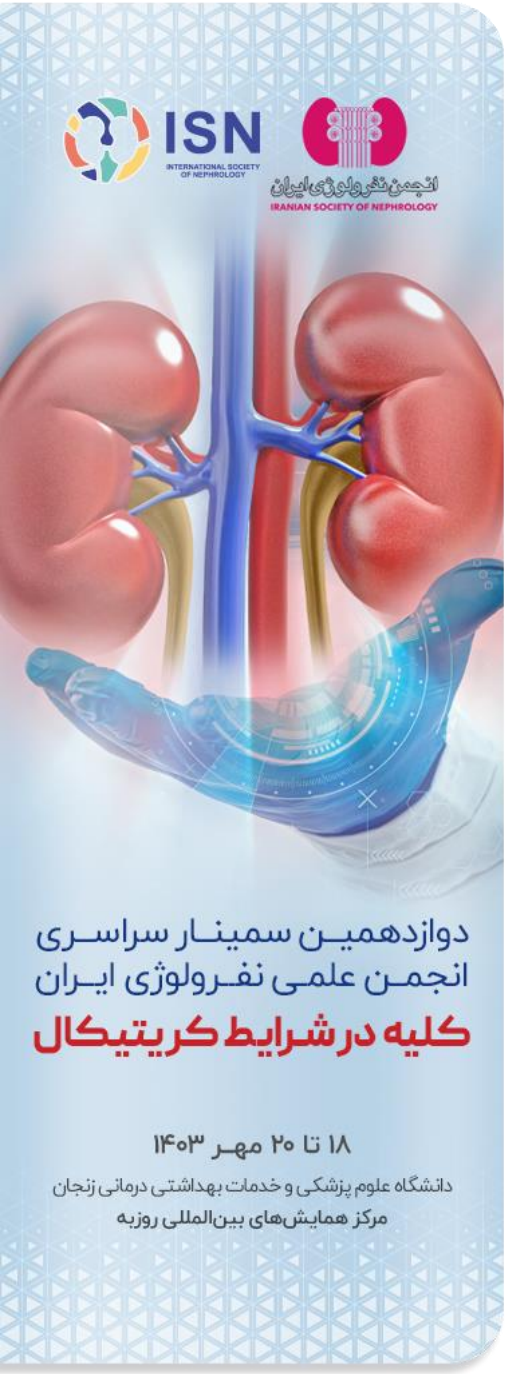

Challenge of Fluid therapy for patients with AKI

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Introduction

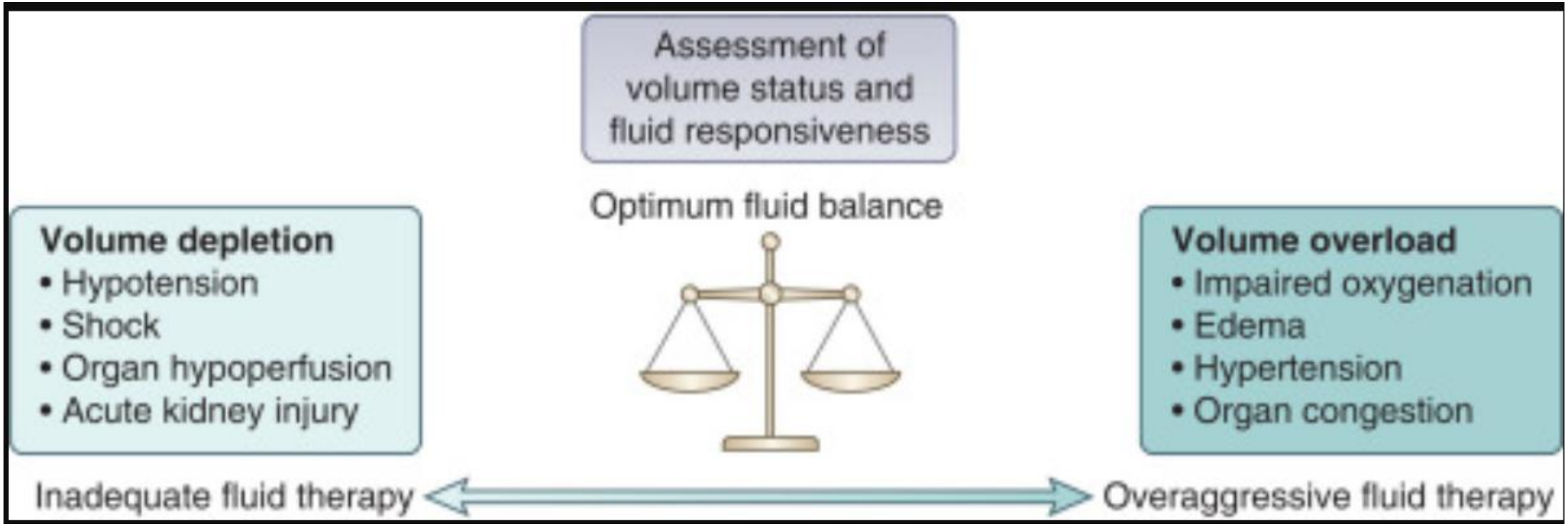
- Acute kidney injury (AKI) is a common problem in both the general hospital population and the critically ill population, affecting >20 and >50% of patients, respectively.
- Fluid administration in AKI should be carefully tailored based on individual haemodynamic status

European Heart Journal: Acute Cardiovascular Care (2022) 11, 788–793

Importance of Fluid Management in AKI

- Optimize renal function
- Prevent volume overload
- Reduce complications

Volume assessment goals



KI Volume 83, 6 June 2013, 1017-1028

Determinants of renal perfusion

- Mean arterial pressure (MAP) is not the only determinant of renal perfusion.
- **Renal blood flow** (RBF) is determined by the pressure gradient between the inflow and the outflow pressures of the kidneys and by the vascular resistance to flow (RBF=$\Delta P/R$).
- The inflow pressure of the kidney is closely related to MAP, while the outflow pressure is determined by the renal venous pressure or intra-abdominal pressure (IAP), depending on which one is higher.

Aims of Fluid Resuscitation

- Optimize intravascular circulating volume
- Increase cardiac output
- Increase perfusion pressure with the aim of improving renal blood flow and glomerular function
- Although hypotension is a strong risk factor for AKI, preservation of systemic arterial pressure alone is not sufficient to ensure adequate renal perfusion.

Types of Fluid

- Fluids are differentiated into crystalloids and colloids.
- Independent of the impact of fluid overload, there is growing evidence that renal function is affected by the type of fluid and that certain fluids are associated with an increased risk of AKI

Commonly Used Colloids

- Albumin 5%
- Albumin 20%
- Haemaccel
- Gelofusine
- Geloplasma
- Dextran 40
- Dextran 70 in NaCl
- Tetraspan 6% HES130/0.42
- Hetastarch 6% HES130/0.4
- Hetastarch 6% HES670/0.75

Commonly Used Crystalloids

- NaCl 0.9%
- NaCl 0.18% /Glucose 4%
- NaCl 0.45%/ Glucose 4%
- Glucose 5%
- Hartmann’s Solution
- Ringer Lactate
- Plasma-Lyte
- Sterofundin Isolyte S
- NaHCO3 1.26%
- NaHCO3 1.4%
- NaHCO3 8.4%
- Ringer Acetate

Colloids

- Containing oncotic macromolecules that largely remain in the intravascular space.
- Preserve intravascular oncotic pressure and expand the intravascular volume more effectively for a longer duration than crystalloids
- However, recent data indicate that their volume-sparing effect (ie, the volume required for restoration of intravascular volume compared with isotonic crystalloid solutions) is only modest, with colloid-to-crystalloid ratios in the range of 1:1.1 to 1:1.4

Colloids

- Some types of colloids have also been found to be nephrotoxic, particularly the hydroxyethyl starches.
- There are only limited data on the benefits and risks of gelatin-based colloids in AKI.
- Administration of gelatin contributes to the development of osmotic nephrosis-induced AKI in critically ill patients.

The potential risks and the absence of clear benefits indicate that **gelatin-based fluids should be avoided in AKI**

Crit Care Med. 2012;40(9):2543-2551

Colloids

- **Albumin** is a natural colloid. When albumin is used for resuscitation, either as a 4%, 5%, or 20% solution, it has not been shown to have a consistent survival benefit compared with the crystalloids.
- A meta-analysis found no difference in the use of RRT with albumin vs crystalloid solutions in patients with sepsis.

Intensive Care Med. 2015;41(9):1561-1571

Colloids

- An RCT in 321 adult patients requiring fluid resuscitation within 48 h of admission to the ICU showed that administration with 20% albumin decreased fluid requirements compared with fluid resuscitation with 4% to 5% albumin.
- There was no difference in the proportion of patients treated with RRT

Intensive Care Med 2018;44(11):1797-1806.

Colloids

- Possible **exceptions for Albumin** are patients with:
- Hepatorenal syndrome, in whom the combination of albumin with a vasopressor analogue may be renoprotective
- Patients with serum albumin levels < 4 mg/dL before undergoing off-pump coronary artery surgery, in whom the preoperative administration of 20% albumin reduces the risk of postoperative AKI.

Anesthesiology. 2016;124(5):1001-1011.

Colloids

- **In conclusion the role of colloids for routine resuscitation in patients at risk of AKI is limited.**
- Current recommendations are to use crystalloids instead of colloids for fluid resuscitation in critically ill patients, including those at risk or with established AKI
- Although hydroxyethyl starches should be avoided,other colloids may be considered in limited quantities for early resuscitation in patients with profound and refractory shock who are fluid responsive and not responding to crystalloids.

Crystalloids

- Saline (0.9% sodium chloride) is still the most commonly used crystalloid in critically ill patients despite the fact that rapid administration of moderate to large volumes can cause hyperchloremia and metabolic acidosis
- The electrolyte composition of (balanced) buffered solutions such as Ringer's lactate, Hartmann's solution, and Plasma-Lyte is similar to human plasma, and there is no reported association with hyperchloremic acidosis
- Although buffered fluids contain potassium in small quantities, this use only poses a risk in patients with severe hyperkalemia.

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

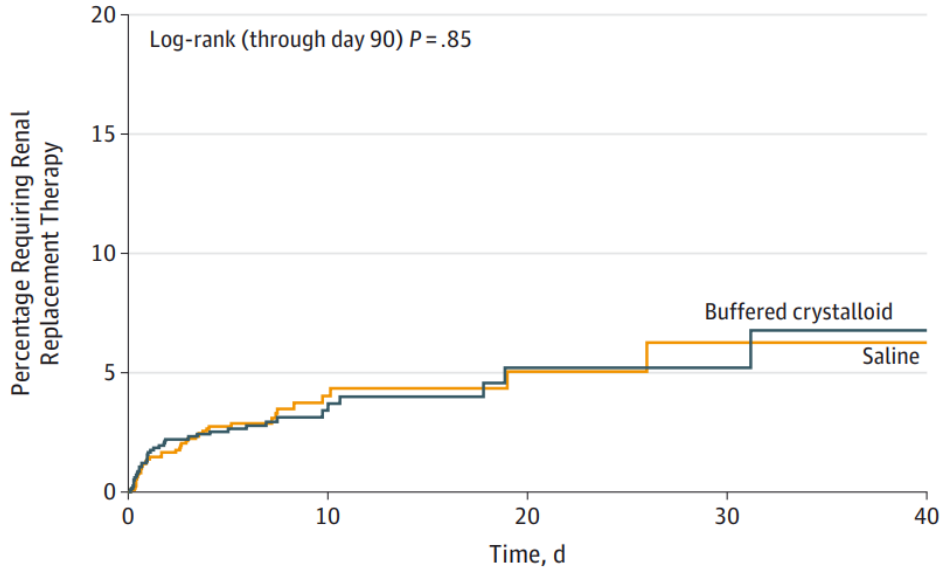
Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit
The SPLIT Randomized Clinical Trial

Paul Young, FCICM; Michael Bailey, PhD; Richard Beasley, DSc; Seton Henderson, FCICM; Diane Mackle, MN; Colin McArthur, FCICM; Shay McGuinness, FANZCA; Jan Mehrtens, RN; John Myburgh, PhD; Alex Psirides, FCICM; Sumeet Reddy, MBChB; Rinaldo Bellomo, FCICM; for the SPLIT Investigators and the ANZICS CTG

- In the (SPLIT) trial, 2,278 ICU patients were randomized to receive Plasma- Lyte 148 vs 0.9% saline
- There was no significant difference in the proportion of patients with moderate to severe AKI.
- This trial included patients with lower comorbid conditions, and the average amount of fluids given was < 2 L

SPLIT randomized clinical trial.
JAMA.2015;314(16):1701-1710

SPLIT TRIAL



- Cumulative Incidence of Patients Requiring Renal Replacement Therapy Until Day 90 After Enrollment in the SPLIT Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults

- The SMART study, showed a lower incidence of major adverse kidney events (MAKE) in those receiving buffered crystalloids (14.3% vs 15.4%; P=.04)
- But there was no significant difference in maximum stage of AKI, need for RRT or proportion of patients with at least a doubling of Scr.
- Among patients with sepsis, the use of buffered crystalloids was associated with a lower 30-day in-hospital mortality compared with use of saline

N Engl J Med. 2018;378(9):829- 839

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

- In [SALT-ED] trial in 13,347 noncritically ill patients admitted to the hospital from the ED (Saline against Lactated Ringer's or Plasma-Lyte
- The number of hospital-free days did not differ between the balanced-crystalloids and saline groups (median, 25 days in each group; adjusted odds ratio with balanced crystalloids, 0.98; 95% confidence interval [CI], 0.92 to 1.04; P=0.41).
- Balanced crystalloids resulted in a lower incidence of major adverse kidney events within 30 days than saline (4.7% vs. 5.6%; adjusted odds ratio, 0.82; 95% CI, 0.70 to 0.95; P=0.01).

N Engl J Med 2018;378:819-828

Crystalloids

- It has been hypothesized that the risk of saline-induced AKI may be dose dependent and only observed in patients receiving large volumes of 0.9% saline
- Recent study in ICU patients receiving large volume fluid resuscitation (> 60 mL/kg per 24 h) showed no association between chloride load and risk of AKI after adjusting for severity of illness
- Based on the current evidence, there is only a limited role for colloids as a therapy to prevent AKI

Crit Care Med. 2016;45(2):e146-e153

Crystalloids

- **To date, no published clinical trials have specifically compared different crystalloid fluids in patients with established AKI**.
- Existing data support the preferential use of buffered solutions for fluid resuscitation of patients at risk of AKI who do not have hypochloremia
- Saline 0.9% is the preferred solution for patients with hypovolemia and hypochloremia (eg, following prolonged vomiting).
- When used, chloride concentrations should be monitored.

Nat Rev Nephrol. 2018;14(9):541-557

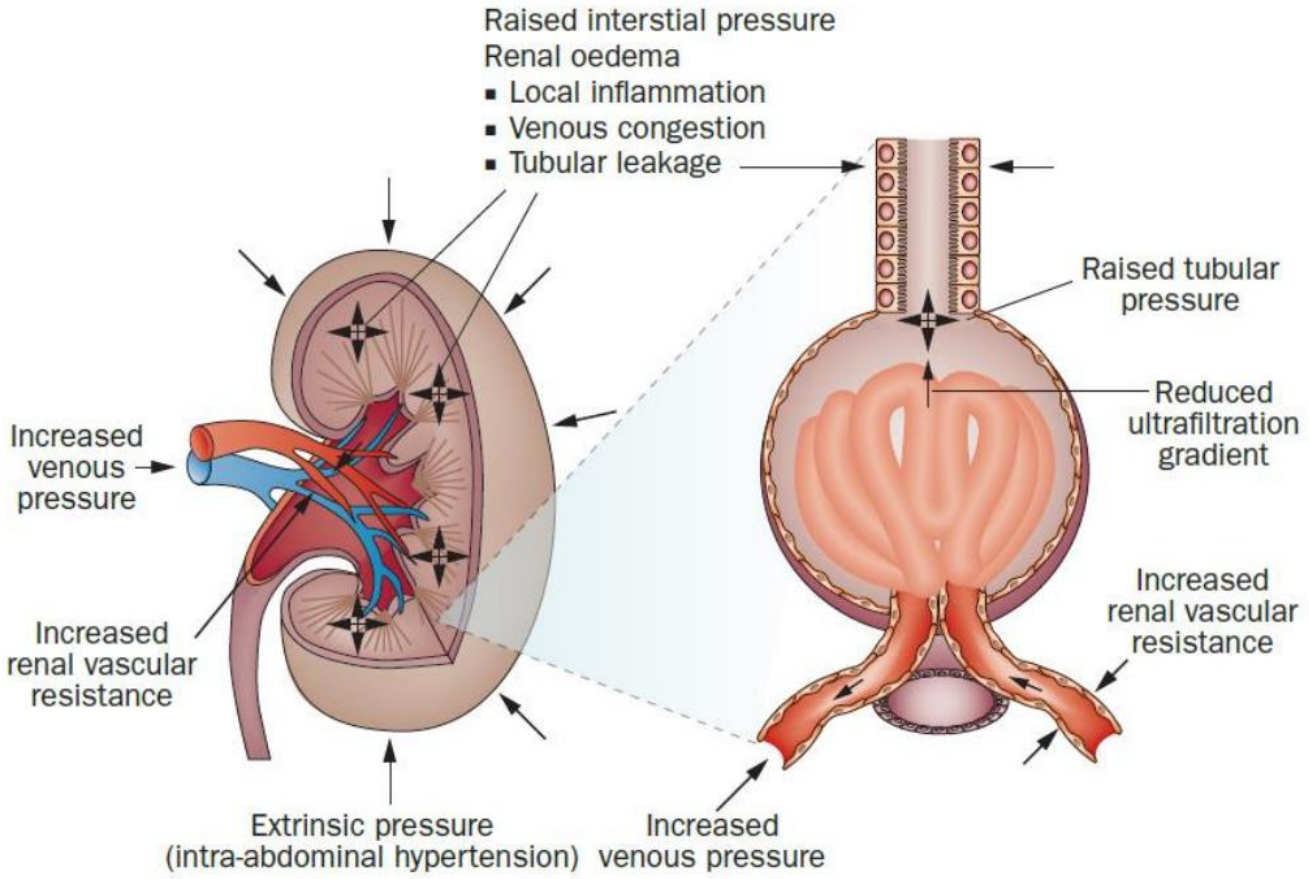
Volume of Fluid

- Fluid loading is indicated in cases of circulatory failure due to intravascular hypovolemia to prevent organ failure, including AKI.
- Excessive fluid administration has also been associated with the development of AKI

Fluids should only be administered until intravascular hypovolemia has been corrected

Volume Overload: Detrimental Effects

The potential mechanisms include **intrarenal compartment syndrome** and **venous congestion** as a result of the kidneys being encapsulated organs.

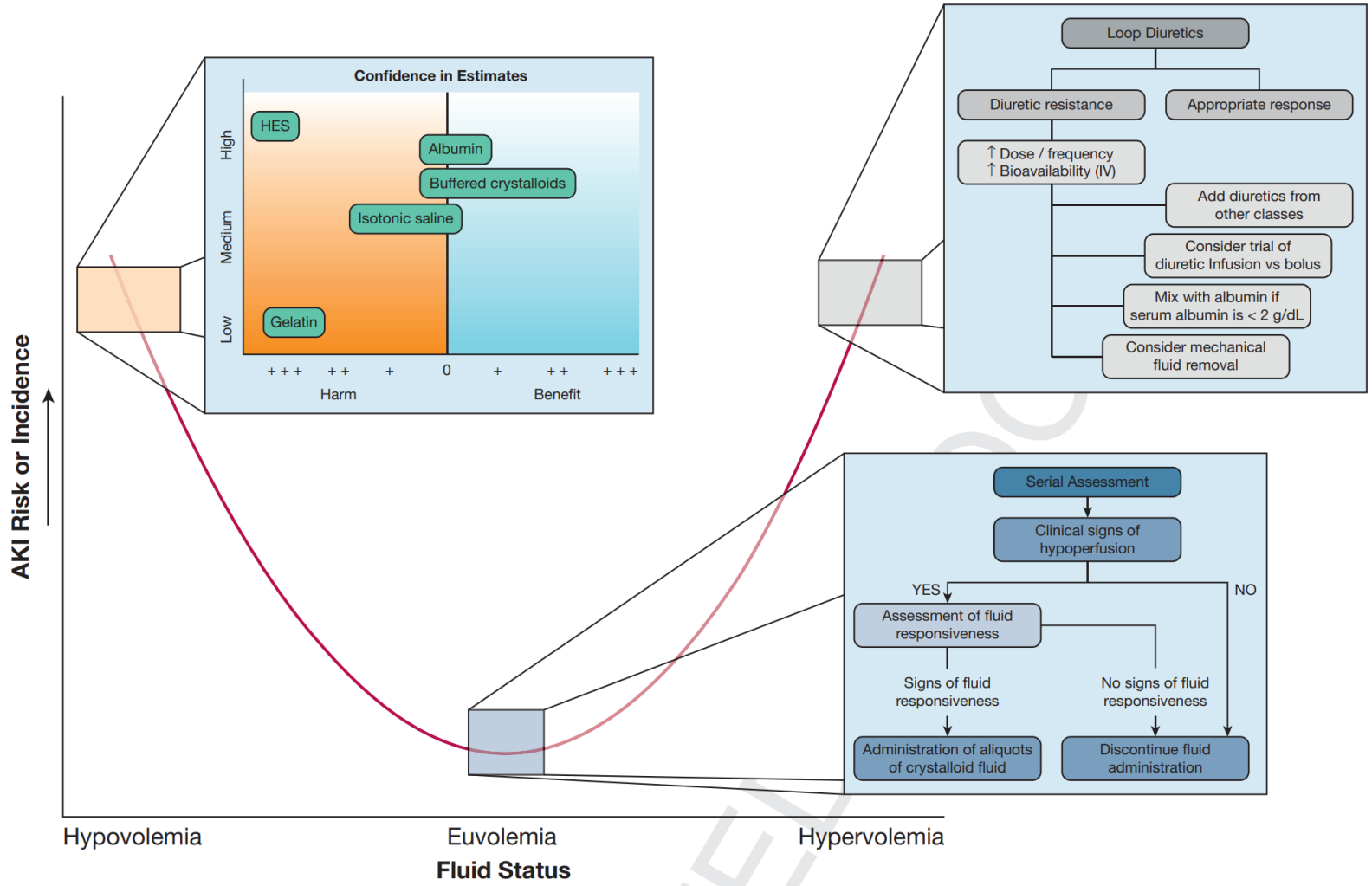


Prowle JR. Nat Rev Nephrol 2010;6:110

Volume of Fluid

- It is desirable to administer the minimum amount of IV fluid required to maintain perfusion and systemic oxygen delivery.
- If fluids are considered necessary, they should be administered in frequent small aliquots and under periodic reassessment of fluid responsiveness and hemodynamic status so that fluid overload is avoided.
- The aim is to achieve and maintain euvolemia.

Fluid administration and the development of AKI



CHEST 2281_ May 2019 -19-0156

Assessment of Volume Status

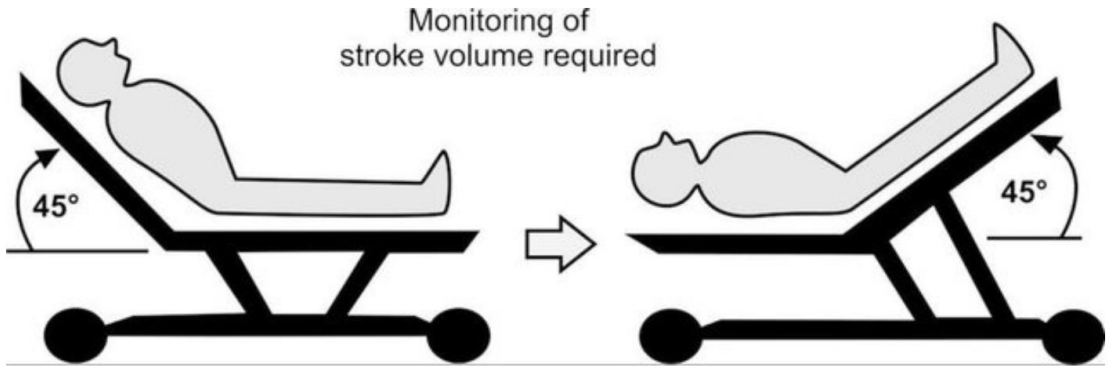
- Fluid responsiveness is often viewed as a surrogate marker of intravascular hypovolemia, and lack of fluid responsiveness is considered as equivalent to euvolemia.
- Classically, the assessment of fluid responsiveness involves giving a fluid challenge to a patient with decreased organ perfusion and checking whether this test increases the cardiac output and improves organ perfusion.

Assessment of Volume Status

Method	Invasive or noninvasive	Static or dynamic	Assess fluid responsiveness	Comments
Historical findings	Noninvasive	Static	No	Of limited value with poor correlation with invasive pressure measurements
Physical exam	Noninvasive	Static and dynamic	Yes	Of limited value but serial examinations may detect changes in organ perfusion
Chest radiograph	Noninvasive	Static	No	Requires use of standardized measures of vascular pedicle width and cardiothoracic ratio. Serial chest X-ray may be helpful in determining effects of fluid therapy
Central venous pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Pulmonary capillary wedge pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Echocardiogram	Noninvasive	Static	No	Single measures of cardiac chamber volume hard to assess. Serial measures may be helpful
Stroke volume or pulse pressure variation	Invasive (pulse oximeter method in noninvasive)	Dynamic	Yes	Requires sedated, mechanically ventilated patient
Esophageal doppler	Invasive	Dynamic	Yes	Not useful for continuous measurements
Vena cava diameter	Noninvasive	Dynamic	Yes	Body habitus dependent
Passive leg raising	Noninvasive (bioreactance end-tidal CO_2) Invasive (FloTrac or PiCCO or LiDOO)	Dynamic	Yes	Unreliable with intra-abdominal hypertension
End-expiratory occlusion	Passive leg raising	Dynamic	Yes	Requires 15-s end-expiratory occlusion
Bioimpedance	Noninvasive	Static	No	Not able to assess intravascular volume

Kalantari K. Kidney Int 2013; 83: 1017

Assessment of Volume Status



- Established noninvasive techniques : the passive leg raise test, ultrasonography, and echocardiography.
- Ideally, the assessment should include dynamic hemodynamic indices such as stroke volume or respiratory variation of pulse pressure rather than static values such as central venous pressure or pulmonary artery occlusion pressure

Assessment of Volume Status

- A typical approach is to ascertain the response of stroke volume or pulse pressure to an increase in preload.
- If a 5% to 15% increase in stroke volume or pulse pressure is seen, it is viewed as an indication that cardiac function lies on the steeper part of the Frank-Starling curve, and the patient is considered to be fluid responsive.

Duration of Fluid Therapy

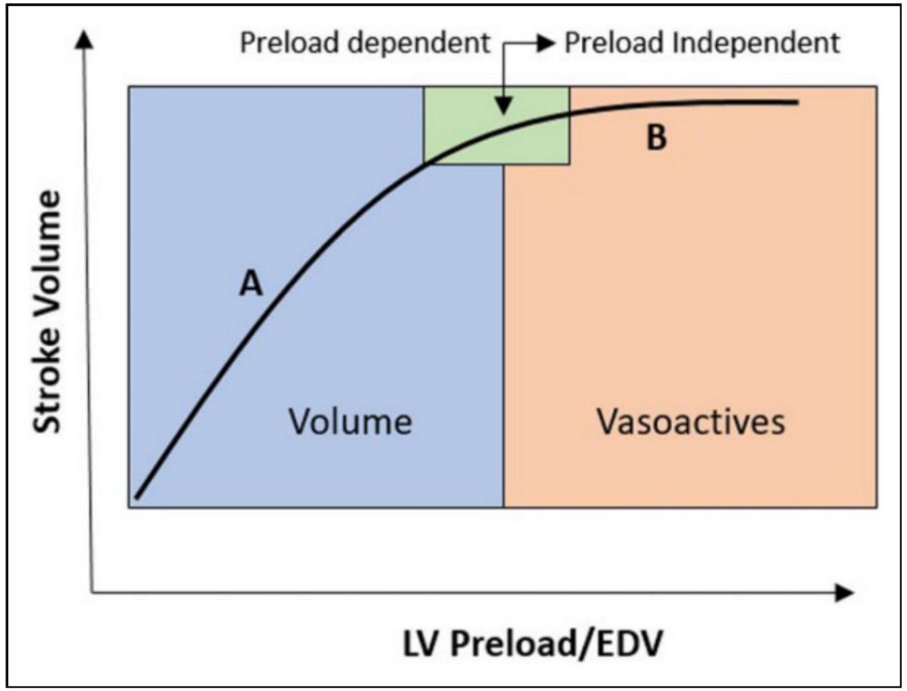
- The overall aim of fluid resuscitation is to correct hypovolemia and optimize preload to maintain renal perfusion.
- In patients with AKI, fluid resuscitation beyond correction of hypovolemia does not increase the chances of renal recovery and may, in fact, hinder recovery of renal function and worsen overall outcomes
- Fluid administration should be stopped when signs of circulatory failure have resolved, early signs of fluid overload appear, and/or dynamic test results indicate that the patient is no longer fluid responsive

Duration of Fluid Therapy

- If the patient remains hemodynamically unstable after hypovolemia has been corrected, support with vasopressors or inotropes should be considered.

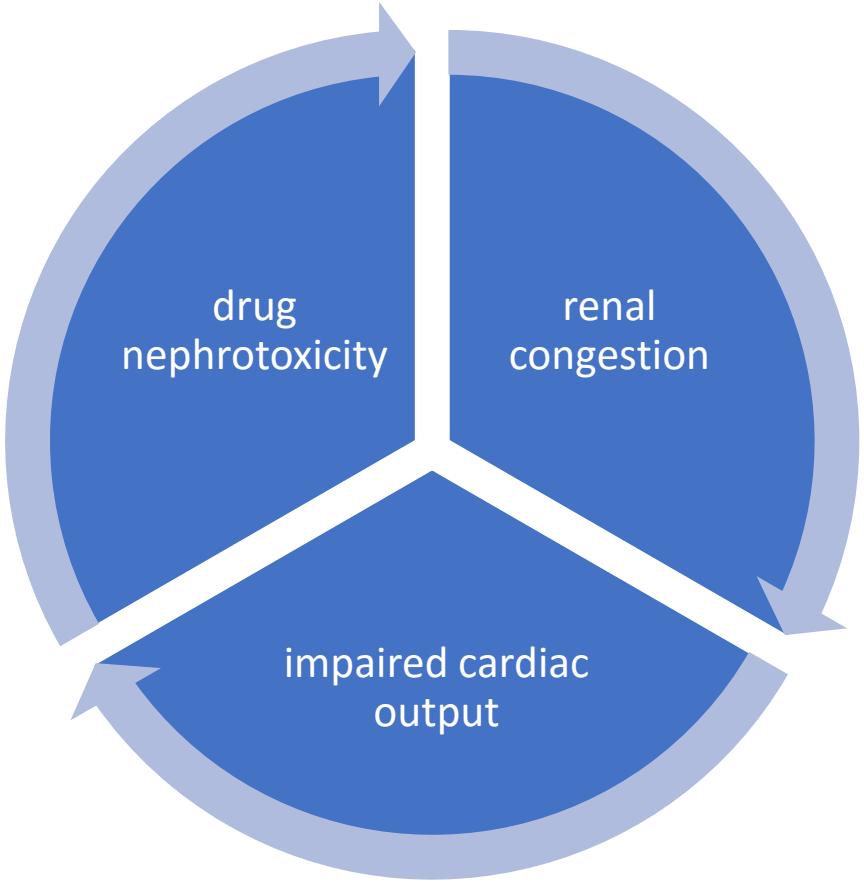
The transition point from volume resuscitation to vasopressor support in treatment for sustained hypotension

- Frank-Starling curve showing the transition point from volume resuscitation (blue shaded) to vasopressor support (red shaded) in treatment for sustained hypotension.



Jaffee W. J Intensive Care Med 2018; 33: 502

AKI in Congestive Cardiac Failure



- In this situation, fluid therapy is only indicated in the case of true intravascular fluid depletion. Support with inotropes and vasopressors is more commonly needed, often in combination with diuretic agents and fluid removal

AKI in Liver Disease

- Patients with liver disease are at high risk of AKI, mainly due to splanchnic vasodilation and relative intravascular hypovolemia.
- Volume expansion in combination with vasoconstrictors is an important component of resuscitation.
- Several studies have confirmed that the combination of a vasopressin analogue and albumin has a beneficial effect on renal function.

Cochrane Database Syst Rev. 2017;9:CD011532.

Obstructive AKI

- In obstructive AKI, resolution of obstruction and correction of intravascular hypovolemia are the mainstay of treatment.
- **physiological diuresis** is the expected response to any relief of urinary obstruction, and excrete excess fluid solutes that may have accumulated while obstructed .
- **postobstructive diuresis** When diuresis continues beyond correction of fluid status due to a degree of **nephrogenic diabetes insipidus**. In this situation, patients need volume fluid resuscitation to keep up with diuresis. Although buffered crystalloid solutions are the preferred fluids, additional electrolyte supplementation is occasionally necessary.

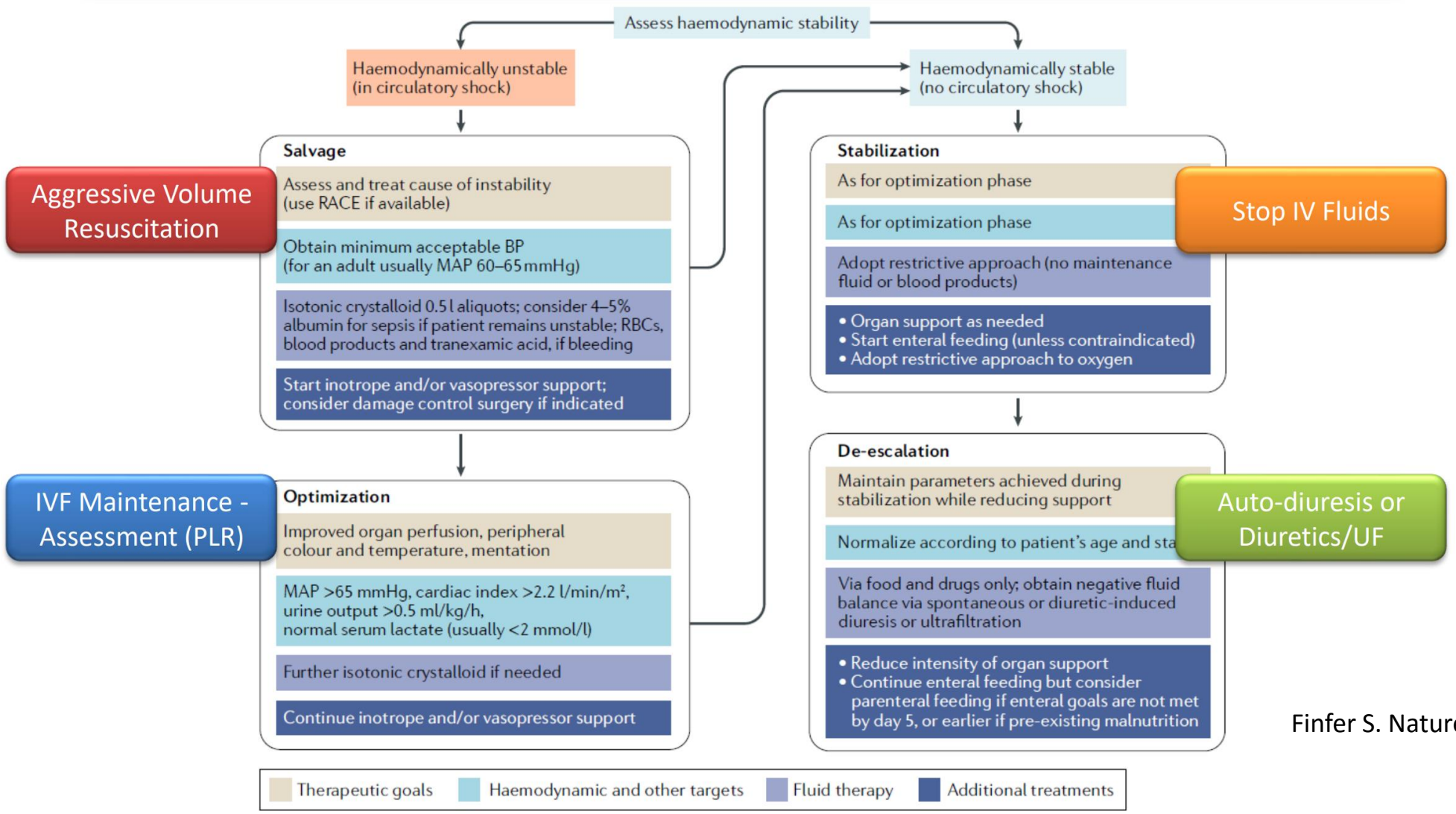
Tumor Lysis Syndrome

- The crystallization of urine acid and/or calcium phosphate in renal tubules together with hypovolemia can lead to AKI, especially in cases of volume depletion.
- The administration of crystalloid fluids (> 100 mL/h) is one of the most important interventions in patients at risk of or with tumor lysis syndrome because it enhances urine flow and allows for rapid clearance of uric acid, potassium, and phosphorus.
- However, volume expansion beyond correction of intravascular hypovolemia is not recommended
- Alkalinization of the urine is no longer recommended

AKI Treated With RRT

- During RRT, fluid management should be guided by the fluid and hemodynamic status of the patient.
- Most patients undergoing RRT need fluid removal, and fluid intake should therefore be minimized.
- Determining the exact volume and speed of fluid removal during RRT is challenging, particularly if patients are hemodynamically unstable

Fluid Management in Shock 4 phases



Aggressive Volume Resuscitation

IVF Maintenance - Assessment (PLR)

Stop IV Fluids

Auto-diuresis or Diuretics/UF

Finfer S. Nature Rev 2018;14:541

Conclusions

Factor	Do	Don't
Indication	Intravascular hypovolemia	Oliguria without hypovolemia
Type of fluid	Crystalloids	Starches
Volume	Boluses of small aliquots	High volumes
Duration	Until hypovolemia corrected	Until AKI resolved

CHEST 2 May 2019 1:51 pm EO: CHEST-19-0156


Thanks for your attention

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