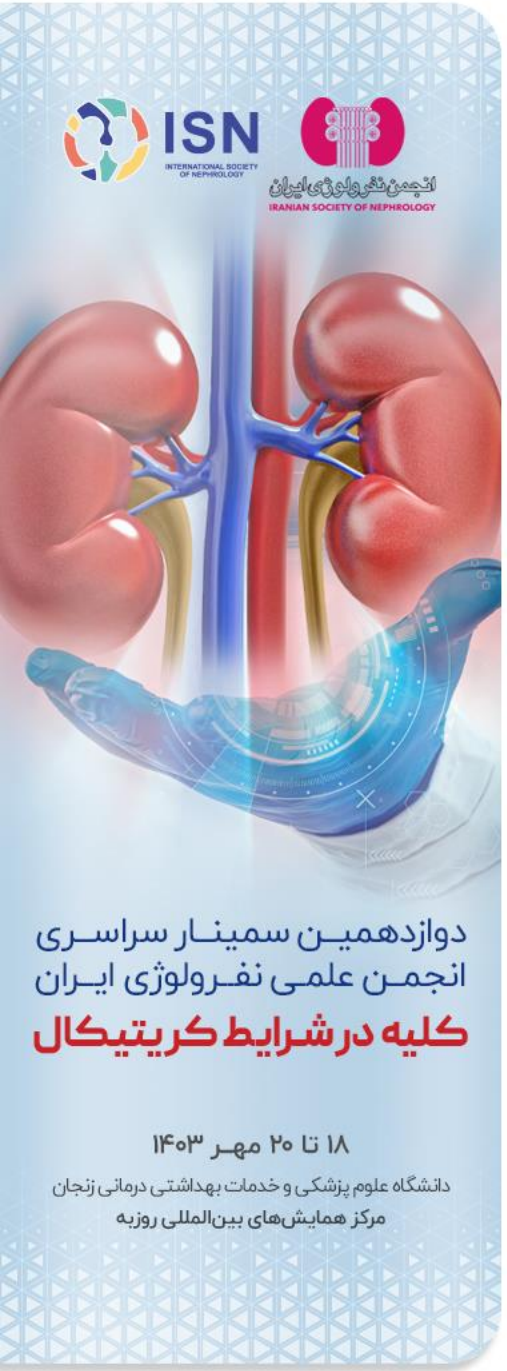
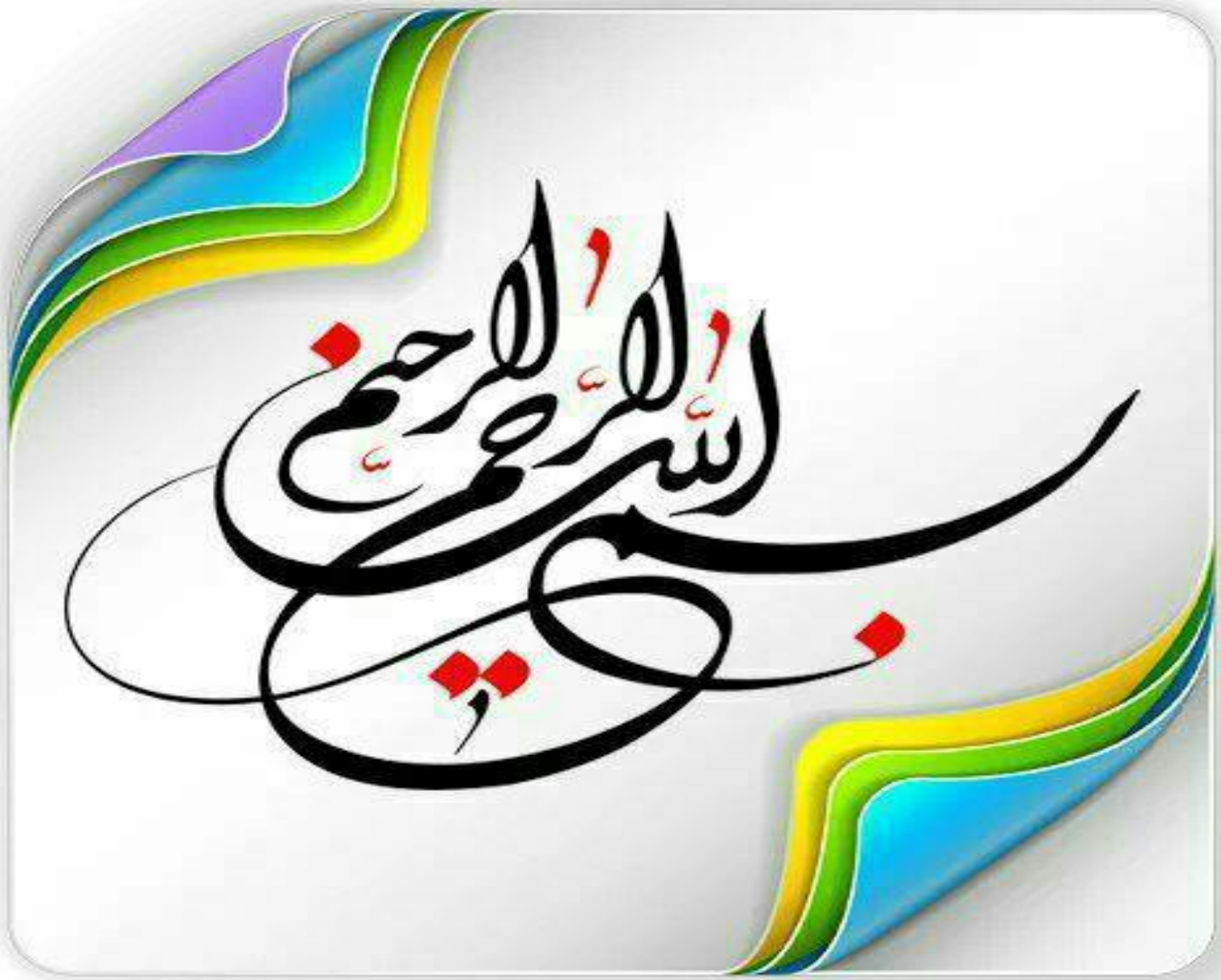
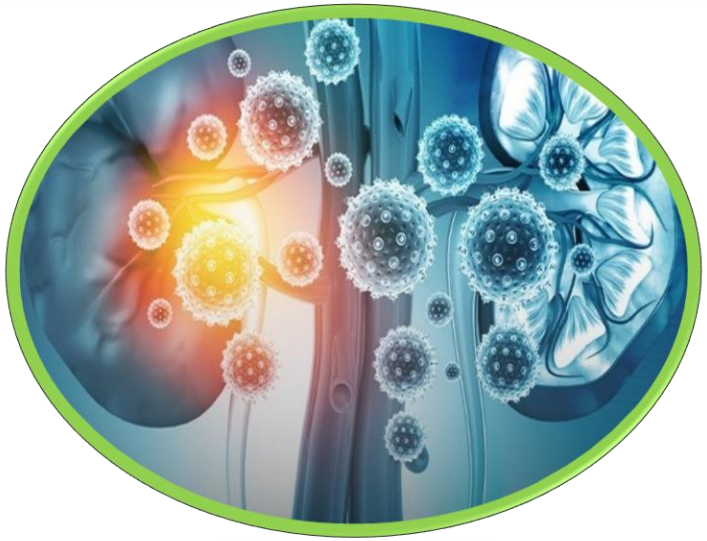

ISN
INTERNATIONAL SOCIETY OF NEPHROLOGY
انجمن نفرولوژی ایران
IRANIAN SOCIETY OF NEPHROLOGY
دوازدهمین سمینار سراسری
انجمن علمی نفرولوژی ایران
کلیه در شرایط کریتیکال
۱۸ تا ۲۰ مهر ۱۴۰۳
دانشگاه علوم پزشکی و خدمات بهداشتی درمانی زنجان
مرکز همایش‌های بین‌المللی روزبه


بسم الله الرحمن الرحیم

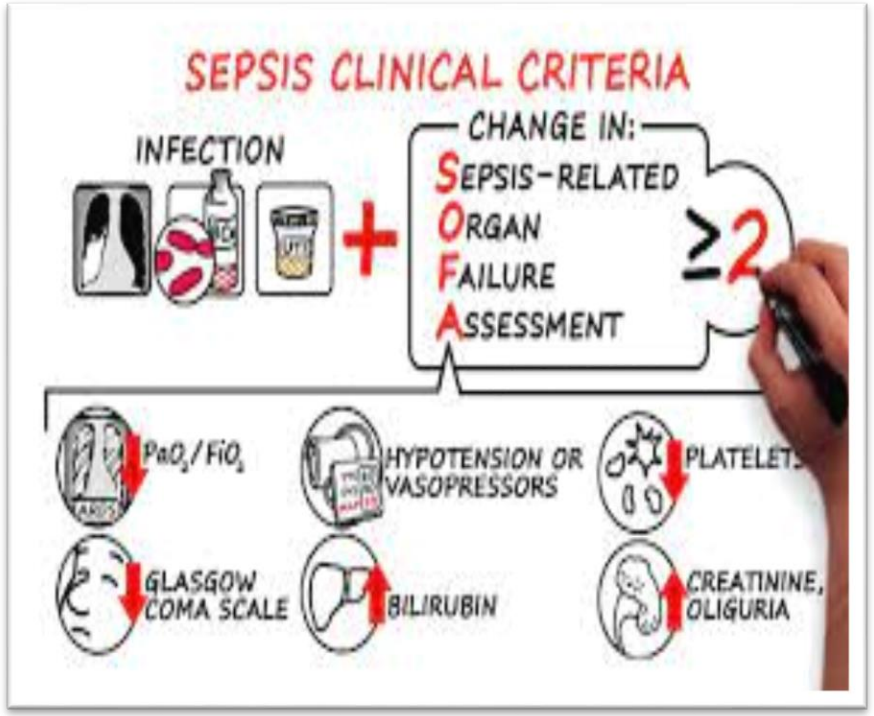
AKI in Patients with Sepsis

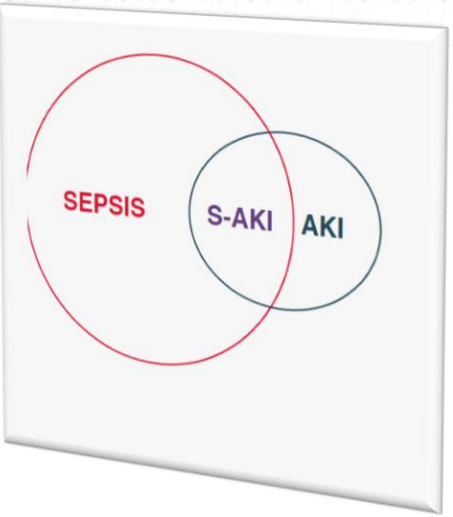


Dr. Maryam Pourkar Jadid

Nephrologist

Sepsis-Associated AKI Definition

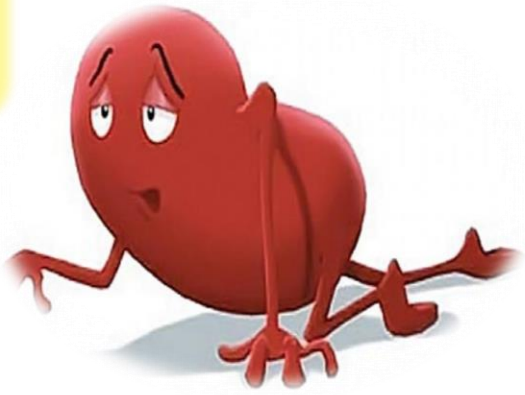




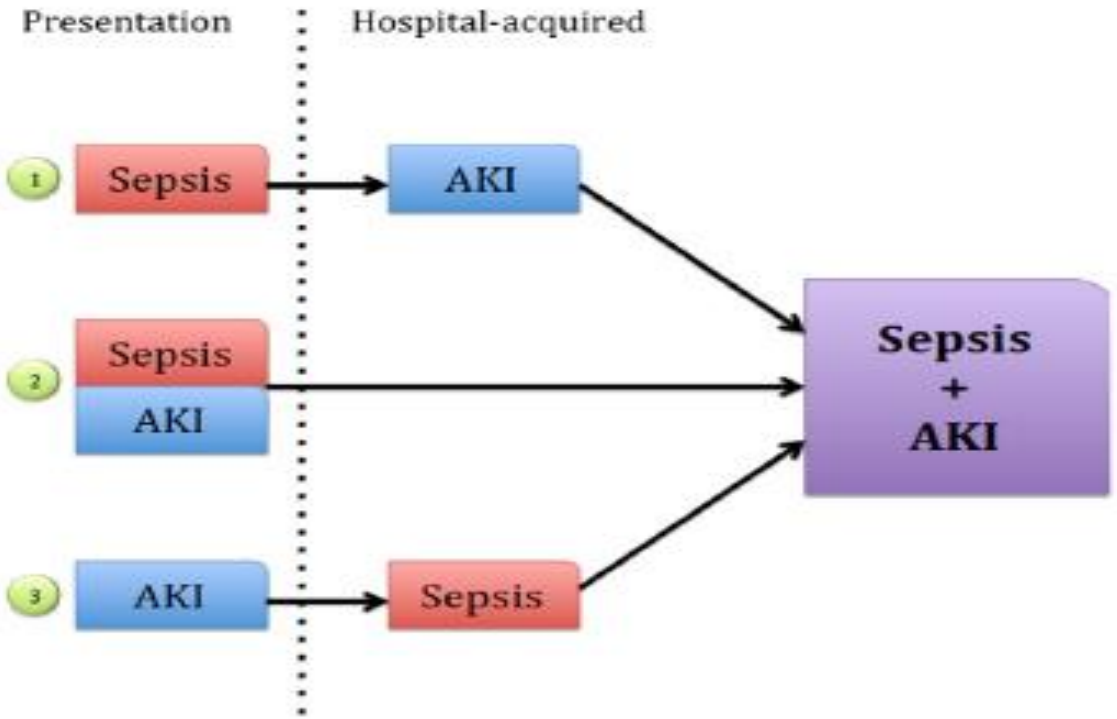
	Serum creatinine	Urine output
STAGE 1	1.5–1.9 times baseline in 7d or increase ≥0.3 mg/dl (≥26.5μmol/l) in 48h	<0.5 ml/kg/h for 6-12 hours
STAGE 2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 hours
STAGE 3	≥3.0 times baseline or creatinine ≥4.0 mg/dl or initiation of RRT or in patients <18 years, eGFR <35 ml/min/1.73m²	<0.3 ml/kg/h for ≥24 hrs or anuria for ≥12 hours

Epidemiology Of SA-AKI

Is the kidney a victim or the cause of the sepsis?

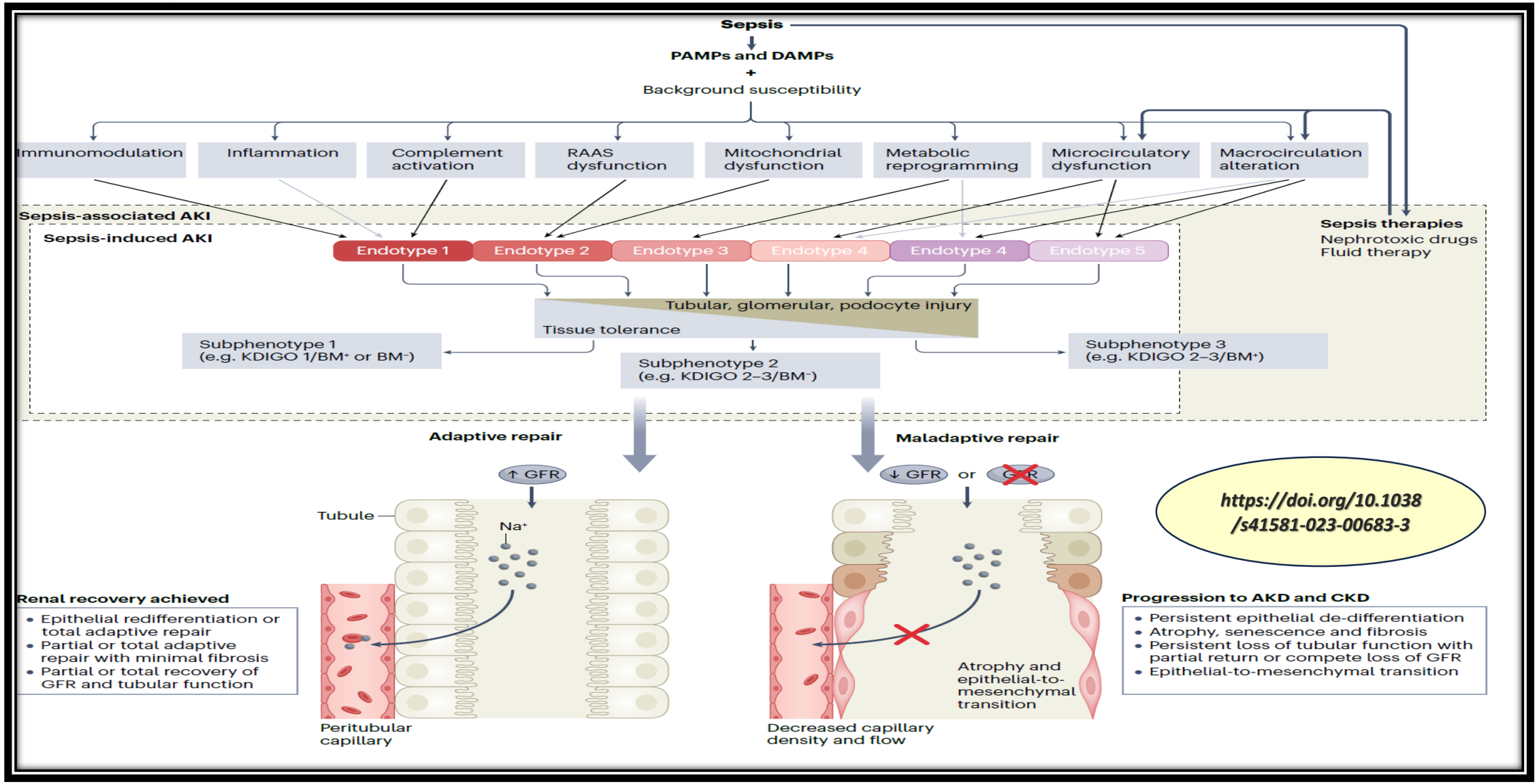


3 Models of Sepsis and AKI



https://doi.org/10.1016/j.semnephrol.2015.01.002


Mitochondrial Dysfunction
Innate Immune Activation
Local Inflammation
Microvascular Dysfunction
Pathophysiologic Mechanisms of SA-AKI
RAAS Dysfunction
Metabolic Reprogramming
Oxidative Stress
Complement Activation

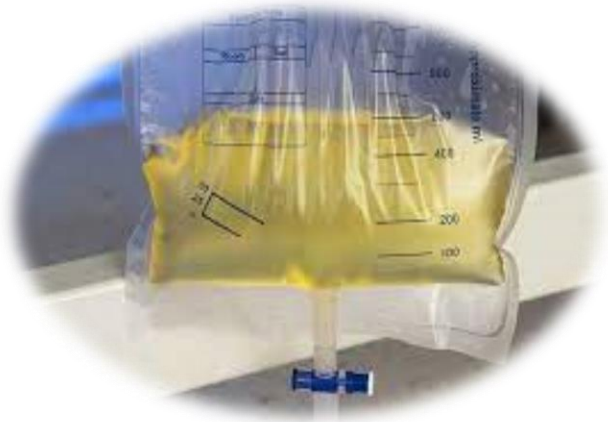


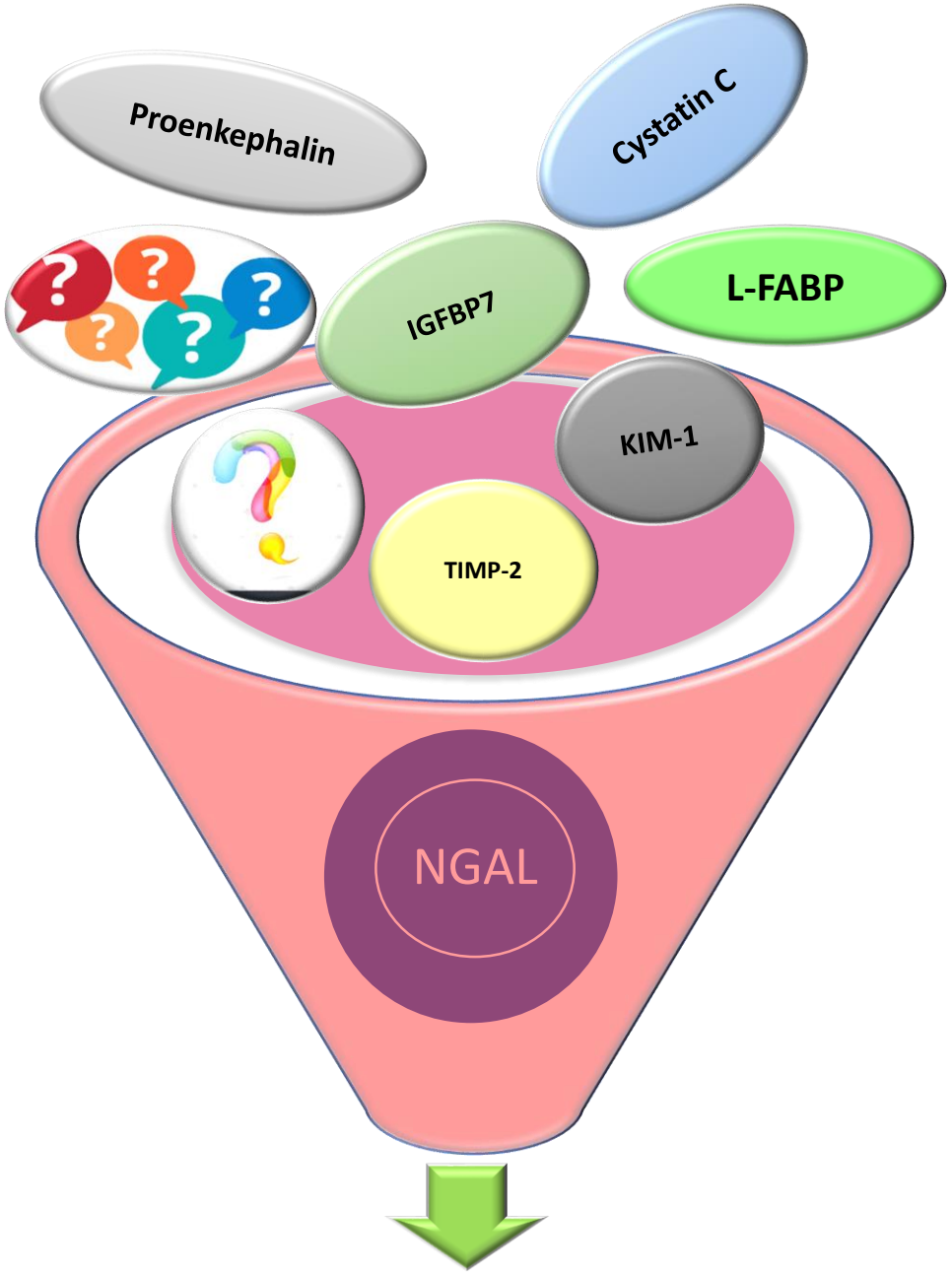
https://doi.org/10.1038/s41581-023-00683-3

Limitations of Define and Diagnosis of SA-AKI

Table 1. Staging of AKI according to KDIGO guidelines.

	Serum Creatinine Criteria	Urine Output
Stage 1	SCr 1.5 to 1.9 times the baseline value OR SCr ≥0.3 mg/dL (≥26.5 μmol/L)	<0.5 mL/kg/h for 6–12 h
Stage 2	SCr 2.0 to 2.9 times baseline	<0.5 mL/kg/h for ≥12 h
Stage 3	SCr rises to 3.0 times baseline OR Increase in SCr to ≥4.0 mg/dL (≥354 μmol/L) OR Need for initiation of renal replacement therapy	<0.3 mL/kg/h for ≥24 h OR Anuria for ≥12 h





Utility Of Biomarkers In SA-AKI

Staging of AKI by ADQI-23 Consensus

Table 1. Proposed New Definition and Staging of Acute Kidney Injury by the ADQI-23 Consensus Conference[a]

KDIGO stage	Functional criteria	Biomarkers	New stage
No AKI	No increased sCr level (≥0.3 mg/dL) in ≤48 h and No increased sCr level (≥1.5 mg/dL from baseline) in 7 d and UO >0.5 mL/kg/h in 6-h period	Negative	No AKI
		Positive	1S
1	Increased sCr level (≥0.3 mg/dL) in ≤48 h or Increased sCr level (1.5-1.9 times baseline) in <7 d or UO <0.5 mL/kg/h for 6-12 h	Negative	1A
		Positive	1B
2	Increased sCr level (2.0-2.9 times baseline) or UO <0.5 mL/kg/h for ≥12 h	Negative	2A
		Positive	2B
3	Increased sCr level (≥3.0 times baseline) or sCr level ≥4.0 mg/dL with acute increase of ≥0.3 mg/dL or UO <0.3 mL/kg/h for ≥24 h or Anuria for ≥12 h or Initiation of kidney replacement therapy	Negative	3A
		Positive	3B

JAMA Network Open. 2022;5(5):e2212709.
doi:10.1001/jamanetworkopen.2022.12709

Biomarkers Roles in SA-AKI

Palmowski et al. Annals of Intensive Care (2024) 14:111
https://doi.org/10.1186/s13613-024-01349-4

Annals of Intensive Care

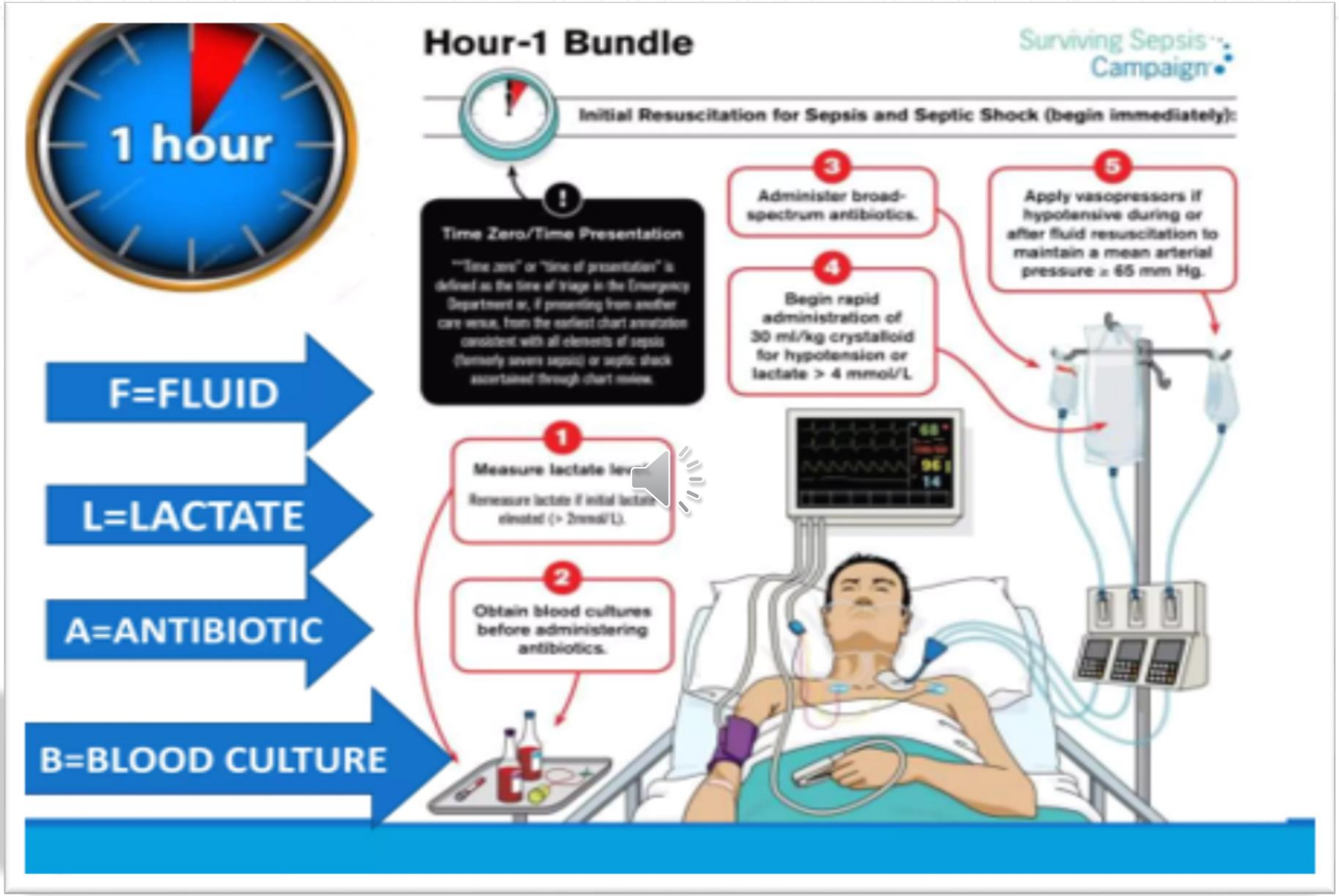
RESEARCH Open Access

Predictive enrichment for the need of renal replacement in sepsis-associated acute kidney injury: combination of furosemide stress test and urinary biomarkers TIMP-2 and IGFBP-7

Lars Palmowski[1†], Simone Lindau[2†], Laura Contreras Henk[3], Britta Marko[1], Andrea Witowski[1], Hartmuth Nowak[1,4], Sandra E. Stoll[5,6], Kai Zacharowski[2], Bernd W. Böttiger[5], Jürgen Peters[7], Michael Adamzik[1], Fabian Dusse[5†] and Tim Rahmel[1*†]

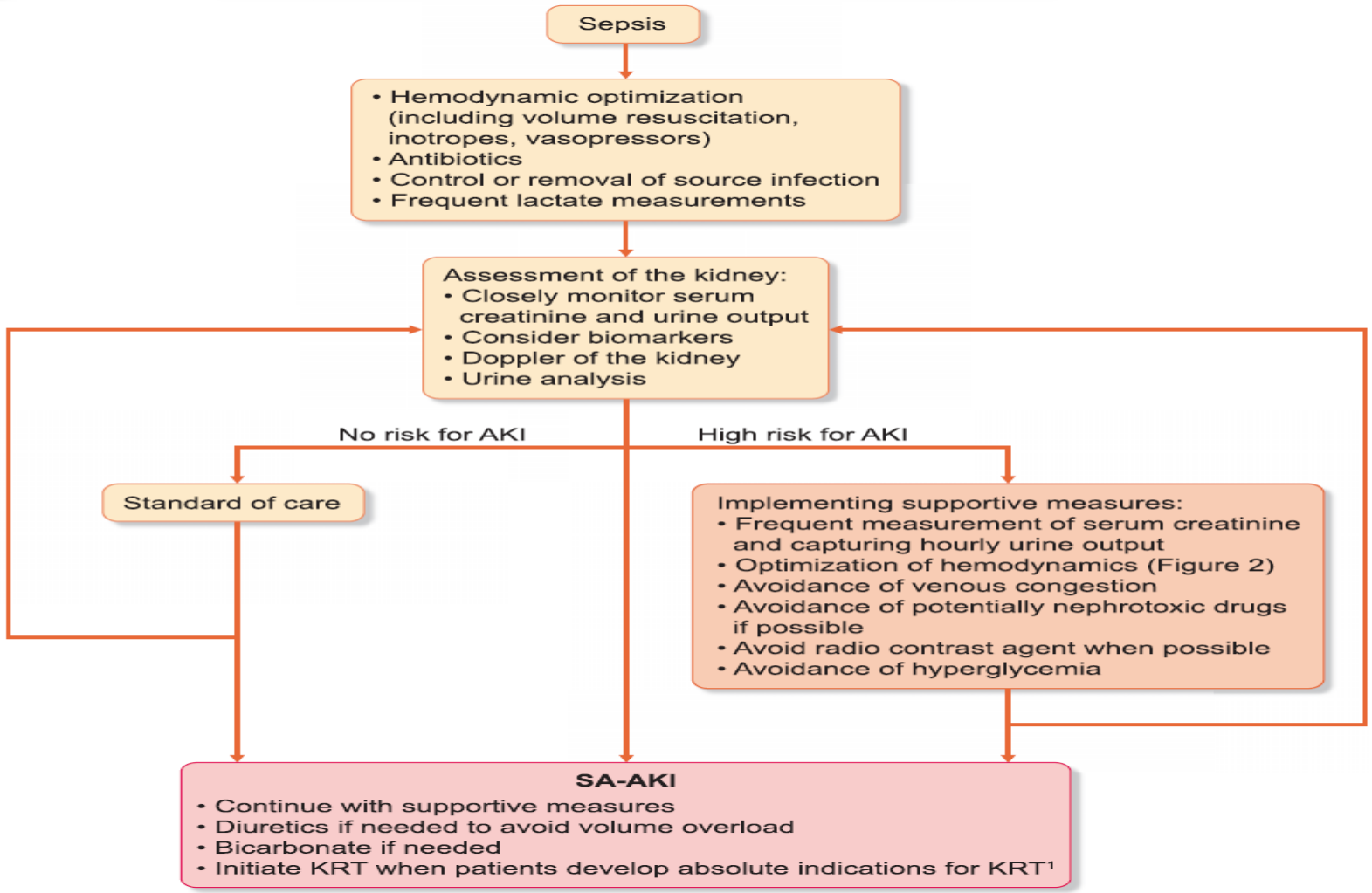
https://doi.org/10.1186/s13613-024-01349-4

Artificial Intelligence(AI) and Machine Learning In SA-AKI


1 hour
Hour-1 Bundle
Surviving Sepsis Campaign
Initial Resuscitation for Sepsis and Septic Shock (begin immediately):
Time Zero/Time Presentation
3
Administer broad-spectrum antibiotics.
4
Begin rapid administration of 30 ml/kg crystalloid for hypotension or lactate > 4 mmol/L
5
Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg.
1
2
Obtain blood cultures before administering antibiotics.
F=FLUID
L=LACTATE
A=ANTIBIOTIC
B=BLOOD CULTURE

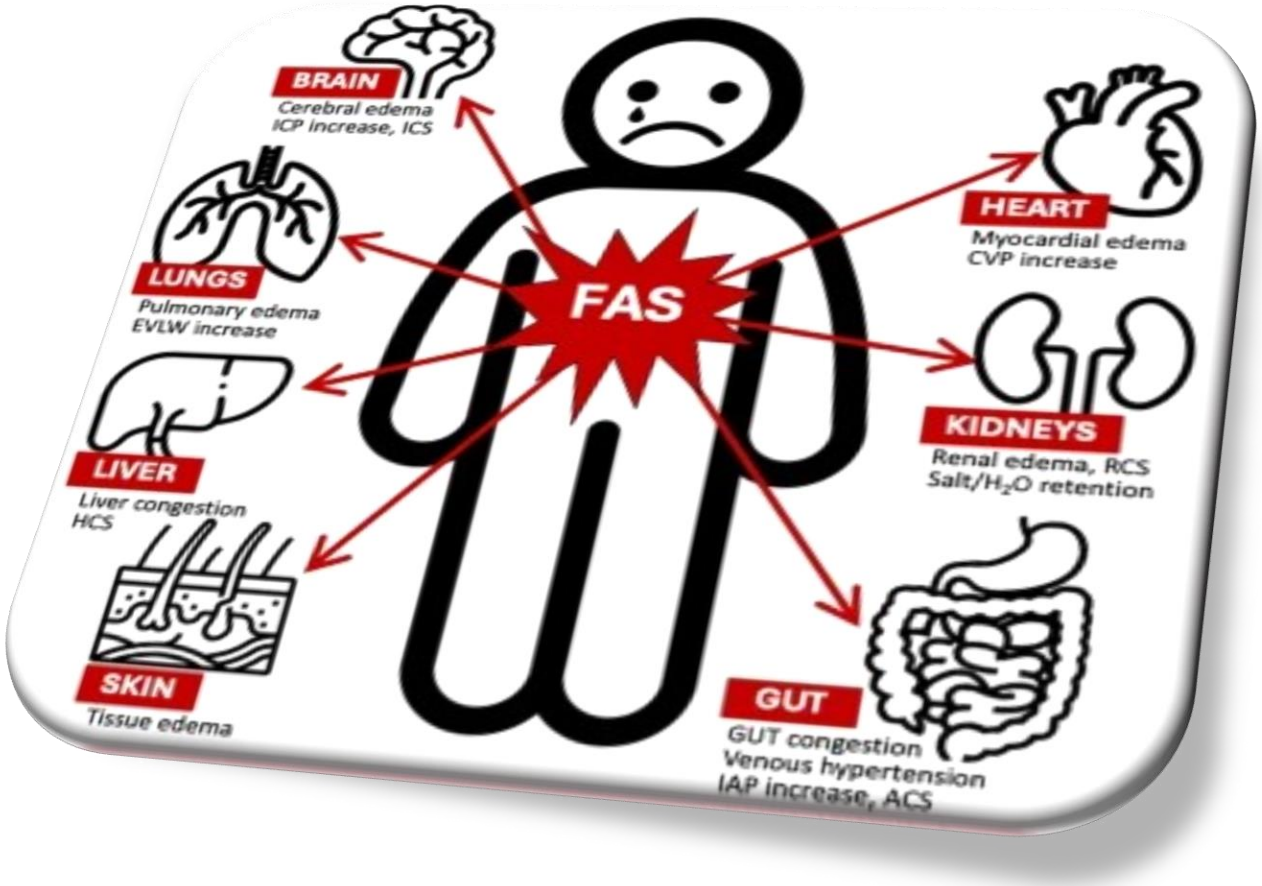
Nephrol Dial Transplant, 2024, 39, 26–35
https://doi.org/10.1093/ndt/gfad142
Advance access publication date: 3 July 2023

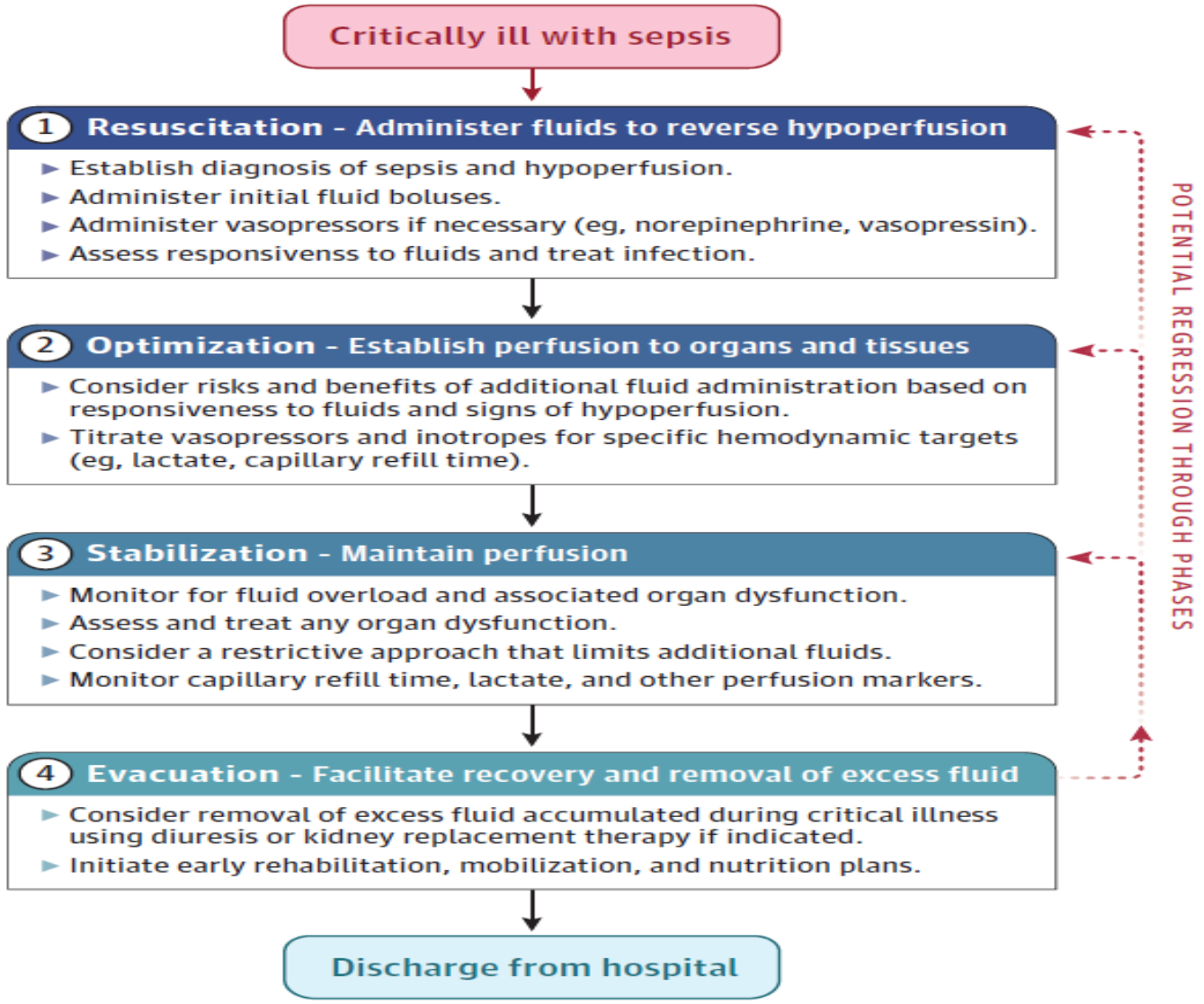
Flow Chart Of The Diagnostic And Treatment Algorithm



Point-Of-Care Ultrasound(POCUS) In SA-AKI

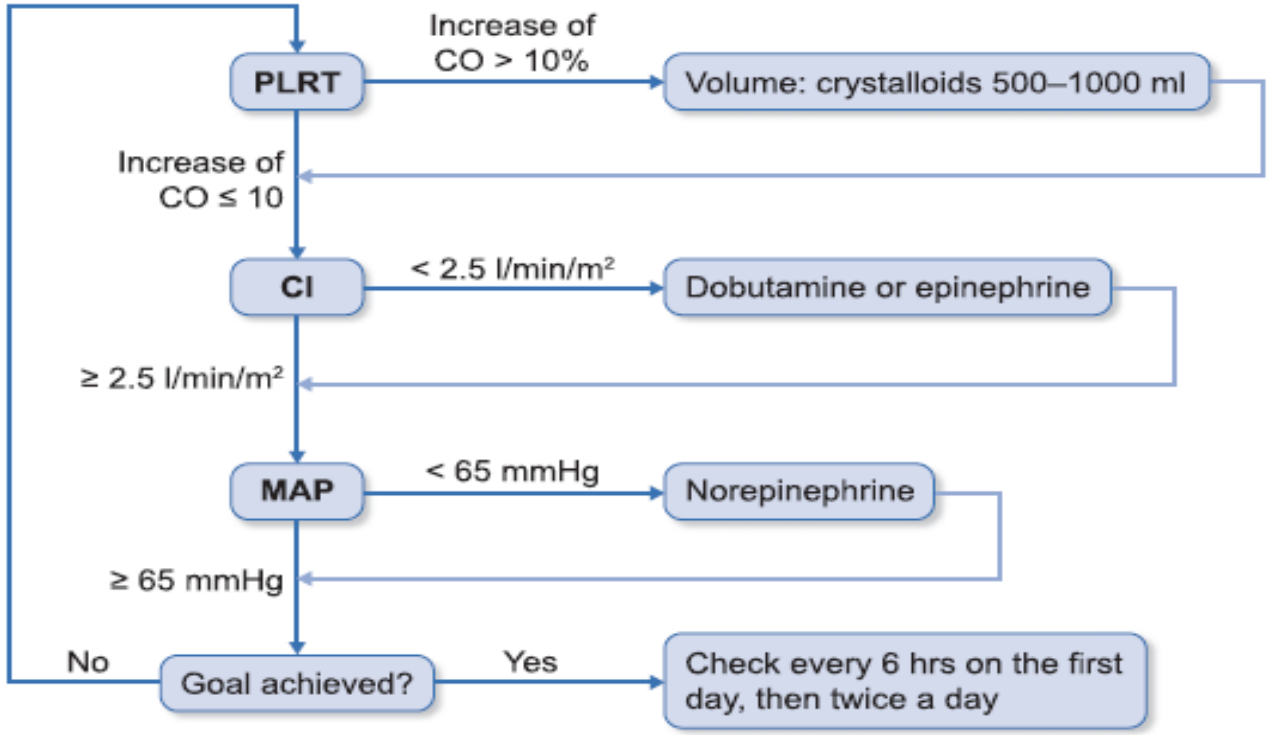
Fluid Accumulation Syndrome



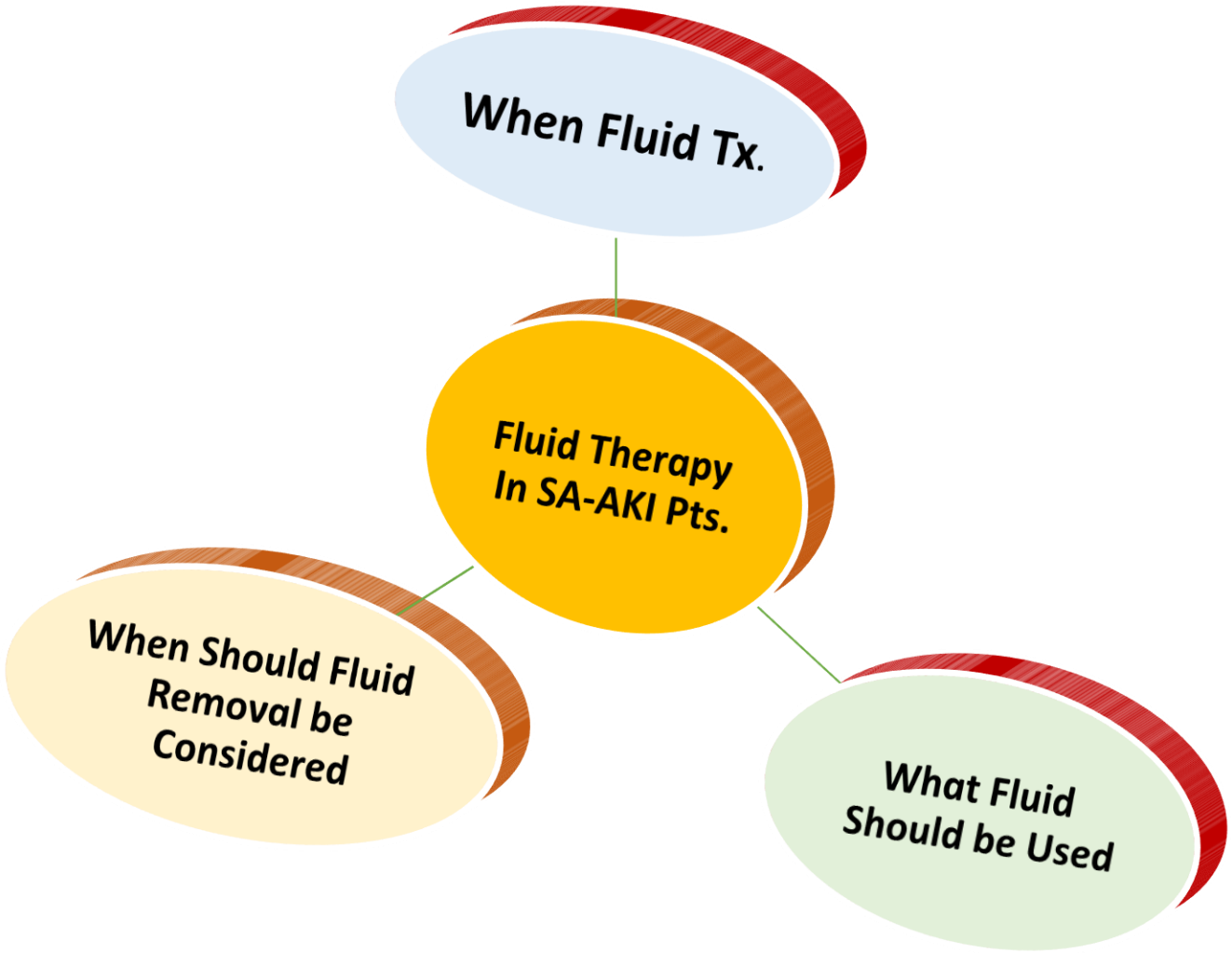


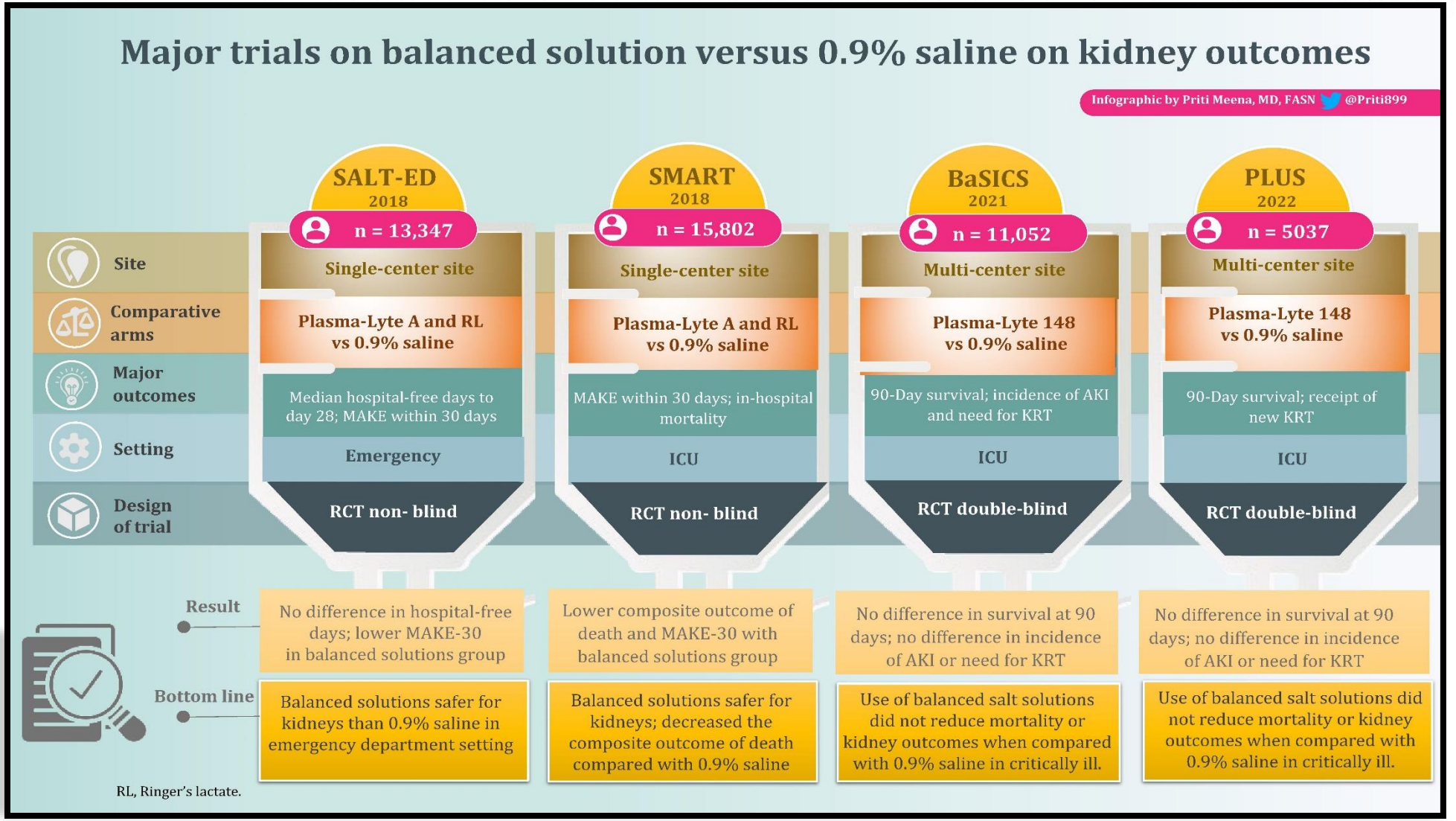
ROSE Protocol

Optimization Of the Volume and haemodynamic Status



Nephrol Dial Transplant, 2024, **39**, 26–35
https://doi.org/10.1093/ndt/gfad142


When Fluid Tx.
Fluid Therapy In SA-AKI Pts.
When Should Fluid Removal be Considered
What Fluid Should be Used


Major trials on balanced solution versus 0.9% saline on kidney outcomes
Infographic by Priti Meena, MD, FASN @Priti899
SALT-ED 2018
n = 13,347
SMART 2018
n = 15,802
BaSICS 2021
n = 11,052
PLUS 2022
n = 5037
Site
Single-center site
Single-center site
Multi-center site
Multi-center site
Comparative arms
Plasma-Lyte A and RL vs 0.9% saline
Plasma-Lyte A and RL vs 0.9% saline
Plasma-Lyte 148 vs 0.9% saline
Plasma-Lyte 148 vs 0.9% saline
Major outcomes
Median hospital-free days to day 28; MAKE within 30 days
MAKE within 30 days; in-hospital mortality
90-Day survival; incidence of AKI and need for KRT
90-Day survival; receipt of new KRT
Setting
Emergency
ICU
ICU
ICU
Design of trial
RCT non- blind
RCT non- blind
RCT double-blind
RCT double-blind
Result
No difference in hospital-free days; lower MAKE-30 in balanced solutions group
Lower composite outcome of death and MAKE-30 with balanced solutions group
No difference in survival at 90 days; no difference in incidence of AKI or need for KRT
No difference in survival at 90 days; no difference in incidence of AKI or need for KRT
Bottom line
Balanced solutions safer for kidneys than 0.9% saline in emergency department setting
Balanced solutions safer for kidneys; decreased the composite outcome of death compared with 0.9% saline
Use of balanced salt solutions did not reduce mortality or kidney outcomes when compared with 0.9% saline in critically ill.
Use of balanced salt solutions did not reduce mortality or kidney outcomes when compared with 0.9% saline in critically ill.
RL, Ringer's lactate.

ALBIOSS-BALANCED trial

(Efficacy of Albumin Replacement and Balanced Solutions in Patients with Septic Shock)

ALBIOSS 2

ALBumin Italian Outcome Septic Shock - BALANCED trial

Pietro Caironi (PI), Antonio Pesenti (co-PI)

2-by-2 factorial reciprocal control design trial in septic shock pts

Hypothesis 1	*Hypothesis 2*
Albumin + Crystalloids *vs.* Crystalloids	Balanced sol. vs. 0.9% NaCl

Septic Shock

Efficacy of Albumin Replacement
Efficacy of Balance Crystalloids

Study design – Multicenter RCT of phase III

ALBIOSS-BALANCED trial

2-by-2 factorial, investigator-initiated, open-label, multicenter, randomized,

Grant from the Italian ministry of Health
RF-2016-02361583

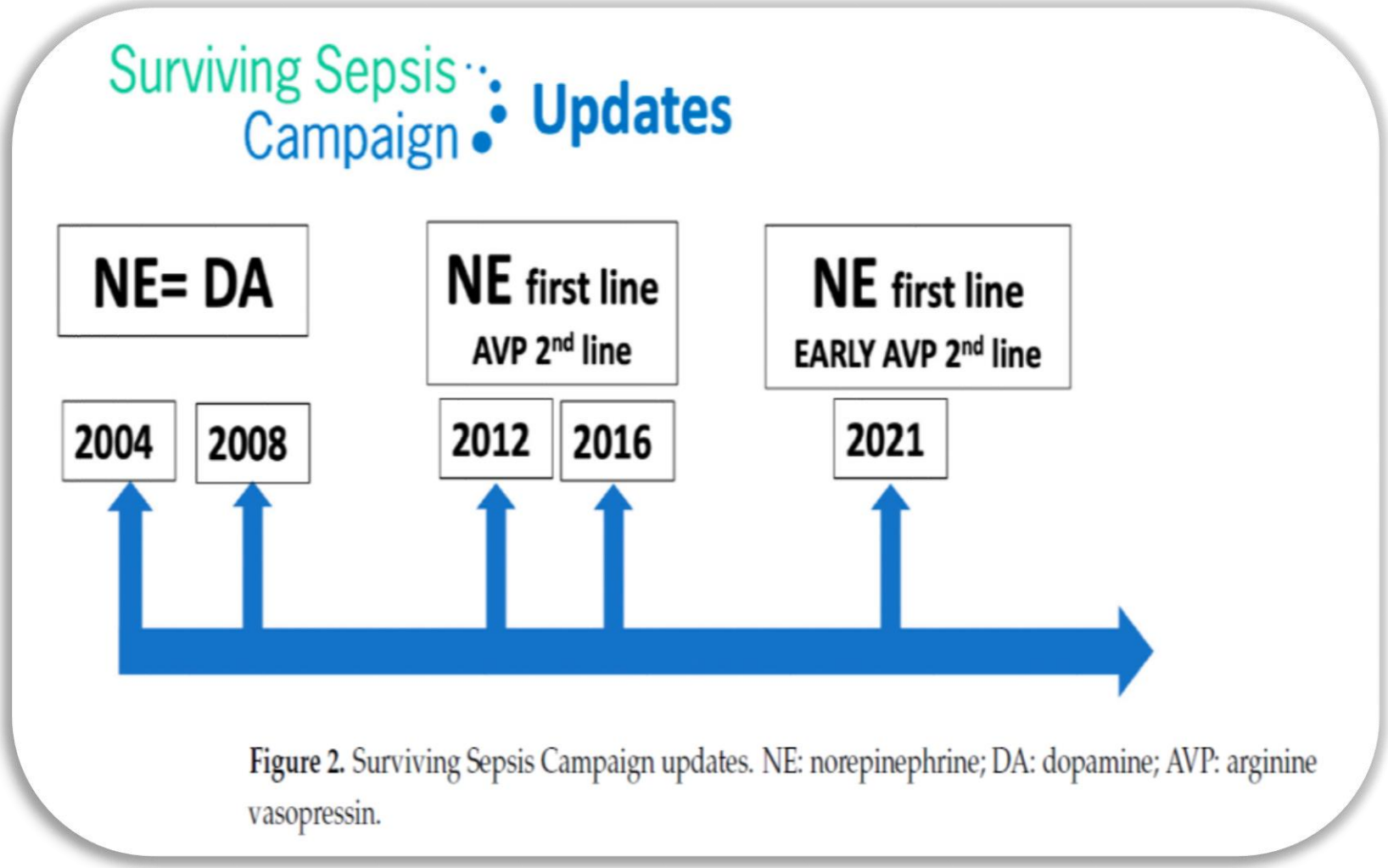
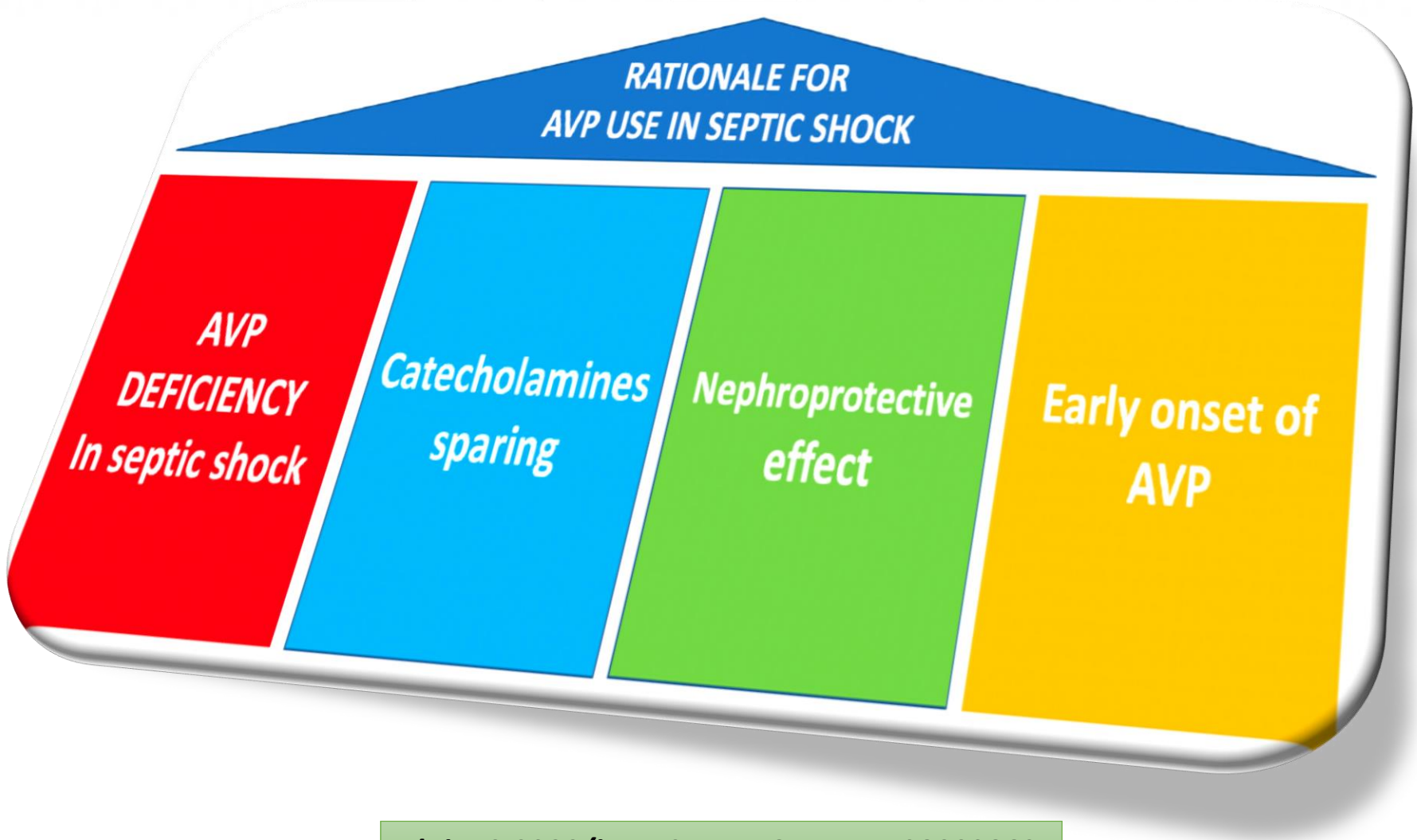
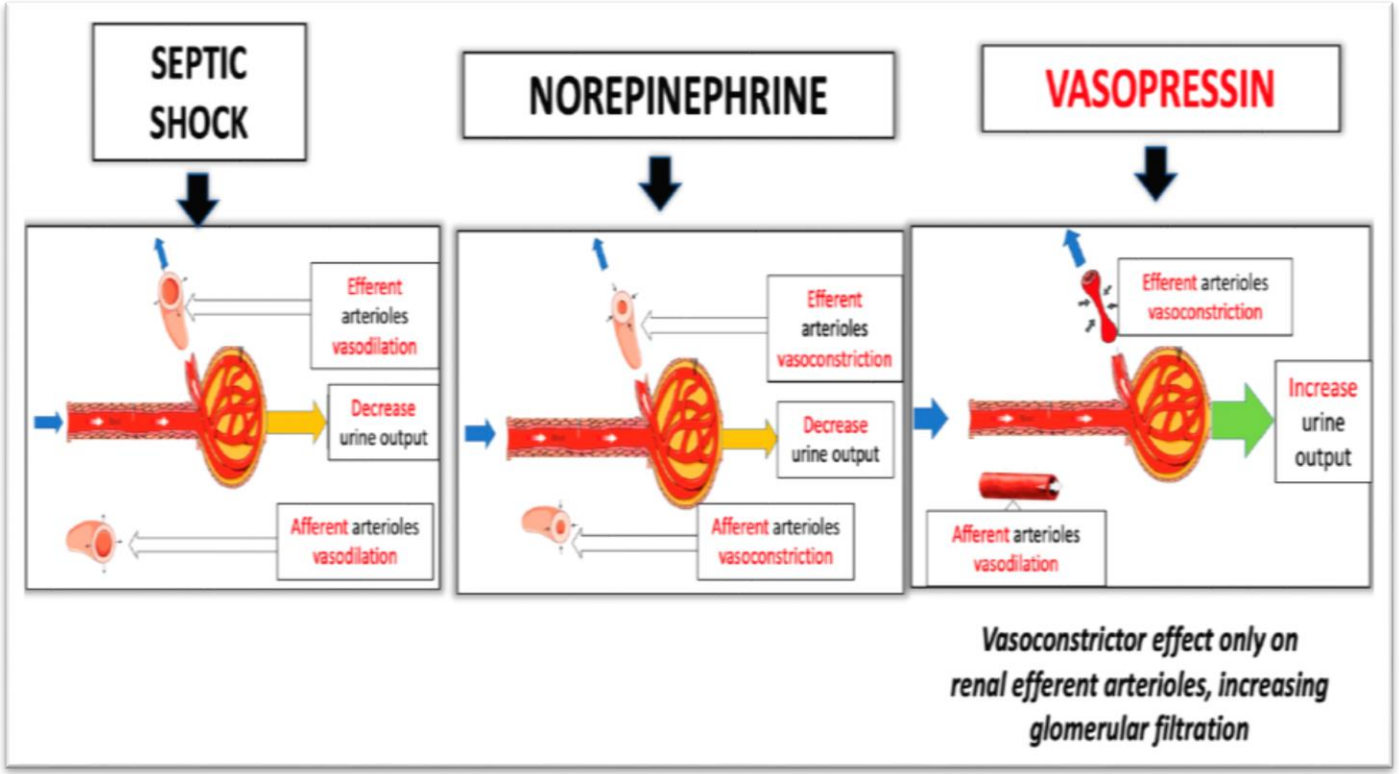


Figure 2. Surviving Sepsis Campaign updates. NE: norepinephrine; DA: dopamine; AVP: arginine vasopressin.

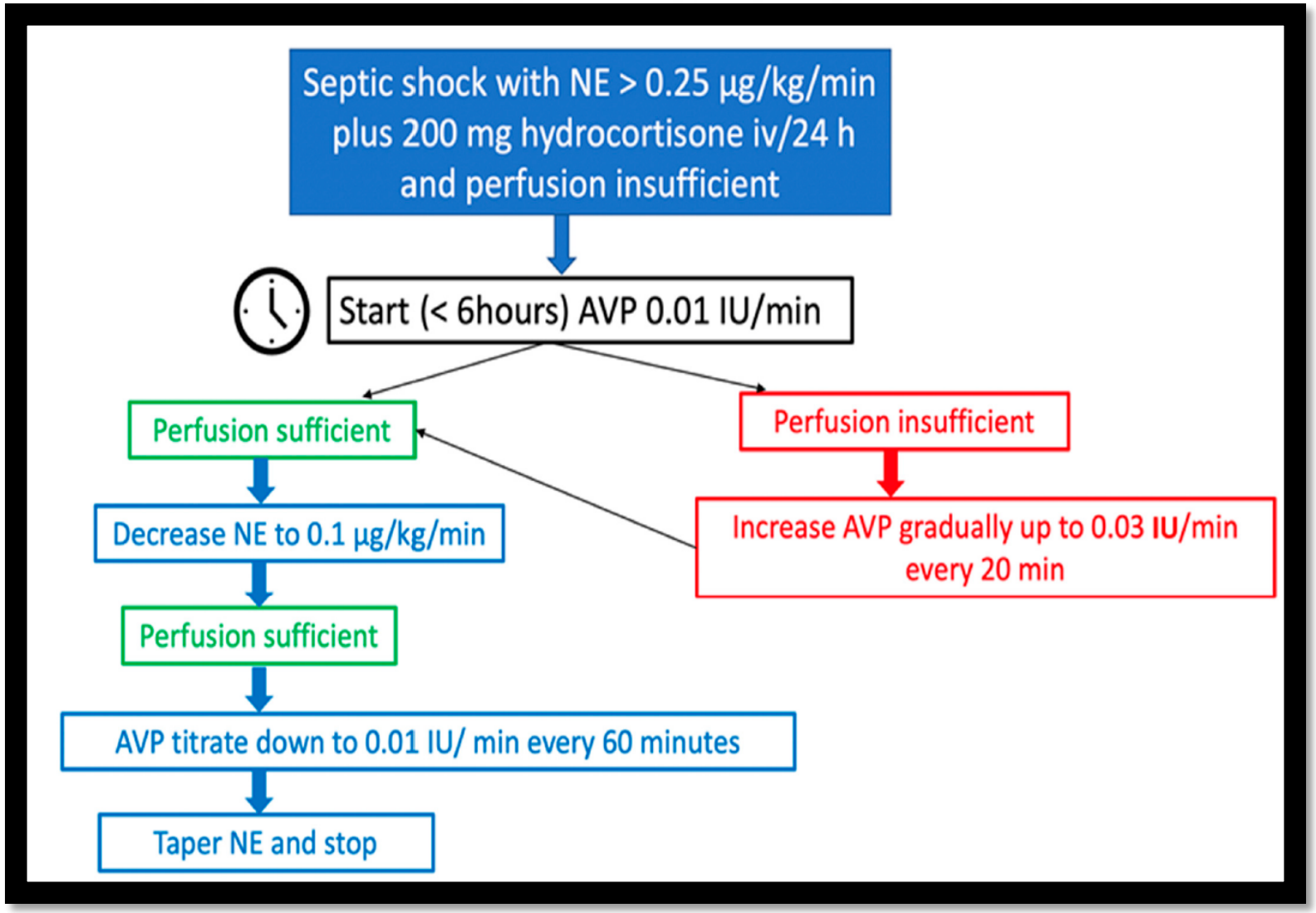


doi: 10.3390/jpm13111548. PMID: 38003863

Nephroprotective Effect Of AVP In Septic Shock



doi: 10.3390/jpm13111548. PMID: 38003863


Septic shock with NE > 0.25 µg/kg/min plus 200 mg hydrocortisone iv/24 h and perfusion insufficient
Start (< 6hours) AVP 0.01 IU/min
Perfusion sufficient
Perfusion insufficient
Decrease NE to 0.1 µg/kg/min
Increase AVP gradually up to 0.03 IU/min every 20 min
Perfusion sufficient
AVP titrate down to 0.01 IU/ min every 60 minutes
Taper NE and stop

Does Bicarbonate Therapy Help Patients with Severe Metabolic Acidemia in the ICU? BICAR-ICU TRIAL

Methods

26 ICUs
n = 389

Pragmatic, Unblinded

Severe Acidemia
pH ≤7·20;
HCO_3 ≤ 20, $PaCO_2$ ≤45)

ACIDIC pH

+

SOFA Score ≥ 4

1: 1 RANDOMIZATION

Intervention

No Bicarb

=

pH < 7.30
n = 144/194

4.2% $NaHCO_3$

=

pH > 7.30
n = 117/195

1ry Composite Outcome

Mortality

+

≥ 1 organ failure

RRT

AKIN ≥ 2

(a-priori subgroup)

Composite Outcome

Mortality

	1ry Composite Outcome	RRT	AKIN ≥ 2 (a-priori subgroup) Composite Outcome	AKIN ≥ 2 (a-priori subgroup) Mortality
No Bicarb	71%	52%	82%	63%
	NS	p = 0.0009	p = 0.04	p = 0.01
4.2% $NaHCO_3$	66%	35%	70%	46%

Conclusion: In patients with severe metabolic acidemia, sodium bicarbonate had no effect on the primary composite outcome. However, it decreased the primary composite outcome and day 28 mortality in the a-priori defined stratum of patients with acute kidney injury.

Jaber S, et al. The Lancet 2018 PMID: 29910040

@divyaa24 for #Lastmonthinnephrology

Mediators

Pathogens

DAMPs

HMGB1

Histones

PAMPs

Bacterial DNA

LPS LPS

dsRNA

Cytokines

TNF IL-1

IL-6

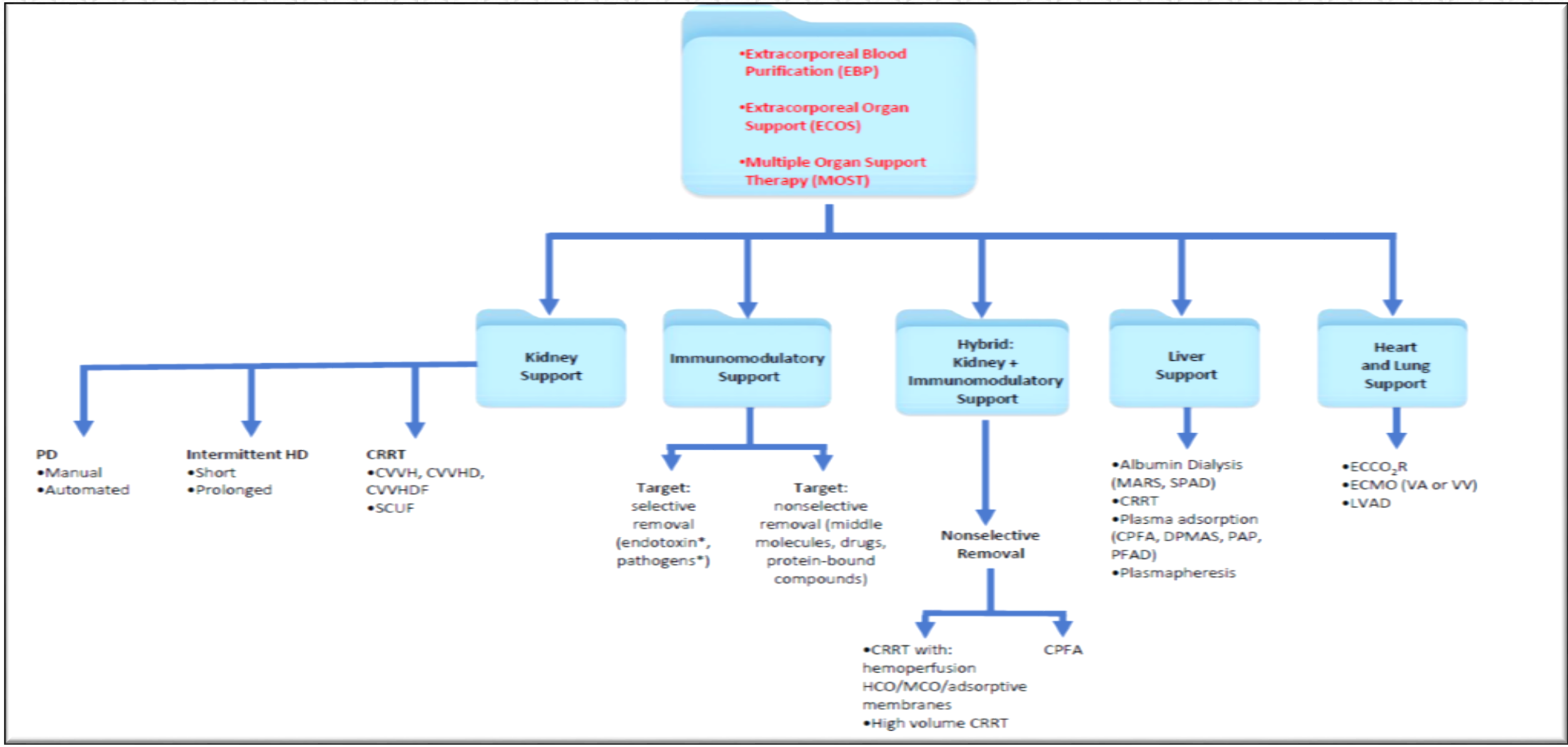
Available Devices

Seraph 100

Polymyxin B Filter

Cytosorb

Jafron – HA380


•Extracorporeal Blood Purification (EBP)
•Extracorporeal Organ Support (ECOS)
•Multiple Organ Support Therapy (MOST)
Kidney Support
Immunomodulatory Support
Hybrid: Kidney + Immunomodulatory Support
Liver Support
Heart and Lung Support
PD
•Manual
•Automated
Intermittent HD
•Short
•Prolonged
CRRT
•CVVH, CVVHD, CVVHDF
•SCUF
Target: selective removal (endotoxin*, pathogens*)
Target: nonselective removal (middle molecules, drugs, protein-bound compounds)
Nonselective Removal
•CRRT with: hemoperfusion HCO/MCO/adsorptive membranes
•High volume CRRT
CPFA
•Albumin Dialysis (MARS, SPAD)
•CRRT
•Plasma adsorption (CPFA, DPMAS, PAP, PFAD)
•Plasmapheresis
•ECCO2R
•ECMO (VA or VV)
•LVAD


THANK YOU
FOR
YOUR
ATTENTION