Optimizing Enteral Nutrition and Drug Therapy in the Critically Ill Patient Requiring Renal Replacement Therapy

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Objectives

- Recognize the importance of nutritional therapy in the critically ill population
- Review the contents of standard enteral formulations
- Assess nutrition requirements in AKI, iHD, and CRRT
- Apply nutritional concepts to a patient case

Patient Case

RG is a 57 YOM admitted 01/25/2019 whose hospital course includes:

- Pancreatitis; Cholecystitis (s/p ERCP, sphincteroplasty, and plastic stent placement)
- STEMI (s/p PCI proximal and mid-LAD)
- AKI (FENa 0.2% - Prerenal)

Allergies: NKDA

PMH: HTN, Diverticulitis with multiple abscesses drained (2018)

SH: (-) Tobacco/illicit; Hx heavy EtOH use

- Consult placed for Nutrition Support Service to manage nutrition after failed PO intake 2/2 necrotizing pancreatitis
- Current Status:
  - MV: off sedation to attempt extubation
  - AKI: planned iHD
- Anthropometrics:
  - Height: 175 cm
  - Weight: 105 kg
  - IBW: 73 kg (140%)
  - BMI: 34 kg/m^2
  - AdjBW: 84 kg

134 | 104 | 71
----------< 249 Ca: 8.8 P: 9.2 Mg: 2.3
5.0 | 13 | 5.90

AST: 14 / ALT: 12 / AlkPhos: 117 / Bili: 0.5 / Prot: 8.3 / Alb: 1.7
ABG: pH: 7.16, pCO2: 42, pO2: 76, HCO3: 15
WBC: 19.20 / Hb: 7.1 / Hct: 23.5 / Plt: 310

Nutrition in the Critically Ill

- *Nutrition Therapy* refers specifically to the provision of either enteral nutrition (EN) by enteral access device and/or parenteral nutrition (PN) by central venous access.

- Critical illness represents a catabolic stress state:
  - Systemic inflammatory response
  - Increased infectious morbidity
  - Multiple organ dysfunction
  - Prolonged hospitalization
  - Disproportionate mortality

JPEN. 2016;40(2):159-211

Nutrition in the Critically Ill, cont.

- Feeding critically ill patients helps to:
  - attenuate the metabolic response to stress
  - prevent oxidative cellular injury
  - favorably modulate immune responses

- Feeding may be increasingly beneficial in patients already malnourished prior to admission

JPEN. 2016;40(2):159-211

Benefits of Enteral Nutrition (EN)

- The specific reasons for providing EN are to:
  - Maintain gut integrity
  - Modulate stress and the systemic immune response
  - Attenuate disease severity
- Outcomes
  - ↓ Mortality (RR = 0.70; 95% CI, 0.49–1.00; *p* = 0.05) (ADD CITATION)
  - ↓ Infectious complications (RR = 0.74; 95% CI, 0.58–0.93, *p* = 0.01) (ADD CITATION)
  - ↓ Length of stay (mean 2.2 days; 95% CI, 0.81–3.63 days; *p* = 0.001) (ADD CITATION)

JPEN. 2016;40(2):159-211

Indications, Contraindications, and Therapy Goals for Enteral Nutrition (EN)

- Indications
  - Unable to meet nutrition requirements PO within 48-72 hours in the ICU
- Contraindications
  - Hemodynamic instability; high dose vasopressor requirements
  - Bowel obstruction, severe and protracted ileus, major GIB, intractable vomiting or diarrhea, GI ischemia, high output fistula
- Goals:
  - Provide > 80% of estimated goal energy and protein within 48–72 hours in the ICU
  - Minimize risk of complications
  - Preserve lean body mass and energy reserve, prevent protein energy wasting, reestablish immune function, reduce mortality, and attenuate the inflammatory response and oxidative stress

Components of Enteral Nutrition (EN)

Component	Purpose	Recommendations	Considerations
Calories	Provide nutrition in the absence of PO intake Preserve lean body mass	25-30 kcal/kg	Malnourishment Obesity
Carbohydrates	Provide glucose	~35-60% of calories Minimum ~100 g/day	Metabolic Syndrome Hyperglycemia
Protein	Promote wound healing Attenuate lean body mass wasting	15-25% of calories Intact proteins	Wounds Acute Kidney Injury Encephalopathy
Fat	Prevent EFAD Maintains the function and integrity of cellular membranes	~30-40% of calories	Hypertriglyceridemia
Vitamins/Minerals/ Micronutrients	Prevent deficiencies Promote healing	Provide RDA	Cholecystitis
Electrolytes	Maintain serum electrolytes WNL	Patient-specific	Acute Kidney Injury
Volume/Free Water	Maintain adequate hydration	30ml/kg of free water	Heart Failure Acute Kidney Injury Dehydration

Savino. *Nutr Clin Pract*. 2018;33(1):90-98

Acute Kidney Injury (AKI)

- AKI is a sudden decline in GFR and UOP
- Accumulation of:
  - Metabolic waste products
  - Toxins
  - Drugs
- AKI is a common complication for hospitalized patients and is associated with high morbidity and mortality

Table 1. Staging System for Acute Kidney Injury.

AKI Stage	Serum Creatinine	Urine Output
I	Increase in serum creatinine ≥ 0.3 mg/dL or increase to ≥ 150%-200% from baseline	<0.5 mL/kg/h for >6 hrs
II	Increase in serum creatinine > 200%-300% from baseline	<0.5 mL/kg/h for >12 hrs
III	Increase in serum creatinine > 300% from baseline or serum creatinine ≥ 4 mg/dL with an acute increase of at least 0.5 mg/dL	<0.3 mL/kg/h for >24 hrs, or anuria for >12 hrs

Adapted from Mehta et al.[9]

McCarthy. *Nutr Clin Pract*. 2014;29(1):56-62

ASPEN Recommendations for Nutrition Therapy in Acute and Chronic Renal Failure

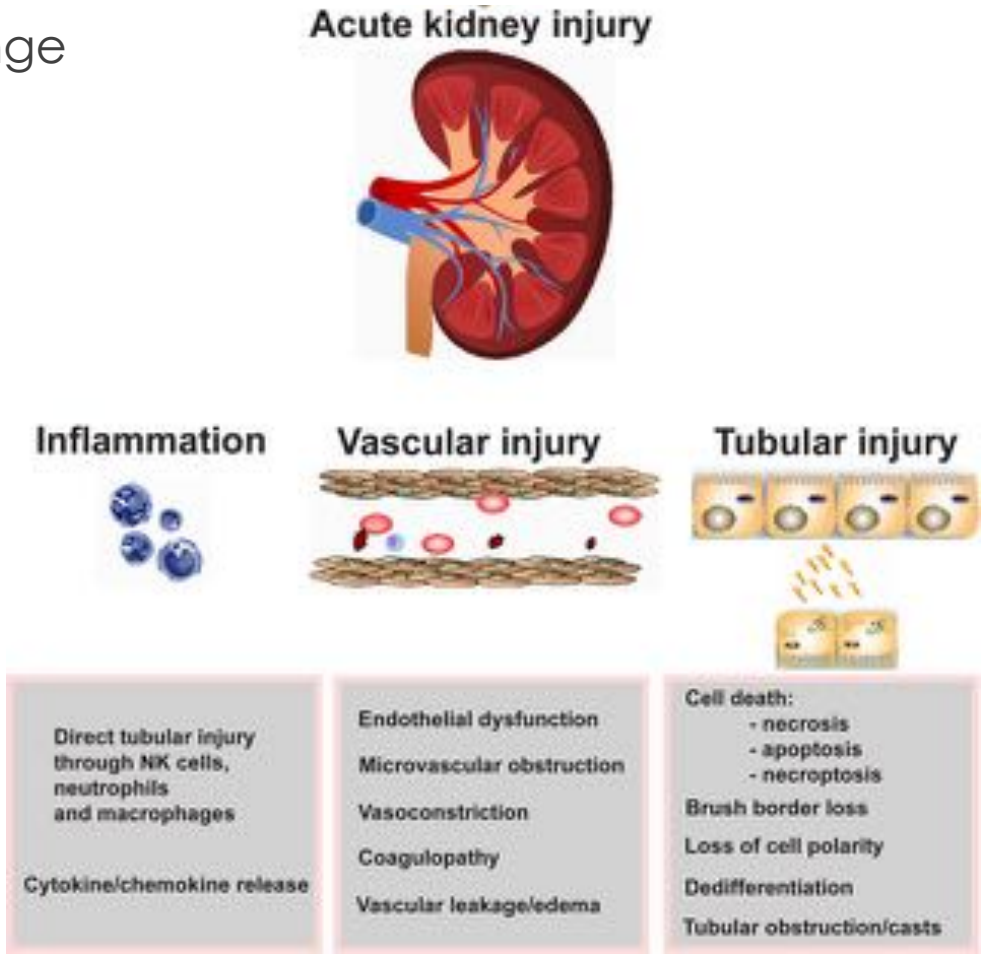
Table 3. Recommendations for Nutrition Therapy in Acute and Chronic Renal Failure.

	Guidelines Recommendation	Grade
1	Patients with renal disease should undergo formal nutrition assessment, including evaluation of inflammation, with development of a nutrition care plan.	D
2	Standard amino acid parenteral nutrition formulations should be used in acute kidney injury	C
3	Intradialytic parenteral nutrition should not be used as a nutrition supplement in malnourished chronic kidney disease–stage V hemodialysis patients	C
4	Patients with renal failure who require nutrition support therapy should receive enteral nutrition if intestinal function permits.	E
5	Energy requirements in patients with renal disease should be evaluated using indirect calorimetry when possible.	D
6	To promote positive nitrogen balance in patients with acute kidney injury, protein intake should be adjusted according to catabolic rate, renal function, and dialysis losses	D
7	Electrolyte intake in patients should be adjusted by monitoring serum concentrations of potassium, magnesium, phosphorus, and calcium	D

Adapted from Brown R, Compher C, ASPEN Board of Directors, ASPEN clinical guidelines: nutrition support in adult acute and chronic renal failure, *JPEN J Parenter Ent Nutr*. 2010;34:366–377, with permission from the American Society for Parenteral and Enteral Nutrition.[7]

Nutrition in AKI

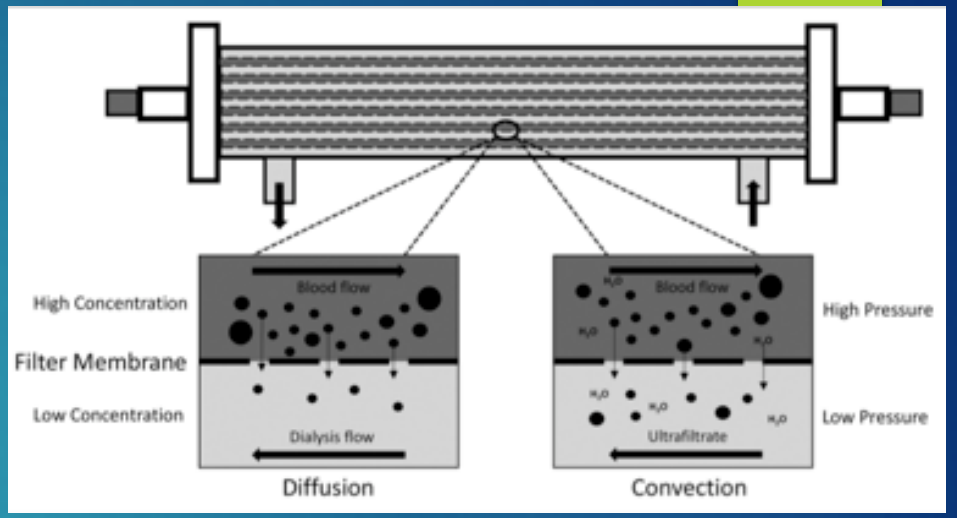
- Optimizing nutrition in AKI is a prevalent clinical challenge
- Varying degrees of fluid accumulation, electrolyte abnormalities, and metabolic derangements
- Common 'sequelae' of AKI
  - Fluid Overload
  - Hyperkalemia, Hypermagnesemia, Hyperphosphatemia
  - Accumulation of creatinine and nitrogen
- Treatment of AKI influences nutritional requirements
  - 'Watch and Wait'
  - Intermittent Hemodialysis
  - Continuous Renal Replacement

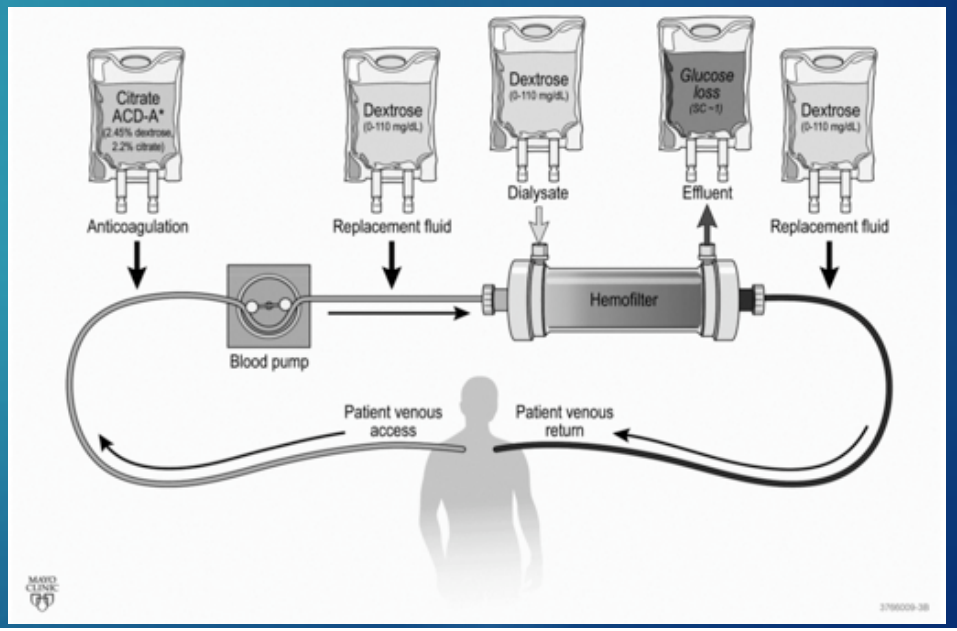


Togel and Westenfelder, 2014

Renal Replacement Therapy

- Intermittent Hemodialysis (iHD)
  - Period of accumulation followed by dialysis
  - Rapid removal, less control of fluid/electrolytes
  - High flow rate; no anticoagulation
  - Risk of hemodynamic instability
- Continuous Renal Replacement Therapy (CRRT)
  - Continuous removal of byproducts
  - Close management of fluid/electrolytes
  - Low flow rate; anticoagulation required
  - Maintains hemodynamics





Nystrom EM. *Nutr Clin Pract*. 2018;33(6):754–766

Nutrition in iHD

Considerations

- Standard ICU recommendations for energy and protein
  - iHD alone produces minimal increases in caloric requirements
- Patients should receive a standard enteral formulation, unless electrolyte abnormalities are present
  - Hyperkalemia, Hypermagnesemia, Hyperphosphatemia
  - Consider renal specific EN product
- Do not restrict protein as means of delaying iHD
  - Protein restriction may be required
- AKI rarely occurs in isolation
  - Usually part of sepsis, multiple organ failure, shock, trauma, or high risk surgery with the resultant hypermetabolism

Recommendations

- Initiate EN within 48 hours of ICU stay
- Calories:
  - 25-30 kcal/kg/day
  - HBE * 1.0-1.3 (Match to other comorbidities)
- Protein
  - Pre-dialysis: 0.6-1.0 g/kg/day
  - Hemodialysis: 1.2-1.3 g/kg/day
- Fats
  - Based on patient need/caloric requirements
- Micronutrients
  - Water soluble vitamin supplementation (MVI)

KDIGO. *Kidney Int*. 2012;2(6):1-138.

Patel. *Nutr Clin Pract*. 2017;32(1_suppl):101S-111S

Patient Case Questions

134 | 104 | 71
----------< 249 Ca: 8.8 P: 9.2 Mg: 2.3
5.0 | 13 | 5.90

Caloric Needs

HBE: 1800 kcal/day (adjBW)

- What stress factor should be applied to assess caloric needs?
  - HBE * 1.0
  - HBE * 1.2-1.3
  - HBE * 1.3-1.6
  - HBE * 0.6-0.8

HBE * 1.2-1.3 = 2160 – 2340 kcal/day
(26-28 kcal/kg adjBW/day)

Protein Needs

Recent surgery, multiple wounds, receiving iHD

- How much protein should we provide?
  - 0.6-0.8 g/kg/day
  - 1.0 g/kg/day
  - 1.2-1.3 g/kg/day
  - 1.5-2.0 g/kg/day

1.2-1.3 g/kg adjBW = 102-110 g/day

Enteral Products

Which product/rate best suits our patients needs?

- **Isosource 1.5 cal** @ 75 mL/hr (2475 kcal; 112 g protein; standard elytes)
- **Diabetasource AC** @ 65 mL/hr (1716 kcal; 86 g protein; standard elytes)
- **Peptamen Intense VHP** @ 55 mL/hr (1210 kcal; 111 g protein; standard elytes)
- **Novasource 2.0** @ 50 mL/hr (2200 kcal; 100 g protein; minimal elytes)

Drug Dosing in iHD

Considerations

- GFR is standard measure of renal function to dose medications, but studies are limited for iHD
- Volume of distribution (V_D)
  - Patients may be edematous
    - Affects water-soluble drugs with small V_D
- Residual Renal Function
- Drug removal by dialysis
  - Drugs will have varying degrees of removal
  - Drugs that exhibit hepatic and renal clearance may shift to the hepatic pathway
  - Small MW, Water soluble, Low protein binding, Non-charged, Small V_D
- Specific Agent Considerations

Dosage Adjustments for RG:

- Cardiovascular Agents
  - Aspirin – No adjustment
  - Atorvastatin – No adjustment
  - Heparin – No adjustment
  - Metoprolol – No adjustment
  - Ticagrelor – No adjustment
- Antimicrobials
  - Piperacillin/Tazobactam
    - 2.25 g every 12 hours; iHD removes 30% to 40% of dose
    - Severe infections: 3.375 g every 12 hours
- Supportive Care
  - Esomeprazole – No adjustment
  - Docusate Sodium – No adjustments

DiPiro, Joseph. "Pharmacotherapy: A Pathophysiologic Approach, Ninth Edition."

Ulldemollins M. *Crit Care*. 2014;18(3):227

Patient Case

RG's renal function continues to get worse on iHD. As a result, he has developed further electrolyte abnormalities.

- Nephrology is consulted and an order is placed for CRRT (CVVHDF)
- Cultures drawn from an abscess due to RG's necrotizing pancreatitis resulted
  - (+) E. coli
  - (+) Enterococcus faecium
- ID consulted and recommends initiation of vancomycin and meropenem
- Team asks NSS to assess the patient's nutritional needs

Nutrition in CRRT

Considerations

- Fluid and electrolyte status resembles normal physiology
- Increased incidence of:
  - Hypokalemia, Hypomagnesemia
- Increased protein requirements
  - CRRT results in a loss of 10-15 g amino acid (protein) per day
- Greater risk of protein and micronutrient losses

Recommendations

- Calories:
  - 25-35 kcal/kg/day
- Protein:
  - 1.5-2.5 g/kg/day
- Lipids – no change
- Micronutrients:
  - Folic Acid (1mg/day)
  - Thiamine(25-100 mg)
  - Selenium (100 µg/day)

McCarthy. *Nutr Clin Pract*. 2014;29(1):56-62

Patient Case Questions

140 | 104 | 38
----------< 384 Ca: 8.0 P: 4.1 Mg: 2.3
3.8 | 13 | 2.6

Caloric Needs

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- What stress factor should be applied to assess caloric needs?
  - HBE * 1.0
  - HBE * 1.2-1.3
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HBE * 1.2-1.3 = 2160 – 2340 kcal/day
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Recent surgery, multiple wounds, receiving CRRT

- How much protein should we provide?
  - 0.6-0.8 g/kg/day
  - 1.0 g/kg/day
  - 1.2-1.3 g/kg/day
  - 1.5-2.0 g/kg/day

1.5-2.0 g/kg adjBW = 126-168 g/day

Enteral Products

Which product/rate best suits our patients needs?

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- **Peptamen Intense VHP** @ 70 mL/hr (1540 kcal; 142 g protein; standard elytes)
- **Novasource 2.0** @ 55 mL/hr (2420 kcal; 110 g protein; minimal elytes)

Drug Dosing in CRRT

Considerations

- Drug dosing for patients with AKI on CRRT is not well defined
- Volume of distribution
  - Dialysis Circuit
    - Affects mostly drugs with low Vd
- Clearance
  - Dialyzable drugs
  - Residual renal function
- Small and larger molecules (~150 k daltons), Water soluble, Low protein binding, Non-charged, Small Vd
- Specific Agent Considerations

Dosage Adjustments for RG

- Cardiovascular Agents
  - Aspirin, Atorvastatin, Metoprolol, Ticagrelor, Heparin
- Antimicrobials
  - Meropenem
    - Consider loading dose of 1 g followed by either 500 mg every 6 to 8 hours **or** 1 g every 8 to 12 hours
  - Vancomycin
    - Loading dose of 15 to 25 mg/kg, followed by either 1,000 mg every 24 hours **or** 7.5 to 10 mg/kg every 12 hours
- Supportive Care
  - Docusate Sodium, Esomeprazole, Melatonin

DiPiro, Joseph. "Pharmacotherapy: A Pathophysiologic Approach, Ninth Edition."

Ulldemollins M. Crit Care. 2014; 18(3): 227.
Scoville B. *Am J Kidney Dis. 2013;*61(3):490-500.

Patient Case Questions

A clot developed in the CRRT circuit…

The team plans to start iHD instead. They ask you dose the vancomycin.

- No changes necessary
- Switch to intermittent dosing
- Decrease the dose
- Increase the dosing interval

RG goes into acute respiratory failure…

RG is intubated and sedated on Propofol at 40 mL/hr for several days. What effect will this have on RGs nutritional requirements?

- No effects
- Increased caloric requirements
- Decreased caloric requirements
- Decreased protein requirements

Summary

- Providing early EN to patients who cannot meet their nutritional needs by mouth helps to maintain gut integrity and modulate the stress response to critical illness.
- Adequately providing nutrition results in decreased mortality, infection, and length of stay.
- Patients with AKI are a clinical challenge regarding nutrition due to comorbidity, variable presentation, and treatment modalities.
- Drug dosing is not well defined in AKI and requires careful attention to detail and patient specific factors.

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