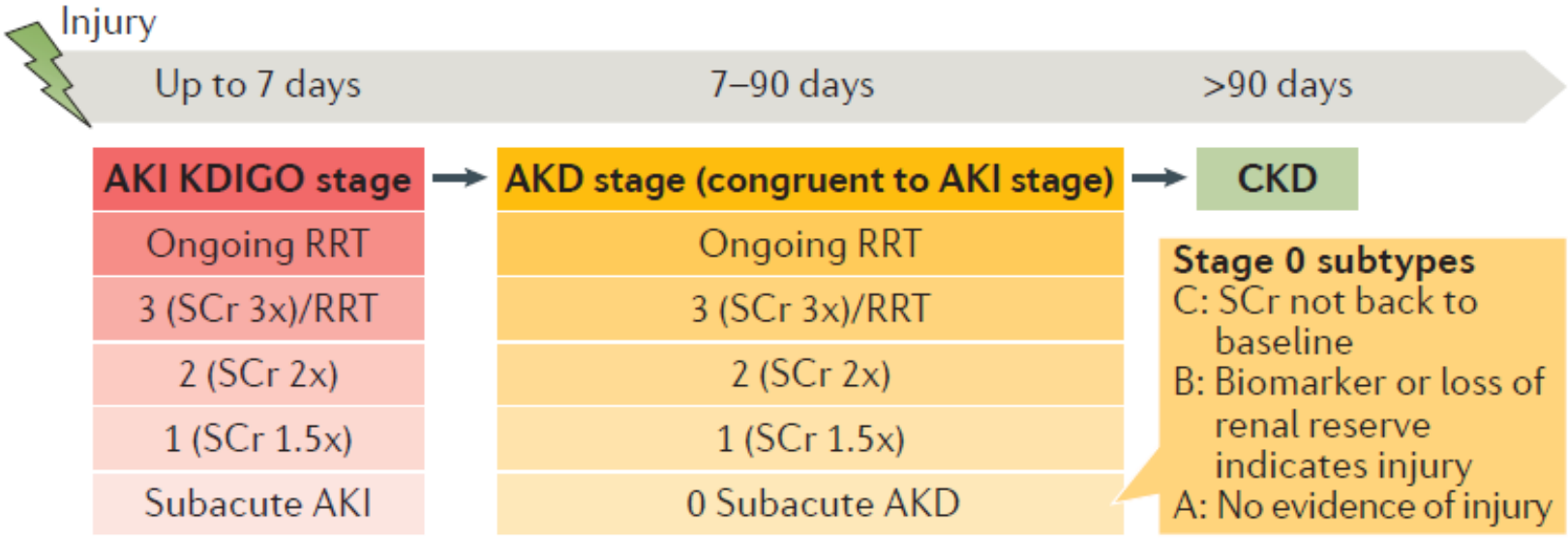
Renal Recovery in patients with AKI who are treated with RRT is defined as sustained (>14days) independence from RRT

Updating and implementing AKD Nomenclature

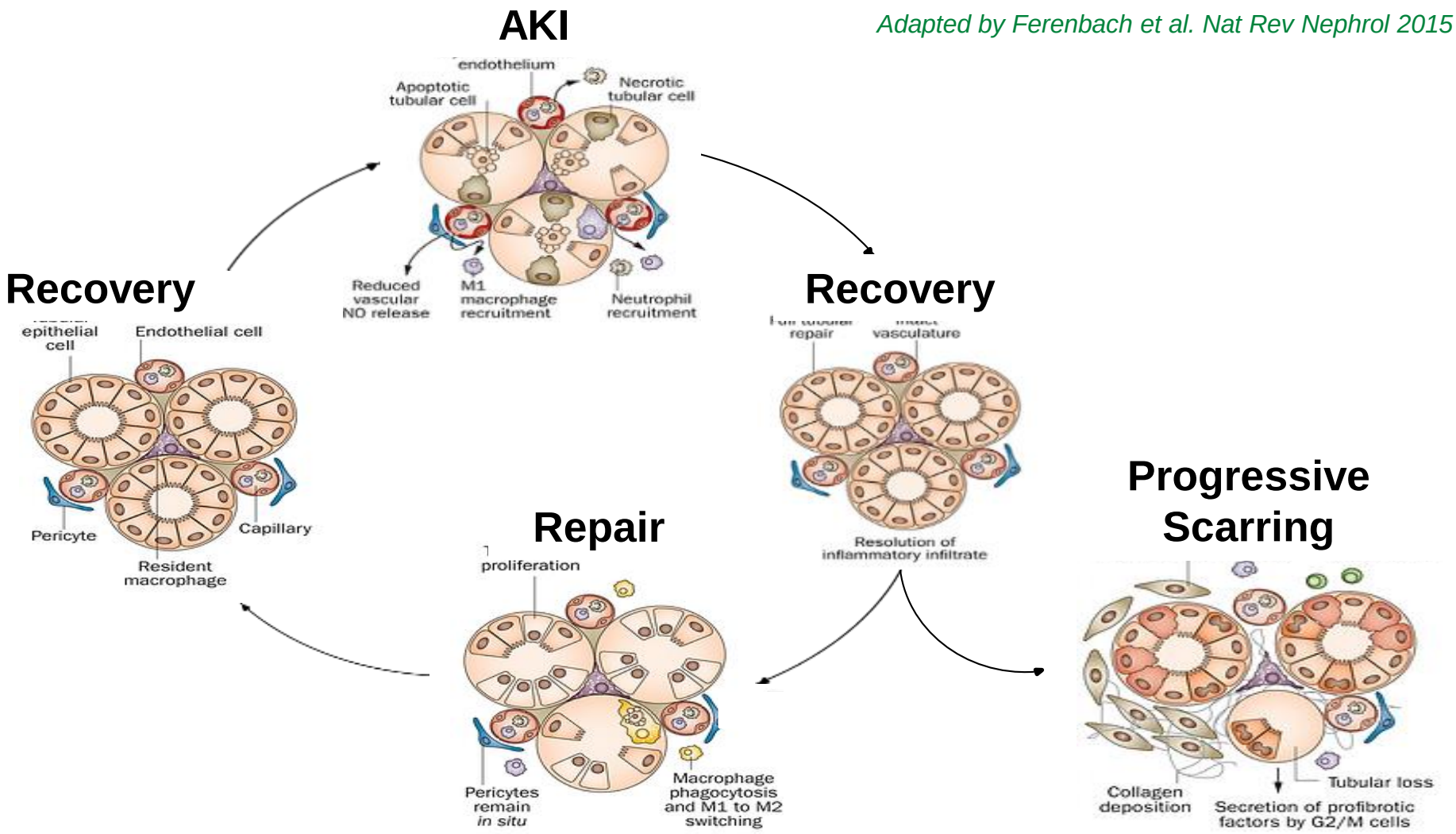
EXPERT CONSENSUS DOCUMENT

Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup





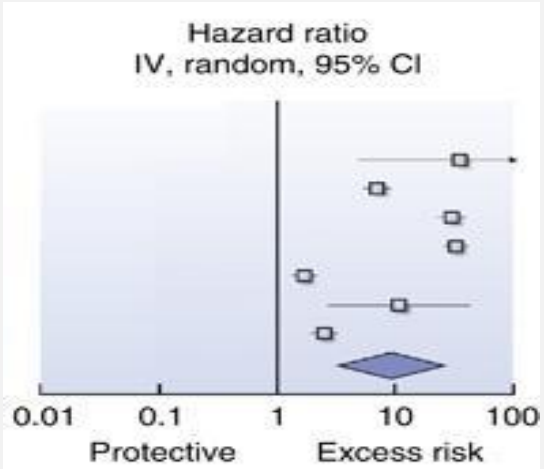
Adapted by Ferenbach et al. Nat Rev Nephrol 2015



CKD and ESRD after AKI

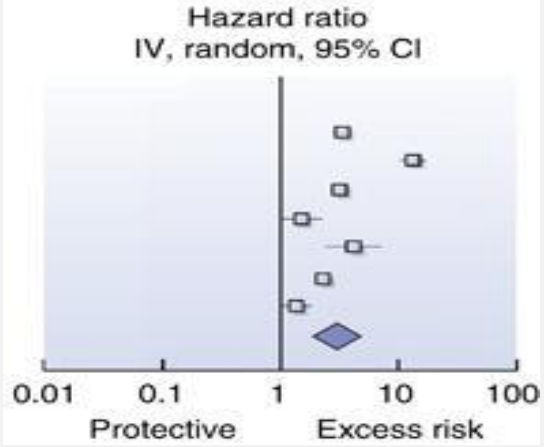
AKI to CKD

HR = 8.8
(95%CI 3.1-25.5)



AKI to ESRD

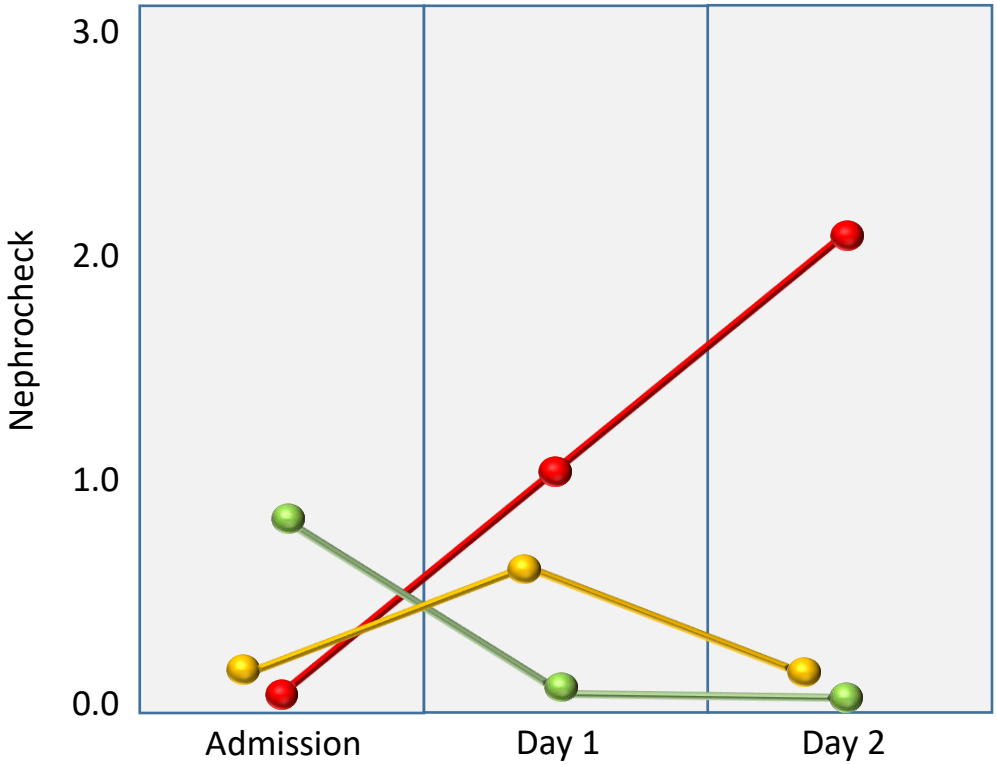
HR = 3.1
(95%CI 1.9-5.0)

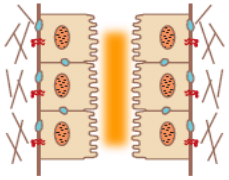


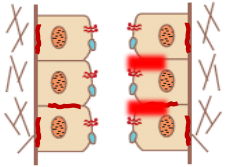
Coca, et al.
Kidney Int 2012

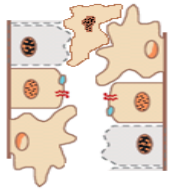
Nephrocheck Curve Study

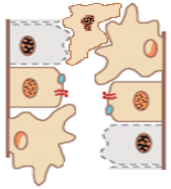
(Vicenza 2017-2018)



A Exposures →  → Stress Biomarkers

B Insult/injury →  → Damage Biomarkers

C Persistent Insult/injury →  → Dysfunction Biomarkers

D AKI Stage 1-2-3 →  → Persistent AKI Biomarkers
RRT very likely needed

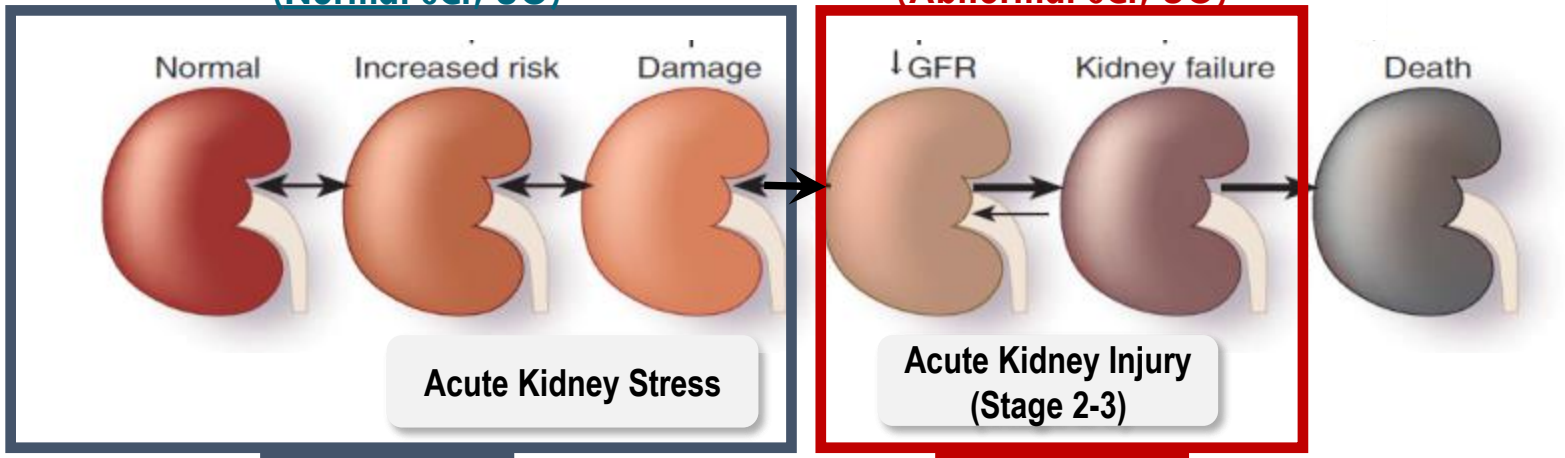
E AKI - AKD →  → CKD progression Biomarkers

NephroClear™ In Symptomatic Patients With Established AKI To Clarify Dialysis Decisions

Complements NephroCheck®, Which Is For Asymptomatic Patients Prior to AKI

Asymptomatic Patients
(Normal sCr, UO)

Symptomatic Patients
(Abnormal sCr, UO)



NephroCheck®

Detects acute kidney stress, prior to AKI

Goal is to prevent AKI and related problems

Find and mitigate source of stress

- Nephrotoxic drugs
- Undiagosed infection
- Perfusion issue (fluid, cardiac output, blood pressure)

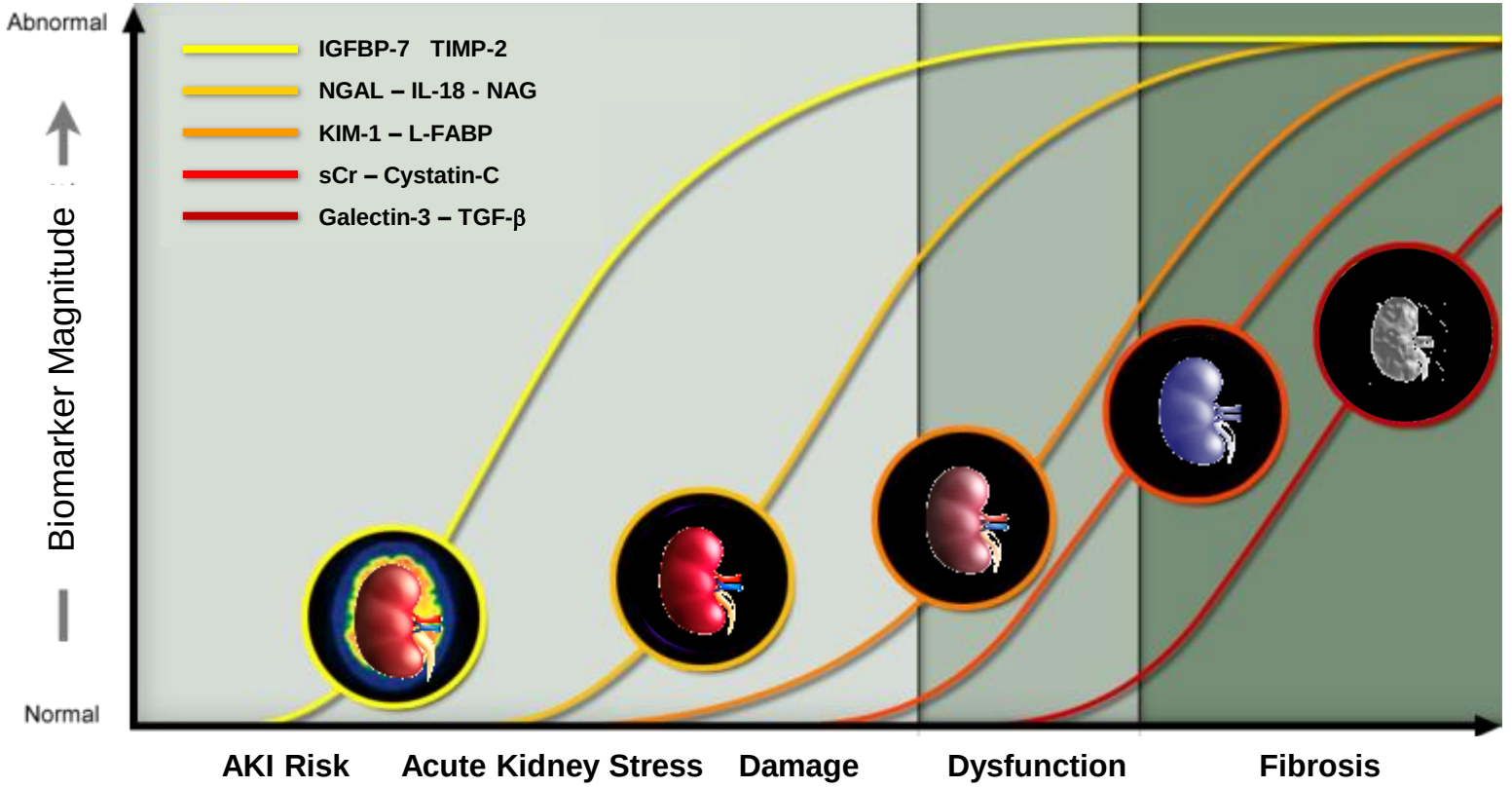
Avoid medication/fluid errors associated with silent AKI

NephroClear™

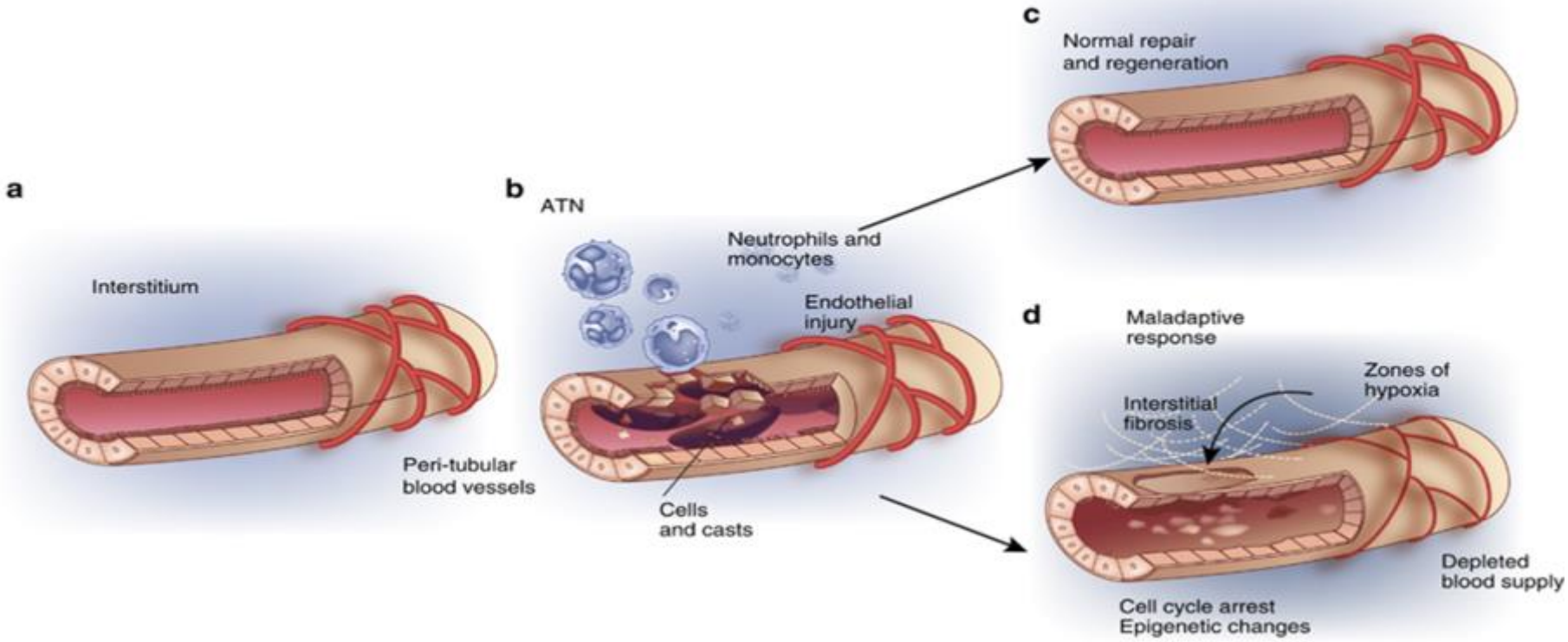
Detects severity of tissue injury to assess likelihood of rapid recovery Goal is to clarify decisions related to renal replacement therapy (RRT)

- Avoid unnecessary RRT in patients likely to recover quickly
- Help identify patients who may need RRT (non-recovery)
- Appropriate timing of RRT (dynamic signal as AKI worsens)

Biomarker Type & Magnitude at different AKI Stage

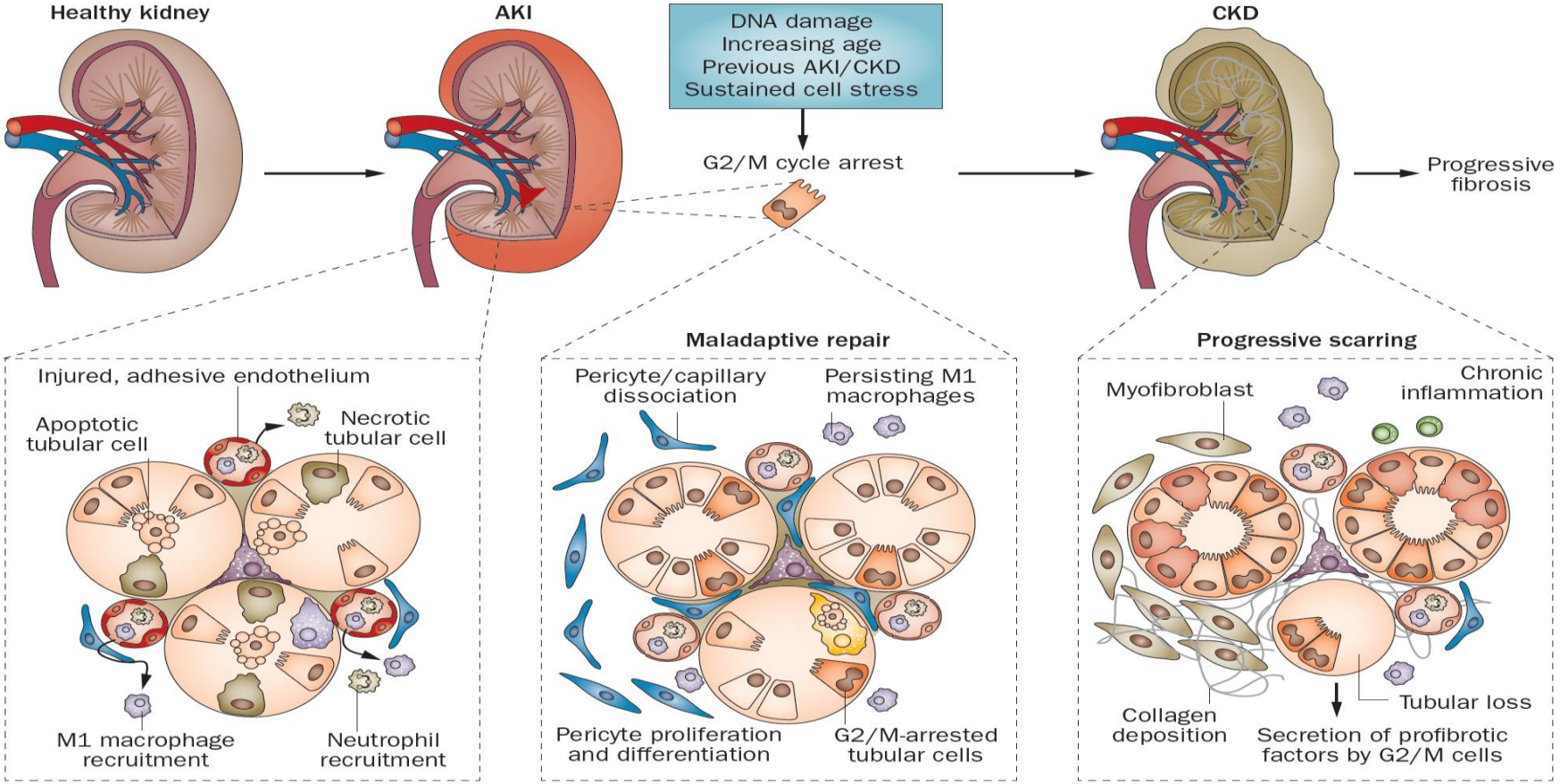


How does AKI progress to CKD?



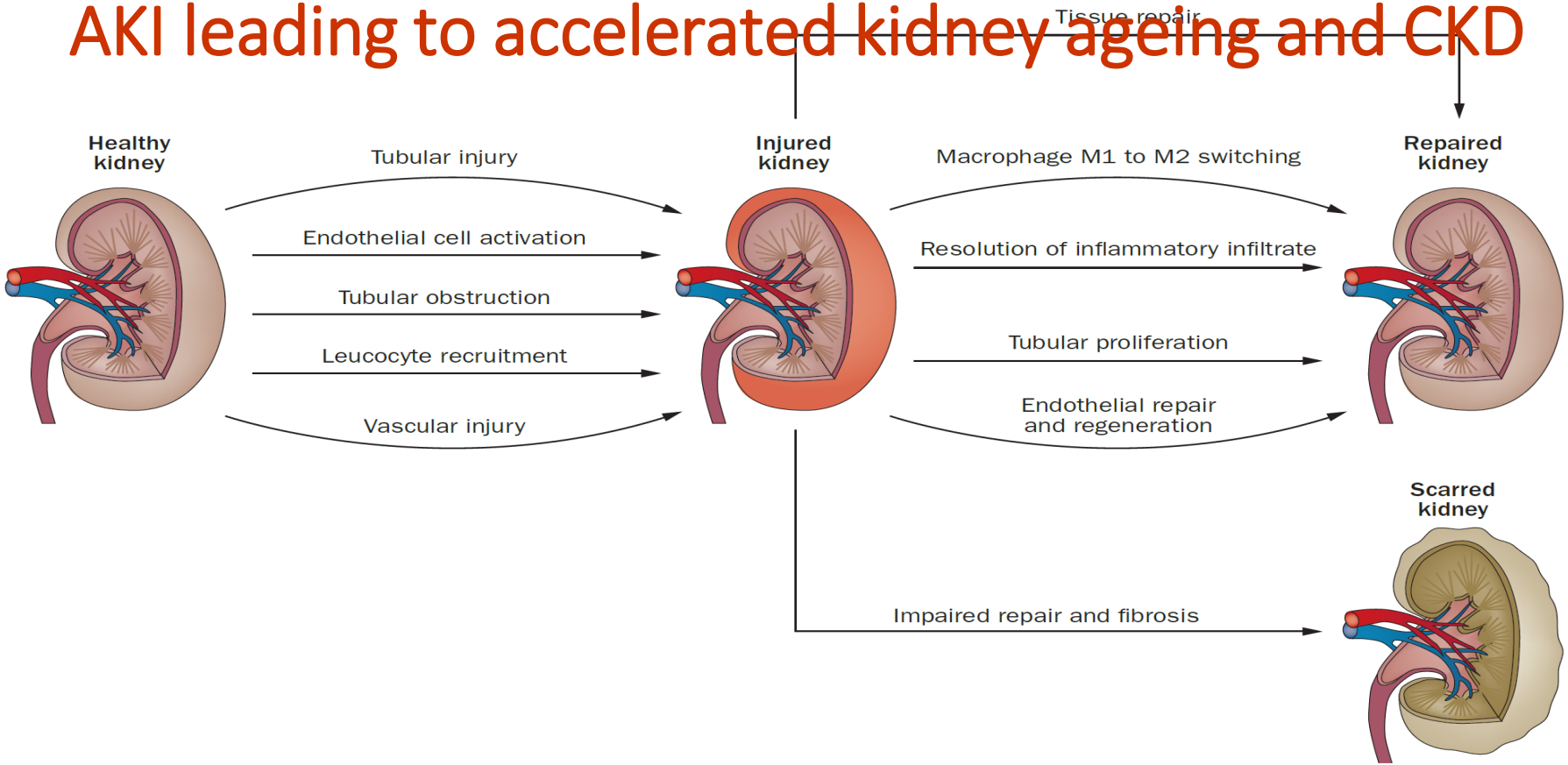
Chawla, Kimmel. Kidney Int 2012

Mechanisms of maladaptive repair after AKI leading to accelerated kidney ageing and CKD



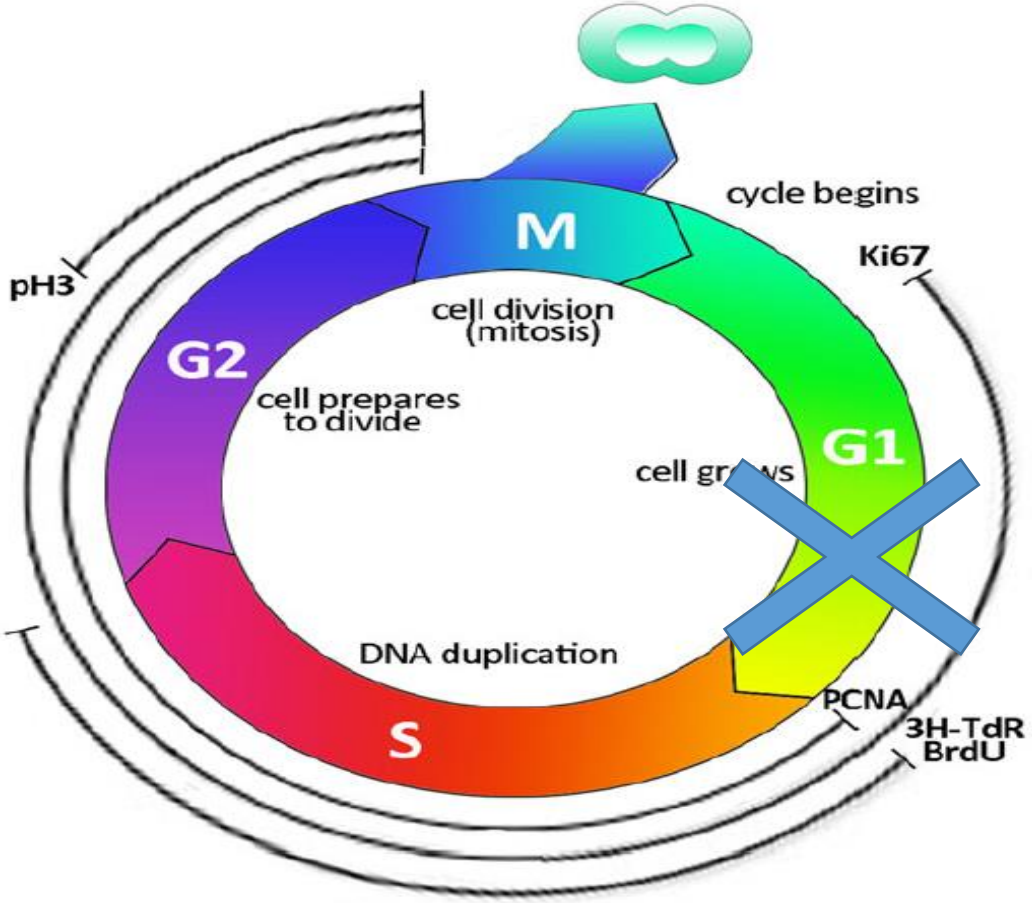
Adapted by Ferenbach et al. Nat Rev Nephrol 2015

Mechanisms of repair and maladaptive repair after AKI leading to accelerated kidney ageing and CKD



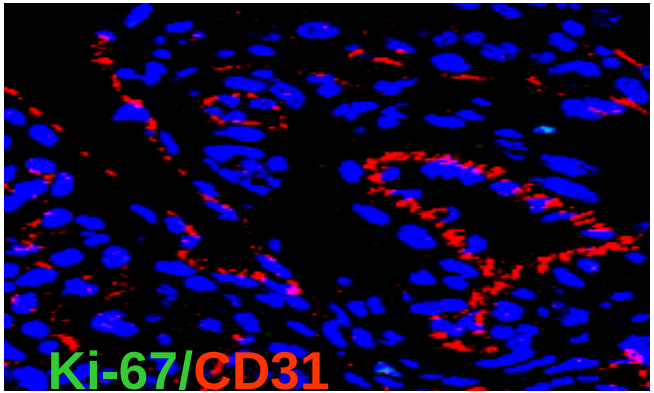
Farenbacj et Al. Nat. Rev. Nephrol. 11, 264–276 (2015

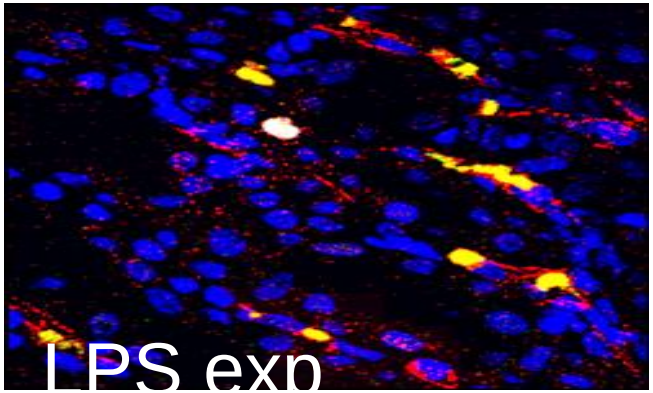
G1/G2 Cell Cycle Arrest and Senescent Phenotype

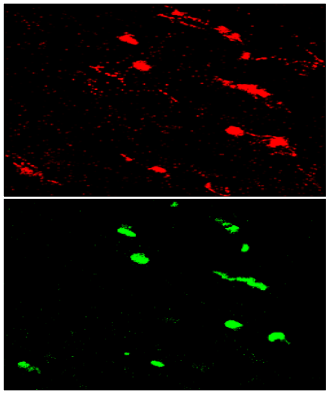


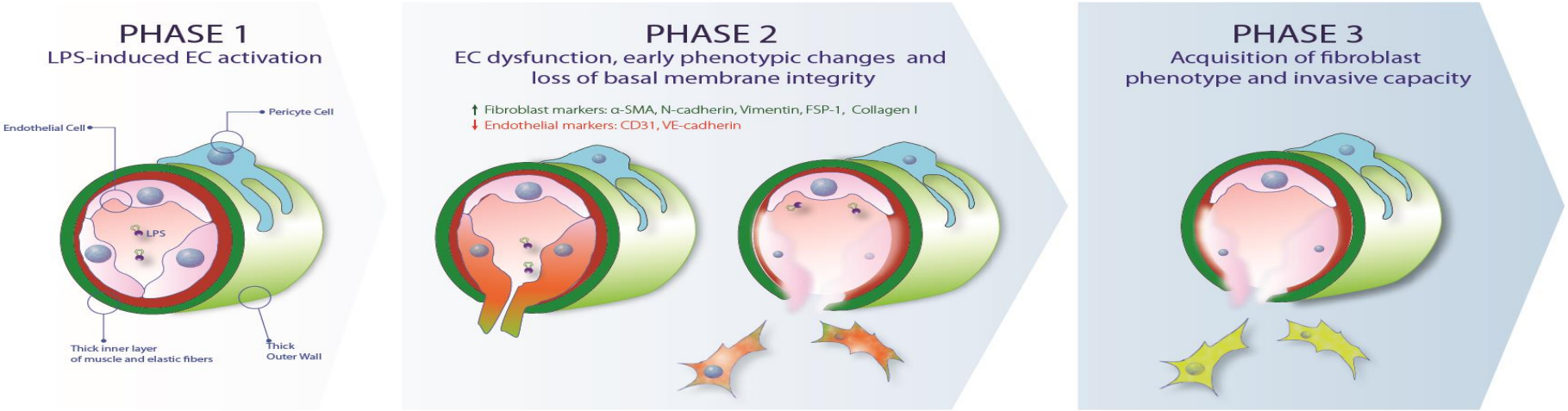
Endothelial/Mesenchymal Transition

Stasi A. & Castellano G., *Review in preparation*

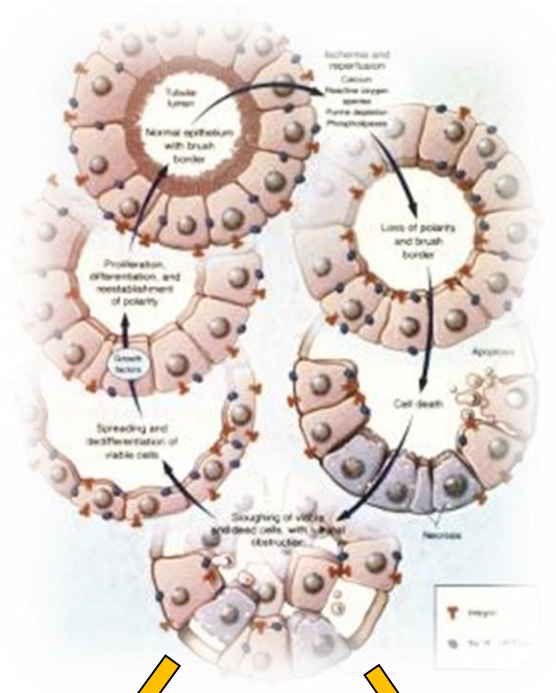








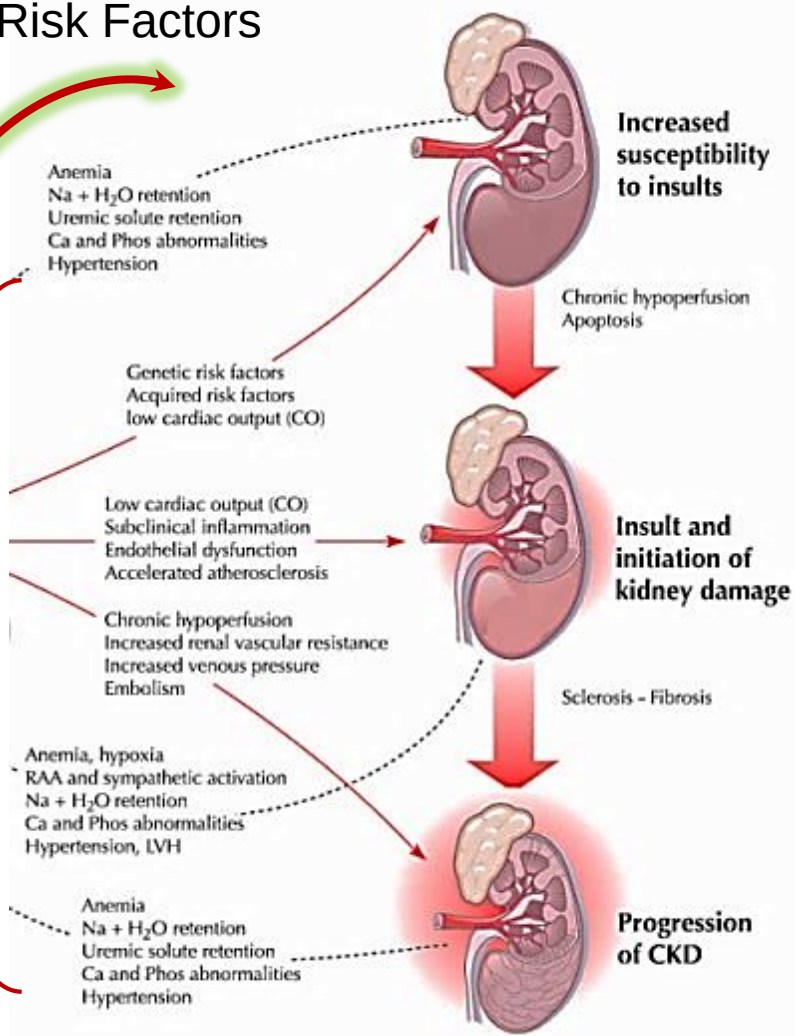
Kidney Attack



Complete Recovery

Partial Recovery

Risk Factors



POST-ACUTE KIDNEY INJURY CARE

EHR TOOLS

AKI sniffers/triggers

Registries and Reports

Patient Education

TELEMEDICINE

Patients to provider

Provider to provider

REMOTE PATIENT MONITORING

Physiologic data to provider care team

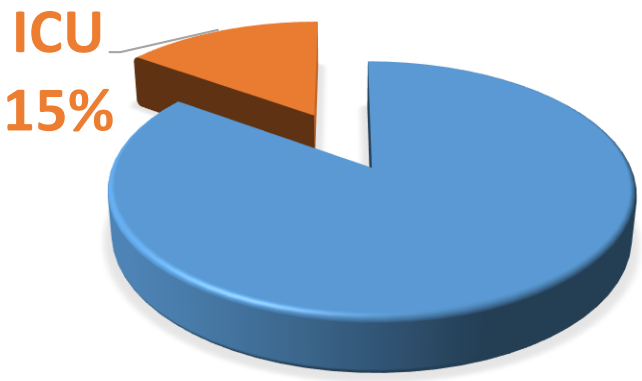
Escalation protocols

DH tools and applications can leverage to realize greater continuity of health and health outcomes for patients

AKI: Changing Pattern

1970-1980

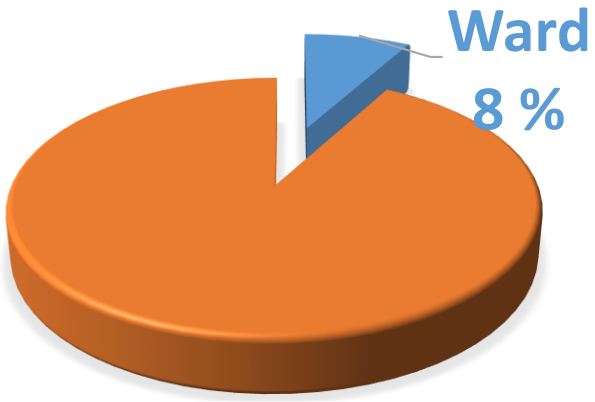
Total number of incident cases = 156



Mortality 58 %

1980-1990

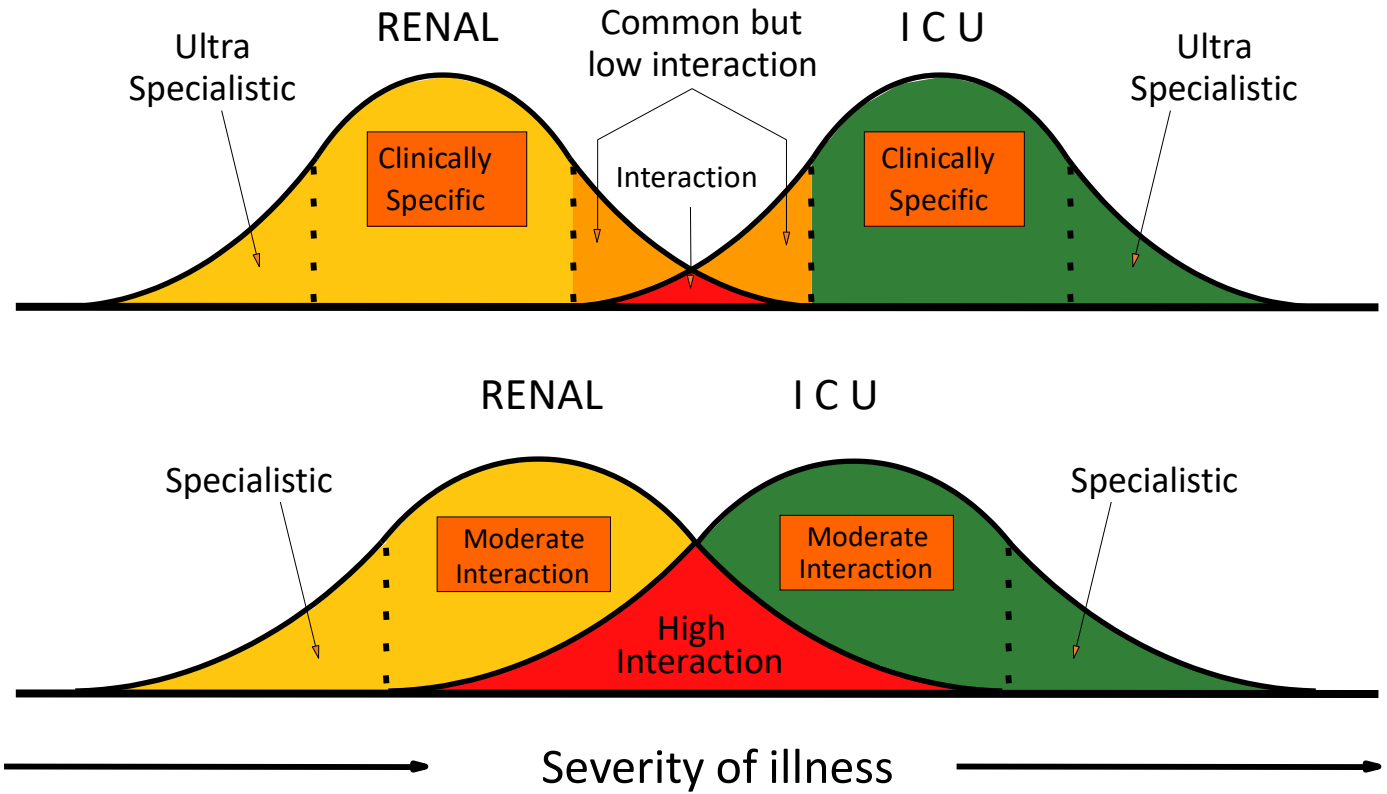
Total number of incident cases = 925



Mortality 54 %

Critical Care Nephrology

FROM SPECIALITY-ORIENTED TO PATIENT-ORIENTED



Nephrology
Dialysis
Transplantation

Claudio Ronco and Rinaldo Bellomo

Critical Care Nephrology: The time has come

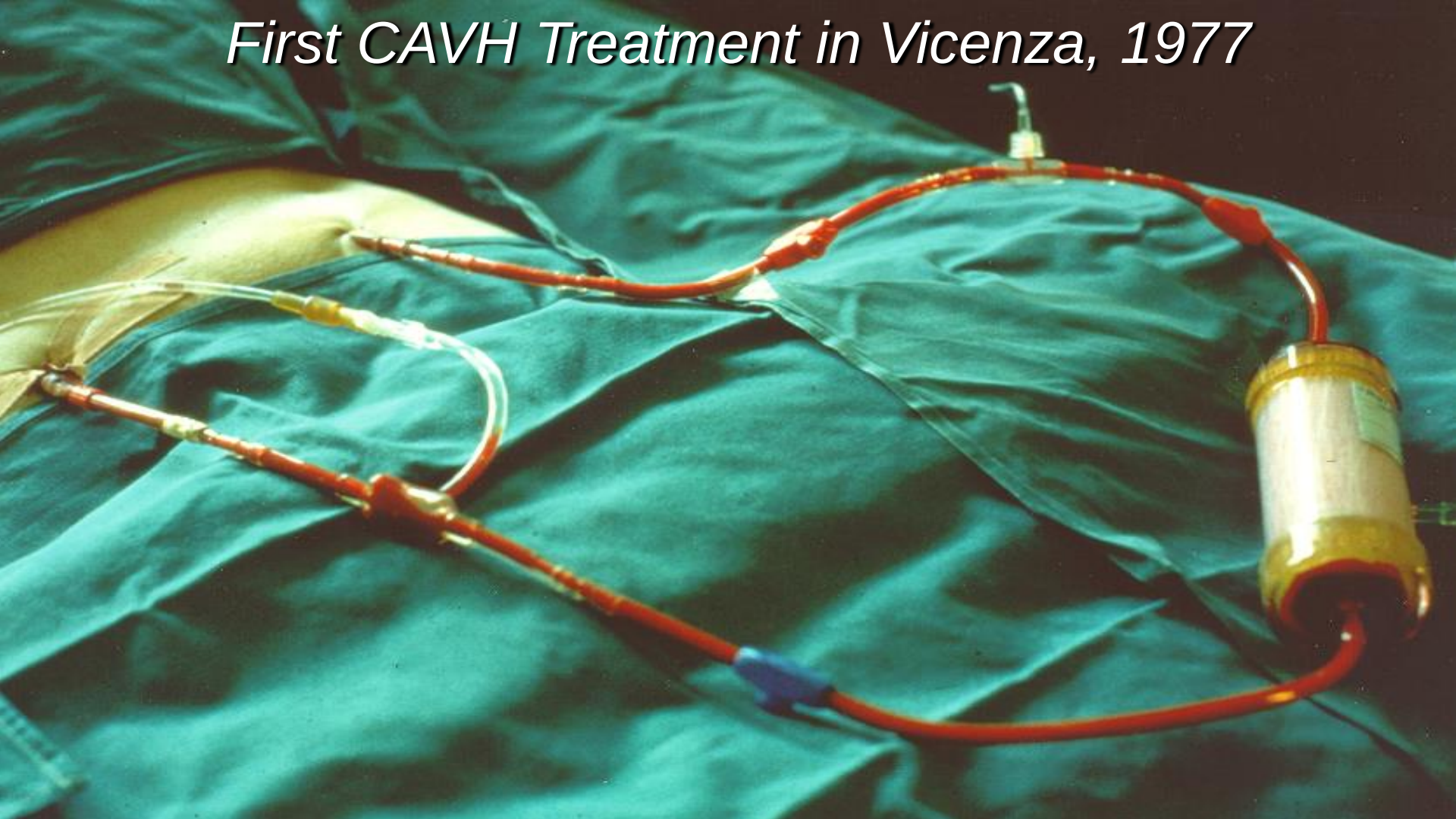
*editorial entitled "*Critical Care Nephrology: the time has come". *It was not so long ago that the term* "critical care nephrology" *was unknown or at least obscure to most physicians both in the nephrological and in the intensive care community; a push was definitely needed to move forward. Today, a few years later, a simple internet query on critical care nephrology leads to more than 157,000 references. For this reason I have decided to dedicate this*

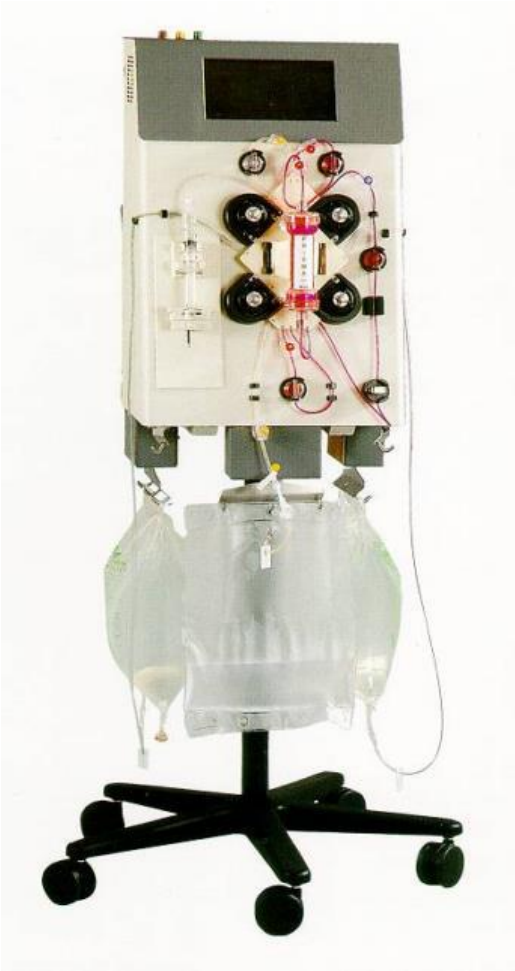
acquired expertise and training in both areas.

In either case, by the late nineties, the formal development of a specialty field called Critical Care Nephrology was seen as something whose time had come.

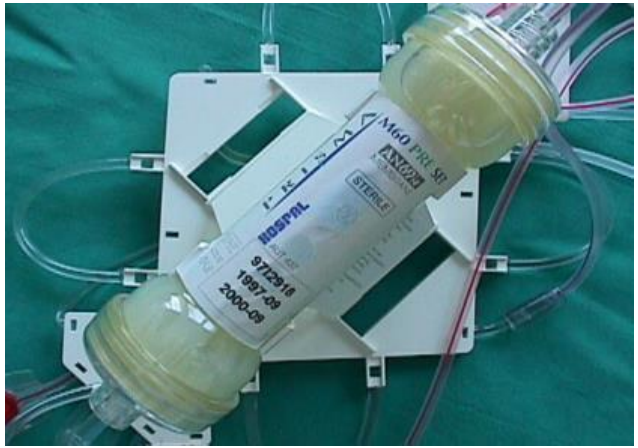
Why had this conceptually simple and effective approach not been developed before? Several issues were raised on the occasion of the First International Course on Critical Care Nephrology held in Vicenza in

First CAVH Treatment in Vicenza, 1977



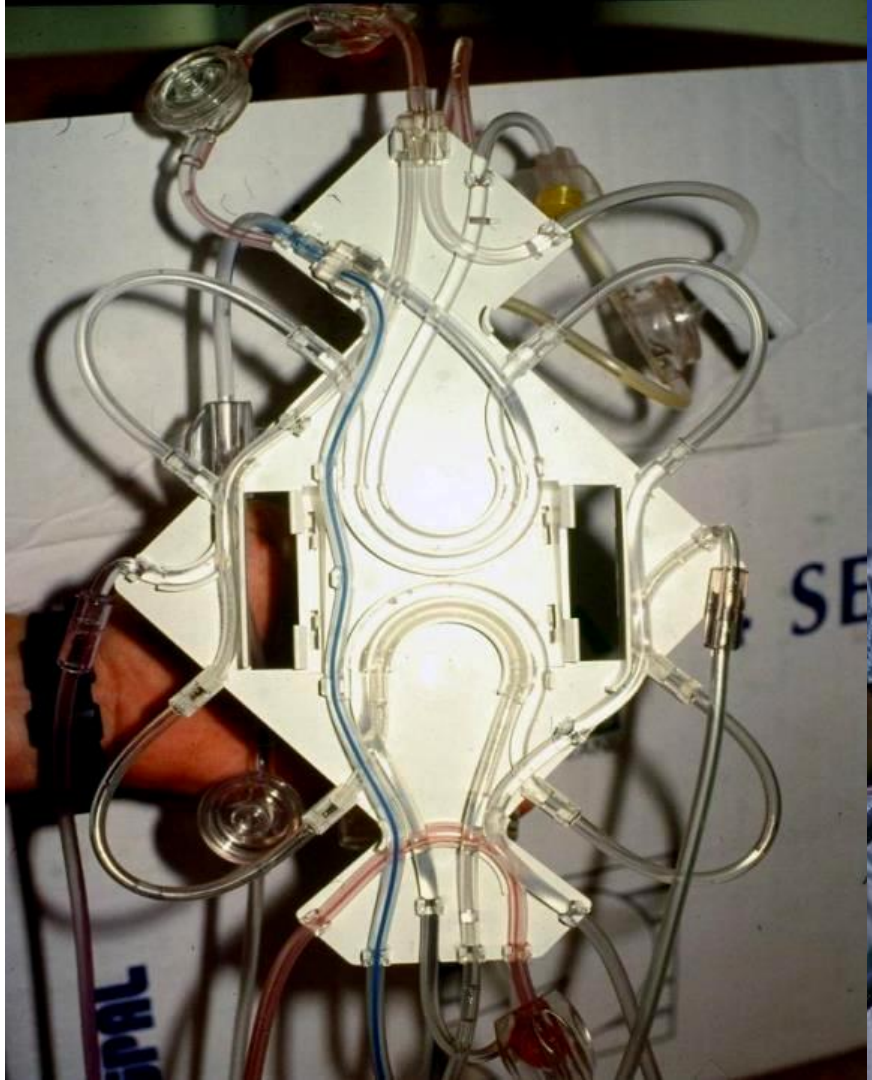


HOSPAL PRISMA



Features:

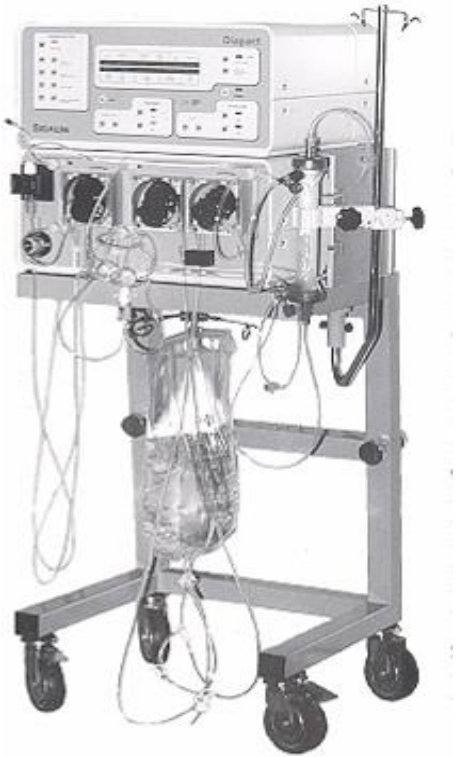
Self loading of lines and autopriming of the circuit. Treatments performed: CVVH-CVVHD - CVVHDF with large capacity of fluid handling. Large display for operations.



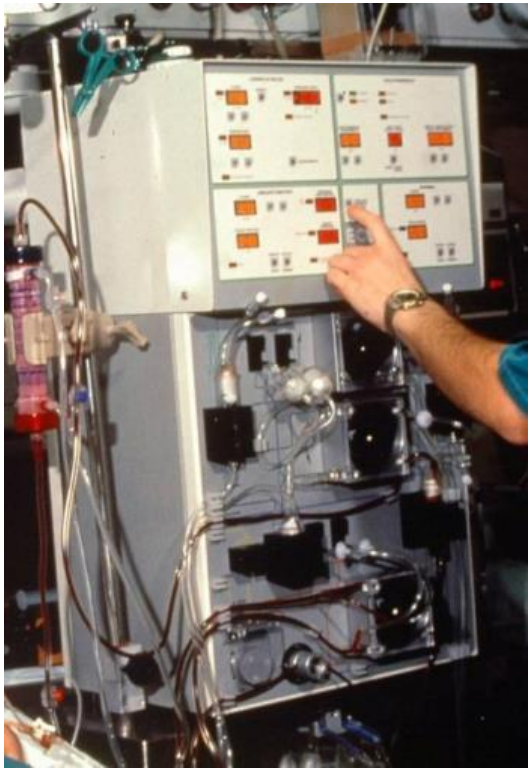

COBE
PRISMA


PRISMA

From ECU to Omni: a long way



1988



1991

1994

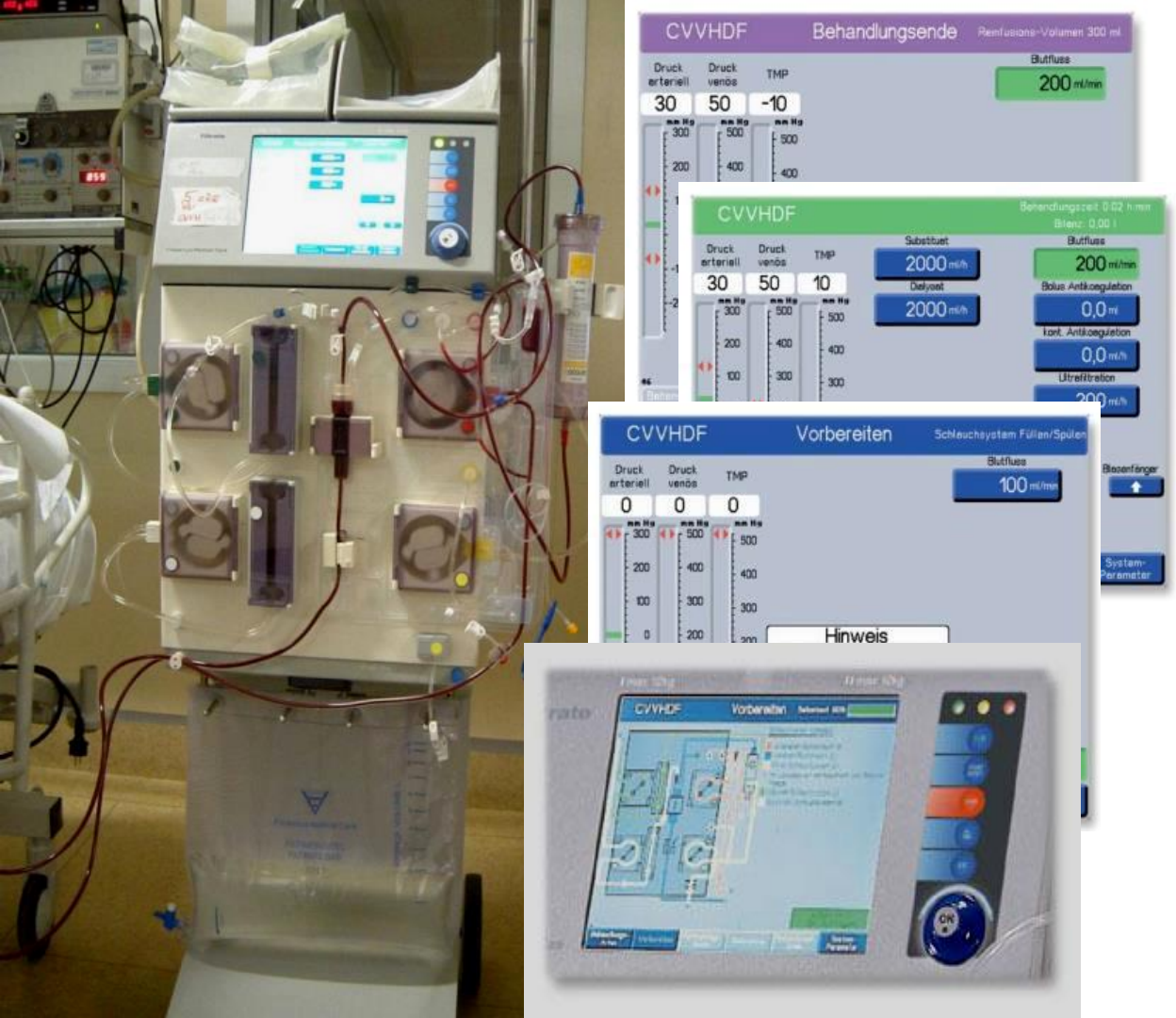

Omni-DL
Emergency Stop
Effluent Bag


OMNI
B.BRAUN

From ECU to Omni: a long way

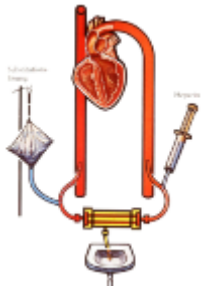
2004

2017


CVVHDF
Behandlungsende
Reinfusions-Volumen 300 ml
Druck arteriell
Druck venös
TMP
30
50
-10
Blutfluss
200 ml/min
CVVHDF
Behandlungszeit 0:02 h:mm
Bilanz: 0,00 l
Druck arteriell
Druck venös
TMP
30
50
10
Substituat
2000 ml/h
Dialysat
2000 ml/h
Blutfluss
200 ml/min
Bolus Antikoagulation
0,0 ml
kont. Antikoagulation
0,0 ml/h
Ultrafiltration
CVVHDF
Vorbereiten
Schlauchsystem Füllen/Spülen
Druck arteriell
Druck venös
TMP
0
0
0
Blutfluss
100 ml/min
Blasenfänger
System-Parameter
Hinweis
CVVHDF
Vorbereiten
ON


FRESENIUS MEDICAL CARE
10 L
Filtrate bag

40 years of CRRT



1977

First CAVH In Gottingen and First CAVH in Vicenza

CAVHD
CAVHDF
Fluid Balance systems

1983

1986

CVVH
CVVHD
and
Adoptive Technology

First generation CRRT machines
CVVH
CVVHD
CVVHDF

1990

1995

Second generation CRRT machines
CVVH
CVVHD
CVVHDF
and
studies on Dose & Adequacy
35 ml/Kg/h

Third generation CRRT machines, Tr. of Sepsis
HVHF & HCO
Membr.

2002

Lung support
ECCO2R
Citrate anticoagulation
Sorbents

2010

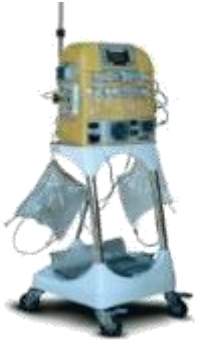
Fourth generation CRRT machines

2017

Liver support
MOST, CPFA





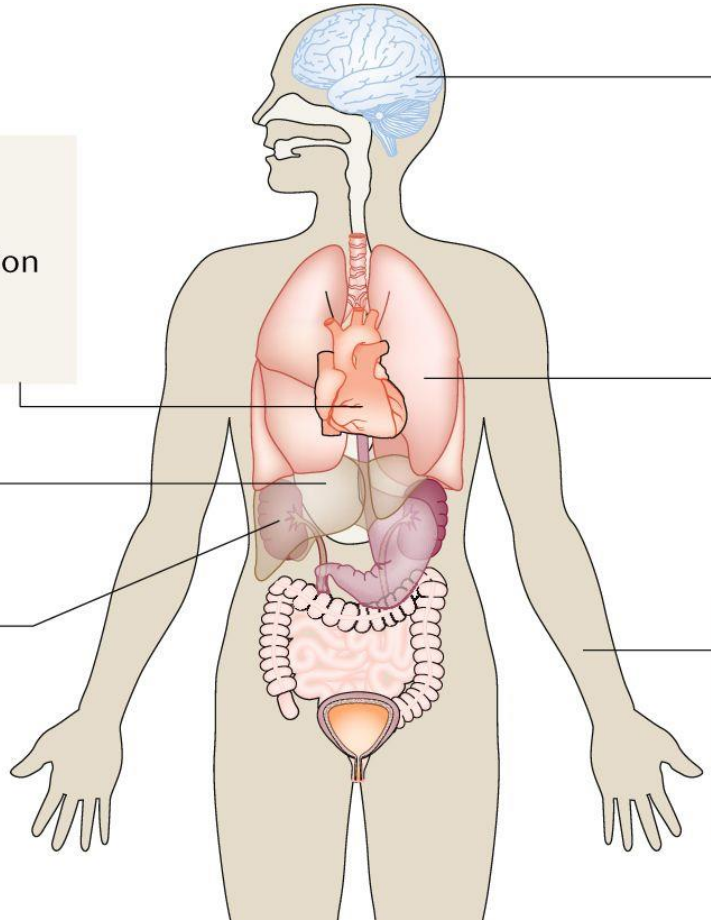










Multiple Organ Dysfunction



Neurological system
- Altered mentation
- Confusion
- Disorientation

Cardiovascular system
- Hypotension
- Mottled skin and altered microcirculation
- ↑ Lactate levels (in septic shock)
- Altered echocardiography variables

Respiratory system
- Hypoxaemia
- ↓ PaO_2:FiO_2 ratio

Hepatic system
- ↑ Bilirubin levels
- ↑ Liver enzymes

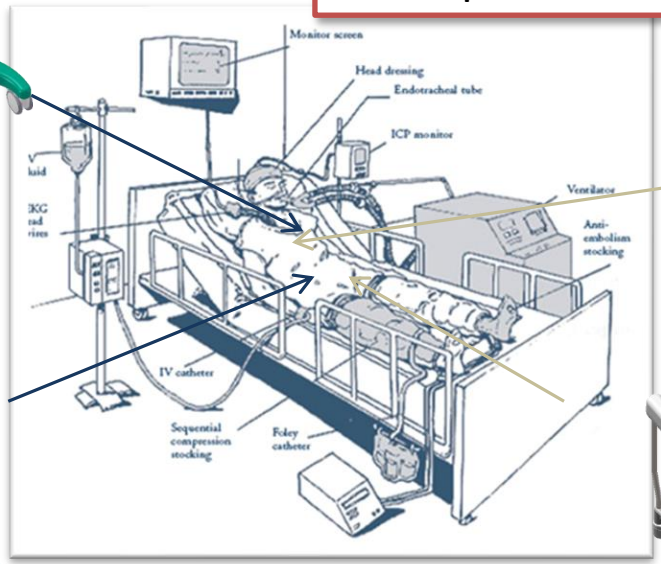
Renal system
- Oliguria
- ↑ Serum creatinine
- ↑ Blood urea nitrogen
- ↑ Biomarkers

Haematological system
- Low platelet count
- Disseminated intravascular coagulation
- Petechiae (in some severe cases)

Precision MOST

Congestive Heart Failure

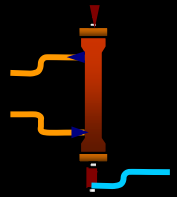
- CO2 Removal
- (ARDS + COBP)
- Plasmapheresis



CRRT

- SIRS
- Sepsis

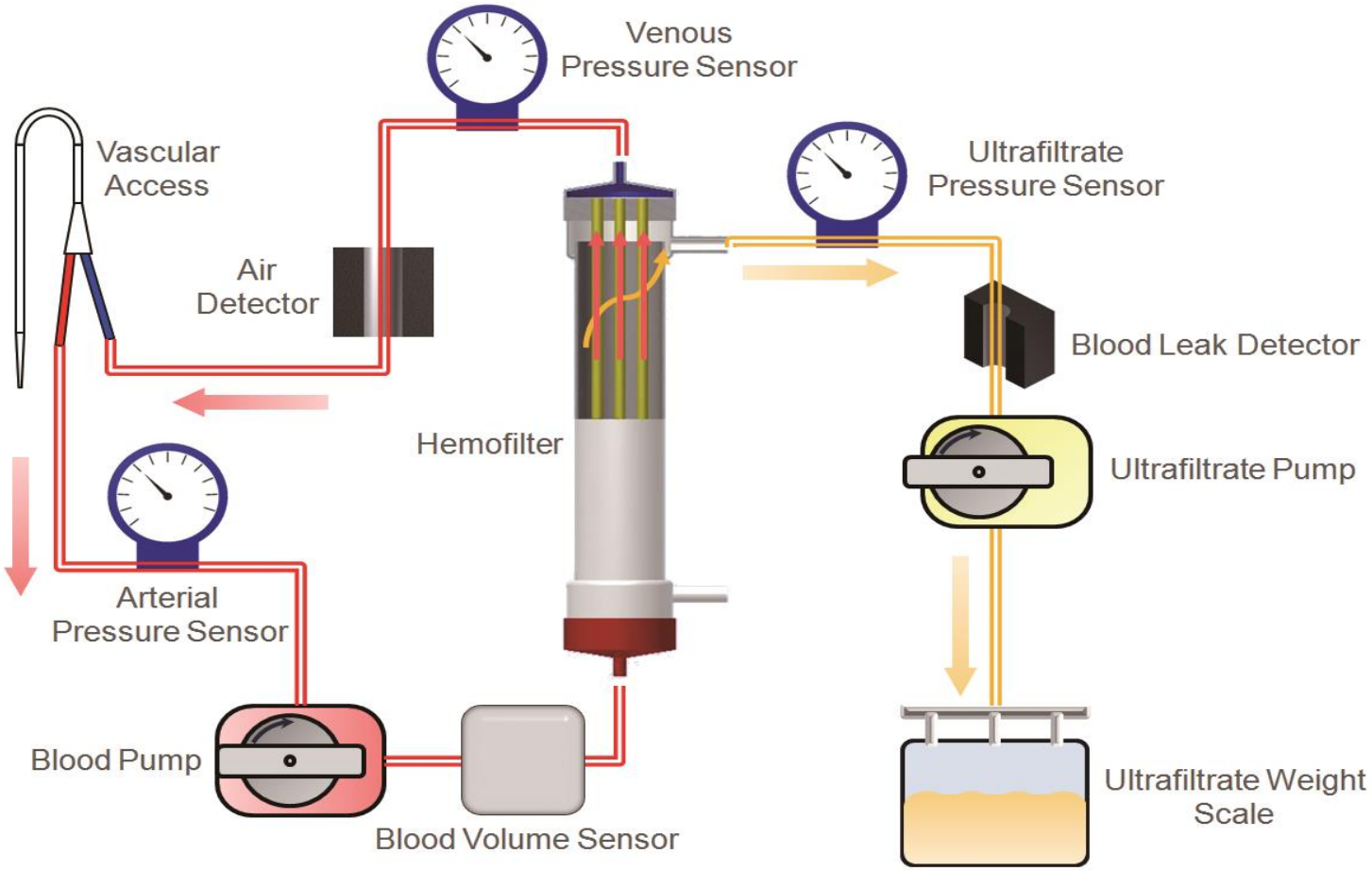
Coping with patient's needs



CRRT

MOST

SCUF


Venous
Pressure Sensor
Vascular
Access
Air
Detector
Ultrafiltrate
Pressure Sensor
Blood Leak Detector
Hemofilter
Ultrafiltrate Pump
Arterial
Pressure Sensor
Blood Pump
Blood Volume Sensor
Ultrafiltrate Weight
Scale

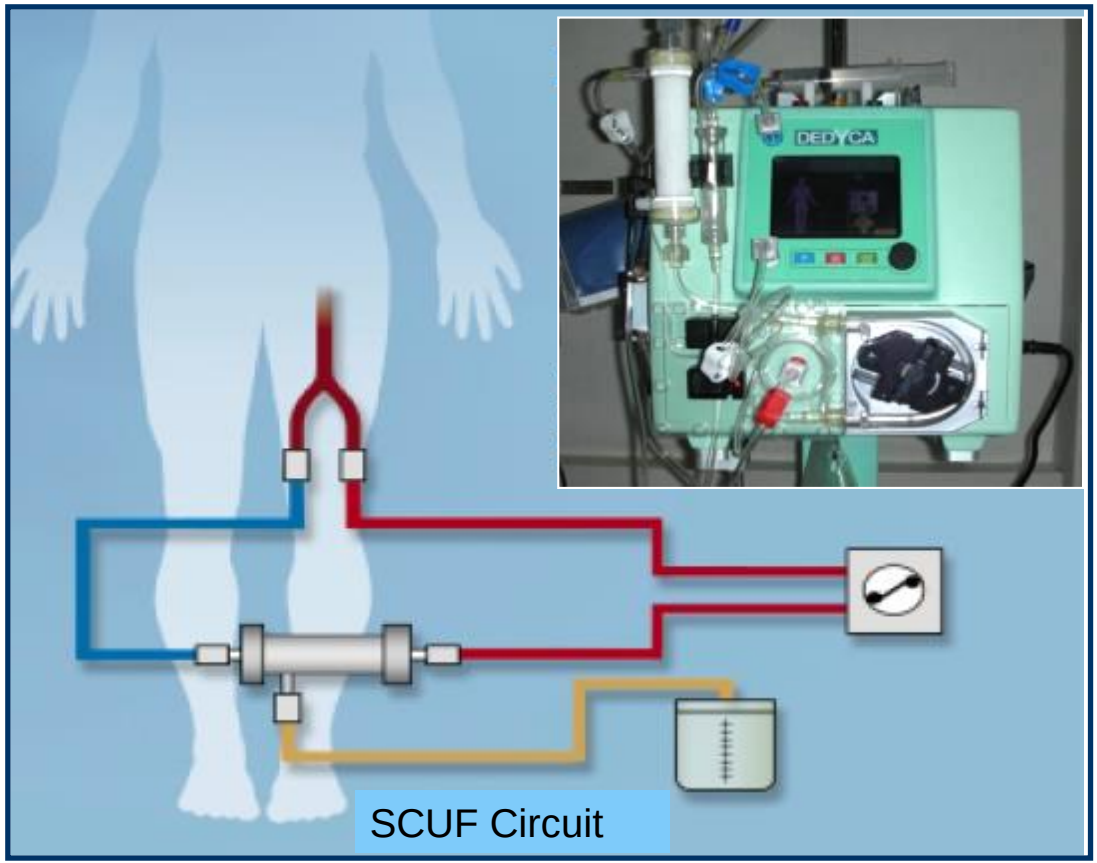


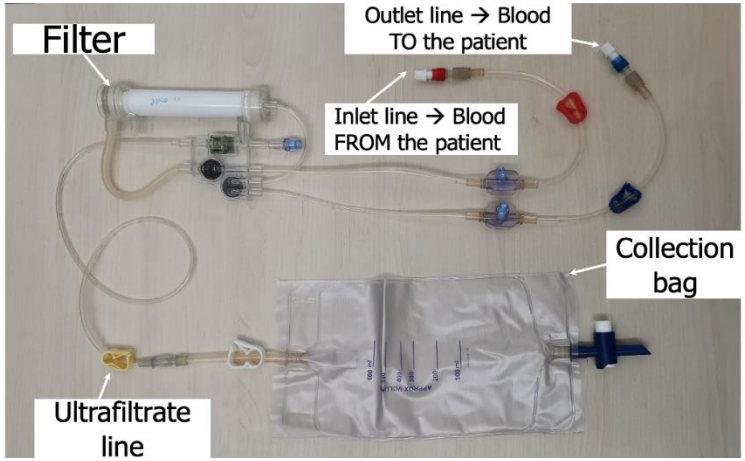
Fig. 2

AQUAPHERESIS

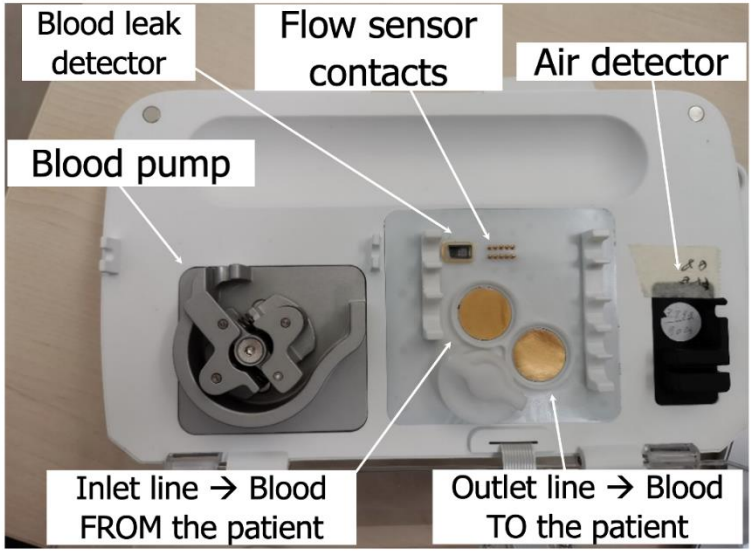
A


AD 1
SCUF system
ON
OFF

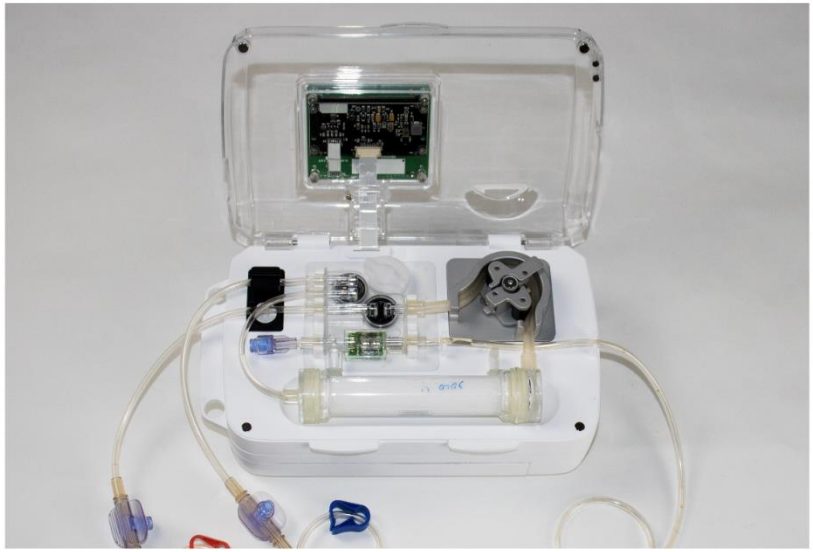
B


Filter
Outlet line → Blood TO the patient
Inlet line → Blood FROM the patient
Collection bag
Ultrafiltrate line

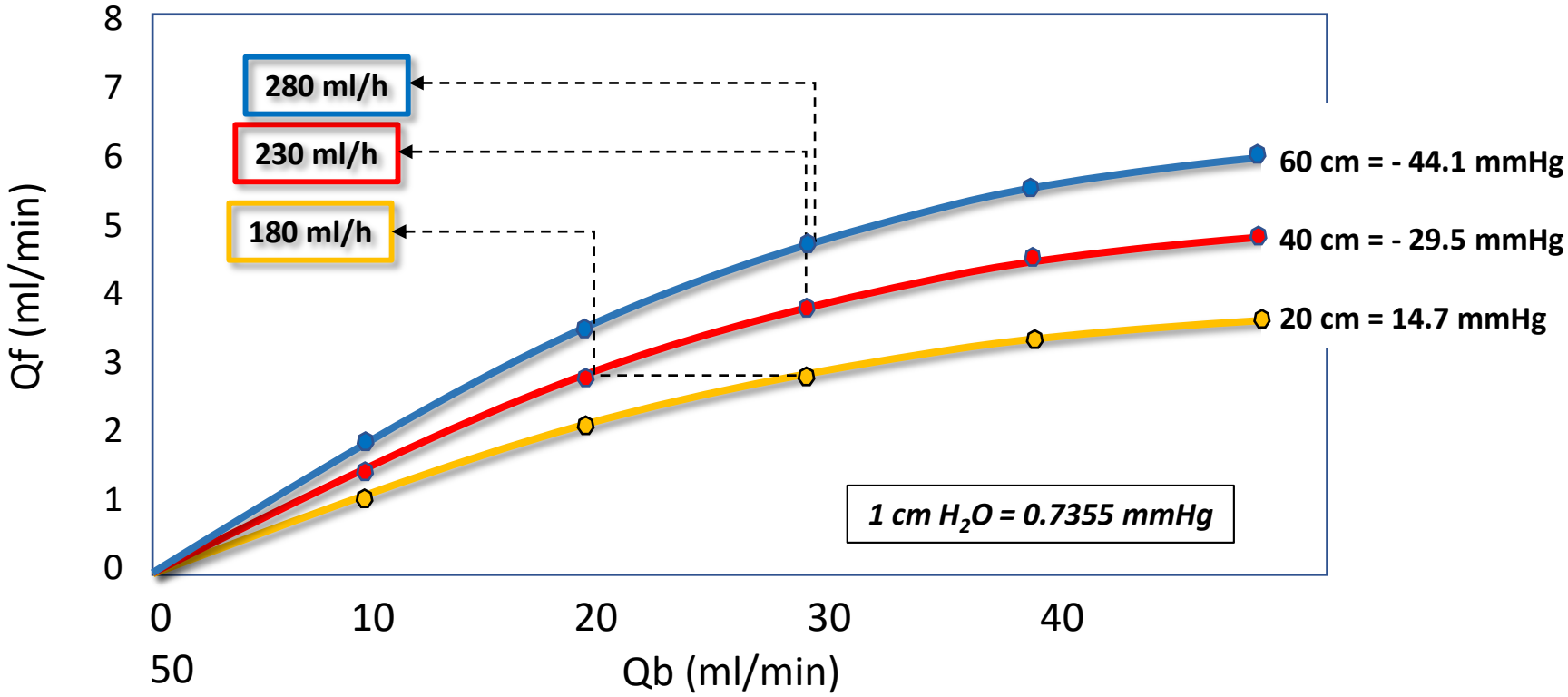
C


Blood leak detector
Flow sensor contacts
Air detector
Blood pump
Inlet line → Blood FROM the patient
Outlet line → Blood TO the patient

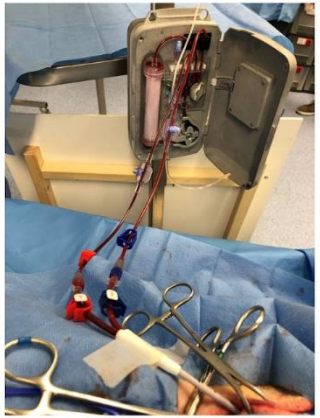
D

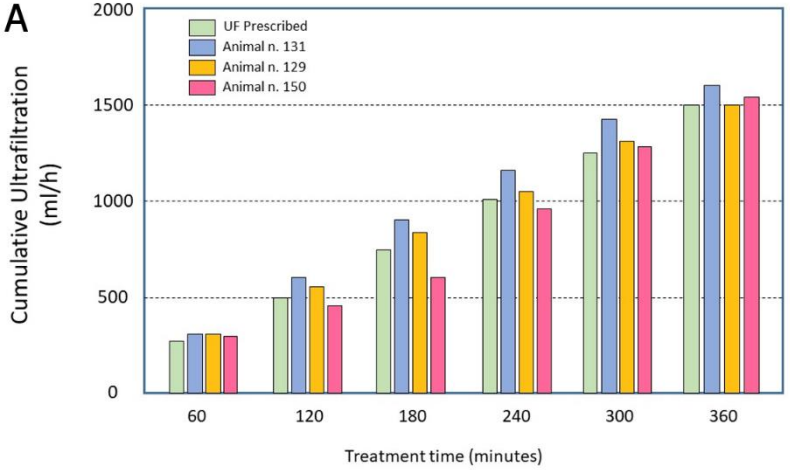


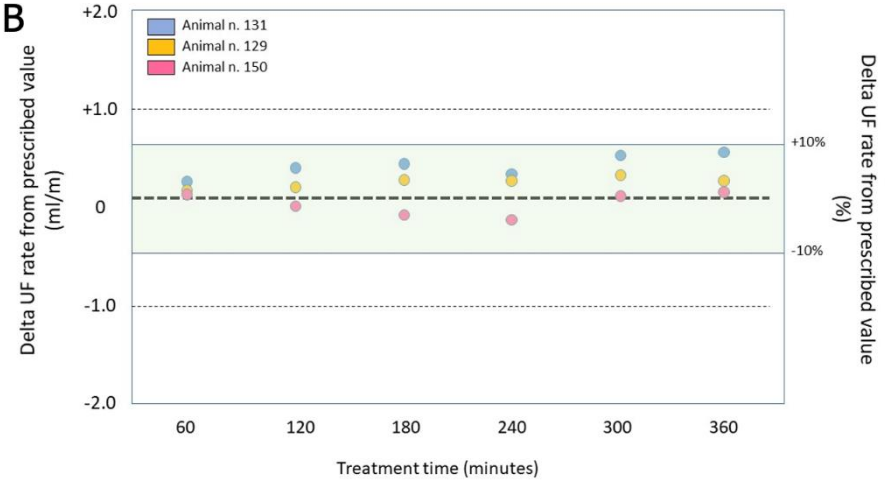
Ultrafiltration rate versus blood flow at different TMP (UF column height)



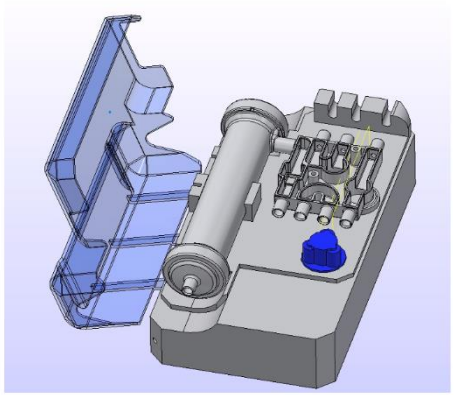
AD1: Animal Studies

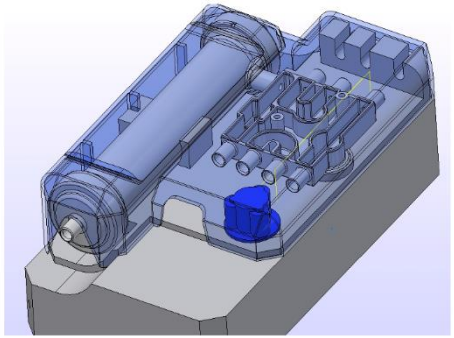






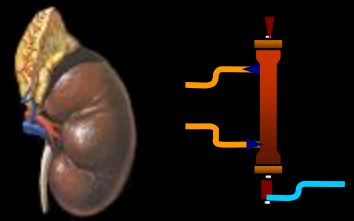
Artificial Diuresis Conceptual Framework



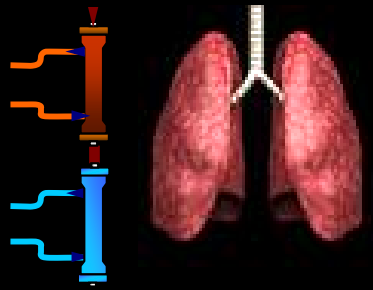


BENEFITS OF AD1

- It is slow and continuous
- It is easy and simple (wards)
- It will reduce complications
- It will reduce treatment costs
- It can be ambulatory (home based)



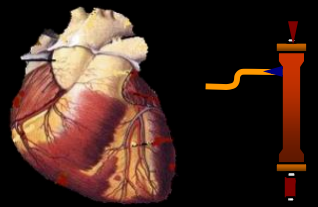
CRRT



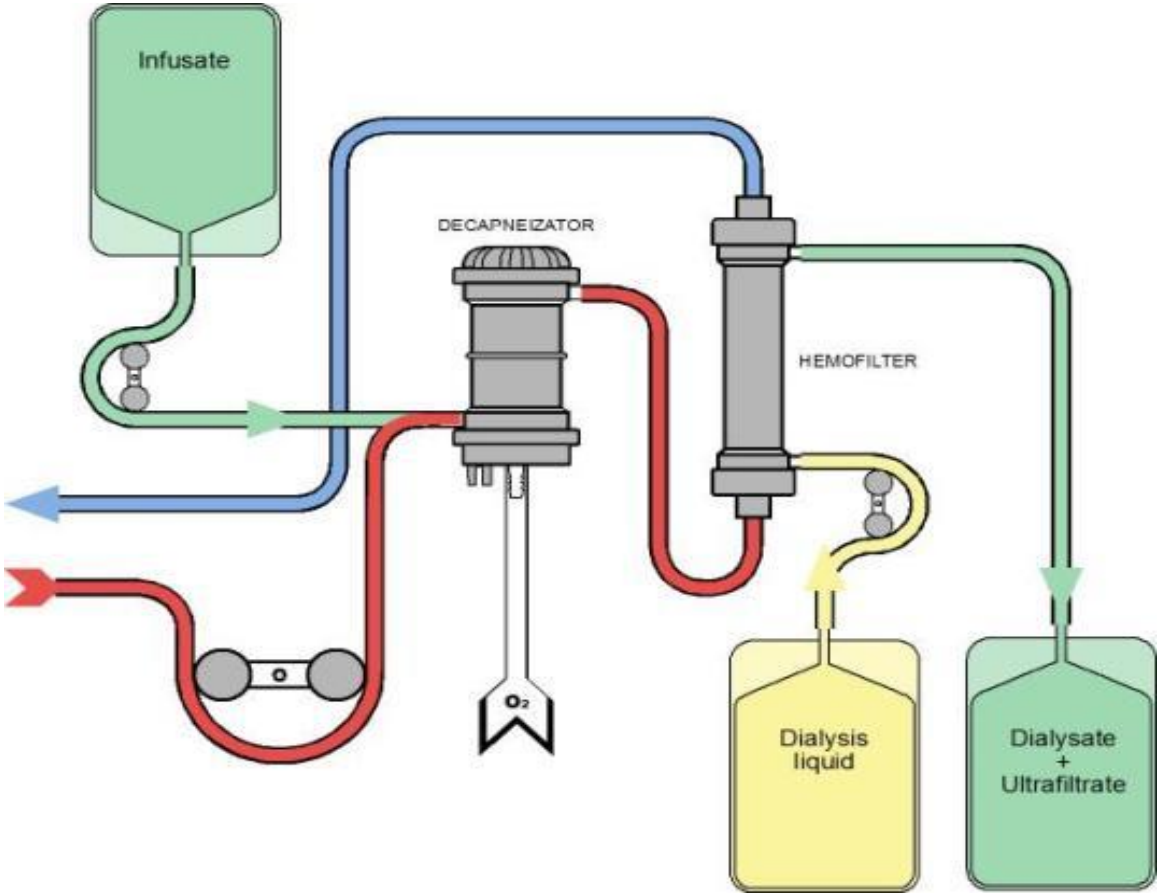
ECLS

MOST

SCUF

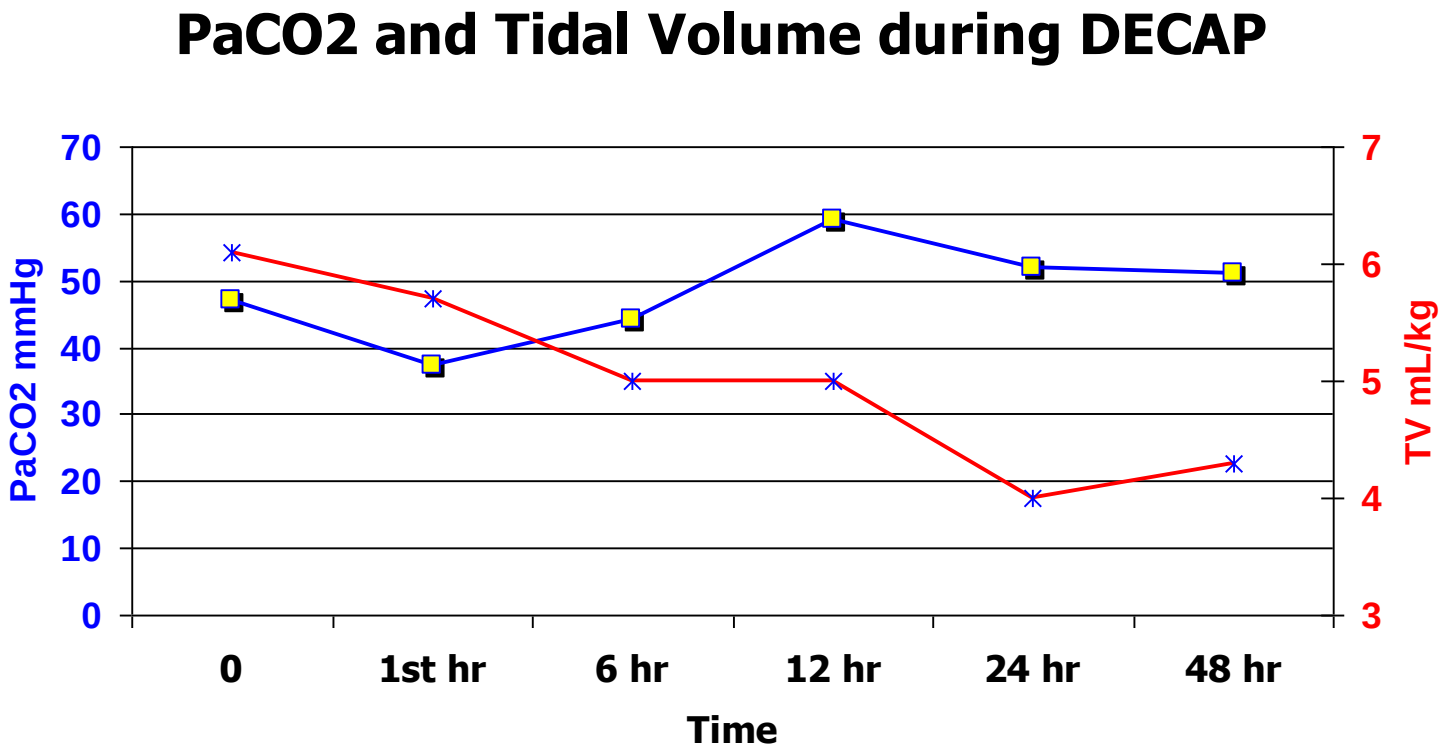


DECAP + CRRT


Infusate
DECAPNEIZATOR
HEMOFILTER
Dialysis liquid
Dialysate + Ultrafiltrate


HEMOFILTEK
MEDICA

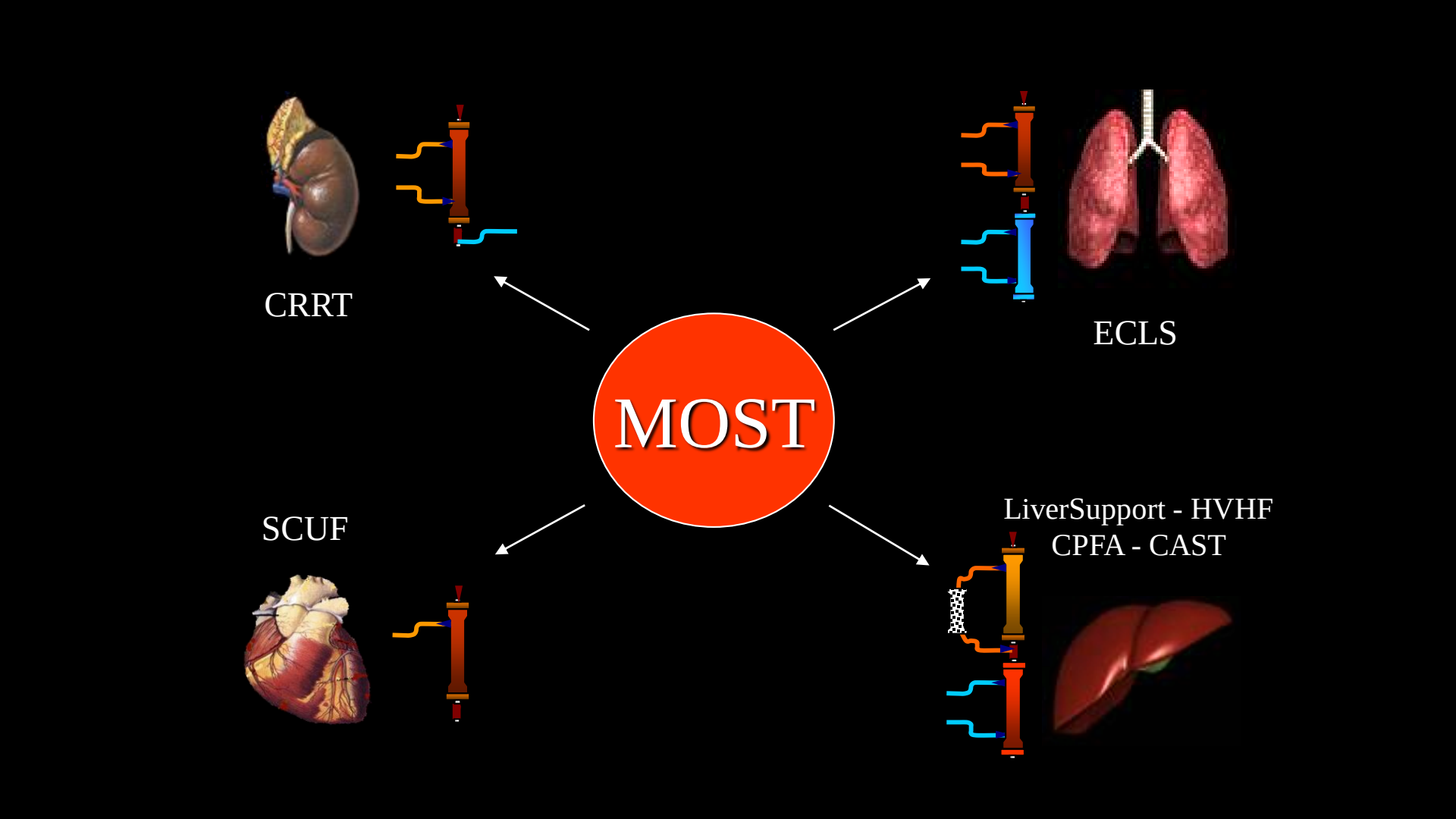
Example: H1N1 respiratory failure and AKI:
Ultra-protective ventilation with CRRT and DECAP



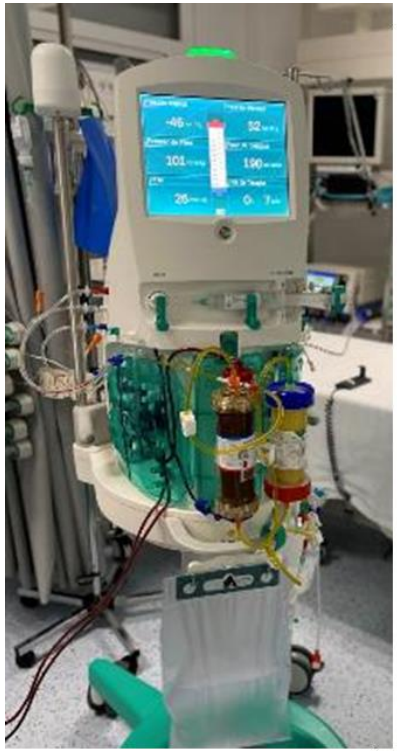
Less invasive approach to mechanical ventilation

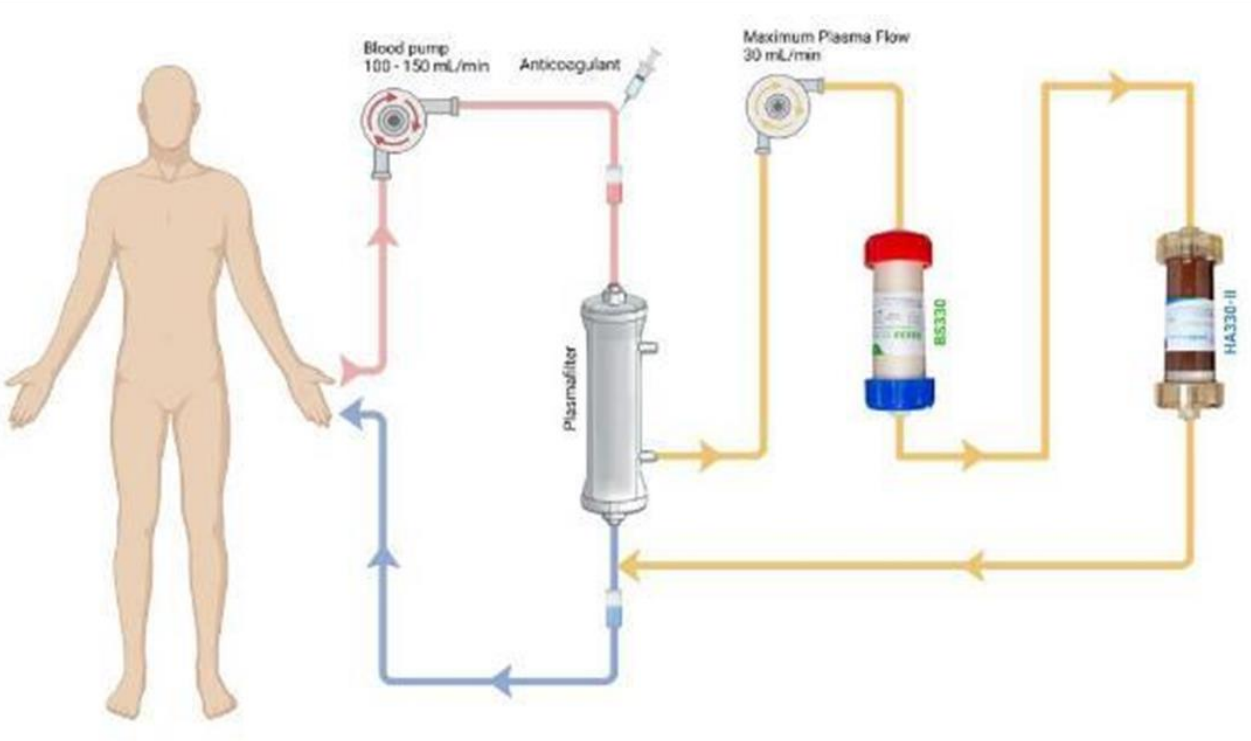
Lower barotrauma and volutrauma

Reduced morbidity due to invasive intubation and shorter stay in the ICU


CRRT
ECLS
MOST
SCUF
LiverSupport - HVHF
CPFA - CAST

Double Plasma Molecular Adsorption System (DPMAS)

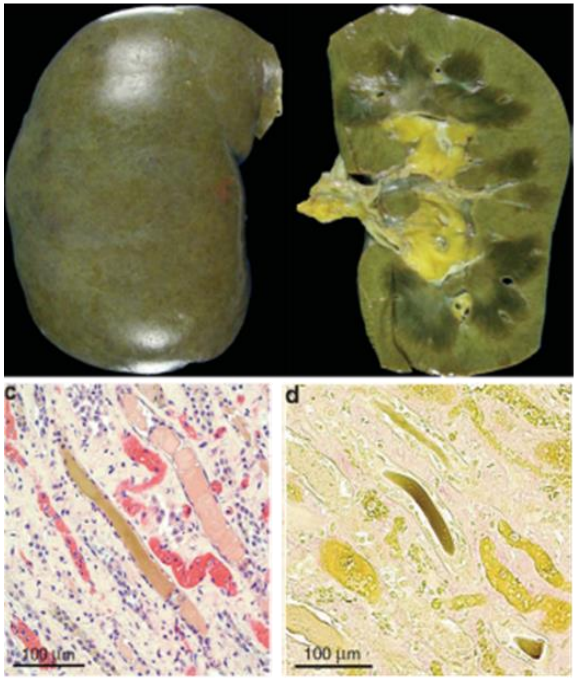




Acute Liver Failure & Decompensated Cyrrhosis

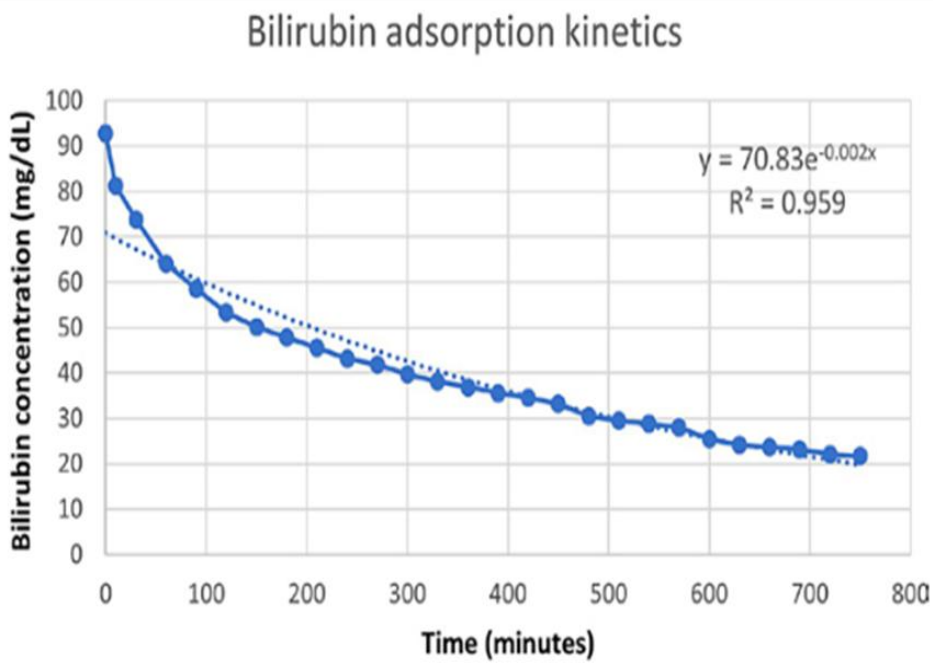
Bile cast nephropathy is a common pathologic finding for kidney injury associated with severe liver dysfunction

Charles M. van Slambrouck[1], Fadi Salem[2], Shane M. Meehan[1] and Anthony Chang[1]

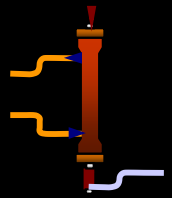


Bilirubin removal by HA Jafron minimodule

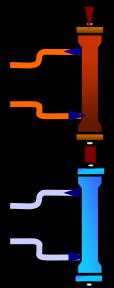
IRRIV Lab test

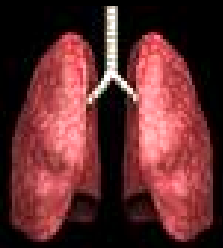


SEPSIS



CRRT





ECLS

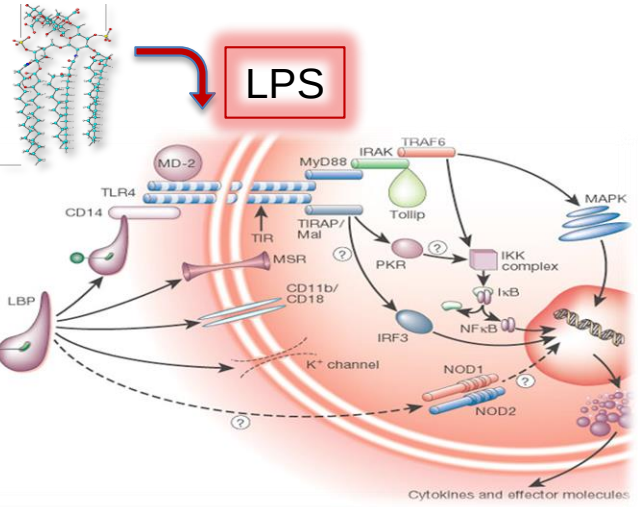
MOST

SCUF

LiverSupport - HVHF
CPFA - CAST

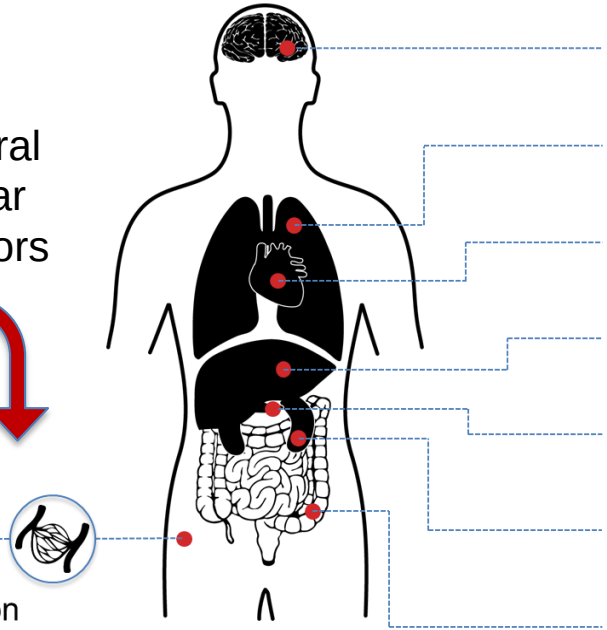
SEPSIS CASCADE

Infection >>> Immuno response >>> Organ Damage



Humoral
Cellular
Effectors

LPS is opsonized and recognised by monocytes through CD14 leading to endothelial cell activation



Microcirculation
- Microvascular thrombosis

Central nervous system
- Confusion

Lungs
- ARDS

Cardiovascular system
- Shock

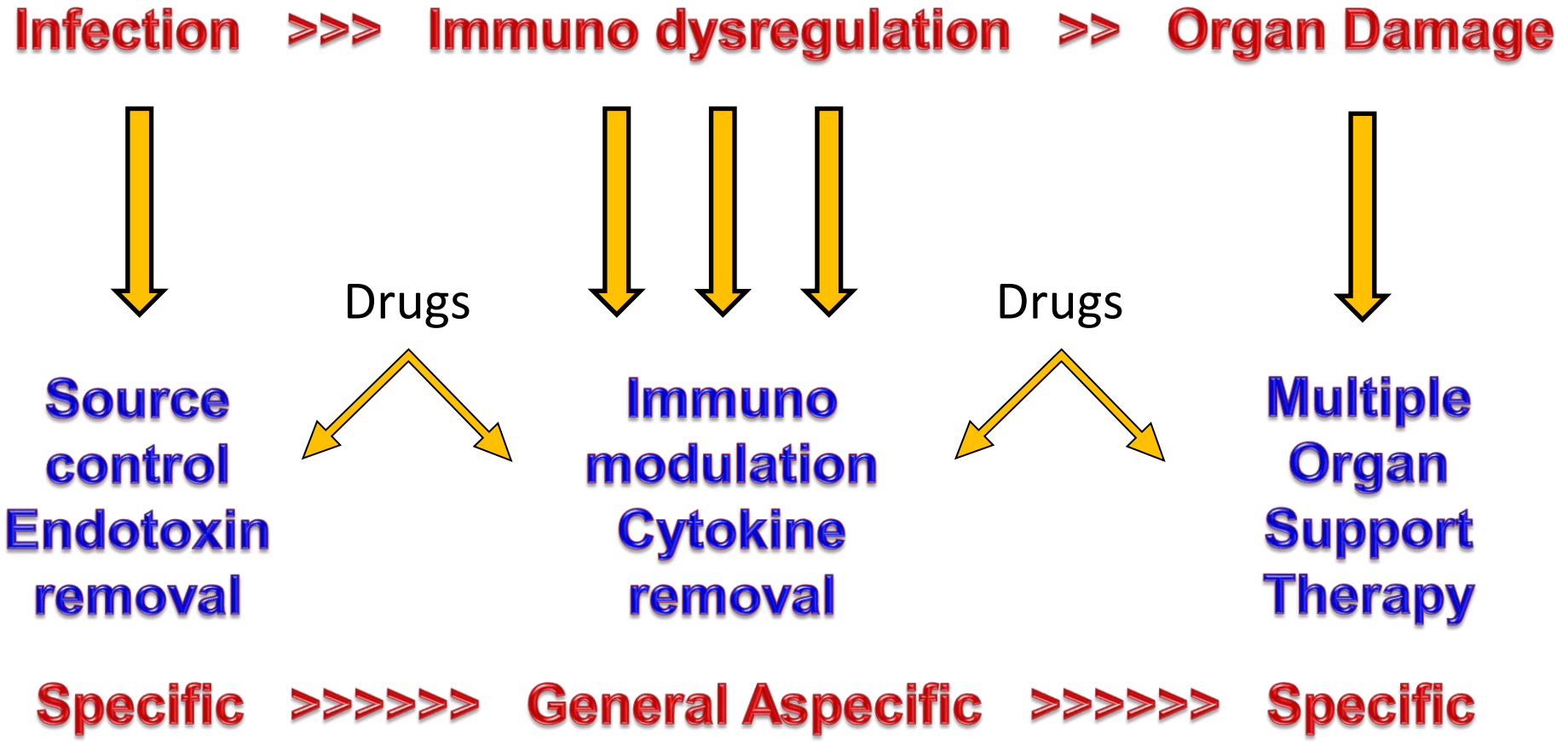
Liver
- Excretory failure

Pancreas
- Hyperglycemia

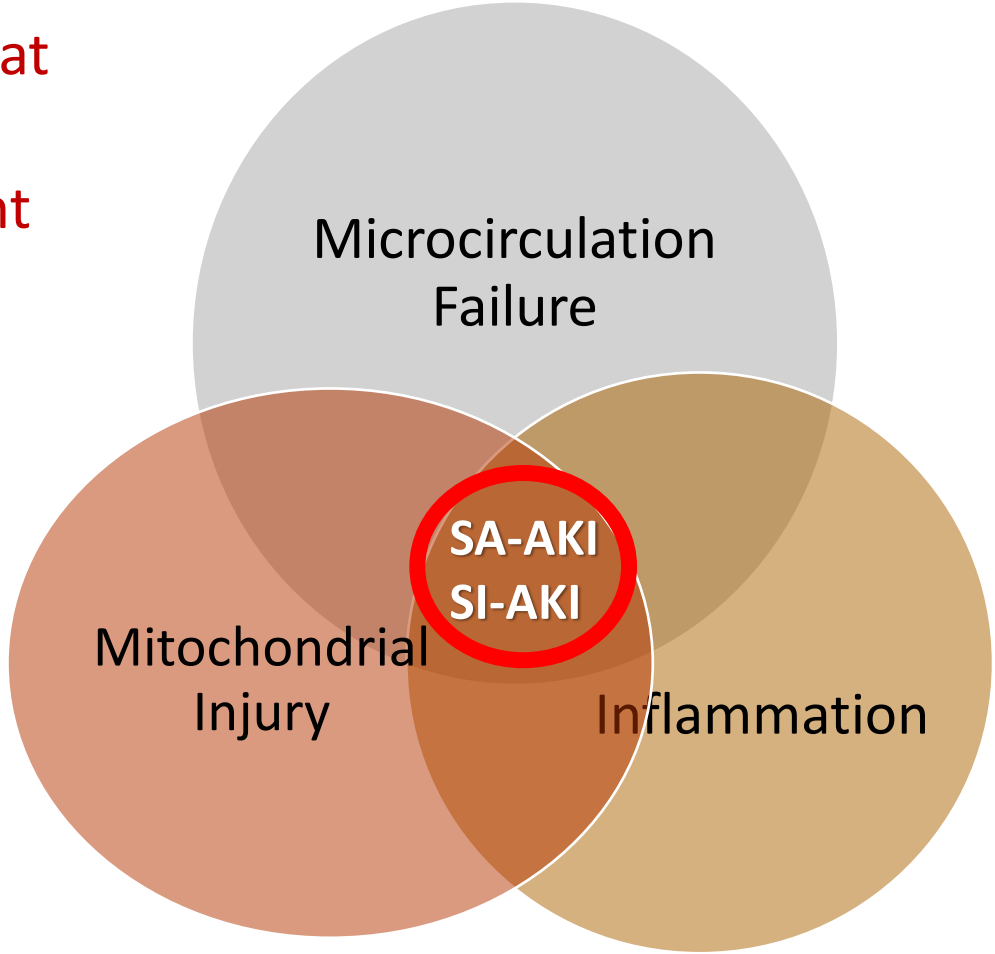
Kidneys
- Oliguria

Gastrointestinal tract
- Loss of barrier function

SEPTIC PATIENT and THERAPEUTIC TARGETS

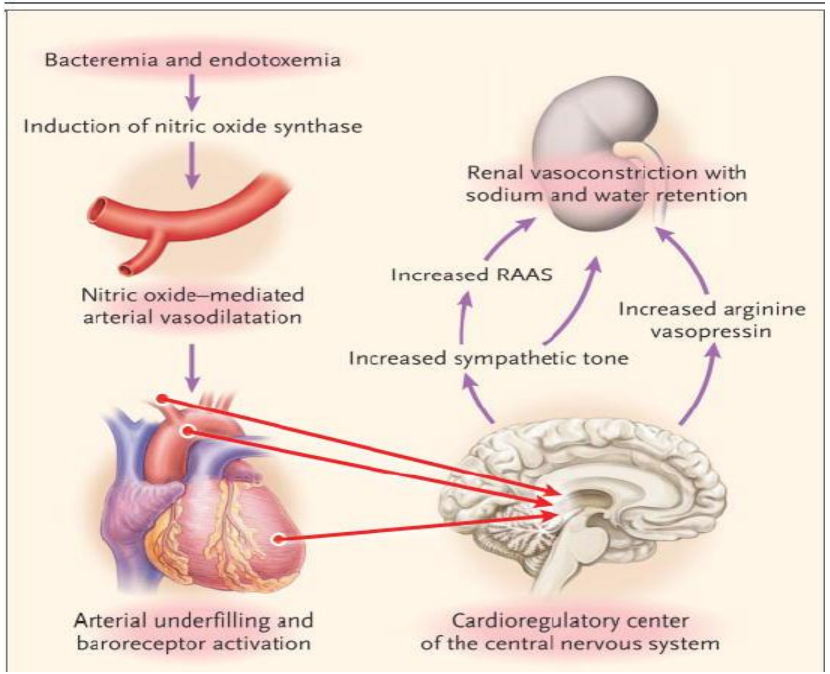


Mechanisms that underlie SA-AKI may be different

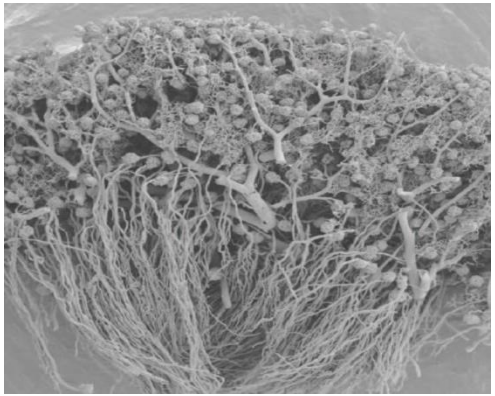


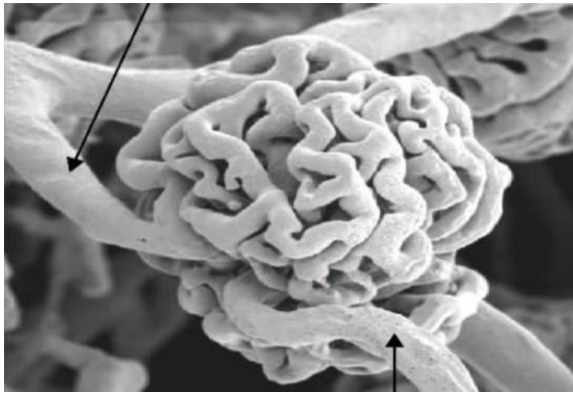
Why does GFR fall in sepsis?

- The NEJM told us (Schrier RW, Wang W. Acute renal failure in sepsis. N Engl J Med 2004; 2004; 351: 159-169)
- "..early in sepsis-related AKI, the predominant pathogenetic factor is renal **vasoconstriction** with intact tubular function…."



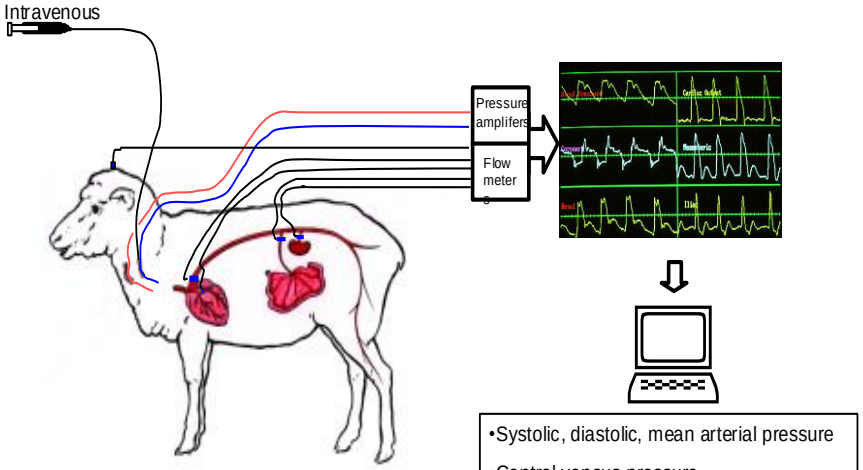
But…..in the same article: "….the hemodynamic hallmark of sepsis is generalized arterial vasodilatation"

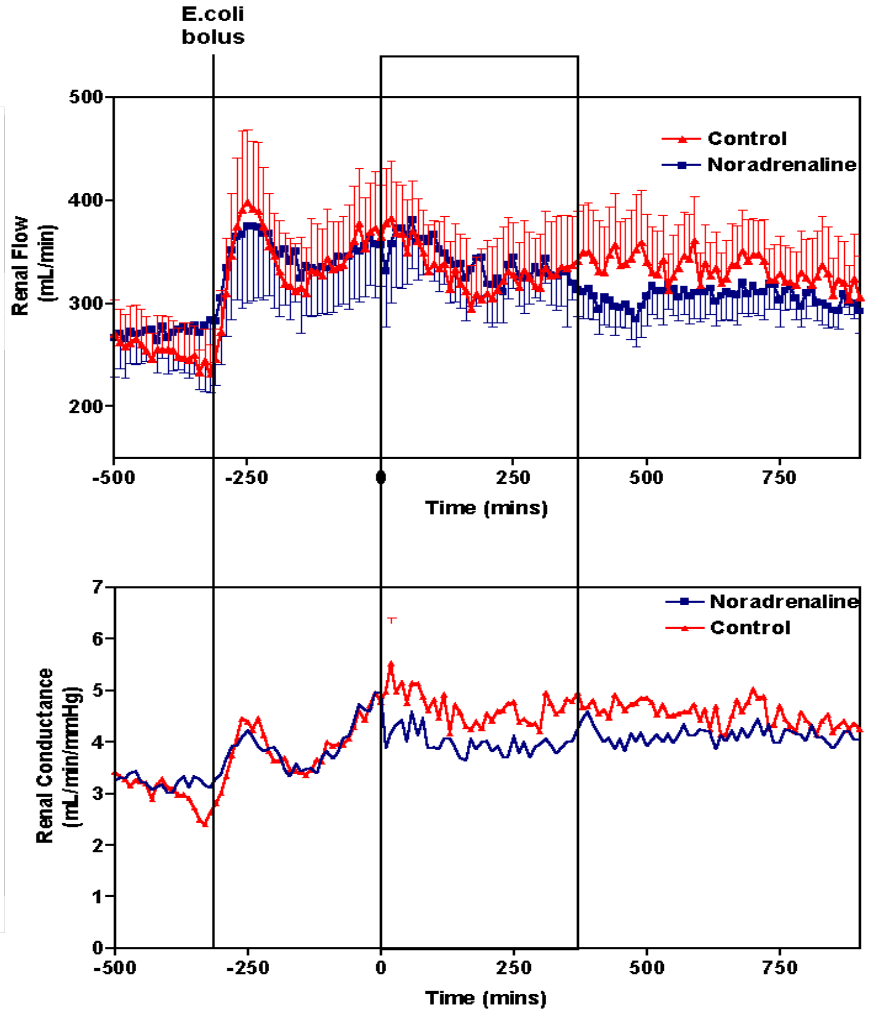




Intensive Care Med 2003; 31: 2509-13

Haemodynamic measurements in conscious sheep





Hyperdynamic Sepsis Model

In a hyperdynamic sepsis model of septic AKI:

- Creatinine may or may not increase
- RBF increases, GFR drops, UO decrease
- Blood flow and Kidney function are dissociated
- There is an important role of mediators on vessell wall

OLIGURIA

New (old) Hypothesis

- There is microcirculatory failure in sepsis. Like other vascular beds the renal bed vasodilates.
- Efferent arteriolar vasodilatation and drop in TMP causes loss of GFR
- Septic AKI is, at least initially, hyperemic not ischemic. GFR drop is due to PAMPS/DAMPS-induced hemodynamic alterations
- If true, besides vasoconstrictors, active correction of **cytokine-induced vasoplegia** should improve GFR and UO in septic AKI

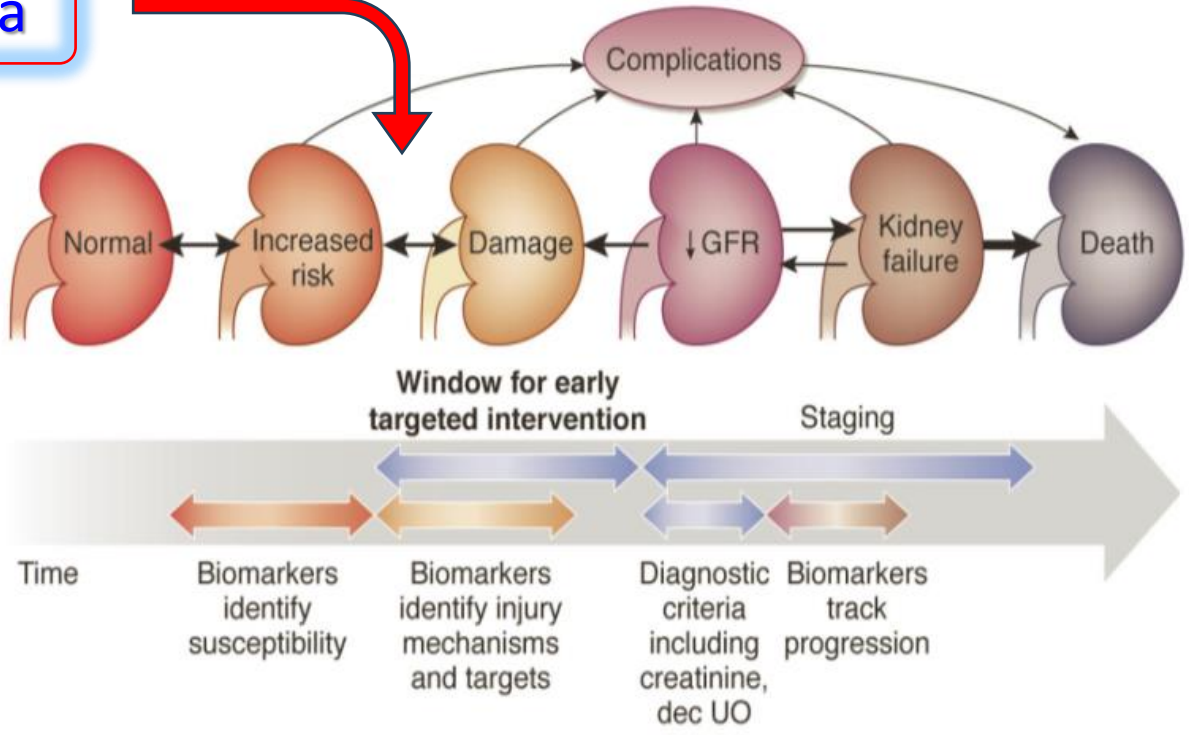
The Continuum of AKI in Sepsis

Sepsis

Oliguria

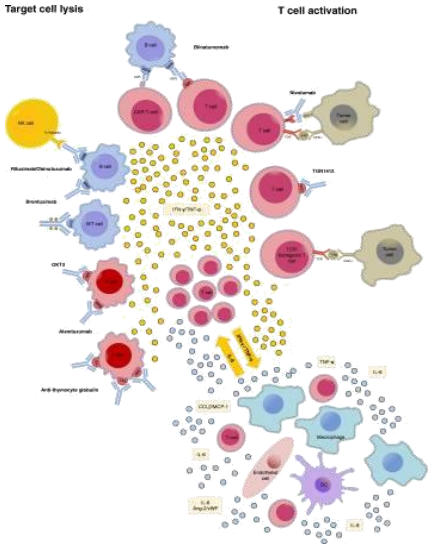
CRS

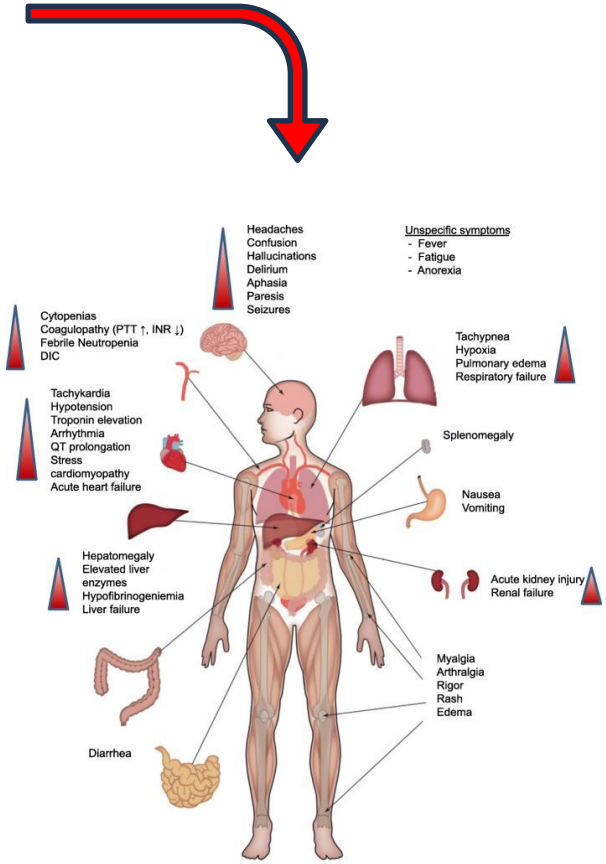
Target for Therapy



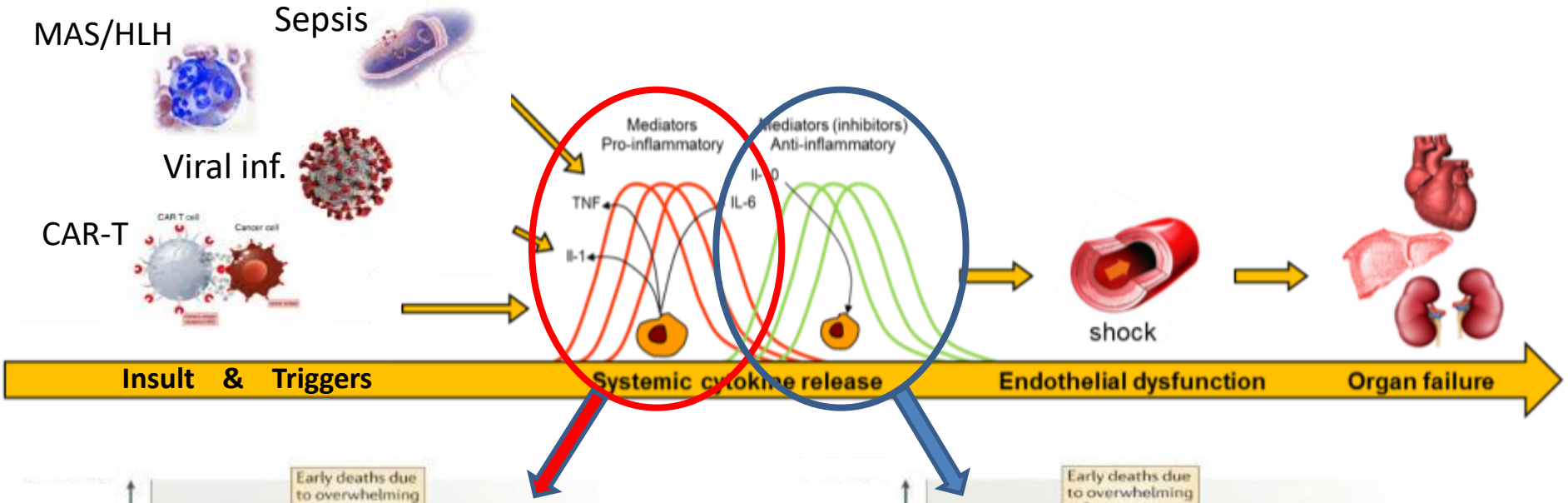
Cytokine Release Syndrome (CRS)

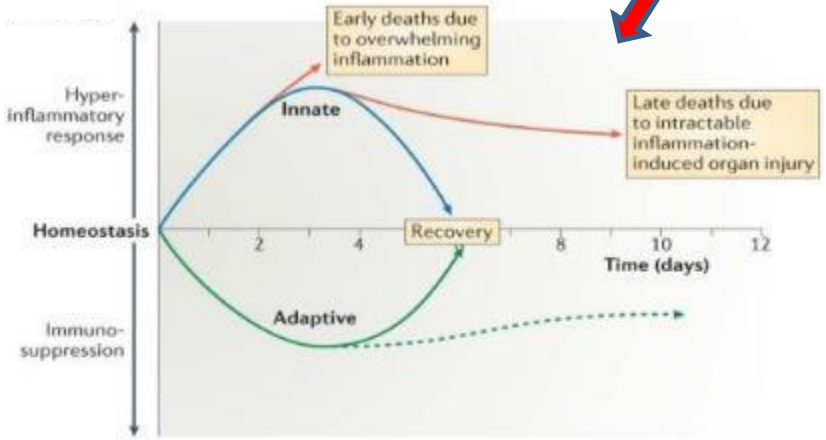
CRS is systemic inflammatory response triggered by infections, drugs, antibody-based therapies or chimeric antigen receptor (CAR)-T cell therapy. Cytokines trigger a cascade with activation of innate immune cells (macrophages and endothelial cells) with further cytokine release.

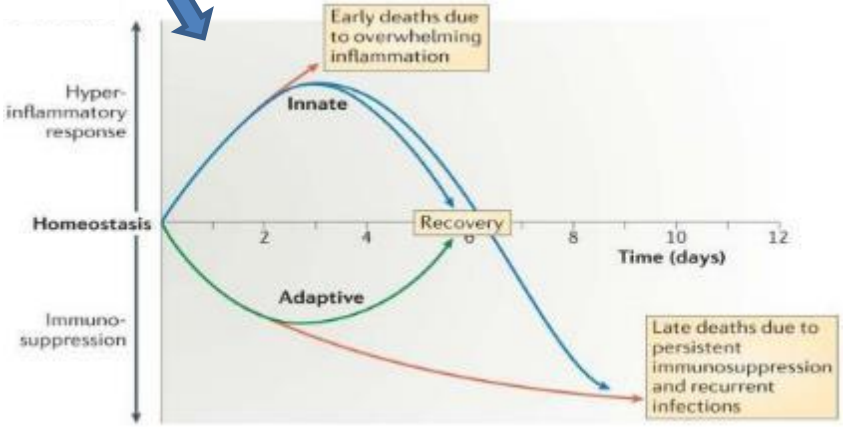




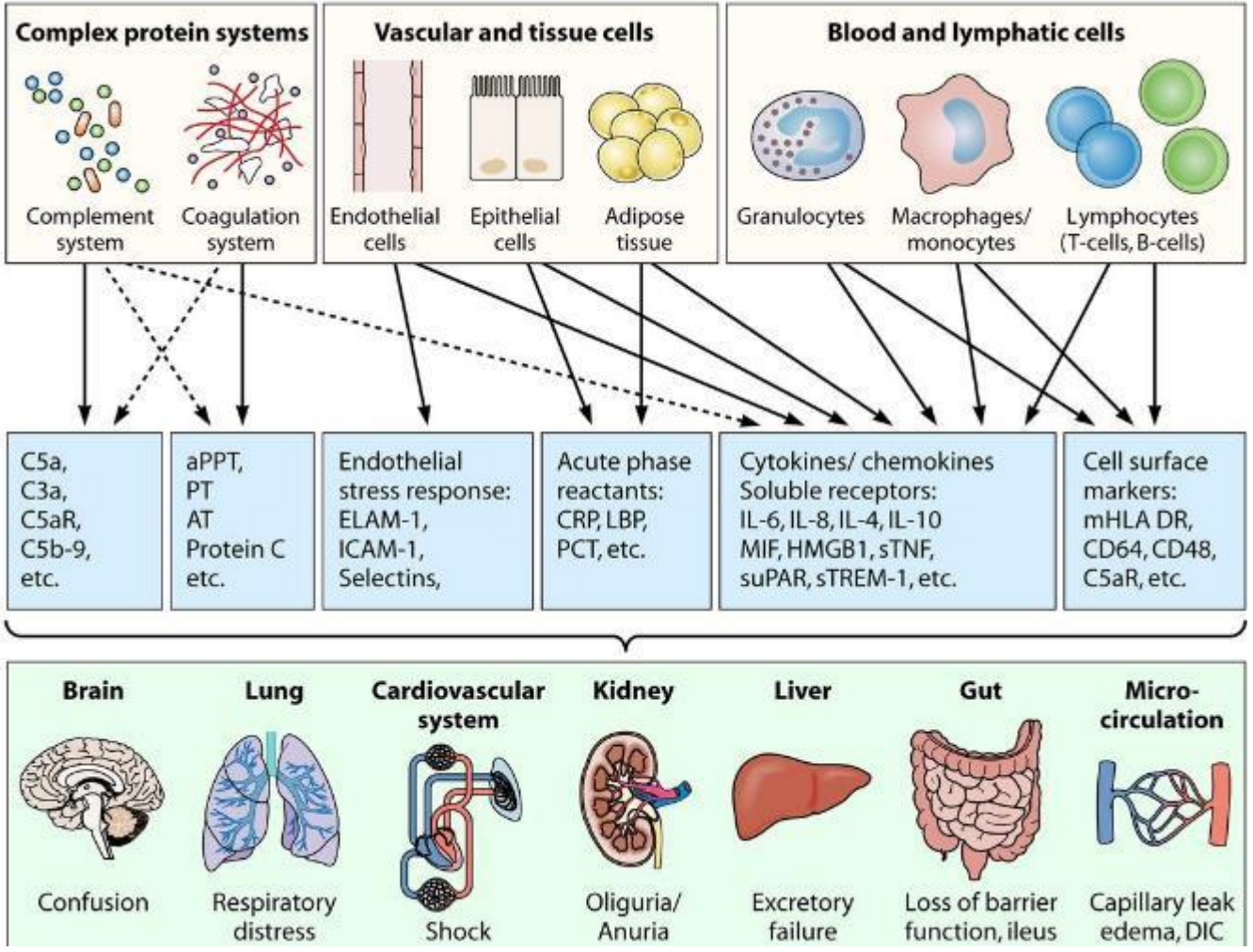
Release of cytokines into the blood is the pathophysiological mechanism of SA-AKI.


MAS/HLH
Sepsis
Viral inf.
CAR-T
CAR T cell
Cancer cell
Mediators
Pro-inflammatory
Mediators (inhibitors)
Anti-inflammatory
TNF
Il-1
IL-6
shock
Insult & Triggers
Systemic cytokine release
Endothelial dysfunction
Organ failure


Early deaths due to overwhelming inflammation
Hyper-inflammatory response
Innate
Late deaths due to intractable inflammation-induced organ injury
Homeostasis
Recovery
2
4
8
10
12
Time (days)
Adaptive
Immuno-suppression

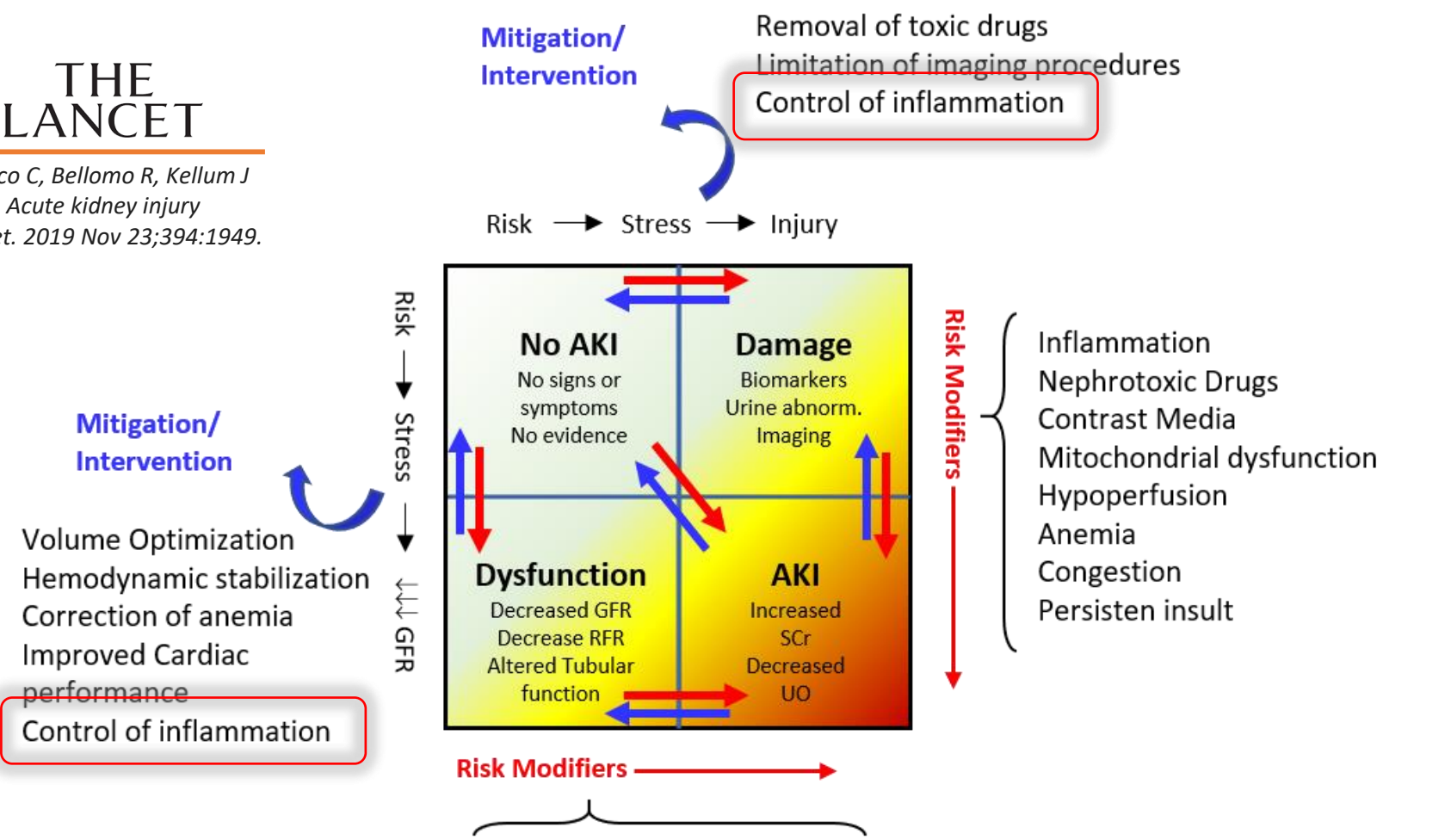

Early deaths due to overwhelming inflammation
Hyper-inflammatory response
Innate
Homeostasis
Recovery
2
4
8
10
12
Time (days)
Adaptive
Immuno-suppression
Late deaths due to persistent immunosuppression and recurrent infections

Insult → **PAMPS & DAMPS**



THE LANCET

Ronco C, Bellomo R, Kellum J
Acute kidney injury
Lancet. 2019 Nov 23;394:1949.



Extracorporeal and novel therapies for sepsis-associated acute kidney injury

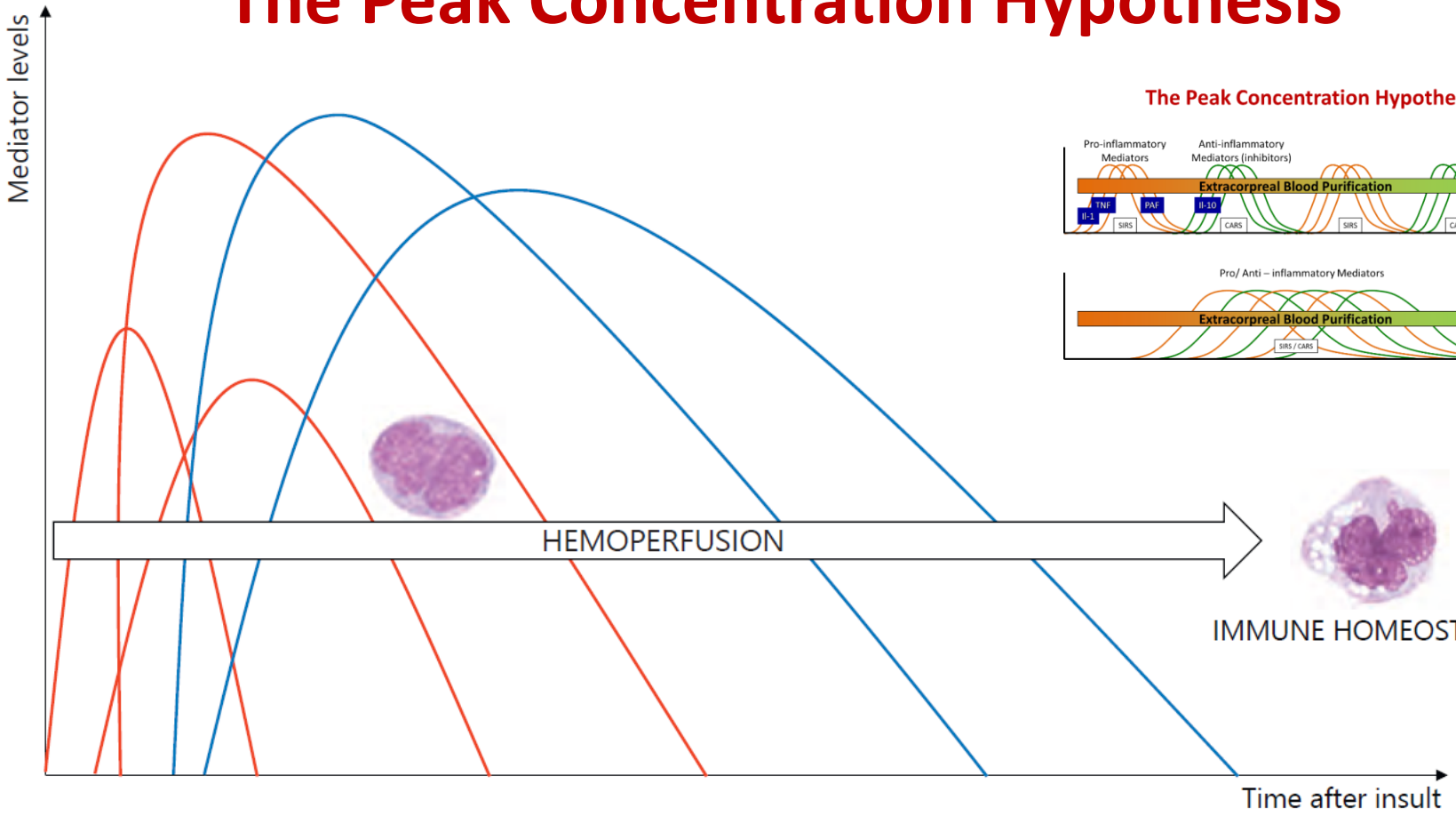
Consensus statement 5a

Extracorporeal blood purification (EBP) techniques can be used to remove pathogens, microbial toxins, inflammatory mediators and toxic metabolites from the blood as well as replenish solutes (grade 1A).

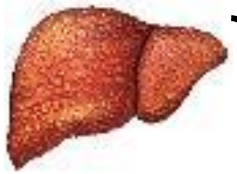
Consensus statement 5d

Initiation of EBP in sepsis might be considered for immunomodulatory molecular patterns and pathogen-associated molecular patterns, as well as other targets of systemic inflammation (not graded).

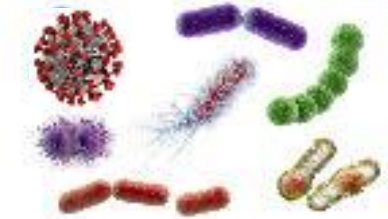
The Peak Concentration Hypothesis



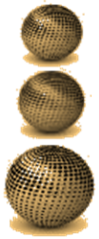
Retention Molecules – PAMPs – DAMPs - Enzyme inhibitors



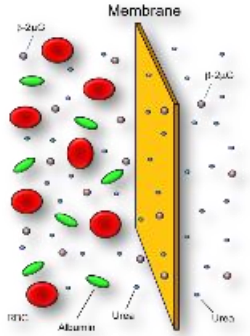
Kidney failure Liver Failure

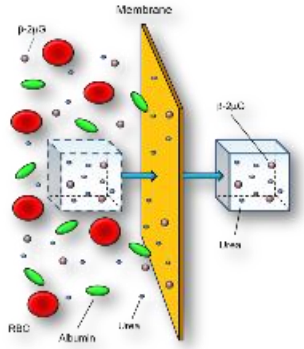


Infections / Inflammation
Sepsis e CRS

Class		SOLUTE	MW (Da)	Action/Effect
Small		Urea Creatinine Vitamin B12	60 125 1250	General toxicity
Middle		β 2 M Leptin Myoglobin	12000 16000 17000	Amiloidosis CTS Malnutrition Organ damage
Large		κ-FLC Prolactin Interleukin-6 Hepcidin Bound P-Cresol Pentraxin-3 λ-FLC TNF-α (Trim)	23000 23000 25000 27000 33500 43000 45000 51000	Toxicity Infertility Inflammation Anemia CV Toxicity Acute Phase Prot. CV Toxicity Inflammation
Essential protein		Albumin	68000	Toxin binding capacity

What Blood Purification Technique?





Diffusion

Hemodialysis
High Flux Dialysis

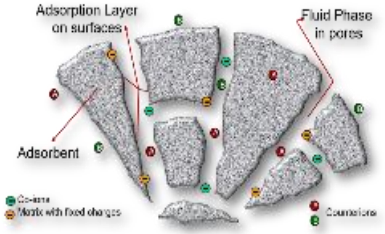
Blood Purification

Convection

Hemofiltration
Hemodiafiltration

Adsorption

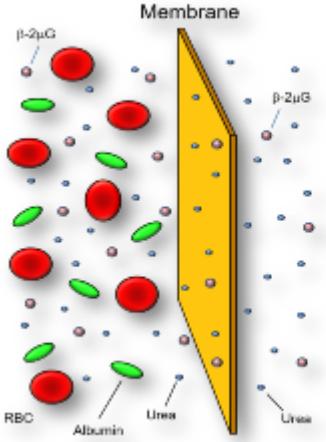
Hemoadsorption
Hemoperfusion



a) Mass separation by barrier (CVVH-CVVHD-CVVHDF)

b) Mass separation by solid agent (Hemoadsorption)

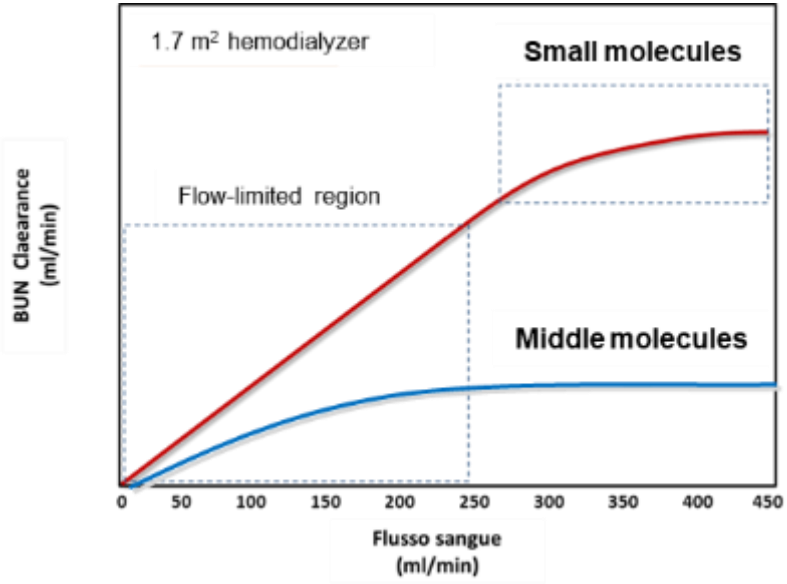
Hemodialyzer



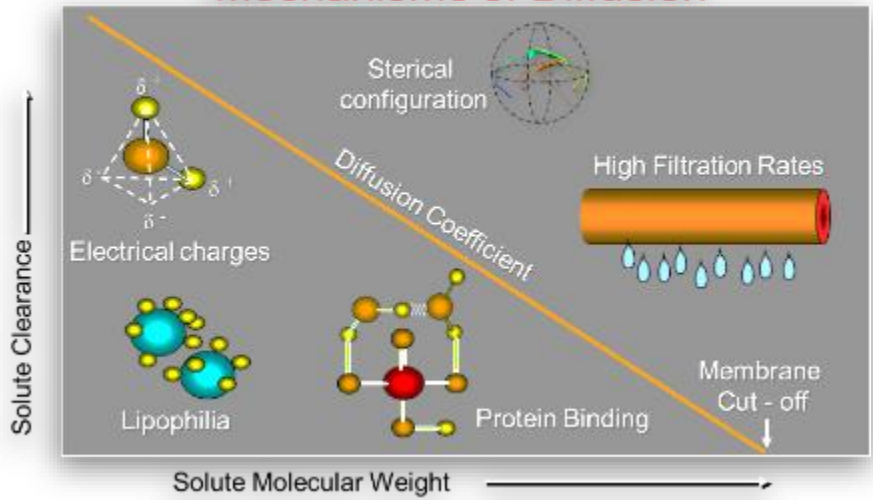
DIFFUSION

$$J_{diff} = D \cdot T \cdot A \cdot (dc/dx)$$

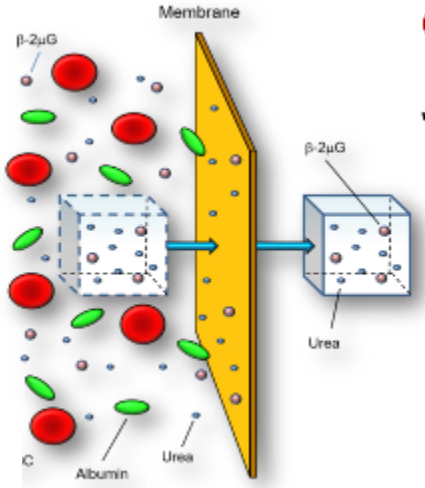
- Distance (Membrane thickness)
- Concentration Gradient
- Membrane Surface Area
- Solution Temperature
- Solute Diffusion Coefficient



Mechanisms of Diffusion



Hemodialyzer



CONVECTION

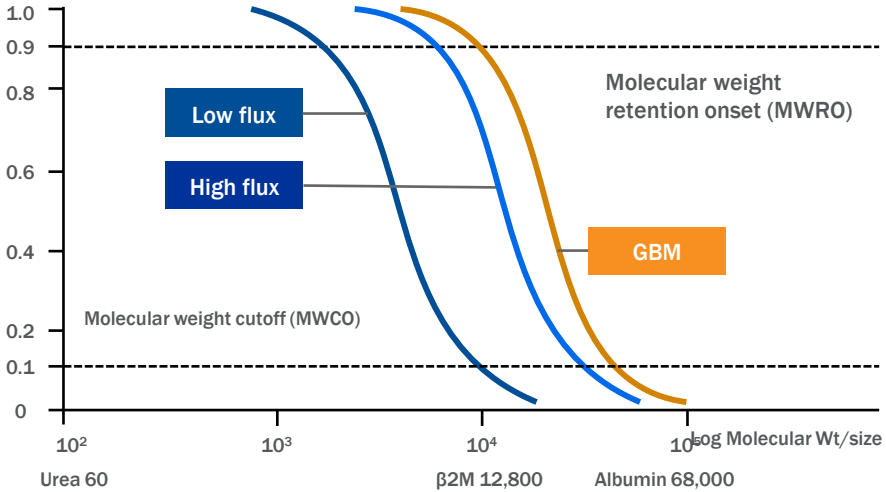
$$J_{conv} = Qf \cdot [uf]/[p]$$

$[uf]/[p] = S$

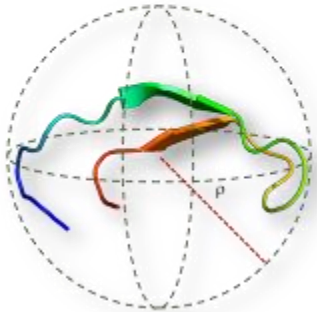
Solute concentration in plasma

Solute concentration in the ultrafiltrate

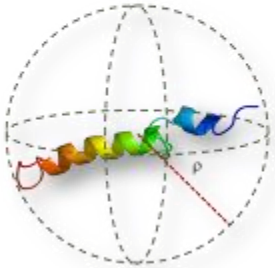
Ultrafiltration rate



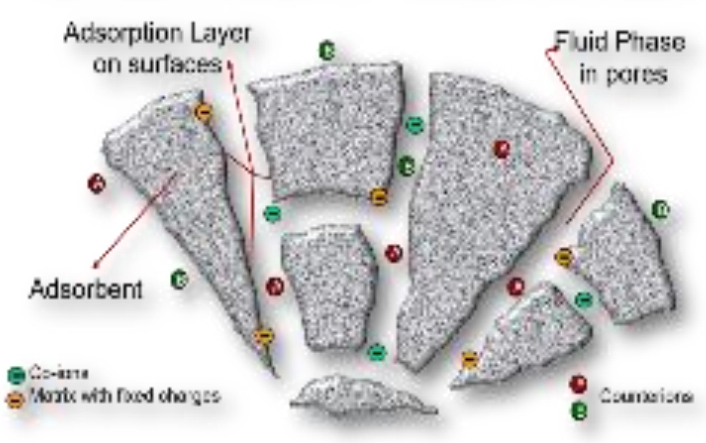
Hepcidin Anti Microbial Peptide
MW: 27000 Da



Parathiroid Hormon
MW: 9300 Da



HEMOADSORPTION



Advantages and Rationale

- Overcoming limitations of HD membranes
- Potential selectivity of the removal
- Placement of sorbent in contact with blood
- No alteration of anticoagulation regime
- No problems of circuit pressure profile

Requirements

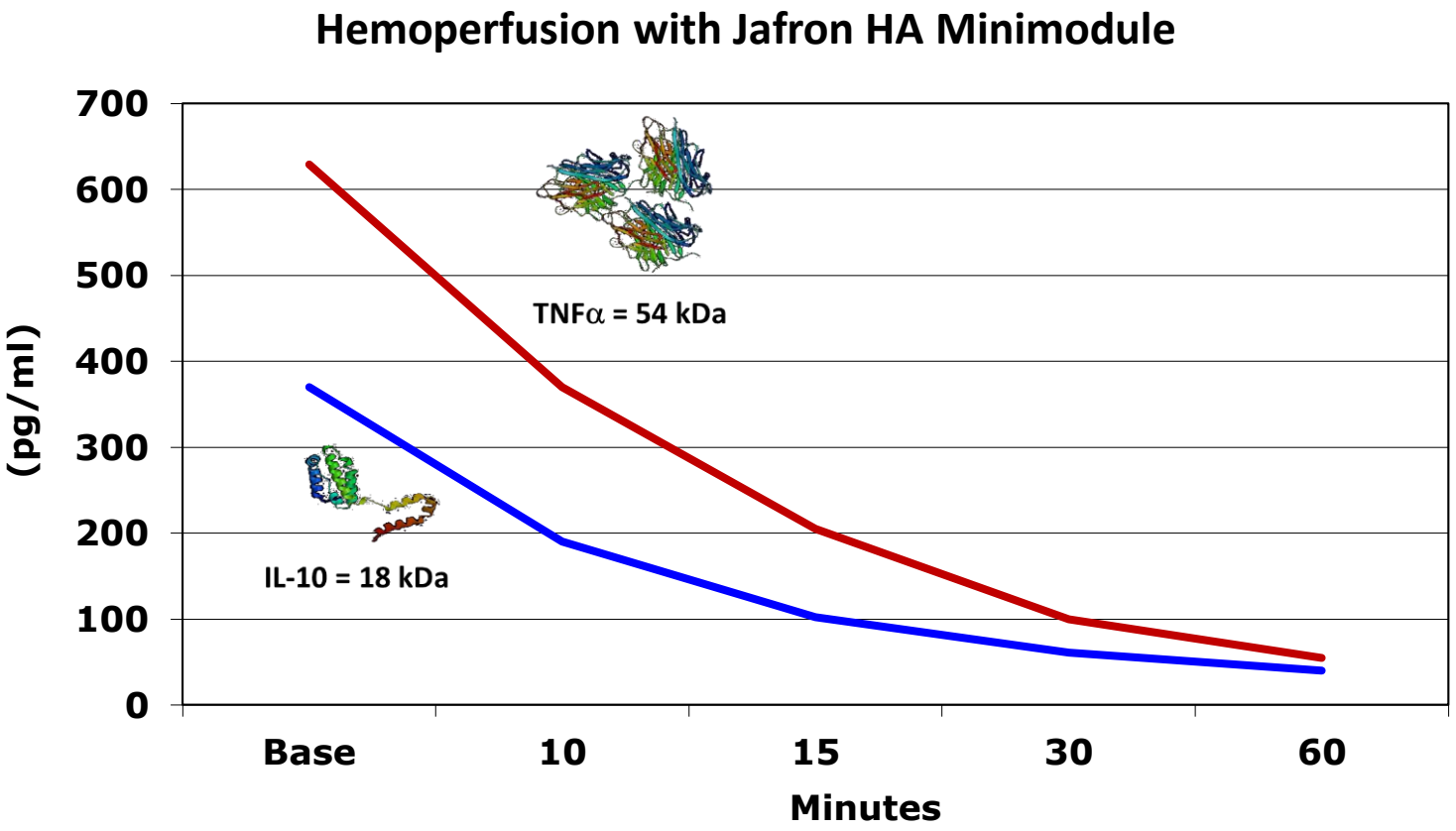
- Demonstrated effectiveness
- Hemocompatibility
- Mechanical strength
- No clotting activation
- Well designed cartridge

Resin Adsorption Range Control

Nano-scale Molecular Sieve Control Technology MAY adjust pore size distribution according to target toxin molecular weight and radius

In Vitro Removal of Cytokines

LPS stimulated U-937 monocytes in Blood

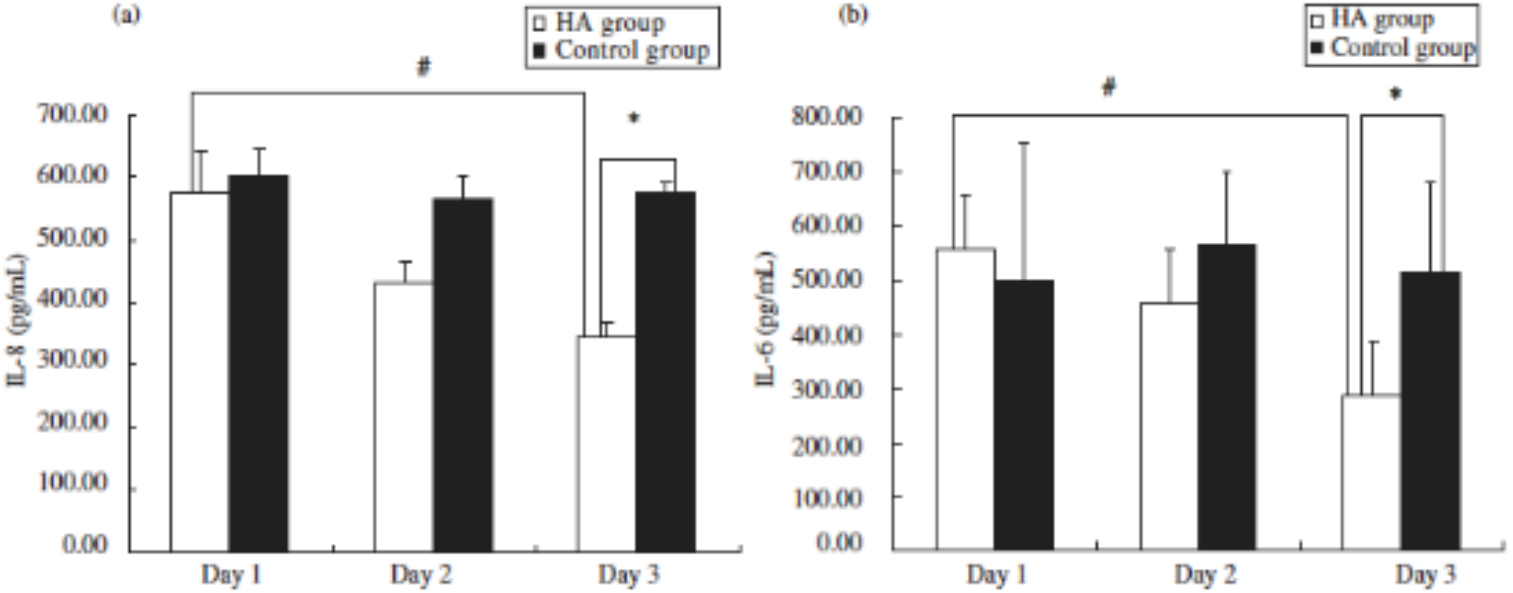


Removal of Humoral Mediators and the Effect on the Survival of Septic Patients by Hemoperfusion With Neutral Microporous Resin Column

Zhao Huang, Si-Rong Wang, Wei Su, and Ji-Yun Liu

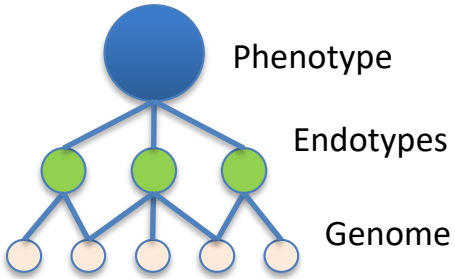
HA 380

- N=44. Severe sepsis/septic shock patients.
- Standard therapy vs standard therapy plus HA (2hr session daily x 3days).



Change in IL-6 and IL-8 and improved SOFA score ($p<0.05$)

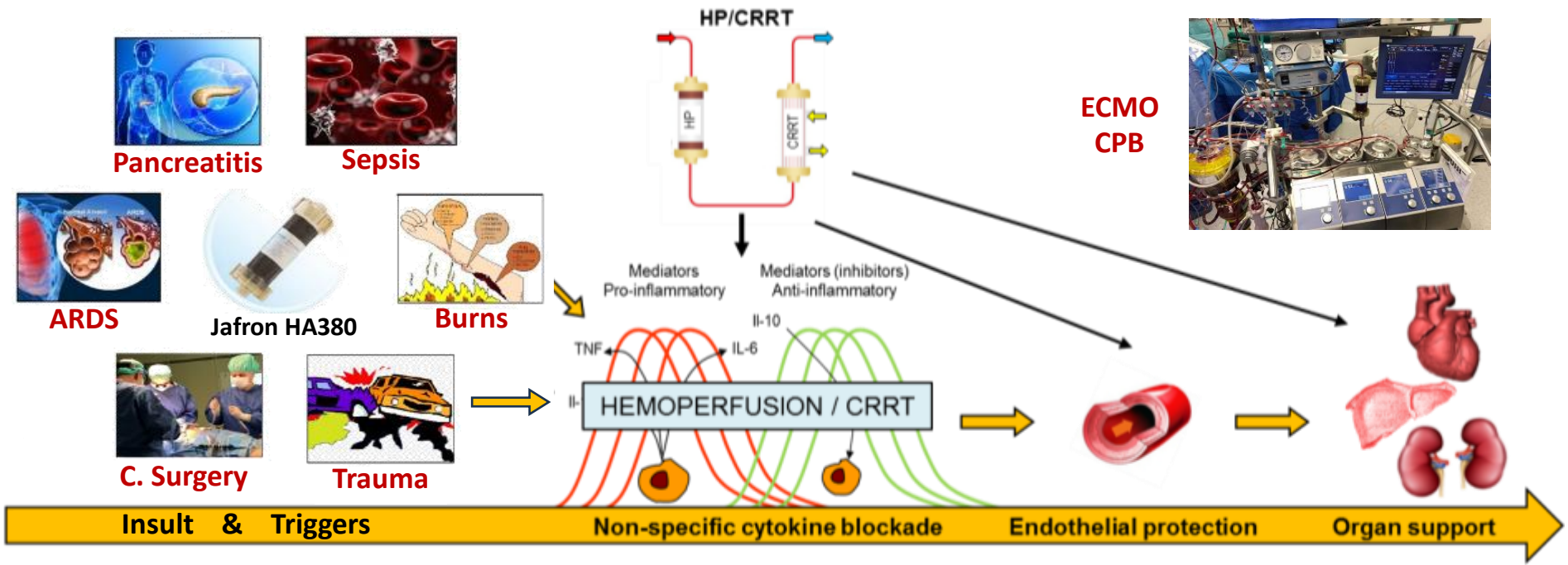
Hemoadsorption Trial design



- Clear indications (inclusion) criteria
- Selection of population
- Identification of sub-phenotypes
- Definition of target effect

Endpoints in Hemoadsorption Trials

- Biochemical *(Different Molecular targets)*
- Biological *(Cellular and tissue effects)*
- Physiological *(Vital parameters)*
- Clinical *(Organ function – Severity scores)*
- Ultimate outcomes *(Recovery - Survival)*



Hemoadsorption in critical illness: Typical Findings

Significant reduction in:

IL-6 (>50%); MCP-1 (>50%); IL-1 RA (>50%);

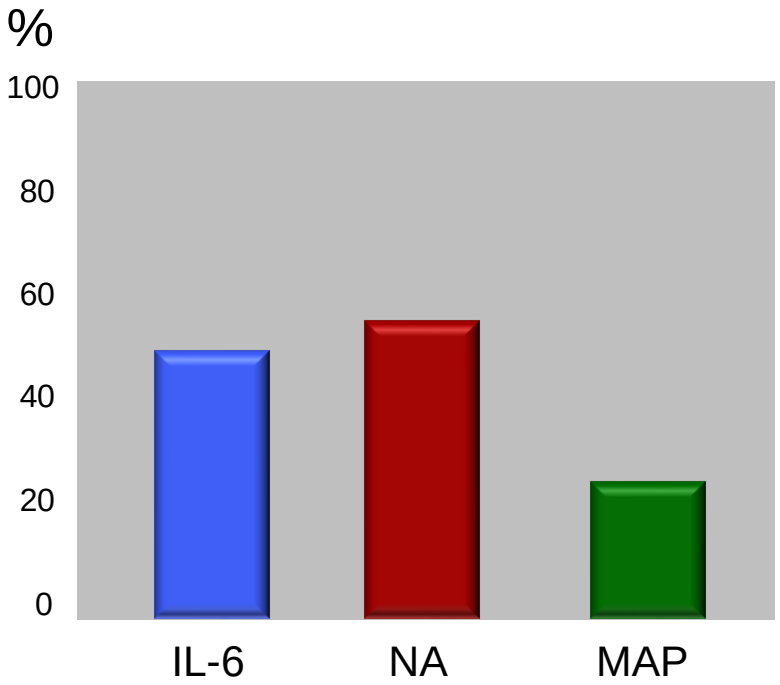
IL-8 (>30%), IL-10 (>50%)

Immediate improvement in patient's hemodynamics

Hemodynamic and Biological Effects of HP

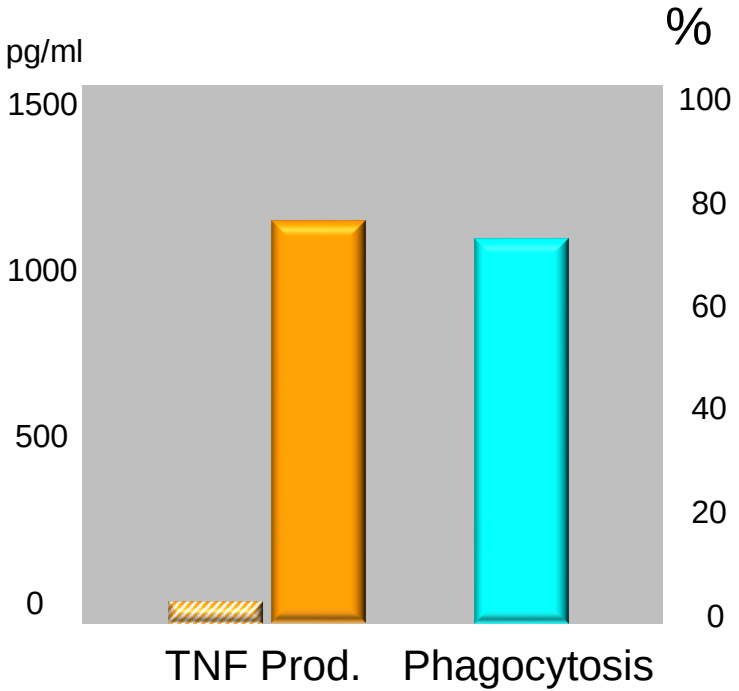
% Delta of IL-6 levels,
NA Dose and MAP

at 10 hours of treatment versus baseline

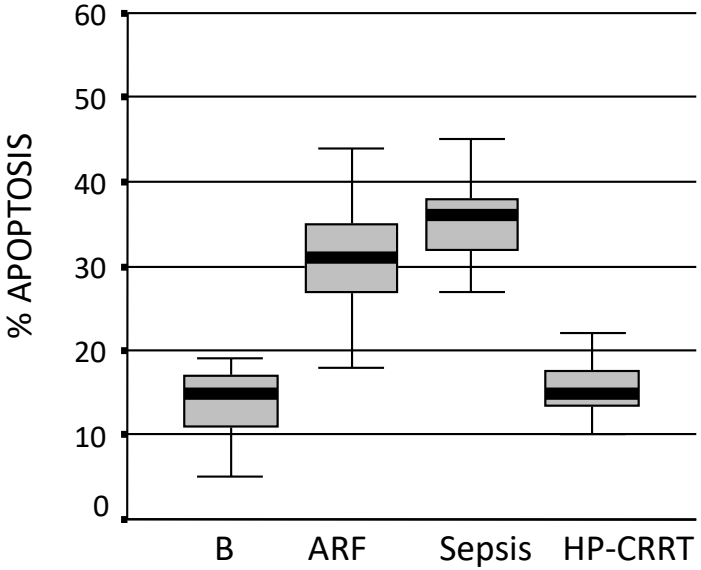


Δ Monocyte TNF production and
Phagocytic Capacity

at 10 hours of treatment versus baseline

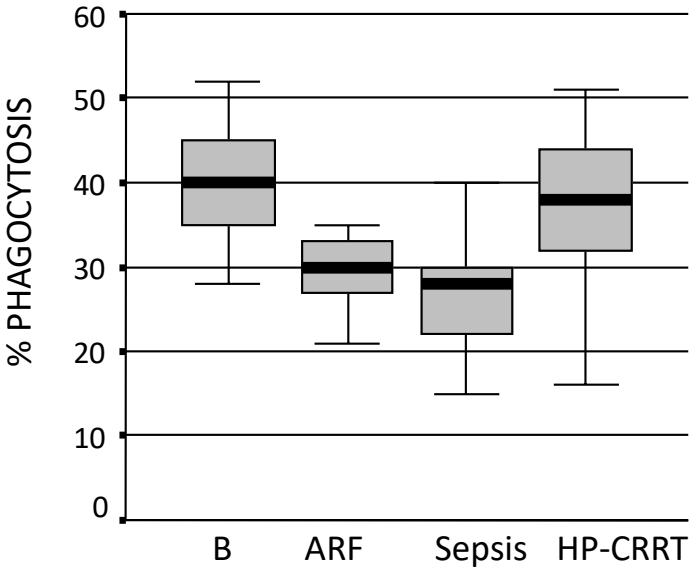


Biological effects: Apoptosis and Phagocytosis



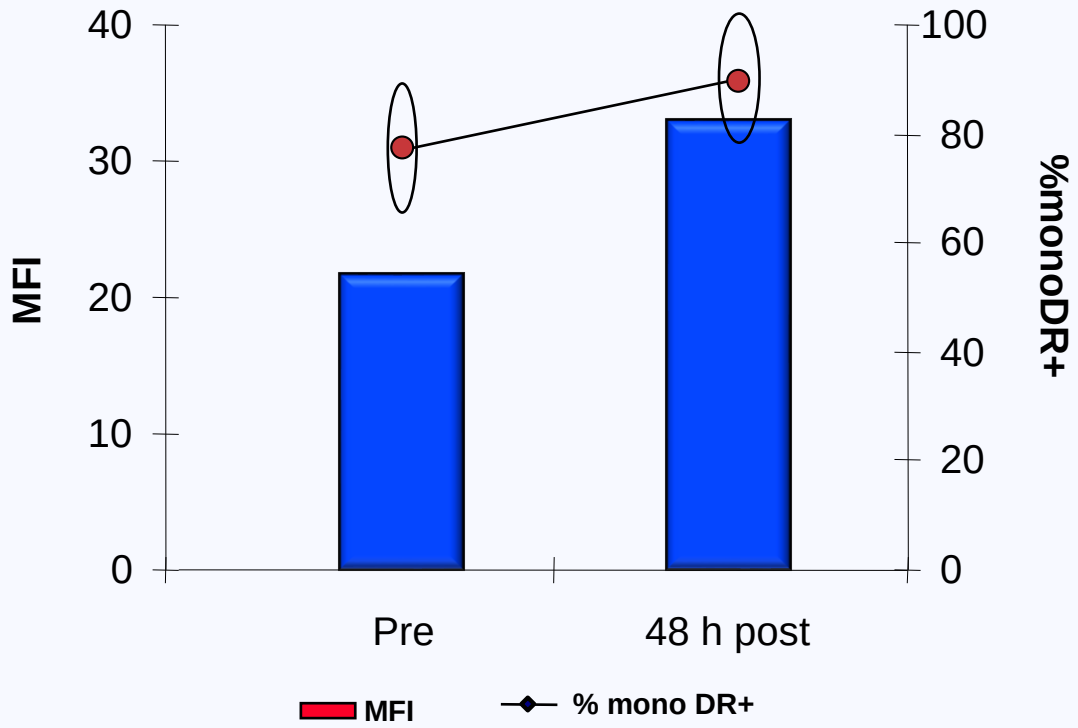
* p<0.05; ** p<0.001

Apoptosis correlated inversely with cell phagocytic function



Patient with Septic Shock and Abdominal Infection

Pre/post HP Tx Antigen Presentation



nature REVIEWS

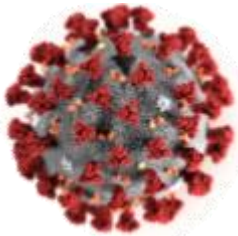
NEPHROLOGY

COMMENT

Kidney involvement in COVID-19 and rationale for extracorporeal therapies

Claudio Ronco[1,2] ✉ *and Thiago Reis*[2,3]

The prevalence of direct kidney involvement in novel coronavirus disease (COVID-19) is low, but such involvement is a marker of multiple organ dysfunction and severe disease. Here, we explore potential pathways of kidney damage and discuss the rationale for extracorporeal support with various blood purification strategies in patients who are critically ill with COVID-19.



> cytokine removal could prevent CRS-induced organ damage

On 11 March 2020, the World Health Organization declared novel coronavirus disease (COVID-19) to be a global pandemic. Among patients who have tested positive for COVID-19 in Italy, approximately 47% have been hospitalized and approximately 6% have required admission to intensive care units (ICUs)[1]. Here, we focus on the mechanisms and management of COVID-19-associated acute kidney injury (AKI).

The available data suggest that the prevalence of AKI

anti-IL-6 monoclonal antibody tocilizumab is widely used to treat CRS in patients who have undergone CAR T cell therapy[3] and is now also being used empirically in patients with severe COVID-19.

Extracorporeal therapies have also been proposed as approaches to remove cytokines in patients with sepsis[6] and could potentially be beneficial in critically ill patients with COVID-19 (REF.[7]). The rationale for use of these therapies is that cytokine removal could prevent

Physiological/clinical effects: COVID-19 patient

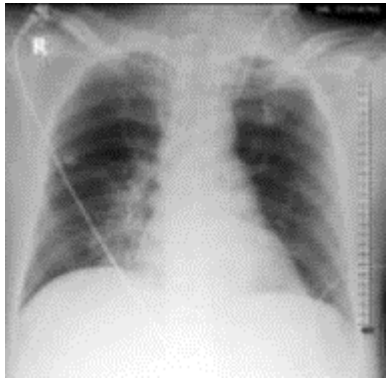
Evidence of CRS

Admission:
Fever
Hypotension
Respiratory failure
> Mech. Ventilation

Hemodynamic instability
High Cytokine Levels
High Ferritin
High CRP
Hypercoagulability

Hemodynamic stabilization
Normalization of Cytokine Levels
Decrease in inflammatory parameters
Improved pulmonary exchanges

Extubation



Day 1

Day 3

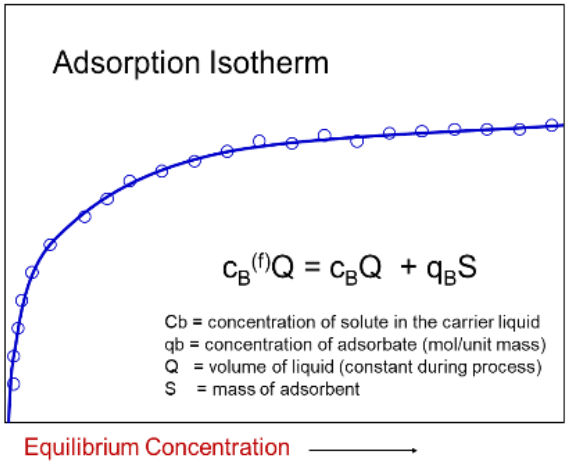
Days 4-5-6

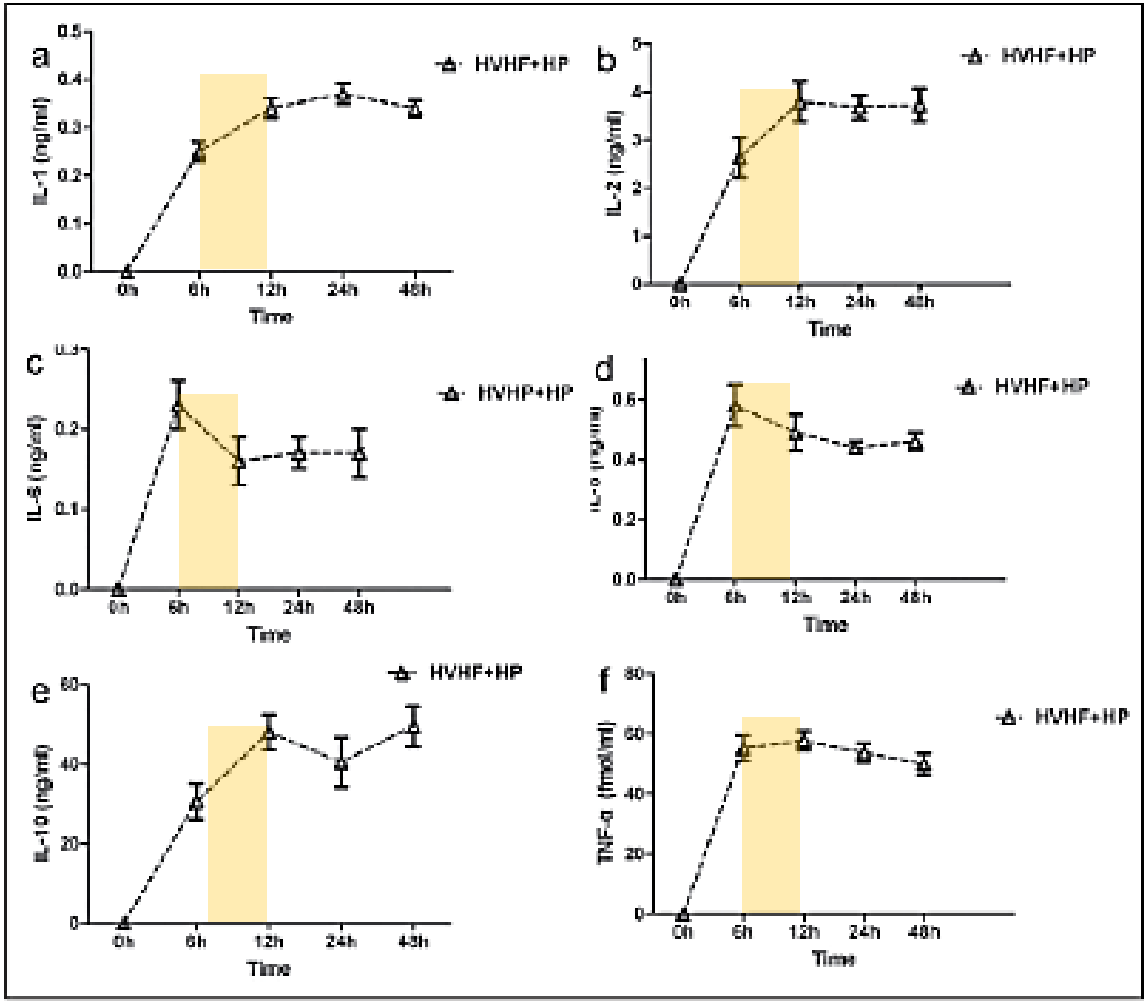
Day 8

Day 12

Cartridge saturation occurs between 6 and 12 hours

Equilibrium Stage for liquid adsorption





HA in Sepsis and CRS

Early application: Patients with signs and symptoms of impensing sepsis and CRS, altered hemodynamics, hyper-inflammatory status, immunodysregulation, requirement of vasopressors

Diagnosis

Day 1

0 6 12 18 24

Day 2

0 6 12 18 24

Day 3

Optional

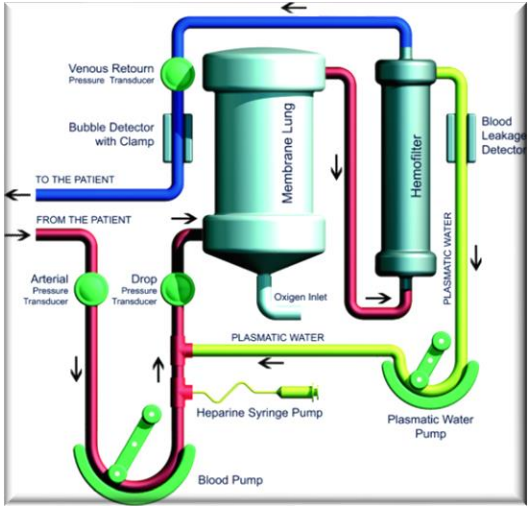
0 6 12 18 24

Multiple Organ Support in Critical Illness and Sepsis

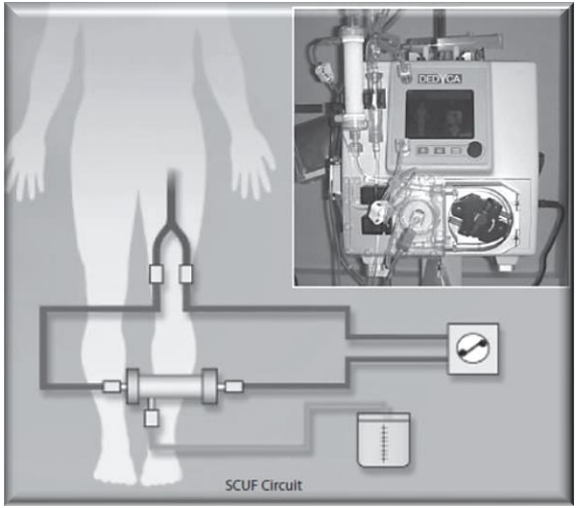
AKI & Sepsis

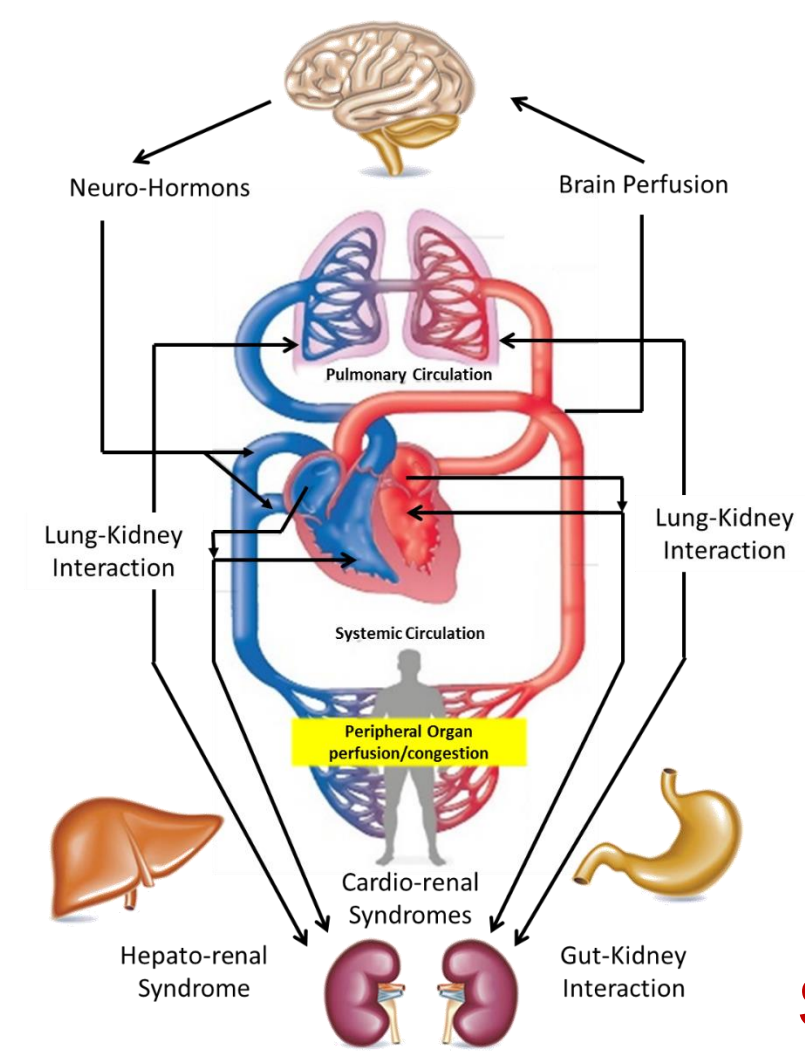
Liver Support

Lung Support $ECCO_2R$

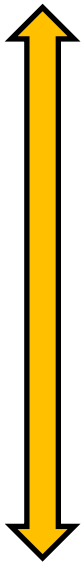


Heart Failure

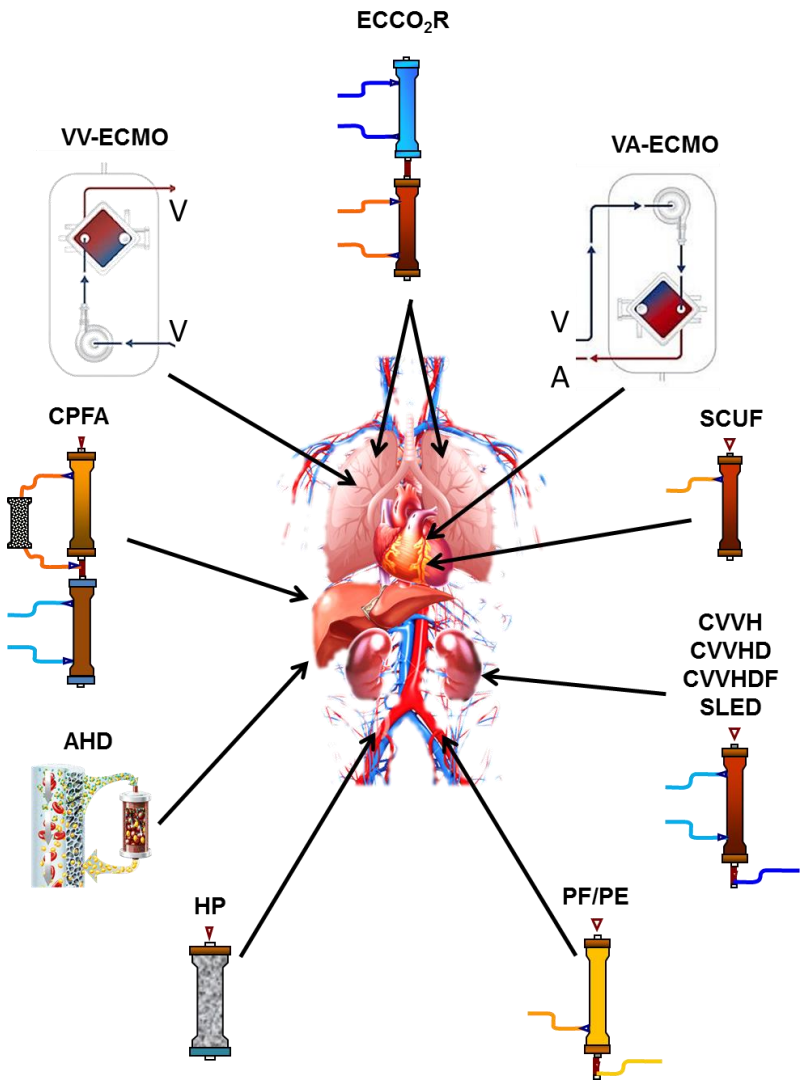




MOST and ECOS

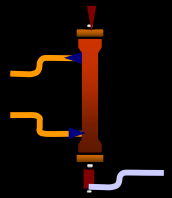


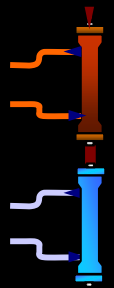
Sepsis

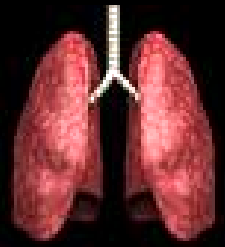


SEPSIS

CRRT







ECLS

MOST

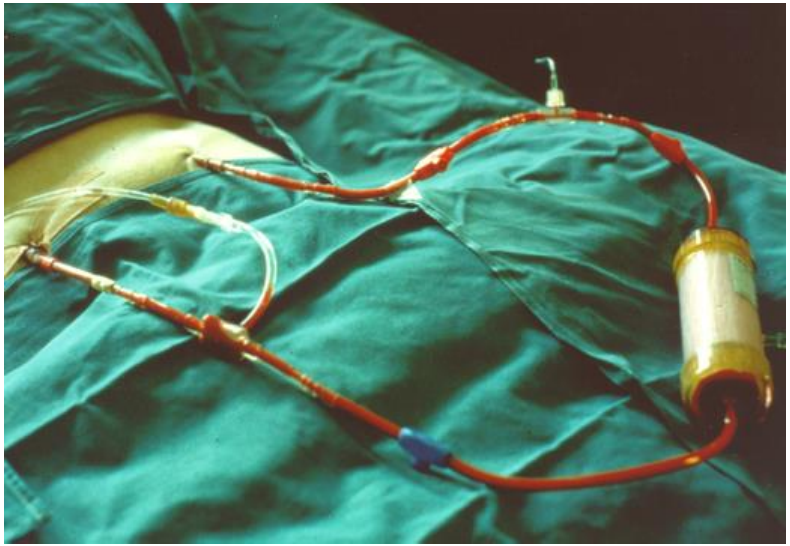
SCUF

LiverSupport - HVHF
CPFA - CAST

PEDIATRICS

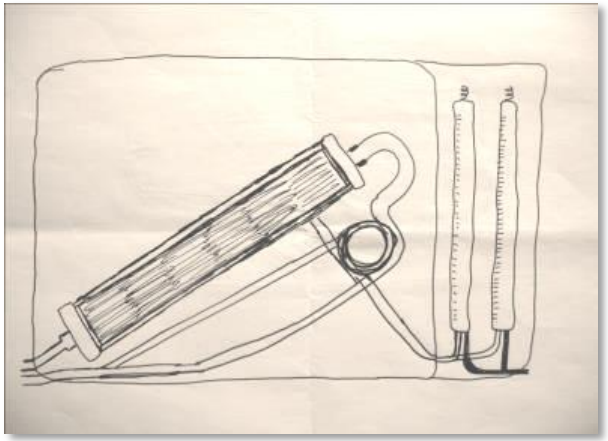
Leading Science of CRRT in Vicenza

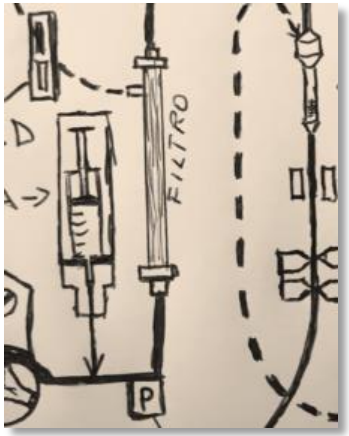
First Adult CAVH in Vicenza 1977

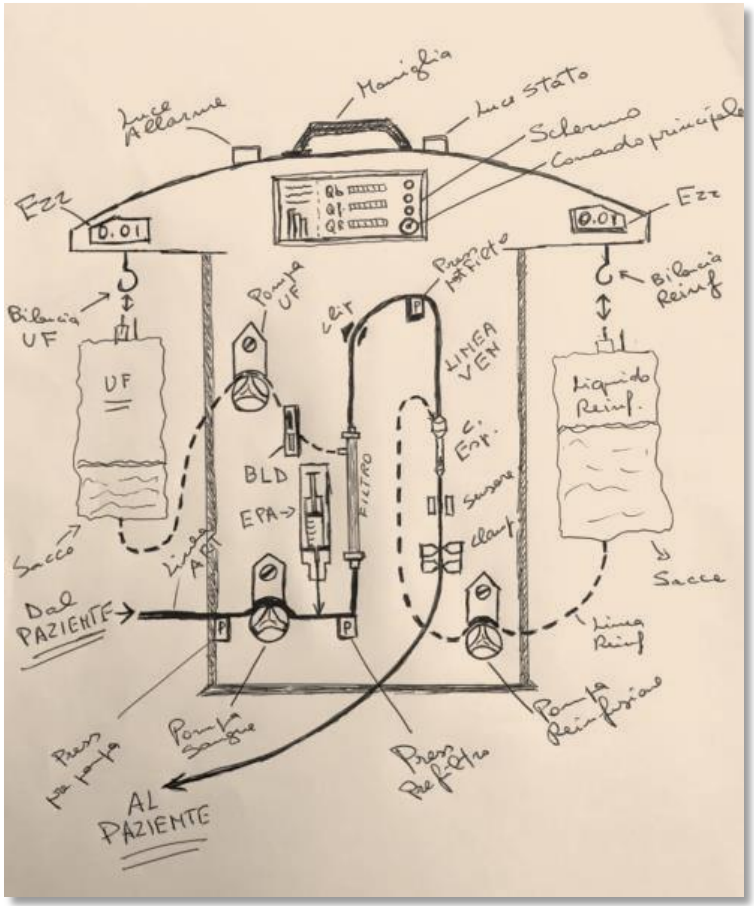


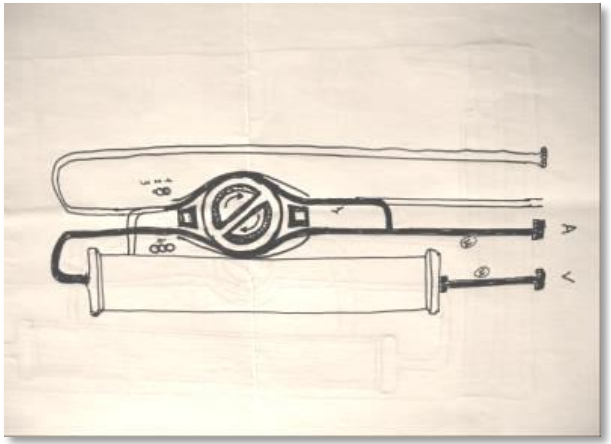
First Neonate CAVH in Vicenza 1982

From a sketch and project to the Final Machine







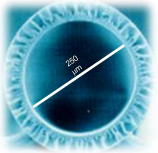



CARPEDIEM

40 years of Pediatric CRRT

1977

Search fo minifilters And visit to Amicon



In Vitro Studies on minifilters and new fiber

1979

1981

First circuit for CAVH in neonate

First world treatment of neonate with CAVH

In Vicenza 1982

1988

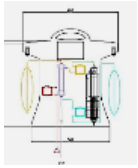
CAVH + ECMO Uf control S. Mini Filter plus and First CAVHD

Pediatric circuits in adult machines

2002

2008

Prototypes and drawing of a neonatal machine

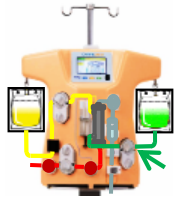


New project CARPEDIEM

2010

2013

First world treatment with CE-Marked CARPEDIEM licensed for human use Vicenza 2013



CVVH-D PE - BE

2017


ADQ
28.08.2000

ADQI

New York 2000

Kidney International, Vol. 62 (2002), pp. 1855–1863

The first international consensus conference on continuous renal replacement therapy

JOHN A. KELLUM, RAVINDRA L. MEHTA, DEREK C. ANGUS, PAUL PALEVSKY, and CLAUDIO RONCO, for the ADQI WORKGROUP[1]

Departments of Critical Care Medicine and Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA; Department of Medicine, University of California, San Diego, CA; Veterans Administration Pittsburgh Healthcare System, Pittsburgh, PA; Department of Nephrology, St. Bortolo Hospital, Vicenza, Italy; and Renal Research Institute, New York, NY, USA

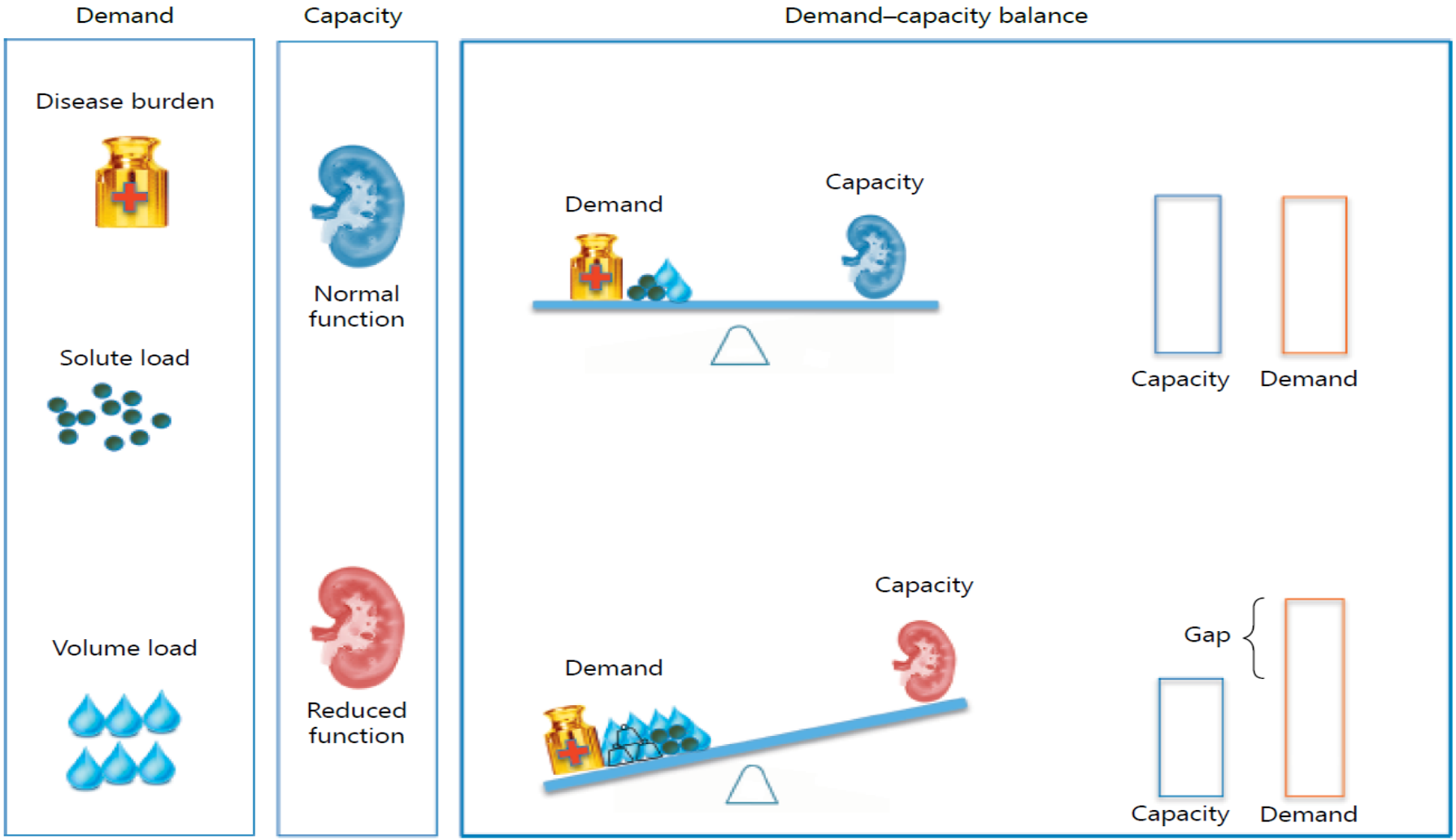
The first international consensus conference on continuous renal replacement therapy.

Background. Management of acute renal failure (ARF) in the critically ill is extremely variable and there are no published standards for the provision of renal replacement therapy in this population. We sought to review the available evidence, make evidence-based practice recommendations, and delineate key questions for future study.

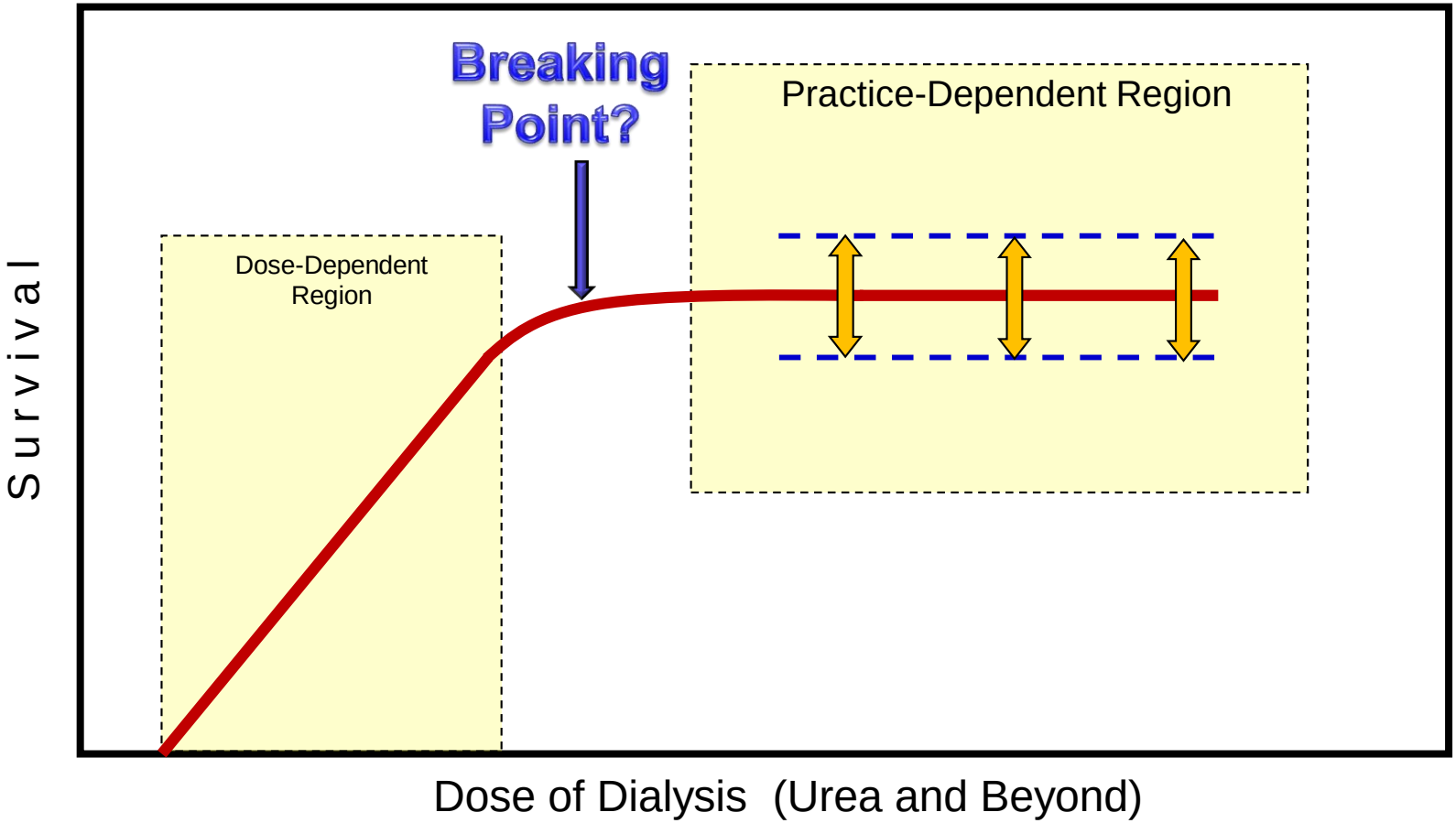
Methods. We undertook an evidence-based review of the literature on continuous renal replacement therapy (CRRT) using MEDLINE searches. We determined a list of key questions and convened a 2-day consensus conference to develop summary statements via a series of alternating breakout and plenary sessions. In these sessions, we identified supporting evidence and generated practice guidelines and/or directions for future research.

Results. Of the 46 questions considered, we found consensus

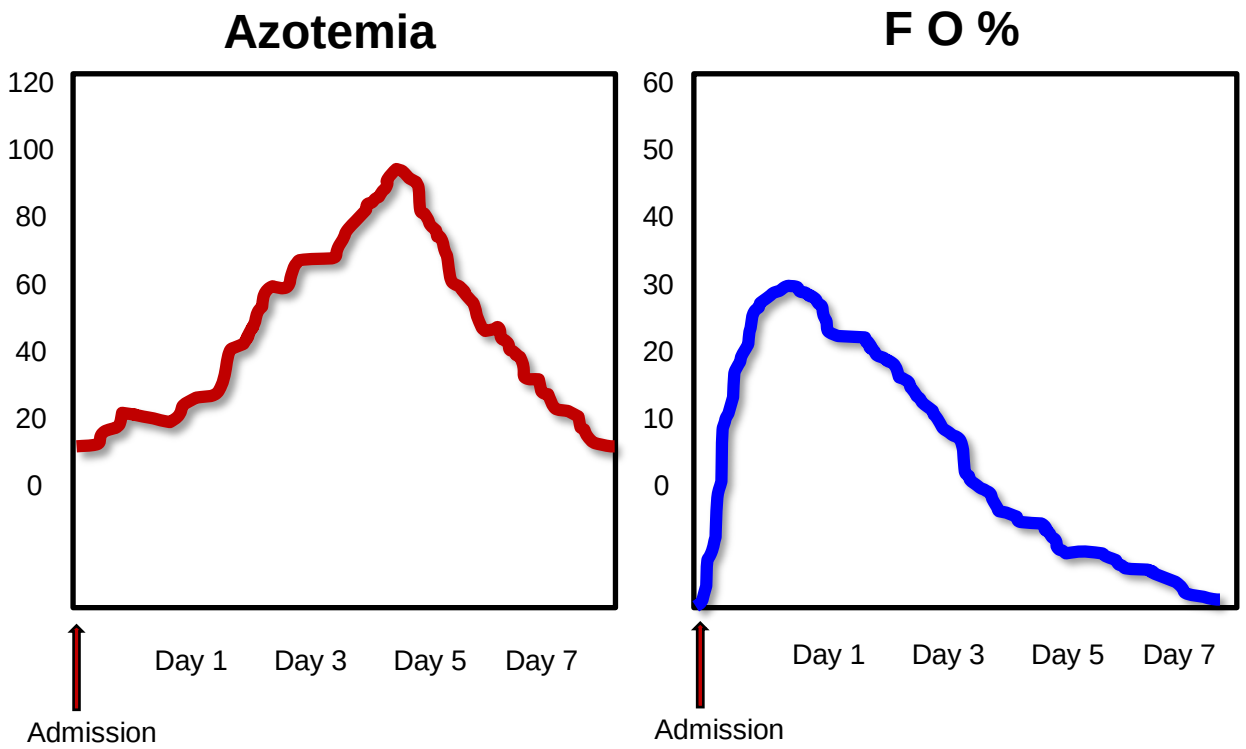
placement therapy (CRRT) [3] and use of this therapy is increasing worldwide. However, there are no standard guidelines for the application of CRRT and practice patterns vary widely between individual centers. Results from recent clinical trials on selection of dialysis membranes [4–7] and dialysis dose [8, 9] provide important evidence to guide therapy. Yet important questions remain unanswered. Finally, the method by which acute organ support is provided can have a profound effect on patient mortality (e.g., transfusion thresholds [10] and ventilator management [11]) supporting the need to identify practice standards and key research questions. The purpose of this consensus conference was to review the available evidence regarding the optimal provision

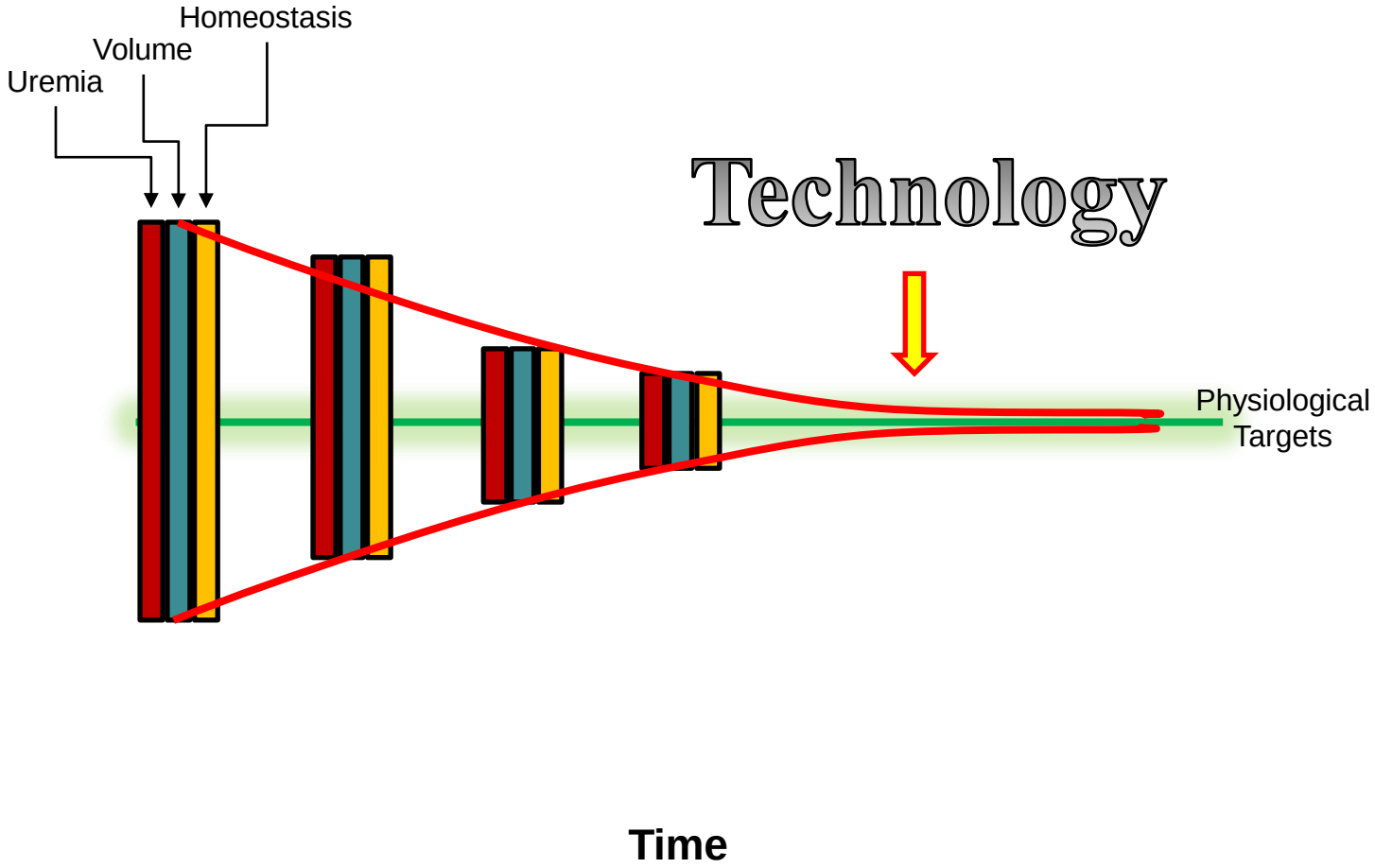

Demand
Capacity
Demand–capacity balance
Disease burden
Solute load
Volume load
Normal function
Reduced function
Demand
Capacity
Capacity
Demand
Demand
Capacity
Gap
Capacity
Demand

Renal Replacement Therapy in AKI

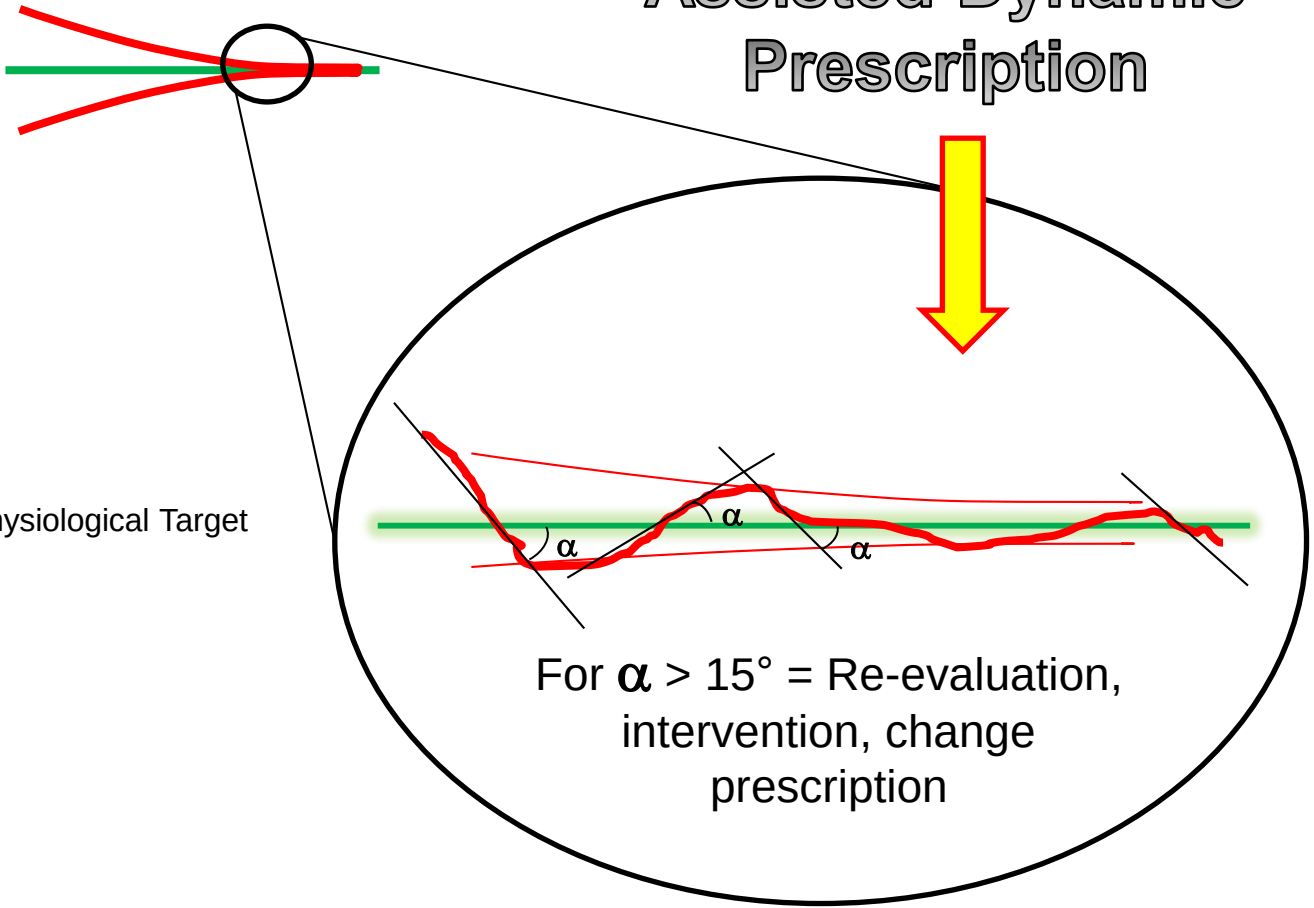


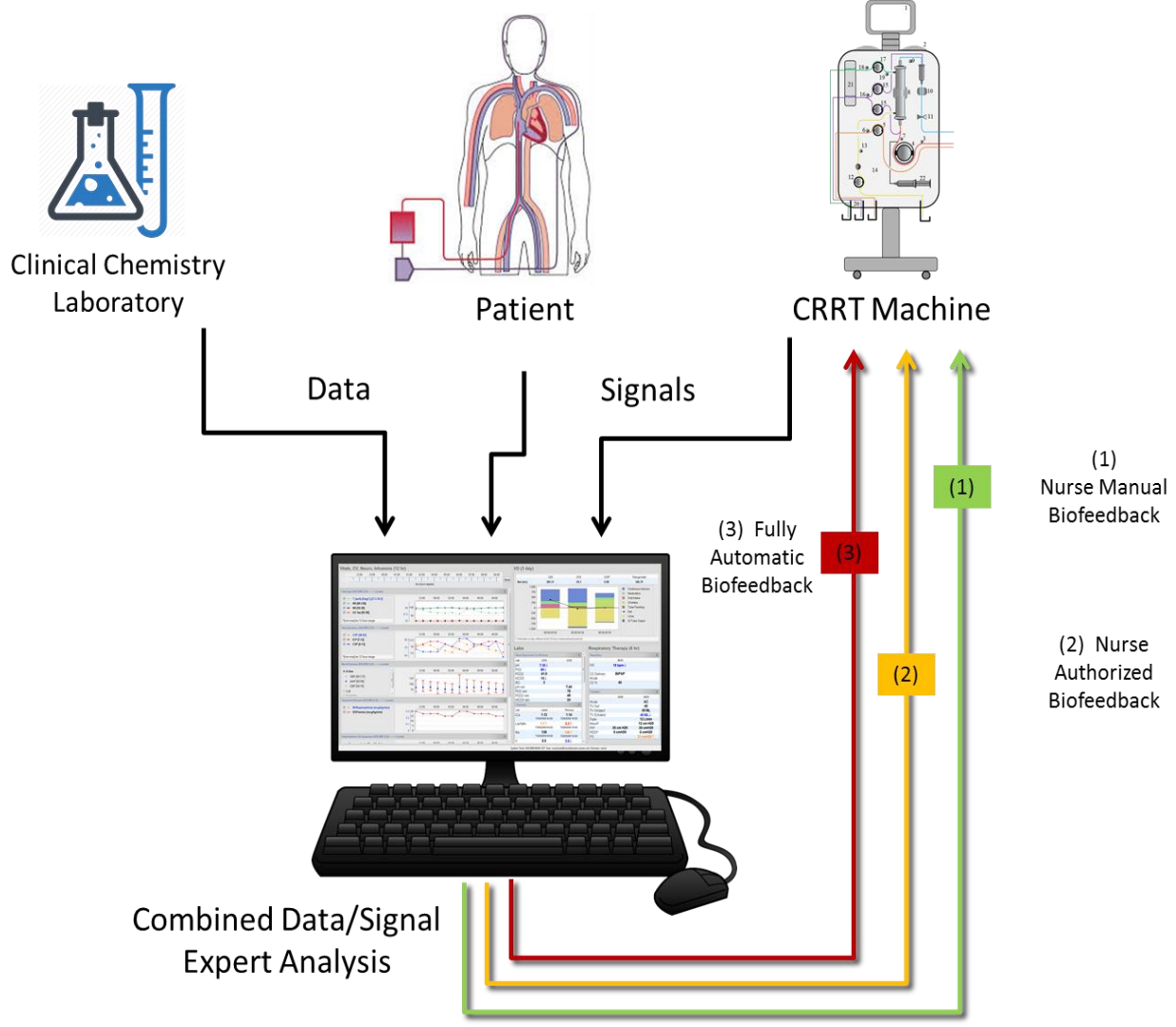
Metabolism and Volume



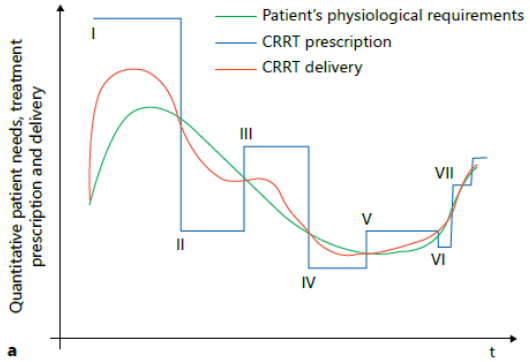

Homeostasis
Volume
Uremia
Technology
Physiological
Targets
Time

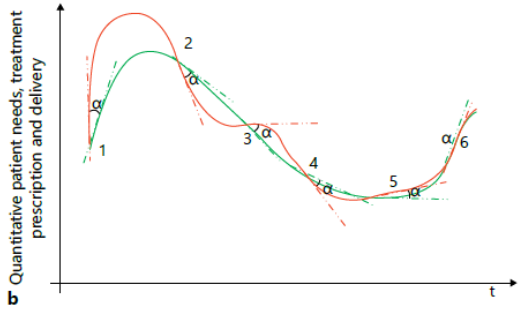
Assisted Dynamic Prescription

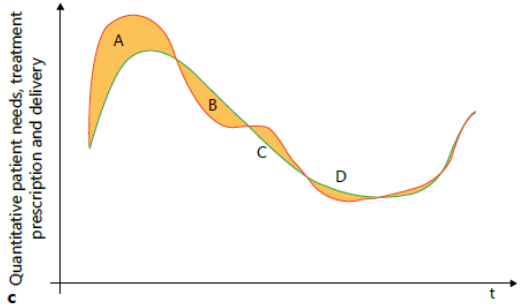



Clinical Chemistry Laboratory
Patient
CRRT Machine
Data
Signals
(3) Fully Automatic Biofeedback
(3)
(1)
(1) Nurse Manual Biofeedback
(2)
(2) Nurse Authorized Biofeedback
Combined Data/Signal Expert Analysis

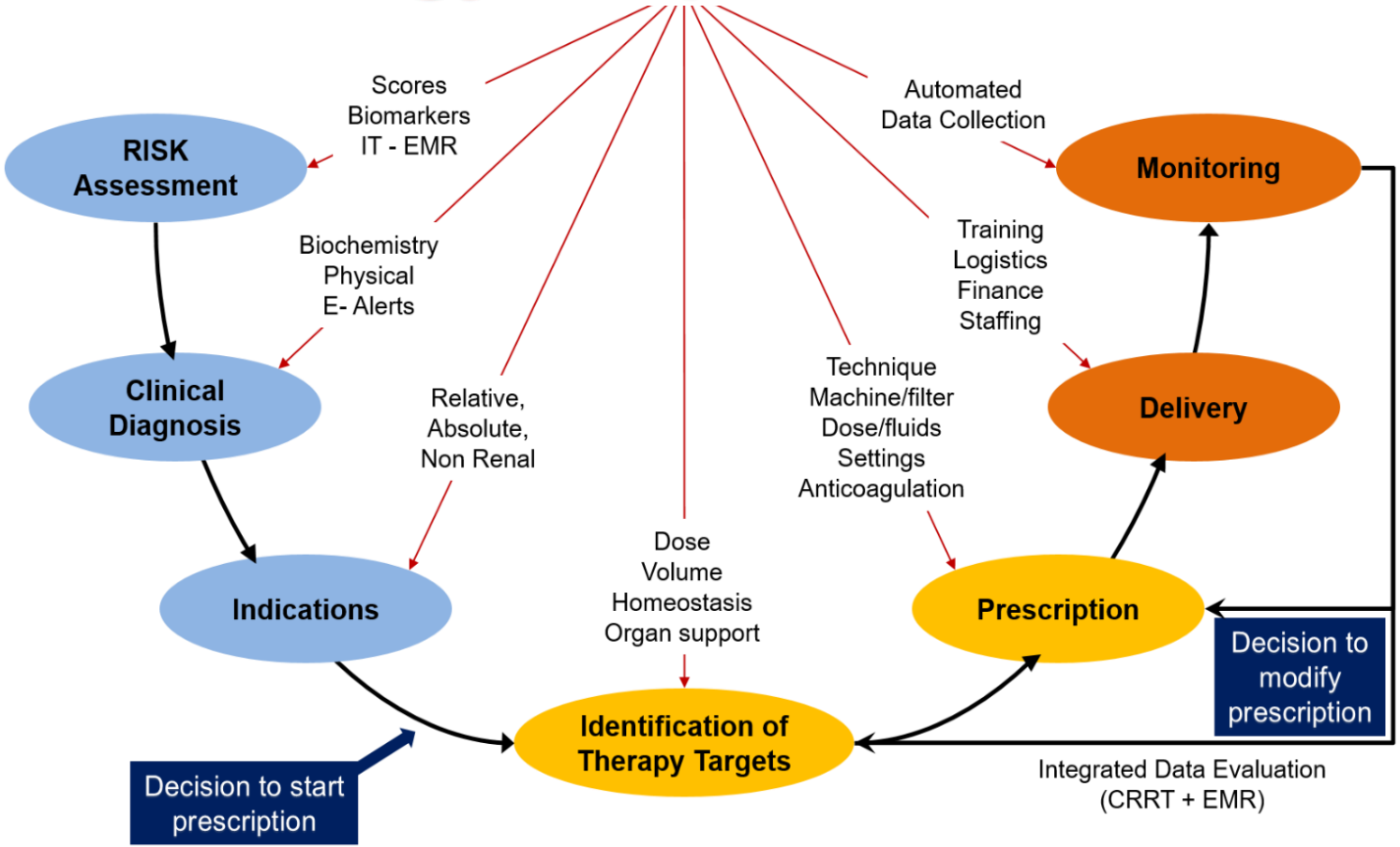

10 L


Patient's physiological requirements
CRRT prescription
CRRT delivery
I
II
III
IV
V
VI
VII
Quantitative patient needs, treatment prescription and delivery
t
a

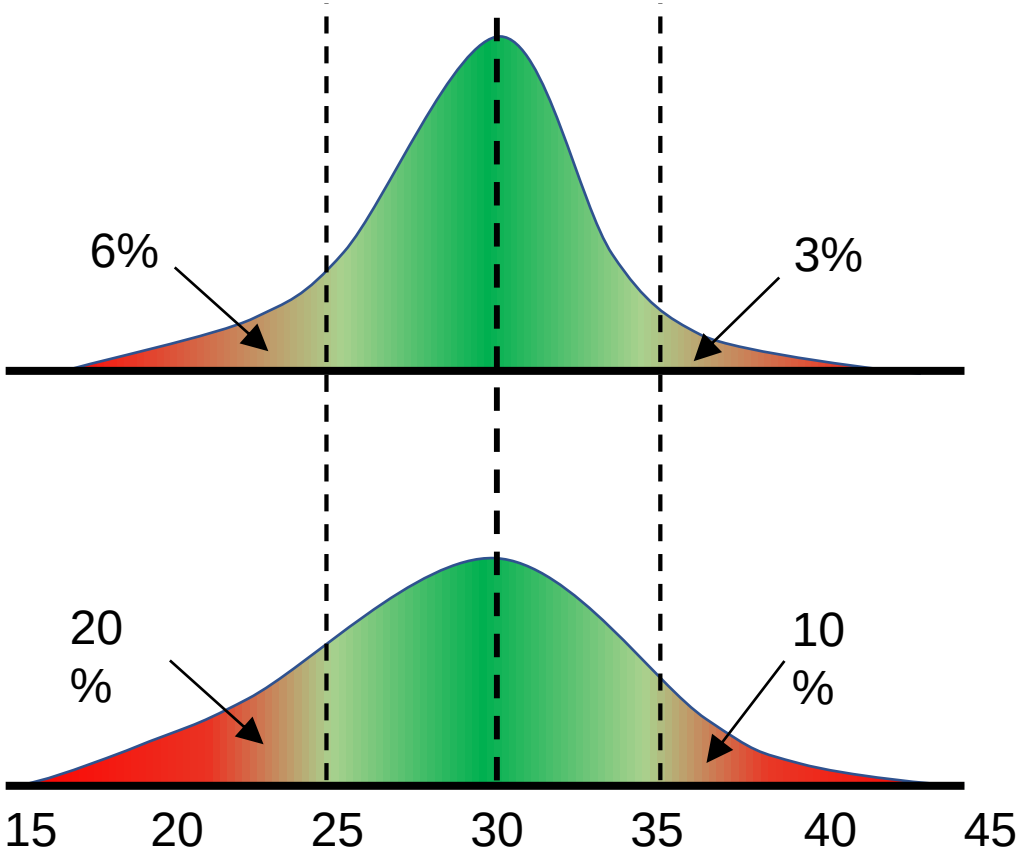

1
2
3
4
5
6
α
Quantitative patient needs, treatment prescription and delivery
t
b


A
B
C
D
Quantitative patient needs, treatment prescription and delivery
t
c

Technology for precision CRRT



Center performance: Quality Control



Control of Outliers

Change of Policy

Hardware Evolution and AI Implementation

From Main Frames to Smart Computers

Electronic Medical Record (EMR)

“Data-fication” in healthcare

Where?

- EMR
- Messages
- Web, Apps, Socials
- Sensors, Monitors
- Biometric/vital data

How big?

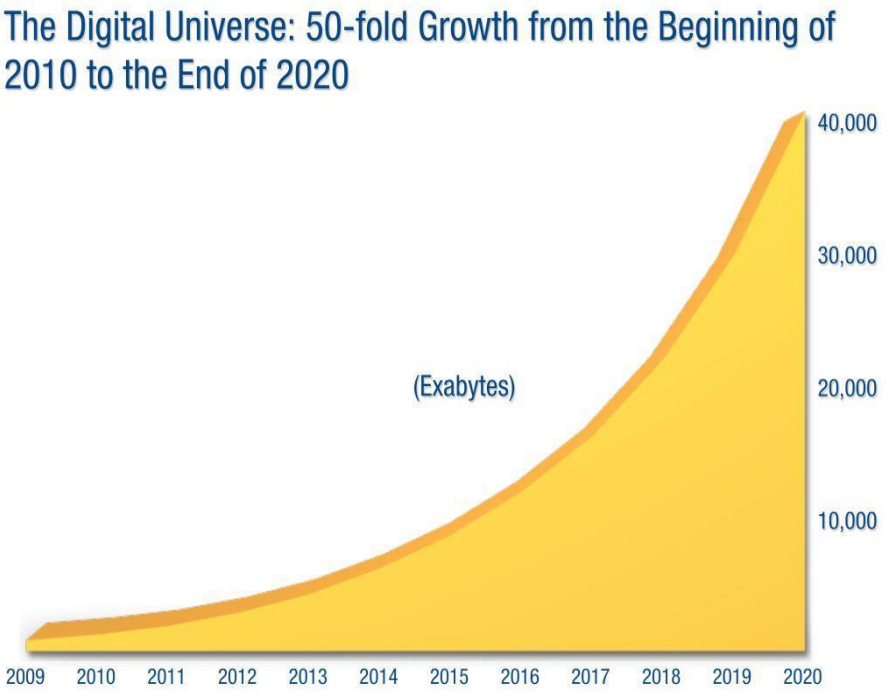
- 1 gigabyte = 1000 megabytes
- 1 terabyte = 1000 gigabytes
- 1 petabyte = 1000 terabytes
- 1 exabyte = 1000 petabytes
- 1 zettabyte = 1000 exabytes

Big Data means …

To have enormous archives that allow for integrative analyses, research operations and clinical care

5 exabites were created until 2005. Today the same amount is generated in 6 hours

Exponential growth of Big Data



How Do Clinicians Make Decisions?

History

Exam

Vitals

Labs

Treatments

CLINICAL DECISION

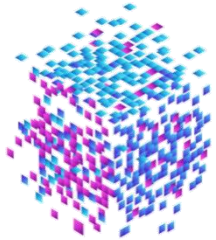
Data

Data Processing

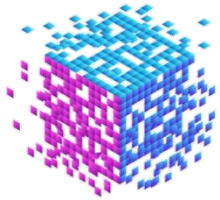
Outcome

Big Data Management

Big Data

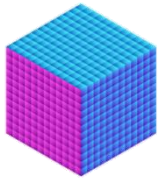


Analisis

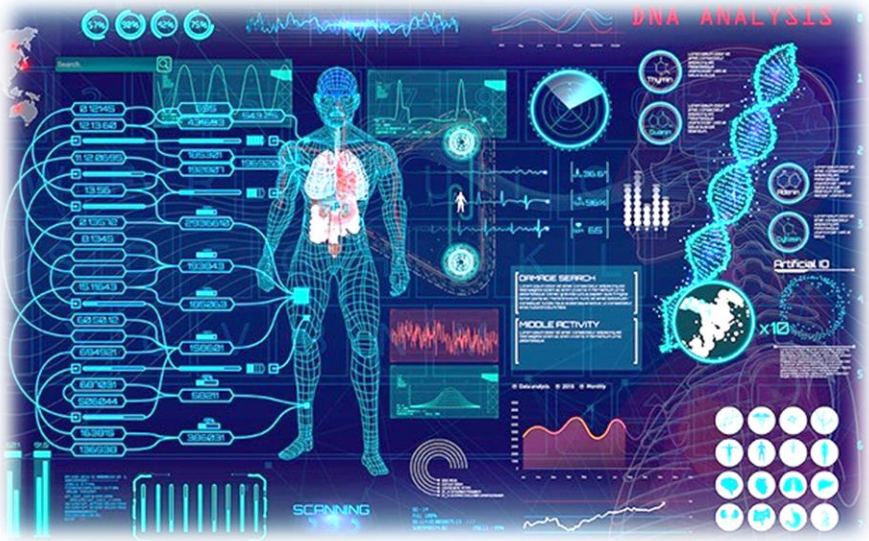


Epidemiology
Correlations and trends
Evidence and trials
Tx Efficacy

Decisions



Health policies
Strategic planning
Research development



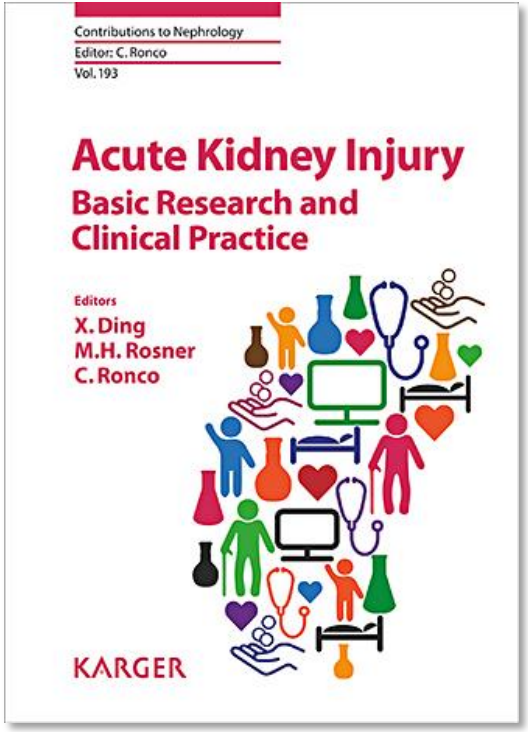
Big Data, DH and AKI

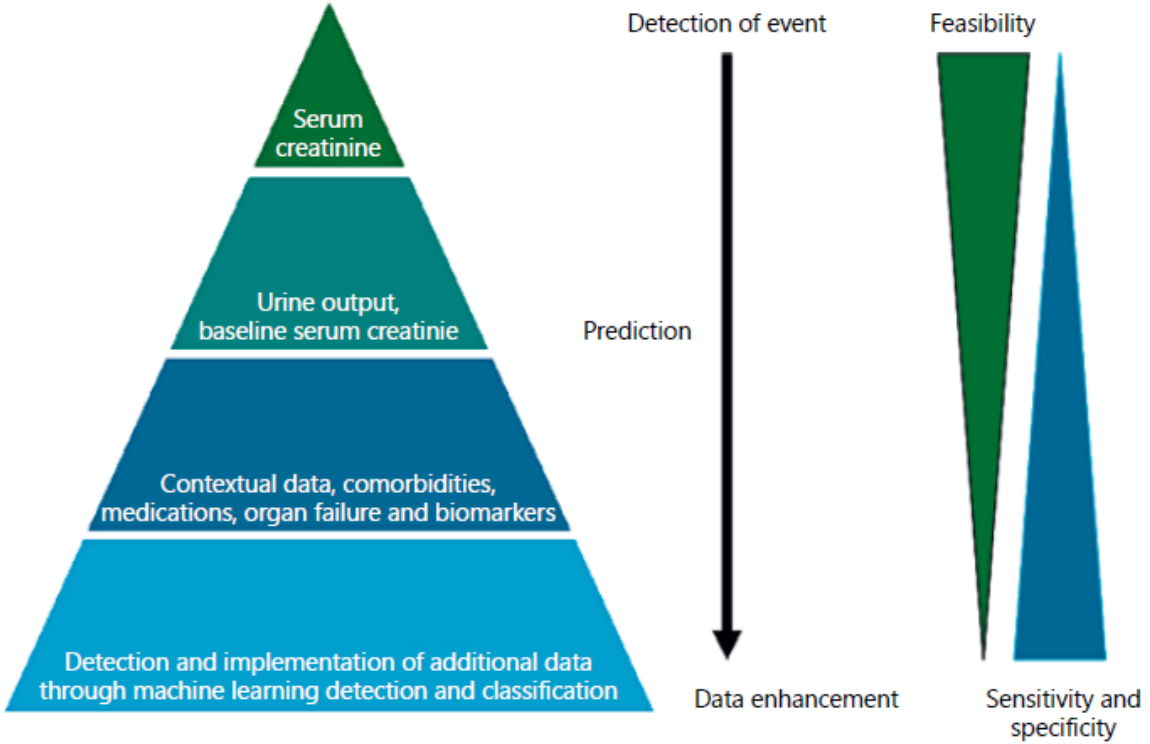
- Use of DH to identify patioents at risk for AKI or complications (sniffers)
- Use of DH to implement personalized therapies, monitoring and interventions (CDS)
- From EMRs to automatic treatment pathways (referrals; clinical decision support)
- Implementation of large pragmatic trials to study different aspects of AKI
- Implementation of training and education programs

Acute Kidney Injury and Big Data

Scott M. Sutherland[a] · Stuart L. Goldstein[b] · Sean M. Bagshaw[c]

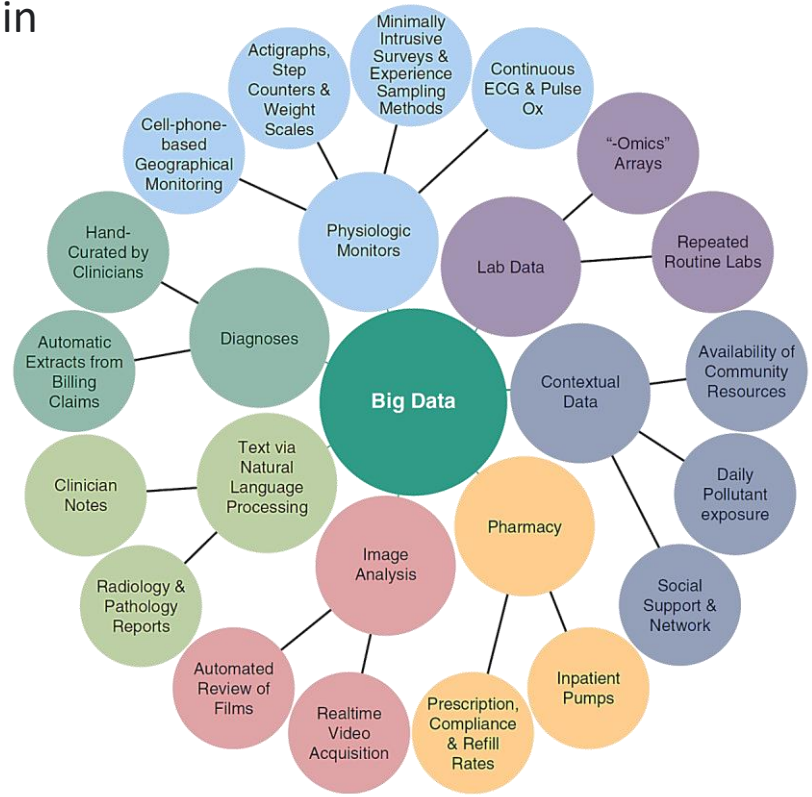
[a]Department of Pediatrics, Division of Nephrology, Stanford University, Stanford, CA, and





Machine Learning (ML) Deep learning and Artificial Intelligence (AI)

Machine learning is AI that can automatically adapt with minimal human interference. Deep learning is a subset of ML using neural networks to mimic the learning process of human brain



ADQI Recommendation

Blood Purification, 2016

- Precision Medicine is suggested in the evaluation of start/stop of renal replacement/support therapies.
- Timing can be variable depending on capacity and demand. Criteria for stopping not defined yet
- More is better until a certain point where the curve of survival reaches the plateau. Dynamic prescription and strict control of delivery is recommended
- Different modalities are today available for CRRT and ECOS
- New technological advances including AI should help clinicians to optimize prescription, delivery and results evaluation.


ANNO
30
IRRIV
International
Renal Research
Institute Vicenza
1994 • 2024


ANNO
30
IRRIV
International
Renal Research
Institute Vicenza
1994 • 2024


10 YEARS
CAPPUCCINO WITH
CLAUDIO RONCO


10 YEARS
CAPPUCCINO WITH
CLAUDIO RONCO


7.1
IRRIV
International Renal Research Institute Vicenza
AXI - CRRT - ECOS